SCIENTIFIC PROGRAM & ABSTRACTS

64th Annual Meeting

March 15-18, 2017

Hilton Orlando Bonnet Creek
Orlando, FL

Continuing Medical Education credit is provided through joint providership with The American College of Obstetricians and Gynecologists.

Society for Reproductive Investigation

Dear Colleagues:

Welcome to the 64th Annual Meeting of the Society for Reproductive Investigation, March 15 - 18, 2017 in Orlando, FL. The theme of the 2017 meeting, “D2D: Data to Discovery,” was chosen to highlight our interest in the most exciting and stimulating basic, translational and clinical research for harnessing the power of scientific data to promote knowledge in reproductive health and medicine.

Sam Mesiano, PhD, our Program Director, has created an excellent program that includes three Presidential Distinguished Lecturers, one trainee plenary session, 24 concurrent oral sessions, 12 minisymposia and 2 Special Symposia. In addition to the scientific sessions, we have also planned complementary activities that advance SRI’s mission. The first is Connection Corners, an event that engages trainees with the more experienced members of the Society. We will also hold three lunch sessions – on Wednesday, we will hold a Diversity Career Development Forum; on Thursday, the topic will be Systems Biology in Pregnancy Health and Research; on Friday, the focus will be Precision Medicine and Women’s Health.

Each of our three Presidential Distinguished Lecturers represents a different aspect of our D2D theme. The Thursday Presidential lecturer is ***Suchi Saria, PhD***, from the Department of Computational Sciences at Johns Hopkins University. Dr Saria is an expert in computational biology and machine learning. She applies her unique knowledge to computational health informatics and predictive modeling in healthcare.

The Friday Presidential lecturer is ***Stephen Quake, PhD***, Lee Otterson Professor in the School of Engineering and Professor of Bioengineering, Applied Physics and Physics at Stanford University. Dr Quake’s recent inventions in the area of prenatal genomics have transformed the field. He will share his innovative research and provide visionary comments about the future of blood based-genomic testing.

David Haig, PhD, George Putnam Professor of Organismic and Evolutionary Biology at Harvard University, will give the Saturday Presidential lecture. Dr Haig will talk about his novel and provocative data synthesis approaches to understanding maternal-fetal conflicts.

The 2017 annual meeting will be held in Orlando, FL, at the Hilton Orlando Bonnet Creek. The science will be inspiring, the camaraderie will be engaging, and the warm sun of Florida will be shining. On behalf of the SRI Council, officers and staff, I invite you to attend the exciting meeting we have planned and connect with our colleagues and friends in SRI!

Yours,

Yoel Sadovsky

Yoel Sadovsky, MD, SRI President 2016-2017

Society for Reproductive Investigation

Executive Council
March 2016 – March 2017

President
Yoel Sadovsky, MD
Pittsburgh, PA, USA

President Elect
Sandra T. Davidge, PhD
Edmonton, AB, Canada

Secretary Treasurer
Mark Phillippe, MD, MHCM
Boston, MA, USA

Immediate Past President
Hugh Taylor, MD
New Haven, CT, USA

President Nominee
Murray D. Mitchell, Dphil, DSc
Brisbane, QLD, Australia

Secretary Treasurer-Elect
Ian M. Bird, PhD
Madison, WI, USA

Council Members
March 2016 – March 2017

Phillip R. Bennett, MD, PhD (2019)
London, United Kingdom

Errol R. Norwitz, MD, PhD (2018)
Boston, MA, USA

In-Training *ad-hoc* Council Member
Emiel Post Uiterweer, MD, PhD
Utrecht, Netherlands

Elizabeth Ann Bonney, MD (2019)
Burlington, VT, USA

Yolanda Smith, MD, MS (2017)
Ann Arbor, MI, USA

Emmet Hirsch, MD (2017)
Evanston, IL, USA

Stacy Zamudio, PhD (2018)
Hackensack, NJ, USA

Program Committee Members

Program Committee Co-Chair
Stephen Matthews, PhD
Toronto, ON, Canada

Elizabeth Ann Bonney, MD, MPH
Burlington, VT, USA

Emiel Post Uiterweer, MD, PhD
Utrecht, Netherlands

Program Committee Co-Chair
Emre Seli, MD
New Haven, CT, USA

William Catherino, MD, PhD
Bethesda, MD, USA

Bo Rueda, PhD
Boston, MA, USA

2017 Program Director
Sam Mesiano, PhD
Cleveland, OH, USA

Sandra Davidge, PhD
Edmonton, AB, Canada

Yoel Sadovsky, MD
Pittsburgh, PA, USA

2018 Program Director
Marilyn Cipolla, PhD
Burlington, VT, USA

Charles Ducsay, PhD
Loma Linda, CA, USA

Stacy Zamudio, PhD
Hackensack, NJ, USA

2019 Program Director
Sarah England, PhD
St. Louis, MO, USA

Leslie Myatt, PhD, FRCOG
Portland, OR, USA

SRI Administration

Executive Director
Anne Krolikowski, CAE
Tel. (414) 918-9888
Email: akrolikowski@sri-online.org

Meetings Manager
Nicole Dahms, CMP
Tel. (414) 918-9888
Email: ndahms@sri-online.org

Associate Executive Director
Leah Miller
Tel: (414) 918-9888
Email: lmiller@sri-online.org

Membership & Communications Coordinator
Morgan Derby
Tel. (414) 918-9888
Email: mderby@sri-online.org

Society for Reproductive Investigation

Presidents' Page

Year	President
1953+	William J. Diekmann
1954+	William J. Diekmann
1955+	Ernest W. Page
1956+	Nicholas S. Assali
1957*	
1958+	Allan C. Barnes
1959+	Russell R. deAlvarez
1960+	Louis M. Hellman
1961+	James T. Bradbury
1962+	Leon C. Chesley
1963+	Charles E. McLellan
1964+	Roger B. Scott
1965+	Jack A. Pritchard
1966+	Ben M. Peckham
1967+	J. George Moore
1968+	Charles H. Hendricks
1969+	Andre E. Hellegers
1970	Edward J. Quilligan
1971+	Joseph Seitchik
1972+	T. Terry Hayashi
1973+	William M. Paul
1974+	C. Donald Christian
1975+	Walter L. Herrmann
1976	Robert B. Jaffe
1977+*	Kenneth J. Ryan
1978+*	Paul C. McDonald
1979+	Thomas H. Kirschbaum
1980+	A. Brian Little
1981+	Pentii K. Siiteri
1982+	Samuel S.C. Yen
1983+	Lawrence D. Longo
1984	James C. Warren
1985+	William N. Spellacy
1986	Roy M. Pitkin
1987	Edward E. Wallach
1988+	Daniel R. Mishell, Jr.
1989+	Howard L. Judd
1990+	Carl J. Pauerstein
1991	Norman F. Gant, Jr.
1992	Frederick Naftolin
1993	W. Ann Reynolds
1994+	Gary D. Hodgen
1995	Alan H. DeCherney
1996	Anne Colston Wentz
1997	James M. Roberts
1998	Rogerio A. Lobo
1999	Joe Leigh Simpson
2000	Eli Y. Adashi
2001	Jennifer R. Niebyl
2002+	Sherman Elias
2003	John R.G. Challis
2004	Jerome F. Strauss, III
2005	Steven G. Gabbe
2006	Gerson Weiss
2007	Linda C. Giudice
2008	Charles J. Lockwood
2009	Felice Petraglia
2010	Leslie Myatt
2011	Robert N. Taylor
2012	Stephen J. Lye
2013	Sarah L. Berga
2014	Kelle H. Moley
2015	Serdar Bulun
2016	Hugh Taylor
2017	Yoel Sadovsky

***No Meeting**
+Deceased

Society for Reproductive Investigation

SRI WOULD LIKE TO THANK THE 2017 ABSTRACT REVIEWERS

Graham Aberdeen
Vikki Abrahams
Kristina Adams Waldorf
Ayman Al-Hendy
Terrence Allen
Lawrence Amesse
Matthew Anderson
Russ Anthony
Dilly Anumba
David Archer
Mira Aubuchon
Samir Babayev
Gordon Bates
Laxmi Baxi
Kelly Bennett
Phillip Bennett
Sarah Berga
Lia Bernardi
Karin Blakemore
Zeev Blumenfeld
Silvina Bocca
Elizabeth Bonney
Jerry Bouma
Catalin Buhimschi
Irina Burd
Heather Burkin
Maria Bustillo
Erkan Buyuk
Egle Bytautiene
Byron Calhoun
Eden Cardozo
Alison Care
Steve Caritis
Sandra Carson
Jorge Carvajal
Patrick Catalano
Marcelle Cedars
John Challis
Setsuko Chambers
Peter Chang
Boonsri Chanrachakul
Madhu Lata Chauhan
Niraj Chavan
Dongbao Chen
Frank Chervenak
Edward Chien
Fumihisa Chishima
SiHyun Cho
Gregory Christman
Pasquapina Ciarmela
Tereza Cindrova-Davies
Marilyn Cipolla
Erin Clark
Charles Coddington
Mariano Colon-Caraballo
Jennifer Condon
Kirk Conrad
Stephen Contag
Carolyn Coulam
Hilary Critchley
Barbara Croy
Gaurang Daftary
Anna David
Sandra Davidge
Alan DeCherney
Maria Delivoria-Papadopoulos
Francesco DeMayo
Gernot Desoye
Lawrence Devoe
Michael Diamond
Evdokia Dimitriadis
William Dodson
Xuesen Dong
Maurice Druzin
Charles Ducsay
Jennifer Eaton
Andrea Edlow
Sarah England
Anna Euser
Michael Fassett
Maisa Feghali
Helen Feltovich
Liping Feng
Enrico Ferrazzi
Jorge Figueroa
Clare Flannery
Idhaliz Flores
Stephen Ford
Martin Frasch
Henry Galan
Hilary Gammill
Haijun Gao
Juan Garcia-Velasco
Caroline Gargett
Shari Gelber
William Gibbons
Sylvie Girard
Linda Giudice
Dino Giussani
Laura Goetzl
Natalia Gokina
Alan Golichowski
Nardhy Gomez-Lopez
Frank Gonzalez
Styliani Goulopoulou
Ernie Graham
Michael Gravett
Erin Greaves
Lucy Green
Anthony Gregg
Chad Grotegut
Seth Guller
Mounira Habli
Lisa Halvorson
Shannon Hawkins
Oskari Heikinheimo
Ryan Heitmann
Debra Heller
Karin Hellner
Denise Hemmings
Jennifer Herington
Guadalupe Herrera-Garcia
Katherine Himes
Alison Holloway
Mariko Horii
Iffath Hoskins
Gloria Huang
Hong-yuan Huang
Se-Te Joseph Huang
Carl Hubel
K. Joseph Hurt
Nicholas Illsley
Mohamad Irani
Hiroaki Itoh
Margit Janát-Amsbury
Patricia Jimenez
Helen Jones
Lisa Joss-Moore
Tu'uhevaha Kaitu'u-Lino
Amanda Kallen
Caleb Kallen
Tomi Kanninen
Sinem Karipcin
Helen Kay
Meredith Kelleher
Matt Kemp
Asma Khalil
Omid Khorram
Ludwig Kiesel
J. Julie Kim
Soon Ok Kim
Yoon Ha Kim
Hamid-Reza Kohan-Ghadr
Justin Konje
Brian Koos
Graciela Krikun
Seung-Yup Ku
Shathiyah Kulandavelu
Deepak Kumar
Sathish Kumar
Satu Kuokkanen
Michelle Kutzler
Andrés López Bernal
Antonio Simone Laganà
Hannele Laivuori
Uwe Lang
Martha Lappas
Louise Laurent
Joop Laven
Yan Li
Sean Limesand
Marshall Lindheimer
Stefano Luisi
Daniel MacPhee
Thomas Magee
Ronald Magness
Mala Mahendroo
Monica Mainigi
Shintaro Makino
Alina Maloyan
Chiara Mando
Adina Maniu
Tracy Manuck
Anna Maria Marconi
Mark Martens
Aymara Mas Perucho
Keiichi Matsubara
Thomas McElrath
Elizabeth McGee
Erin McGillick
Lynda McGinnis
Peter McGovern
Ramkrishna Mehendale
K.M.J. Menon
Ramkumar Menon
Brian Mercer
Zaher Merhi
Murray Mitchell
Tiffany Moore Simas
Alexandros Moraitis
Molly Moravek
Terry Morgan
Jude Morton
Ozgul Muneyyirci-Delale
Sribalasubashini Muralimanoharan
Amy Murtha
David Mutch
Levent Mutlu
Leslie Myatt
Jenny Myers
Indira Mysorekar
Frederick Naftolin
Manubai Nagamani
Peter Nathanielsz
Nihar Nayak
Genevieve Neal-Perry
Guiying Nie
Jane Norman
Errol Norwitz
Warren Nothnick
Perrie O'Tierney-Ginn
Sergio Oehninger
Kutluk Oktay
Sara Ornaghi
George Osol
Yutaka Osuga
Charlotte Oyston
Jeyasuria Pancharatnam
Samuel Parry
Kristiina Parviainen
Mary Ellen Pavone
William Pearce
Donald Peebles
Louis Peeters
Gerald Pepe
Margaret Petroff
Sophie Petropoulos
Mark Phillippe
Margareta Pisarska
Alex Polotsky
Robert Powers
Eva Pressman
Jelmer Prins
J. Gerald Quirk
Karen Racicot
Nilufer Rahmioglu
Augustine Rajakumar
Jay Ramadoss
John Randolph
E. Albert Reece
Kathryn Reed
Torsten Reinheimer
John Repke
Bryan Richardson
Paolo Rinaudo
James Roberts
Victoria Roberts
Jared Robins
Charles Rosenfeld
Paul Rozance
Bo Rueda
Yoel Sadovsky
Alessandro Santin
Joaquin Santolaya-Forgas
Philippa Saunders
Danny Schust
Amy Schutt
James Segars
Panicos Shangaris
Oksana Shynlova
Robert Silver
Melissa Simon
Joe Leigh Simpson
Donna Slater
Ov Slayden
Roger Smith
Robert Sokol
Francesca Soncin
Floortje Spaans
Jessica Spencer
Aleksandar Stanic
Eric Steegers
Julie Stilley
Pamela Stratton
Jennifer Straughen
Aaron Styer
Junichi Sugawara
Motoi Sugimura
Daniel Surbek
Lynne Sykes
Reshef Tal
Anthony Taylor
Robert Taylor
Kari Teramo
Larry Thaete
Michael Thomas
Loren Thompson
Mancy Tong
Stephen Tong
Rachel Tribe
John Tsibris
Jason Umans
Felipe Vadillo-Ortega
Ignatia Van Den Veyver
Vladimir Vargas
Anthony Vintzileos
Joris Vriens
Ganesa Wegienka
Tracey Weissgerber
Wendy White
Deborah Wing
Ruth Ann Word
Daliao Xiao
Qing Xue
Simcha Yagel
Liliya Yamaleyeva
Qiwei Yang
Lynn Yee
Bruce Young
Roger Young
Bo Yu
Liang Yu
Hong Wa Yung
Pavel Zagadailov
Jing Zheng
Chi Zhou
Erin Zinkhan
Krina Zondervan

Society for Reproductive Investigation

THE SRI WOULD LIKE TO THANK THE 2016 SRI ANNUAL MEETING POSTER DISCUSSANTS
MARCH 16-19 - MONTREAL, QC, CANADA

Kristina Adams Waldorf, MD
Ayman Al-Hendy, MD, PhD
Beth J Allison, PhD
Dilly Anumba, MD, FRCOG, LLM
Philip Baker, BMedSci, BM, BS, FRC
Kelly A Bennett, MD,MSc,FRCSC
Phillip R Bennett, MD, PhD
Ira M Bernstein, MD
Karin Blakemore, MD
Zeev Blumenfeld, MD
Silvina Bocca, MD, PhD, HCLD,CC
Irina Burd, MD, PhD
Eden Cardozo, MD
Alison S Care, PhD
Niraj Chavan, MD, MPH
Dongbao Chen, PhD
Julian K Christians, PhD
Jennifer Condon, PhD
(B)-Anne Croy, PhD
Leandro De Oliveira, MD, PhD
Mina Desai, PhD
Lucien Daniel Durosier, MD, MSc
Esther Eisenberg, MD MPH
Amelie Fassbender, PhD
Helen Feltovich, MD
Liping Feng, MD
Clare Flannery, MD
Caroline E Gargett, PhD
Styliani Goulopoulou, PhD
Chad Grotegut, MD
Cynthia Gyamfi-Bannerman, MD, MSc
Erica Hammer, MD
Oskari Heikinheimo, MD, PhD
Iffath A Hoskins, MD
K. Joseph Hurt, MD, PhD
Jeffrey A Keelan, PhD
Matthew Kemp, PhD
Sathish Kumar, DVM, PhD
Satu Kuokkanen, MD, PhD
Uwe Lang, MD, PhD
Monica Mainigi, MD
K.M.J. Menon, PhD
Ramkumar Menon, PhD
Molly B Moravek, MD
Terry Morgan, MD, PhD
Janna Morrison, PhD
Nihar Nayak, DVM, PhD
Michael J Paidas, MD
Mana Parast, MD, PhD
Margareta D Pisarska, MD
Jelmer R Prins, MD, PhD
Augustine Rajakumar, PhD
Bryan S Richardson, MD
Danny Schust, MD
Emre Seli, MD
Oksana Shynlova, PhD
Robert J. Sokol, MD
Aleksandar Stanic-Kostic, MD, PhD
Pamela Stratton, MD
Aaron Styer, MD
Daniel Surbek, MD, Prof
Lynne Sykes, BSc, MBBS, PhD
Robert N. Taylor, MD, PhD
Loren P Thompson, PhD
Rachel M Tribe, PhD
Angela Vinturache, MD, PhD
Tracey L Weissgerber, PhD
Wendy White, MD, MPH
Deborah Wing, MD, MBA
Hung Winn, MD, JD, MBA
Qing Xue, MD, PhD
Chih-Feng Yen, MD
Steven L Young, MD, PhD
Tamas Zakar, MD, PhD
Stacy Zamudio, PhD

Society for Reproductive Investigation

On-Site Meeting Registration

All scientific sessions, satellite sessions and poster sessions will be held at the Hilton Orlando Bonnet Creek in Orlando, FL. Entry to all sessions (including guests at the poster sessions) requires a paid registration and the wearing of a name badge.

Registration Hours

Tuesday, March 14	2:00 p.m. – 7:00 p.m.
Wednesday, March 15	7:00 a.m. – 7:00 p.m.
Thursday, March 16	7:00 a.m. – 6:00 p.m.
Friday, March 17	7:00 a.m. – 6:30 p.m.
Saturday, March 18	7:00 a.m. – 1:00 p.m.

Registration Fees

	ON SITE
Member	$680.00
Associate Member	$580.00
In-Training Member	$430.00
Non-Member	$905.00
*In-Training Non-Member (Must have support letter)	$580.00
In-Training Non-Member: ASRM or SMFM Member	$522.00
Emeritus Member	$680.00
Emeritus Member 70+	Complimentary *(SRI registration only)*
Guest	$50.00

Session Fees:

Satellite Meetings
(Wednesday, March 15, 2017) $100.00

* All In-Training Non Member registrations must be accompanied by a letter from the trainee's supervisor confirming the status of the registrant.

Speaker Ready Room

Participants and Speakers who are scheduled to give oral presentations may preview their presentations prior to their lectures. The Speaker Ready Room is located in Hilton Orlando Bonnet Creek, Desoto Room. **Please note that all presentations will be in Microsoft PowerPoint format. USB Flash Drives, USB Thumb Drives and USB Pen Drives containing presentations must be provided to the AV Technicians in the Speaker Ready Room at least 4 hours prior to the oral session or the day before for morning presentations.**

SRI Cancellation Policy:

Meeting registration cancellations must be in writing to the SRI administrative office in Milwaukee, WI

555 East Wells Street, Suite 1100
Milwaukee, WI 53202

Registration fees will be refunded, less a $165.00 administrative fee if the request is made in writing prior to February 17, 2017. **No Refunds** will be made on registration cancellations after February 17, 2017.

Host Hotel

Hilton Orlando Bonnet Creek
14100 Bonnet Creek Resort Lane
Orlando, FL 32821
Tel: +1-407-597-3600
Reservations: 1-888-353-2013

Awards and Their Meanings

The SRI Lifetime Distinguished Service Award is intended to recognize an individual who has made outstanding service contributions to the Society for Reproductive Investigation and significant contributions to the field of reproductive medicine and women's health. *Past awardees include Alan DeCherney (2016).* The 2017 award recipient will be announced at the meeting.

The SRI Distinguished Scientist Award is made annually to a senior member of the Society who has made significant and lasting contributions to the Society and to scientific research in reproductive medicine. The recipient is selected by the President, with the advice of officers and other members. As of 2012, this award is generously sponsored by the Giorgio Pardi Foundation in honor of Professor Giorgio Pardi, a distinguished former member of the SRI. Past awardees include *Nicholas S. Assali* (1982); *Willard M. Allen* (1983); *Edward H. G. Hon* (1984); *Donald H. Barron* (1985); *James T. Bradbury* and *Leon Chesley* (1986); *Louis Hellman* and *Elizabeth Ramsey* (1987); *Jack A. Pritchard* (1988); *Kenneth J. Ryan* (1989); *Paul C. MacDonald* (1990); *Giacomo Meschia* (1991); *Samuel S. C. Yen* (1992); *Robert B. Jaffe* (1993); *Daniel R. Mishell, Jr.* (1994); *Paul G. McDonough* (1995); *Lawrence D. Longo* (1996); *Pentti K. Siiteri* (1997); *Edward J. Quilligan* (1998); *Orlando J. Miller* (1999); *Howard W. Jones, Georgeanna Seegar Jones, James R. Scott* and *Robert K. Creasy* (2000); *Frederick P. Zuspan* (2001); *Joe Leigh Simpson* (2002); *Frederick Naftolin* (2003); *Luigi Mastroianni, Jr.* (2004)*; Maria Delivoria-Papadopoulous* (2005); *Jerome F. Strauss, III (2006); D. Michael Nelson (2007); Linda C. Giudice (2008); John R.G. Challis (2009); Gautam Chaudhuri (2010); James M. Roberts (2011); Peter Nathanielsz (2012); Charles J. Lockwood (2013); Carole Mendelson (2014); Eli Adashi (2015); Roberto Romero (2016).* The 2017 award recipient will be announced at the meeting.

The President's Achievement Award is made annually to a member of the Society whose record in scientific investigation is outstanding and assures a continued productive research career in the future. The recipient is selected by the President, with the advice of officers and other members. Past awardees include *Gary D. Hodgen* (1983); *Evan R. Simpson* (1984); *John R.G. Challis* (1985); *Joe Leigh Simpson* (1986); *A. H. DeCherney* (1987); *Aaron J.W. Hsueh* (1988); *Eli Y. Adashi* (1989); *Jerome F. Strauss* (1990); *Murray D. Mitchell* (1991); *Roberto Romero* (1992); *Maria Delivoria-Papadopoulos* (1993); *Robert Schenken* and *M. Linette Casey* (1994); *Rogerio A. Lobo* (1995): *Linda C. Giudice* (1996); *Stephen J. Lye* (1997); *Deborah J. Anderson* (1998); *Mark I. Evans* (1999); *Ricardo Azziz, Sarah L. Berga* and *Richard S. Legro* (2000); *Katherine D. Wenstrom* (2001); *Serdar Bulun* (2002); *Sandra Davidge* (2003); *Yoel Sadovsky* (2004); *Philip Baker* (2005); *Sam Mesiano (2006); Kelle Moley (2007); Hugh Taylor (2008); Fiona Lyall and Jane Norman (2009); Marilyn Cipolla (2010); Lisa M. Halvorson (2011); Stephen Matthews (2012); Caroline Gargett (2013); Anil Sood (2014); Ayman Al-Hendy and Emily Su (2015); Emre Seli (2016).* The 2017 award recipient will be announced at the meeting.

The Frederick Naftolin Award for Mentorship was established in 2003 to recognize the contributions of a member of the society to training and career development of investigators in the field of reproductive and women's health. The award is named in honor of Dr. Naftolin, a former President of the society and past recipient of the President's Distinguished Scientist Award. Dr. Naftolin a staunch advocate for creating a mechanism for the society to celebrate outstanding service to our scientific community through excellence in mentoring. The award was endowed by generous contributions from members of the society, Dr. Naftolin's colleagues and trainees. The awardee is selected by the Council, in consultation with the Past Presidents and members of the society. The first recipient of this award was *Lawrence D. Longo* (2004); *Edward J. Quilligan* (2005); *Mortimer Levitz (2006); Philip J. DiSaia (2007); James Roberts (2008); B.C.J.M. Fauser (2009); Louis Peeters (2010;) James C. Rose (2011); John R.G. Challis (2012); Joan Hunt (2013); Leslie Myatt (2014); Linda Giudice (2015); Jerome F. Strauss (2016).* The 2017 award recipient will be announced at the meeting.

The Rogerio A. Lobo Award was established in 2007 to recognize the most outstanding contribution to *Reproductive Sciences* by a member of the Society for Reproductive Investigation. The award is named in honor of Dr. Lobo, a former President of the society and former Editor in Chief of the *Journal of the Society for Gynecologic Investigation (JSGI)* which is now *Reproductive Sciences*. Recipients of this award were: *Michael G. Ross and Omid Khorram (2008); Joan S. Hunt (2009); Carolyn Y. Muller (2010); Linda C. Giudice (2011); Nasser Chegini (2012); Kelle Moley (2013); Felice Petraglia (2014); Ayman Al-Hendy (2015); Hilary Critchley (2016).* The 2017 award recipient will be announced at the meeting.

The SRI President's Presenter's Awards recognizes the four highest ranked abstracts chosen for presentation at the President's New Investigator Plenary Session. The recipients of the award will each be presented with a $1,000 travel award at the Awards Ceremony. The 2017 award recipient will be announced at the meeting.

The Laxmi Baxi Awards was established in 2013 and will be awarded to PhD individuals only who are either graduate students still in training or postdoctoral fellows within 5 years of their PhD degree. Two $1,000 travel awards will be given to the top abstracts in basic reproductive science and in translational reproductive science. The awardees will receive a plaque, check and they will be honored at the SRI annual meeting Awards Ceremony. This award is made possible by a generous, long-standing member of SRI, Dr. Laxmi Baxi, and was created to encourage young PhD trainees to present their research at our meeting. The 2017 award recipient will be announced at the meeting.

The Pfizer-SRI President's Presenter's Awards were originally established in 1996 as the Wyeth President's Presenter Award to recognize the 25 most meritorious abstracts (either poster or oral presentation) submitted by individuals still in training. Fellows and those in both pre and post-doctoral training are eligible to receive the award. The 25 awardees will receive a certificate and a check, and they and their training directors will be honored at an awards ceremony. The Society has always sought a means by which to encourage young investigators to present their research at our meeting. We anticipate the SRI President's Presenter's Award will encourage more abstract submissions and higher quality abstracts by the very people who need encouragement to consider a research career. The 2017 award recipient will be announced at the meeting.

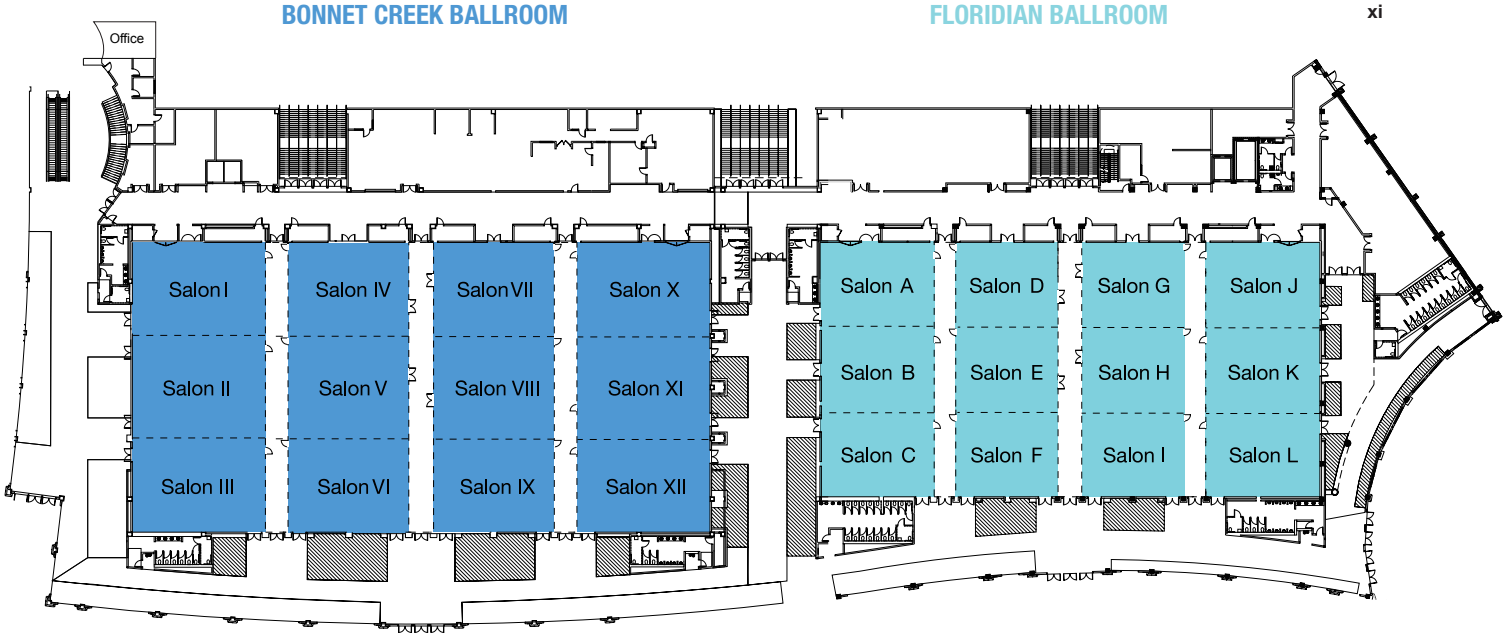
The Thomas McDonald Award acknowledges the highest ranked abstract by an investigator in training within the field of fetal neuroscience. This award honors the legacy of Dr. McDonald, whose immense contributions to the field of obstetrics and gynecology focused upon the neuroendocrinology of the developing fetus, placental function, fetal brain development, and the uterine contractility. The award will be presented at the Award Ceremony during the SRI Annual Scientific Meeting.

The Giorgio Pardi Foundation Awards provide a monetary award to a Junior Researcher, as well as to the best young worthy investigator coming from an Italian University. The award winners will be presented at the Award Ceremony during the SRI Annual Scientific Meeting.

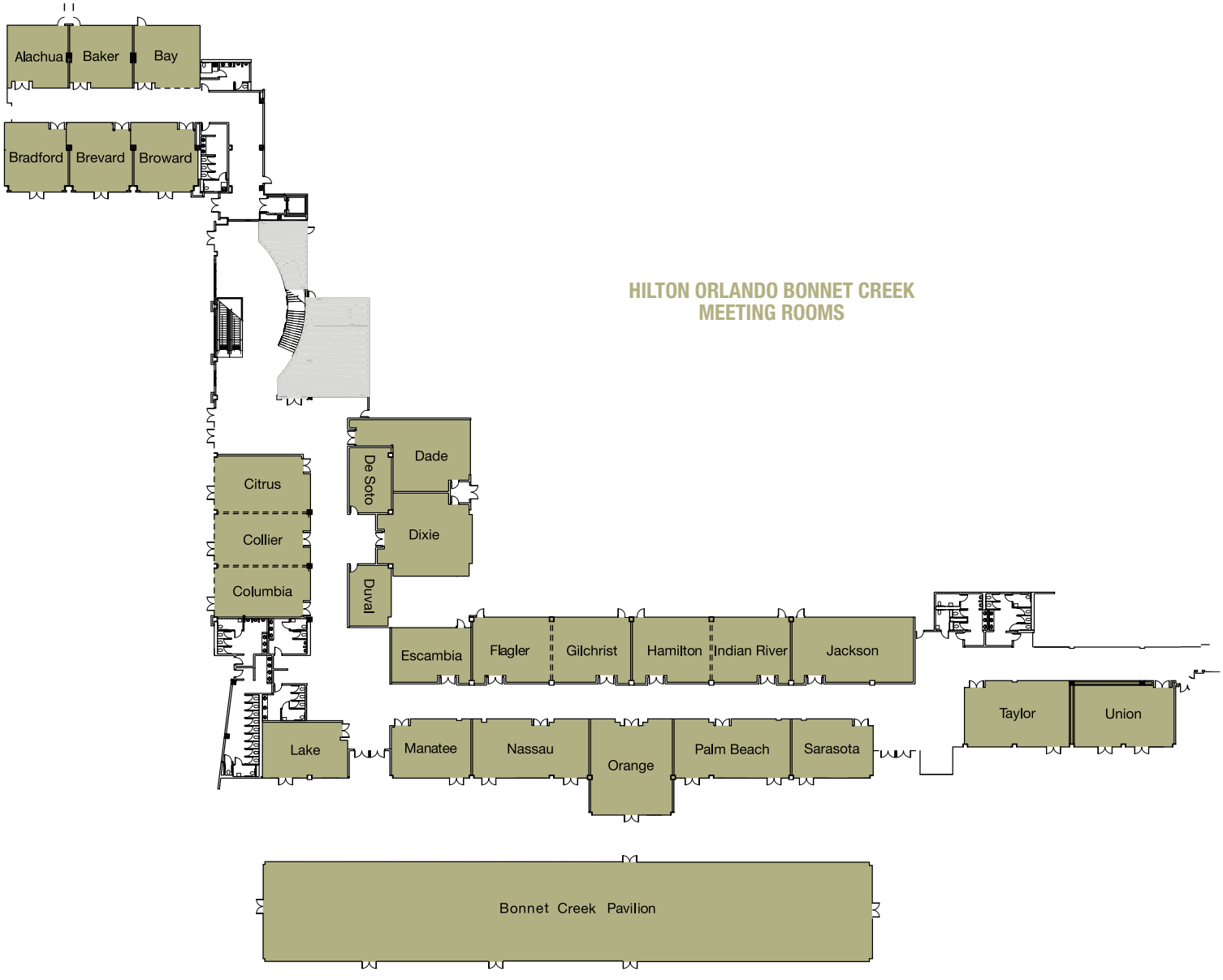
The SRI Poster Awards were initiated at the 2010 SRI Annual Meeting in Orlando, Florida. Two senior investigators will be discussing/judging posters presented by Investigators-In-Training. The Poster Presenter will summarize their work for the judges, followed by questions from the poster discussants/judges. Awards will be given to the best 20 posters at the SRI Annual Scientific Meeting Awards Ceremony.

HILTON ORLANDO BONNET CREEK
BONNET CREEK BALLROOM

HILTON ORLANDO BONNET CREEK
FLORIDIAN BALLROOM



HILTON ORLANDO BONNET CREEK
MEETING ROOMS



SRI Annual Scientific Meeting

D2D: Data to Discovery

March 15 – 18, 2017

Orlando, FL

	Wednesday, March 15	Thursday, March 16	Friday, March 17	Saturday, March 18
Morning	**7:00 a.m. – 7:00 p.m.** Registration **7:30 a.m. – 8:30 a.m.** Career Development Session – Mid-Career Researcher **8:30 a.m. – 5:00 p.m.** Satellite Meetings	**7:00 a.m. – 6:00 p.m.** Registration **8:00 a.m. – 10:00 a.m.** President's Welcome Address, President's Distinguished Lecture I, New Investigator Plenary **10:00 a.m. – 11:30 a.m.** Poster Session I	**7:00 a.m. – 6:30 p.m.** Registration **7:15 a.m. – 8:00 a.m.** SRI Business Meeting (Members only) **8:00 a.m. – 9:00 a.m.** President's Distinguished Lecture II **9:15 a.m. – 10:45 a.m.** Concurrent Oral Presentations II **10:45 a.m. – 12:15 p.m.** Poster Session II	**7:00 a.m. – 1:00 p.m.** Registration **8:00 a.m. – 9:00 a.m.** President's Distinguished Lecture III **9:00 a.m. – 10:30 a.m.** Poster Session III **10:30 a.m. – 12:00 p.m.** Concurrent Oral Presentations IV
Afternoon	**8:30 a.m. – 5:00 p.m.** Satellite Meetings **12:15 p.m. – 1:15 p.m.** Career Development Session - Diversity & Inclusion **12:00 p.m. – 1:00 p.m.** *Reproductive Sciences* Editorial Board Meeting	**12:00 p.m. – 1:30 p.m.** Special Symposia I **1:45 p.m. – 3:45 p.m.** Mini Symposia I **4:00 p.m. – 6:00 p.m.** Concurrent Oral Presentations I	**12:30 p.m. – 2:00 p.m.** Special Symposia II **12:30 p.m. – 2:00 p.m.** Pfizer-SRI President's Awards (By Invite Only) **2:15 p.m. – 3:45 p.m.** Concurrent Oral Presentations III **4:00 p.m. – 6:00 p.m.** Mini Symposia II	**12:15 p.m. – 1:45 p.m.** Hot Topics & Awards Ceremony (Lunch Included) **2:00 p.m. – 4:00 p.m.** SRI Council Meeting (Council Members Only)
Evening	**5:15 p.m. – 6:45 p.m.** Career Development Session-In-Training and Early Career Researcher **6:45 p.m. – 8:00 p.m.** Welcome Reception	**6:15 p.m. – 7:45 p.m.** Connection Corners	**6:15 p.m. – 7:45 p.m.** Presidential Address, Awards and Wine and Cheese Reception	

Society for Reproductive Investigation

64th Annual Meeting of the Society for Reproductive Investigation

"D2D: Data to Discovery"

Hilton Orlando Bonnet Creek, Orlando, FL

March 15 – 18, 2017

Wednesday, March 15, 2017

7:00 a.m. – 7:00 p.m.	**Registration** Bonnet Creek Foyer
7:30 a.m. – 8:30 a.m.	**Career Development Session – Mid-Career Researcher** Floridian E - F Mid-Career Researcher Breakfast **Navigating a Changing Landscape: Mid-Career in Reproductive Science**
Moderators:	Elizabeth A. Bonney, MD, MPH University of Vermont Jared Robins, MD Northwestern University
8:30 a.m. – 5:00 p.m.	**Endometrium Satellite Meeting – Endometriomics in Health and Disease** Floridian C
Organizers:	Peter A.W. Rogers, PhD University of Melbourne Asgi T. Fazleabas, PhD Michigan State University
Morning Session:	**8:30 a.m. – 12:00 p.m.**
8:30 a.m. – 9:30 a.m.	**Mouse Models for Uncovering Estrogen and ER Actions in the Uterus** Kenneth S. Korach, PhD National Institute of Environmental Health Sciences/ National Institute of Health
9:30 a.m. – 10:00 a.m.	**Break**
10:00 a.m. – 10:30 a.m.	**Steroid Hormone-Epigenome Interplay in the Human Endometrium** Sahar Houshdaran, PhD University of California, San Francisco
10:30 a.m. – 11:00 p.m.	**The Endometrial Cistrome: Identifying Novel Targets of the Glucocorticoid Receptor** Shannon D. Whirledge, PhD Yale School of Medicine
11:00 a.m. – 12:00 p.m.	**Roles of Non-Coding RNA in Endometrial-Embryo Interactions** Eva Dimitriadis, PhD Hudson Institute of Medical Research
12:00 p.m. – 1:30 p.m.	**Lunch**
Afternoon Session:	**1:30 p.m. – 5:00 p.m.**
1:30 p.m. – 2:30 p.m.	**Addressing Neglected Diseases: Innovative Ways to Relieve Women From the Burden of Endometriosis** Markus Koch, PhD Bayer Pharma
2:30 p.m. – 3:00 p.m.	**Profiling Endometrial Pericytes Reveals Roles in Endometrial Repair** Phoebe Kirkwood, PhD Student MRC Centre for Inflammation Research, University of Edinburgh
3:00 p.m. – 3:30 p.m.	**Decidualization Defect as a Possible Maternal Cause of Preeclampsia** Tamara Garrido, PhD University of Valencia, Igenomix/ INCLIVA
3:30 p.m. – 4:00 p.m.	**Break**
4:00 p.m. – 5:00 p.m.	**Obesity, Decidualization and Autophagy - The Perfect Storm** Kelle Moley, MD Washington University
8:20 a.m. – 5:00 p.m.	**Fetal Physiology Satellite Meeting – Integration of Environmental Signals During Development** Bonnet Creek X
Organizer:	Sean W. Limesand, PhD University of Arizona
Morning Session:	**8:20 a.m. – 12:00 p.m.**
Moderator:	Sean W. Limesand, PhD University of Arizona
8:20 a.m. – 8:30 a.m.	**Welcome**
8:30 a.m. – 9:30 a.m.	**Hypoxia Stress, and Fetal Inflammation: What's the Microbiome got to Do With It?** Charles E. Wood, PhD University of Florida
9:30 a.m. – 10:00 a.m.	**Break**

10:00 a.m. – 11:00 a.m. **Developmental Programming by IUGR: Common Outcomes and Gaps in Knowledge From Animal Models**
Kathryn L. Gatford, PhD
University of Adelaide

11:00 a.m. – 12:00 p.m. **Lactocrine Signaling and the Maternal Environmental Continuum**
Frank "Skip" F. Bartol, PhD
Auburn University

12:00 p.m. – 1:30 p.m. **Lunch**

Afternoon Session: **1:30 p.m. – 5:00 p.m.**

Moderator: Dustin T. Yates, PhD
University of Arizona

1:30 p.m. – 2:00 p.m. **Modulation of Fetal Adipogenesis by Endocrine Disrupting Chemicals**
Almudena Veiga-Lopez, DVM, PhD
Michigan State University

2:00 p.m. – 2:30 p.m. **Amino Acids Regulate Paracrine Signaling and Development of the Pancreatic Islet in IUGR Fetuses**
Paul J. Rozance, MD
Children's Hospital Colorado

2:30 p.m. – 3:00 p.m. **Intrauterine Inflammation and Infection: Journey to Center of the Fetal Brain**
Irina Burd, MD, PhD
Johns Hopkins Medicine

International Collaborative Ovine Network (ICON) Session
International Collaborative Ovine Network was established to promote sheep as a valuable animal model for biomedical and physiological research.

Organizer: Matthew Kemp, PhD
University of Western Australia

3:00 p.m. – 3:30 p.m. **The Artifical Placenta: Development and Application**
Masatoshi Saito, MD, PhD
Tohoku University Hospital

3:30 p.m. – 4:00 p.m. **Break**

4:00 p.m. – 4:30 p.m. **Ultrasound in Preclinical Models of Pregnancy**
Sarah Stock, MBChB, PhD
University of Edinburgh

4:30 p.m. – 5:00 p.m. **Manipulating Gene Expression in the Sheep Placenta**
Russ Anthony, PhD
Colorado State University

8:30 a.m. – 5:00 p.m. **Myometrium/Parturition Satellite Meeting**
Floridian B

Organizers: Rachel Tribe, PhD
King's College London
R. Ann Word, MD
University of Texas Southwestern Medical Center

Morning Session: **8:30 a.m. – 12:00 p.m.**

Moderator: Rachel Tribe, PhD
King's College London

8:30 a.m. – 9:00 a.m. **Heat Shock Proteins: Renaissance Molecules for the Myometrium**
Daniel MacPhee, PhD
University of Saskatchewan

9:00 a.m. – 9:30 a.m. **The Uterine Unfolded Protein Response Regulates Gestational Length**
Jennifer Condon, PhD
Wayne State University School of Medicine

9:30 a.m. – 10:00 a.m. **Break**

10:00 a.m. – 10:30 a.m. **Regulation of Inflammation and Innate Immune Cells in Preterm Birth**
Karen Racicot, PhD
Michigan State University College of Medicine

10:30 a.m. – 11:00 a.m. **The Role of Adrenomedullin in Establishing and Maintaining the Maternal-Fetal Interface**
Brooke Matson, MD, PhD
University of North Carolina at Chapel Hill

11:00 a.m. – 11:30 a.m. **Epigenetic Sensitization to African American Commensal Bacteria in Preterm Labor**
Scott Walsh, PhD
Virginia Commonwealth University

11:30 a.m. – 12:00 p.m. **TrpV4 Channels and Preterm Labour**
David Cornfield, MD
Stanford University

12:00 p.m. – 1:30 p.m. **Lunch**

Afternoon Session: **1:30 p.m. – 5:00 p.m.**

Moderator: R. Ann Word, MD
University of Texas Southwestern Medical Center

1:30 p.m. – 2:30 p.m. **Mechanisms of Dysfunctional Quiescence in Spontaneous Preterm Labor**
Ian Buxton, PhD
University of Nevada

2:30 p.m. – 3:00 p.m. **New Paradigms in Cervical Tissue Structure and Function**
Joy Vink, MD
Columbia University Medical Center

3:00 p.m. – 3:30 p.m. **Optical and Mass Spectral Analysis of the Cervix During Pregnancy**
Jeff Reese, MD
Vanderbilt University

3:30 p.m. – 4:00 p.m. **Break**

4:00 p.m. – 5:00 p.m. **Hypoxia and Myometrial Function: Something Old and Something New**
Susan Wray, PhD
University of Liverpool

8:30 a.m. – 5:00 p.m. **Ovarian Biology Satellite Meeting – Biomarkers of Embryo Viability and Implantation in the Era of Precision Medicine**
Floridian A

Organizers: Richard T. Scott, MD,
Reproductive Medicine Associates
New Jersey
Emre Seli, MD
Yale School of Medicine

Morning Session: **8:30 a.m. – 12:00 p.m.**

Moderator: Emre Seli, MD
Yale School of Medicine

Non-Invasive Strategies for Embryo Assessment

8:30 a.m. – 9:30 a.m. **Non-Invasive Strategies to Assess Embryo Viability**
Emre Seli, MD
Yale School of Medicine

9:30 a.m. – 10:00 a.m. **Break**

Invasive Strategies for Embryo Assessment

10:00 a.m. – 11:00 a.m. **Pre-Implantation Genetic Screening (PGS) for Aneuploidy: Promises and Pitfalls**
Richard T. Scott, MD
Reproductive Medicine Associates
New Jersey

11:00 a.m. – 11:30 a.m. **Next Generation Sequencing for Embryo Diagnostics**
Dagan Wells, PhD
Oxford University

11:30 a.m. – 12:00 p.m. **Mitochondrial DNA Copy Number as a Predictor of Embryo Implantation**
Elpida Fragouli, PhD
Oxford University

12:00 p.m. – 1:30 p.m. **Lunch**

Afternoon Session: **1:30 p.m. – 5:00 p.m.**

Moderator: Richard T. Scott, MD
Reproductive Medicine Associates
New Jersey

Endometrial Predictors of ART Outcome

1:30 p.m. – 2:30 p.m. **Transcriptomic Assessment of Endometrial Receptivity: ERA Testing**
Carlos Simon, MD, PhD
Fundacion IVI

2:30 p.m. – 3:00 p.m. **Endometrial Microbiome and Assisted Reproduction**
Jason Franasiak, MD
Reproductive Medicine Associates
New Jersey

3:00 p.m. – 3:30 p.m. **Endometrial Proteome as a Predictor of Implantation**
Francisco Dominguez, PhD
Fundacion IVI

3:30 p.m. – 4:00 p.m. **Break**

Big Data and Personalized Reproductive Medicine

4:00 p.m. – 4:30 p.m. **Using Prediction Model-Based Clinical Solutions to Expand Patients' Access to IVF and PGS and Improve IVF Success Rates**
Mylene Yao, MD
Univfy

4:30 p.m. – 5:00 p.m. **Big-Data Analytics and Genomics to Optimize Infertility Treatment**
Mark Adams, PhD
Celmatix

8:30 a.m. – 5:00 p.m. **Placental Association of the Americas Satellite Meeting**
Bonnet Creek XI

Organizer: Thomas Jansson, MD, PhD
University of Colorado Anschutz Medical Campus

Session 1: **8:30 a.m. – 12:00 p.m.**

Moderator: Johann Urschitz, PhD
Thomas Jansson, MD, PhD

Utero-Placental Gene-Targeting *In Vivo*: From Mice to Humans

8:30 a.m. - 9:30 a.m. **Lentiviral Vector-Mediated Placenta-Specific Gene Manipulation in Mice**
Masahito Ikawa, PhD
Osaka University

9:30 a.m. – 10:00 a.m. **Break**

10:00 a.m. – 10:30 a.m. **PiggyBac Transposase-Mediated Gene Modulation in the Placenta**
Johann Urschitz, PhD
University of Hawaii

10:30 a.m. – 11:00 p.m. **Nano-Particle Mediated Placental IGF-1 Therapy in IUGR**
Helen N. Jones, PhD
Cincinnati Children's Hospital Medical Center

11:00 a.m. – 12:00 p.m. **Uterine Artery Adenovirus-Mediated Delivery of VEGF to Improve Utero-Placental Flow in IUGR**
Anna David, PhD
University College London

12:00 p.m. – 1:30 p.m. **Lunch**

Session 2: **1:30 p.m. – 4:30 p.m.**

Moderator: Anna Euser, MD, PhD
Thaddeus G. Golos, PhD

Zika and the Placenta

1:30 p.m. – 2:15 p.m.	**Mechanisms of Antiviral Defense at the Maternal- Fetal Interface** Carolyn Coyne, PhD University of Pittsburgh
2:15 p.m. – 3:00 p.m.	**Zika GO: Tracking ZIKV in the Placenta** Indira Mysorekar, PhD Washington University
3:00 p.m. – 3:30 p.m.	**Zika Virus Infects Human Placental Macrophages** Rana Chakraborty, MD Emory University
3:30 p.m. – 4:00 p.m.	**Break**
4:00 p.m. – 4:30 p.m.	**Transplacental Innate Immune Defense and Transmission of ZIKV** Jennifer Stencel-Baerenwald, PhD University of Washington
Session 3:	**4:30 p.m. – 5:00 p.m.**
Moderator:	Leslie Myatt, PhD, FRCOG

The Human Placental Project: An Update

4:30 p.m. – 5:00 p.m.	**The Human Placenta Project: Progress and Future Directions** David Weinberg, PhD NICHD

8:30 a.m. – 5:00 p.m.	**Preterm Birth International Satellite Symposium** Bonnet Creek XII

Preterm Birth International Collaborative (PREBIC)

Organizer:	Ramkumar Menon, PhD University of Texas Medical Branch at Galveston
Morning Session:	**8:30 a.m. – 12:00 p.m.**
Moderators:	Hanns Helmer, MD President - PREBIC Medical University Vienna
8:30 a.m. – 9:00 a.m.	**Placental Aging and Stillbirth** Roger Smith, AM. MBBS, Hons., PhD, FRACP, FRANZCOG, FRSB University of Newcastle
9:00 a.m. – 9:30 a.m.	**Clocks, Alarms and the Onset of Parturition** Robert N. Taylor, MD, PhD Wake Forest School of Medicine
9:30 a.m. – 10:00 a.m.	**Coffee Break**
10:00 a.m. – 10:30 a.m.	**Novel Targets for Preventing Spontaneous Preterm Birth** Martha Lappas, PhD University of Melbourne
10:30 a.m. – 11:00 a.m.	**Infection, Inflammation and Preterm Birth: Pharmacological Prevention and Treatment Strategies** Jeffrey Keelan, PhD University of Western Australia

PREBIC Keynote Lecture

11:00 a.m. – 11:45 a.m.	**Cell Fate Diversity and Aging** Judith Campisi, PhD University of Southern California
11:45 a.m. – 12:00 p.m.	**Discussion**
12:00 p.m. – 1:30 p.m.	**Lunch**
Afternoon Session:	**1:30 p.m. – 5:00 p.m.**
Moderator:	Nanbert Zhong, MD, PhD Secretary General, PREBIC New York State Institute for Basic Research in Developmental Disabilities
1:30 p.m. – 2:00 p.m.	**Can Risk Prediction Models be Clinically Useful in Identifying Women at Risk of Preterm Birth?** Jane Hirst, MD University of Oxford
2:00 p.m. – 2:30 p.m.	**Evaluation of the Systemic Inflammatory Response Associated to Air Pollutants Exposure During Pregnancy** Felipe Vadillo-Ortega, MD Instituto Nacional de Medicina Genomica
2:30 p.m. – 3:00 p.m.	**Cell-Based Non-Invasive Prenatal Testing Using Fetal Cells Isolated From Maternal Blood** Ripudaman Singh, PhD, MBA ARCEDI Biotech ApS

Progesterone Debate

3:00 p.m. – 3:30 p.m.	**Progesterone - Exploiting its Action to Prevent Preterm Birth** Sam Mesiano, PhD Case Western Reserve University
3:30 p.m. – 4:00 p.m.	**Coffee Break**
4:00 p.m. – 4:20 p.m.	**Progesterone - Why it Still Has a Role in Preterm Birth Prevention** Cynthia Gyamfi-Bannerman, MD, MSc Columbia University
4:20 p.m. – 4:45 p.m.	**Progesterone - Why We Shouldn't Depend on it to Prevent Preterm Birth** Jane E. Norman, MD, FRCOG, FRCPE, FMedSci University of Edinburgh MRC Centre for Reproductive Health, Queen's Medical Research Institute
4:45 p.m. – 5:00 p.m.	**Discussion**

12:00 p.m. – 1:00 p.m.	**Reproductive Sciences Editorial Board Meeting** Palm Beach

12:15 p.m. – 1:15 p.m. **Career Development Session – Diversity Symposium**
Floridian E - F
Maps Where Children Matter
Marie Lynn Miranda, PhD
Rice University

5:15 p.m. – 6:45 p.m. **Career Development Session – In-Training and Early Career Investigators**
Floridian A
Job Search and Negotiation

6:45 p.m. – 8:00 p.m. **Welcome Reception**
Signature Island

Thursday, March 16, 2017

7:00 a.m. – 6:00 p.m. **Registration**
Bonnet Creek Foyer

8:00 a.m. – 10:00 a.m. **President's Welcome Address, President's Distinguished Lecture I, New Investigator Plenary**
Floridian D - I

8:00 a.m. – 8:10 a.m. **Welcome Address**
Yoel Sadovsky, MD
SRI President

8:10 a.m. – 9:00 a.m. **President's Distinguished Lecture I**
*Eligible for **1.0 AMA PRA Category 1 Credits™**/1.0 Category 1 College Cognate Credits*
Suchi Saria, PhD
Assistant Professor, Department of Computational Sciences
Johns Hopkins University

9:00 a.m. – 10:00 a.m. **New Investigator Plenary Session**

10:00 a.m. – 11:30 a.m. **Poster Session I**
Bonnet Creek I - IX

12:00 p.m. – 1:30 p.m. **Special Symposia I: Systems Biology in Pregnancy Health and Research**
Floridian D - I

Moderators: Mark Chance, PhD
Nathan Price, PhD

12:00 p.m. – 12:30 p.m. **Network Biology Tools for Translational Research**
Mark Chance, PhD

12:30 p.m. – 1:00 p.m. **Systems Analysis of OMICS Data in Pregnancy Conditions**
Nathan Price, PhD

1:00 p.m. – 1:30 p.m. **Genestation: A Powerful Platform for Integrating Diverse Types of OMICS Data to Understand Pregnancy and its Pathologies**
Antonis Rokas, PhD

1:45 p.m. – 3:45 p.m. **Mini Symposia I**

The Influence of Circadian Rhythms on Reproductive Outcomes
*Eligible for **2.0 AMA PRA Category 1 Credits™**/ 2.0 Category 1 College Cognate Credits*
Bonnet Creek X

Moderator: Sarah K. England, PhD

1:45 p.m. – 2:15 p.m. **The Influence of Chronodisruption on Risk of Preterm Birth**
Sarah K. England, PhD

2:15 p.m. – 2:45 p.m. **The Ability of Light to Suppress Contractions in Late-Term Pregnant Women; Mechanisms for Melatonin Action in the Human Uterus**
Elizabeth B. Klerman, MD, PhD

2:45 p.m. – 3:15 p.m. **Circadian Rhythms in the Fetus**
Claudia Torres-Farfan, PhD

3:15 p.m. – 3:45 p.m. **Estrogenic Modulation of Activity Rhythms in Development and Adulthood**
Megan M. Mahoney, PhD

Fundamental and Translational Aspects of Extracellular Vesicles: Focus on the Female Reproductive System
*Eligible for **2.0 AMA PRA Category 1 Credits™**/ 2.0 Category 1 College Cognate Credits*
Bonnet Creek XI

Moderator: Thomas E. Spencer, PhD

1:45 p.m. – 2:15 p.m. **Extracellular Vesicles and Ovarian Function and Disease**
Lane Christenson, PhD

2:15 p.m. – 2:45 p.m. **Extracellular Vesicles as Important Mediators of Uterine Function**
Thomas Spencer, PhD

2:45 p.m. – 3:15 p.m. **Human Endometrial Exosomes Influence Trophectodermal Cells to Promote Implantation**
Lois Salamonsen, PhD

3:15 p.m. – 3:45 p.m. **ExRNAs as Biomarkers for Placental Dysfunction**
Louise C. Laurent, MD, PhD

Fetal Membranes Weakening and Rupture-Understanding PPROM in Four Dimensions
*Eligible for **2.0 AMA PRA Category 1 Credits™**/ 2.0 Category 1 College Cognate Credits*
Floridian B

Moderator: John Moore, MD

1:45 p.m. – 2:15 p.m. **Preterm Premature Rupture of Membranes - Clinical Perspectives**
Brian Mercer, MD

2:15 p.m. – 2:45 p.m. **Novel Targets for Inhibition of Inflammation for the Prevention of PPROM**
Martha Lappas, PhD

2:45 p.m. – 3:15 p.m. **Deformation and Rupture of Fetal Membranes - Microstructural Mechanisms Which May Account for Their Toughness or Brittleness**
Edoardo Mazza, PhD

3:15 p.m. – 3:45 p.m. **Insight Gained From a Human In-Vitro Model System of Fetal Membrane Weakening**
Deepak Kumar, MD

The -OMICS Revolution in Understanding of Uterine Leiomyomas, and the Future of Therapy
*Eligible for **2.0 AMA PRA Category 1 Credits™**/ 2.0 Category 1 College Cognate Credits*
Bonnet Creek XII

Moderator: William H. Catherino, MD, PhD

1:45 p.m. – 2:15 p.m. **The Genetics and Genomics of Leiomyomas**
William H. Catherino, MD, PhD

2:15 p.m. – 2:45 p.m. **Developmental Epigenetics and Uterine Fibroids**
Ayman Al-Hendy, MD, PhD

2:45 p.m. – 3:15 p.m. **Pathogenesis and Etiology of Uterine Fibroids: Opportunities for Research**
James Segars, MD

3:15 p.m. – 3:45 p.m. **What is Effective Fibroid Treatment?**
Elizabeth Stewart, MD

An Applied System Biology to Study the Endometrial Receptivity
*Eligible for **2.0 AMA PRA Category 1 Credits™**/ 2.0 Category 1 College Cognate Credits*
Floridian A

Moderator: Jose Antonio Horcajadas, PhD

1:45 p.m. – 2:15 p.m. **The Transcriptomics of the Endometrium: A 15 Year Data Experience**
Jose Antonio Horcajadas, PhD

2:15 p.m. – 2:45 p.m. **The Proteomic Interactome of the Endometrial Receptivity**
Francisco Dominguez, PhD

2:45 p.m. – 3:15 p.m. **A System Biology Approach to Understand the Endometrium's Physiology and the Endometrial Receptivity**
Andres Salumets, PhD

3:15 p.m. – 3:45 p.m. **Endometrial Receptivity Tests: Advanced Molecular Tools to Study the Endometrial Receptivity**
Sergio C. Oehninger, MD, PhD

Delineating Contributors to the Genesis and/or Treatment Resistance Properties of Gynecologic Cancers
*Eligible for **2.0 AMA PRA Category 1 Credits™**/ 2.0 Category 1 College Cognate Credits*
Floridian C

Moderator: Bo R. Rueda, PhD

1:45 p.m. – 2:15 p.m. **Unbiased Molecular Analysis of Progesterone Receptor Action in Cancer Identifies Novel Mechanisms and Processes**
J. Julie Kim, PhD

2:15 p.m. – 2:45 p.m. **Clinicopathologic Significance of Mismatch Repair Defects in Endometrial Cancer and Promise for Immune Checkpoint Blockade-Based Therapies**
Paul Goodfellow, PhD

2:45 p.m. – 3:15 p.m. **Epithelial Cell Plasticity and the Origins of Ovarian Cancer**
Barbara Vanderhyden, PhD

3:15 p.m. – 3:45 p.m. **Ovarian Cancer Stem Cells Display Resistance to PARP Inhibitor Treatment**
Bo. R. Rueda, PhD

3:45 p.m. – 4:00 p.m. **Coffee Break**
Bonnet Creek I - IX

4:00 p.m. – 6:00 p.m. **Concurrent Oral Presentations I**
a) Reproductive Biology I - Floridian A
b) Parturition I - Bonnet Creek XII
c) Gynecology I - Floridian B
d) Clinical Perinatology I - Bonnet Creek X
e) Preeclampsia I - Bonnet Creek XI
f) Maternal Biology and Health - Floridian C

6:15 p.m. – 7:45 p.m. **Connection Corners**
New, Early and Mid-Career Investigators are invited to come meet and 'connect' with Senior Investigators about jobs, career advice or just some friendly banter. Drinks and light appetizers provided.
Bonnet Creek Pavilion

2017 Table Topics:
1. From Trainee to PI
2. Your First SRI Meeting
3. From the Bench to the Bedside
4. Finding a Good Mentor - Mentor in the Cloud
5. Networking Tips
6. Negotiating: Getting What You Need to Succeed
7. Clinical Grantsmanship
8. Basic Science Grantsmanship
9. Publishing Tips and Tricks
10. Physician-Scientist: Is There Time to Sleep?
11. A Healthy Work-Life Balance
12. Careers Outside of Academia

Friday, March 17, 2017

7:00 a.m. – 6:30 p.m. **Registration**
Bonnet Creek Foyer

7:15 a.m. – 8:00 a.m. **SRI Business Meeting**
(Members Only) Breakfast Provided
Floridian D - I

8:00 a.m. – 9:00 a.m. **President's Distinguished Lecture II**
Molecular Stethoscope in Pregnancy
*Eligible for **1.0 AMA PRA Category 1 Credits™**/1.0 Category 1 College Cognate Credits*
Floridian D - I
Stephen Quake, PhD
Lee Otterson Professor in the School of Engineering and Professor of Bioengineering, of Applied Physics, and, By Courtesy, of Physics
Stanford University

9:15 a.m. – 10:45 a.m. **Concurrent Oral Presentations II**
a) Developmental Programming I - Floridian C
b) Fetus I - Bonnet Creek X
c) Parturition II - Bonnet Creek XII
d) Gynecology II - Floridian B
e) Placenta I - Bonnet Creek XI
f) Reproductive Endocrinology and Infertility I - Floridian A

10:45 a.m. – 12:15 p.m. **Poster Session II**
Bonnet Creek I - IX

12:30 p.m. – 2:00 p.m. **Special Symposia II: Precision Medicine and Women's Health**
Floridian D - I

Moderator: Diana Bianchi, MD

12:30 p.m. – 1:00 p.m. **Precision Medicine and Women's Health**
Linda Guidice, MD, PhD, MSc

1:30 p.m. – 1:30 p.m. **Fetal Precision Medicine**
Diana Bianchi, MD

1:30 p.m. – 2:00 p.m. **Precision Medicine for Gynecologic Cancers**
Gordon Mills, MD

12:30 p.m. – 2:00 p.m. **Pfizer-SRI President's Presenter's Award Lunch**
Orange

2:15 p.m. – 3:45 p.m. **Concurrent Oral Presentations III**
a) Reproductive Biology II - Floridian A
b) Gynecologic Oncology - Floridian B
c) Gynecology III - Floridian C
d) Clinical Perinatology II - Bonnet Creek X
e) Preeclampsia II - Bonnet Creek XI
f) Epidemiology, Population Health and Global Health - Focus on Zika - Bonnet Creek XII

4:00 p.m. – 6:00 p.m. **Mini Symposia II**

Mining Big Data to Reveal Biomarkers and Pathophysiology of Preterm Birth
*Eligible for **2.0 AMA PRA Category 1 Credits™**/ 2.0 Category 1 College Cognate Credits*
Bonnet Creek XII

Moderator: Stephen Lye, PhD

4:00 p.m. – 4:30 p.m. **Maternal Peripheral Blood Leukocytes as Biomarkers of Preterm Birth**
Oksana Shynlova, PhD

4:30 p.m. – 5:00 p.m. **Multi-Omic Data Integration and Interrogation to Discover Network Signatures of Preterm Birth**
Doug Brubaker, PhD

5:00 p.m. – 5:30 p.m. **In Richness and In Health: The Role of Vaginal Microbiota in Pregnancy**
David MacIntyre, PhD

5:30 p.m. – 6:00 p.m. **The Use of Next-Generation Sequencing and Family Studies to Uncover Rare Genetic Variants Associated with Preterm Birth**
Wei Ang, MSc

Molecular Biology of Implantation and Recurrent Pregnancy Loss
*Eligible for **2.0 AMA PRA Category 1 Credits™**/ 2.0 Category 1 College Cognate Credits*
Floridian A

Moderator: Vikki M. Abrahams, PhD

4:00 p.m. – 4:30 p.m. **Molecular Regulation of Endometrial Plasticity in Implantation and Recurrent Pregnancy Loss**
Jan J. Brosens, MD, PhD

4:30 p.m. – 5:00 p.m. **Role of Endogenous Retroviruses in the Establishment and Maintenance of Pregnancy**
Neal S. Rote, PhD

5:00 p.m. – 5:30 p.m. **MicroRNA Regulation of Immunotolerance in Early Pregnancy**
Sarah A. Robertson, PhD

5:30 p.m. – 6:00 p.m. **Novel Mechanisms of Placental Inflammation in Obstetric Antiphosolipid Syndrome**
Vikki M. Abrahams, PhD

Immune Cell Contributions to Endometrial and Cervical Health and Disease
*Eligible for **2.0 AMA PRA Category 1 Credits™**/ 2.0 Category 1 College Cognate Credits*
Bonnet Creek X

Moderator: Chandrakant Tayade, DVM, PhD

4:00 p.m. – 4:30 p.m. **Modulation of Inflammatory Responses in the Female Reproductive Tract**
Charles Wira, PhD

4:30 p.m. – 5:00 p.m. **Immune Basis of Infertility**
Bruce Lessey, MD, PhD

5:00 p.m. – 5:30 p.m. **Tissue Resident Uterine Immune Cells**
Dorothy K. Sojka, PhD

5:30 p.m. – 6:00 p.m. **Immune Cell Contributions to Initiation of Endometriosis**
Chandrakant Tayade, DVM, PhD

Gamete Biology and Gene Editing
*Eligible for **2.0 AMA PRA Category 1 Credits™**/ 2.0 Category 1 College Cognate Credits*
Floridian B

Moderator: Kyle Orwig, PhD

4:00 p.m. – 4:30 p.m. **Mitochondrial Replacement Therapy**
David L. Keefe, MD

4:30 p.m. – 5:00 p.m. **iPSC-Mediated Germline Gene Therapy**
Renee A. Reijo Pera, PhD

5:00 p.m. – 5:30 p.m. **Mitochondrial Diseases and Mitochondrial Replacement Therapy**
Michio Hirano, MD

5:30 p.m. – 6:00 p.m. **Germline Gene Therapy with Spermatogonial Stem Cells**
Kyle Orwig, PhD

Frontiers in Diagnosis, Treatment and Prevention of CMV and ZIKA in Pregnancy
*Eligible for **2.0 AMA PRA Category 1 Credits™**/ 2.0 Category 1 College Cognate Credits*
Bonnet Creek XI

Moderator: Simcha Yagel, MD

4:00 p.m. – 4:30 p.m. **Ex-Vivo Model of CMV Transmission**
Simcha Yagel, MD

4:30 p.m. – 5:00 p.m. **Placental Trophoblasts and Viral Resistance in Recipient Cells**
Yoel Sadovsky, MD

5:00 p.m. – 5:30 p.m. **Patterns of CMV and ZIKV Infection in the Uterine- Placenta Interface and Routes of Vertical Transmission**
Lenore Pereira, PhD

5:30 p.m. – 6:00 p.m. **Vaccine Development to Control CMV Disease: Immune Manipulation by the Virus**
Edward Mocarski, PhD

Linking Early Life Exposures to Later Pathology
*Eligible for **2.0 AMA PRA Category 1 Credits™**/ 2.0 Category 1 College Cognate Credits*
Floridian C

Moderator: Dino A. Giussani, PhD, ScD, FRCOG

4:00 p.m. – 4:30 p.m. **Heart Disease Link to Fetal Hypoxia: An Intergenerational Perspective**
Dino A. Giussani, PhD, ScD, FRCOG

4:30 p.m. – 5:00 p.m. **Maternal Obesity and Offspring Cardiometabolic Disease: Unravelling the Underlying Mechanisms**
Rebecca M. Reynolds, PhD, FRCP, FRCPE

5:00 p.m. – 5:30 p.m. **The Obesity Epidemic: Could it be an Oocyte Issue?**
Kelle H. Moley, MD

5:30 p.m. – 6:00 p.m. **Epigenetic Impact of Prenatal Exposure to Adversity**
Frances A. Champagne, PhD

6:15 p.m. – 7:45 p.m. **President's Address, Awards, and Wine and Cheese Reception**
Floridian D - I

Saturday, March 18, 2017

7:00 a.m. – 1:00 p.m. **Registration**
Bonnet Creek Foyer

8:00 a.m. – 9:00 a.m. **President's Distinguished Lecture III**
Maternal-Fetal Conflict and Cooperation in Human Pregnancy
*Eligible for **1.0 AMA PRA Category 1 Credits™**/1.0 Category 1 College Cognate Credits*
Floridian D - I
David Haig, PhD
George Putnam Professor of Organismic and Evolutionary Biology
Harvard University

9:00 a.m. – 10:30 a.m. **Poster Session III**
Bonnet Creek I - IX

10:30 a.m. – 12:00 p.m. **Concurrent Oral Presentations IV**
a) Developmental Programming II - Floridian B
b) Fetus II - Bonnet Creek X
c) Stem Cells - Floridian C
d) Parturition III - Bonnet Creek XII
e) Placenta II - Bonnet Creek XI
f) Reproductive Endocrinology and Infertility II - Floridian A

12:15 p.m. – 1:45 p.m. **Hot Topics & Awards Ceremony**
Lunch Included
Floridian D - I

Moderators: Emre Seli, MD
Marilyn Cipolla, PhD

Plenary/Oral Sessions	Abstract Numbers	Title Pages	Abstract Pages
Thursday, March 16, 2017, 9:00 AM-10:00 AM			
Presidential Plenary	O-001 – O-004	3A	55A
Thursday, March 16, 2017, 4:00 PM-6:00 PM			
Clinical Perinatology I	O-005 – O-012	4A	56A
Endometriosis, Fibroids and Gynecology I	O-013 – O-020	4A	58A
Maternal Biology and Health	O-021 – O-028	5A	61A
Parturition I	O-029 – O-036	5A	63A
Preeclampsia I	O-037 – O-044	6A	66A
Reproductive Biology I	O-045 – O-052	6A	68A
Friday, March 17, 2017, 9:15 AM-10:45 AM			
Developmental Programming I	O-053 – O-058	7A	71A
Fetus I	O-059 – O-064	7A	73A
Endometriosis, Fibroids and Gynecology II	O-065 – O-070	8A	75A
Parturition II	O-071 – O-076	8A	76A
Placenta I	O-077 – O-082	9A	78A
Reproductive Endocrinology and Infertility I	O-083 – O-088	9A	80A
Friday, March 17, 2017, 2:15 PM-3:45 PM			
Clinical Perinatology II	O-089 – O-094	10A	82A
Epidemiology, Population Health and Global Health - Focus on Zika	O-095 – O-100	10A	84A
Gynecologic Oncology	O-101 – O-106	11A	86A
Endometriosis, Fibroids and Gynecology III	O-107 – O-112	11A	88A
Preeclampsia II	O-113 – O-118	12A	90A
Reproductive Biology II	O-119 – O-124	12A	92A
Saturday, March 18, 2017, 10:30 AM-12:00 PM			
Developmental Programming II	O-125 – O-130	13A	94A
Fetus II	O-131 – O-136	13A	95A
Parturition III	O-137 – O-142	14A	97A
Placenta II	O-143 – O-148	14A	99A
Reproductive Endocrinology and Infertility II	O-149 – O-154	15A	101A
Stem Cells	O-155 – O-160	15A	103A

Poster Sessions	Abstract Numbers	Title Pages	Abstract Pages
Thursday, March 16, 2017, 10:00 AM-11:30 AM			
Basic Parturition	T-001 – T-015	16A	105A
Clinical Perinatology	T-035 – T-054	17A	115A
Developmental Programming	T-070 – T-087	19A	126A
Epidemiology	T-088 – T-091	20A	132A
Fetus	T-092 – T-105	20A	133A
Global Health	T-106 – T-106	21A	137A
Gynecologic Oncology	T-107 – T-109	21A	138A
Endometriosis, Fibroids, and Gynecology	T-110 – T-127	22A	138A
Maternal Biology and Health	T-128 – T-137	23A	144A
Placenta	T-138 – T-158	23A	147A
Population Health	T-159 – T-160	24A	154A
Preeclampsia	T-161 – T-178	25A	154A
Reproductive Biology	T-179 – T-194	26A	160A
Reproductive Endocrinology and Infertility	T-195 – T-208	26A	165A
Stem Cells	T-209 – T-212	27A	169A
Friday, March 17, 2017, 10:45 AM-12:15 PM			
Basic Parturition	F-001 – F-017	28A	170A
Clinical Perinatology	F-036 – F-052	29A	181A
Developmental Programming	F-071 – F-088	31A	192A
Epidemiology	F-089 – F-092	32A	197A
Fetus	F-093 – F-105	33A	198A
Gynecologic Oncology	F-106 – F-109	33A	202A
Endometriosis, Fibroids, and Gynecology	F-110 – F-127	34A	203A
Maternal Biology and Health	F-128 – F-136	35A	209A
Placenta	F-137 – F-157	35A	212A
Population Health	F-158 – F-159	36A	218A
Preeclampsia	F-160 – F-178	37A	219A
Reproductive Biology	F-179 – F-195	38A	225A
Reproductive Endocrinology and Infertility	F-196 – F-208	38A	230A
Stem Cells	F-209 – F-212	39A	234A
Saturday, March 18, 2017, 9:00 AM-10:30 AM			
Basic Parturition	S-001 – S-018	40A	235A
Clinical Perinatology	S-035 – S-052	41A	246A
Developmental Programming	S-069 – S-087	43A	257A
Epidemiology	S-088 – S-090	44A	262A
Fetus	S-091 – S-103	45A	263A
Global Health	S-104 – S-104	45A	267A
Gynecologic Oncology	S-105 – S-108	45A	267A
Endometriosis, Fibroids, and Gynecology	S-109 – S-126	46A	268A
Maternal Biology and Health	S-127 – S-135	47A	274A
Placenta	S-136 – S-156	47A	276A
Population Health	S-157 – S-158	48A	283A
Preeclampsia	S-159 – S-176	49A	283A
Reproductive Biology	S-177 – S-193	49A	289A
Reproductive Endocrinology and Infertility	S-194 – S-207	50A	294A
Stem Cells	S-208 – S-211	51A	299A

Scientific Program Schedule

64th Annual Scientific Meeting

Thursday, March 16, 2017 - Plenary

9:00 AM-10:00 AM **Plenary**

PRESIDENTIAL PLENARY

Floridian D - I

Yoel Sadovsky, 2016 - 2017 SRI President
Sandra T Davidge, 2017 - 2018 SRI President

9:00 O-001 **MiR-200b Mediates the Teratogenic Effect of Maternal Diabetes Leading to Neural Tube Defects by Suppressing Autophagy and Inducing Endoplasmic Reticulum Stress.**
Daoyin Dong, Wei-Bin Shen, and Peixin Yang. Baltimore, MD, USA.

9:15 O-002 **SOX17 Governs the Indian Hedgehog to Promote Female Fertility via Uterine Epithelial-Stromal Interactions.**
Xiaoqiu Wang, Xilong Li, Nyssa R Adams, San-Pin Wu, Rainer B Lanz, John P Lydon, Jae-Wook Jeong, and Francesco J DeMayo. RTP, NC, USA; Houston, TX, USA; and Grand Rapids, MI, USA.

9:30 O-003 **Cervical Gene Delivery of Human Beta-Defensin-3(HBD-3) Prevents Ascending Bacterial Infection in Pregnant Mice.**
Natalie Suff, Rajvinder Karda, Mona Bajaj-Elliott, Suzanne MK Buckley, Mark Tangney, Simon N Waddington, and Donald Peebles. London, United Kingdom; and Cork, Ireland.

9:45 O-004 **Maternal Lifestyle Impairs Embryonic Growth: A Prospective Periconception Cohort Study.**
Matthijs R Van Dijk, Nicole V Borggreven, Sten P Willemsen, Anton HJ Koning, Regine PM Steegers-Theunissen, and Maria PH Koster. Rotterdam, Zuid-Holland, Netherlands.

Thursday, March 16, 2017 - Concurrent Session I

4:00 PM-6:00 PM **Concurrent Oral Session**

CLINICAL PERINATOLOGY I

Bonnet Creek X

Jeff Reese and Deepak Kumar

4:00 O-005 **Non-Invasive Assessment of Fetal CMV Infection and Injury via Fetal Neuronal Exosomes: A Non-Human Primate Model.**
Laura Goetzl, Nune Darbinian, Nana Merabova, Kinari Patel, Alice F Tarantal, and Peter A Barry. Philadelphia, PA, USA; and Davis, CA, USA.

4:15 O-006 **The New Triple I Classification Scheme and Outcomes Among Term Infants.**
Christina A Herrera, Julie Shakib, Erin AS Clark, Michael W Varner, and Bob Silver. Salt Lake City, UT, USA.

4:30 O-007 **Network Analysis of Maternal Genes Implicated in Preterm Birth.**
Maria Schmoll, Ravindu Gunatilake, Avinash Patil, and Annabeth Barnard. Indianapolis, IN, USA; and Phoenix, AZ, USA.

4:45 O-008 ***Futurebirth*™- Prediction by 12w of Future Preterm Birth (PTB)<33w Using a Novel Test of Cell Free Plasma (cfp) RNA.**
Carl Weiner, Helen Zhou, Howard Cuckle, Argyro Syngelaki, Kypros Nicolaides, and Yafeng Dong. Kansas City, KS, USA; Tel Aviv, Israel; and London, United Kingdom.

5:00 O-009 **Altered Acylcarnitine Metabolism in the Placenta in Spontaneous Preterm Birth.**
Summer Elshenawy, Paschalis T Doulias, Samuel Parry, Michael Bennett, Harry Ischiropolous, and Rebecca A Simmons. Philadelphia, PA, USA.

5:15 O-010 **PreImplantation Factor (PIF*) Prevents Fetal Loss by Modulating LPS Induced Inflammatory Response.**
Martin Mueller, Nicoletta Di Simone, Fiorella Di Nicuolo, Riccardo Marana, Roberta Castellani, Francesco Ria, Manuela Veglia, Giovanni Scambia, Daniel Surbek, and Eytan Barnea. Rome, Italy; Bern, Switzerland; Cherry Hill, NJ, USA; and New Haven, CT, USA.

5:30 O-011 **Genetic Deficiency in IL-6 Modifies Sex-Related Differences in Neonatal Mouse Mortality in Response to Influenza Infection.**
Elizabeth A Bonney, Jenna E McQuesten, Kendall Krebs, and Mercedes Rincon. Burlington, VT, USA.

5:45 O-012 **Healthy, Infection-Free Growth of Preterm Lambs Maintained with Ex-Vivo Uterine Environment (EVE) Therapy for One Week.**
Haruo Usuda, Shimpei Watanabe, Eleanor Woodward, Masatoshi Saito, Gabrielle C Musk, Suhas G Kallapur, Judith Rittenschober-Böhm, Hideyuki Ikeda, Shinichi Sato, Takushi Hanita, Tadashi Matsuda, John P Newnham, and Matthew W Kemp. Perth, WA, Australia; Sendai, Miyagi, Japan; and Cincinnati, OH, USA.

4:00 PM-6:00 PM **Concurrent Oral Session**

ENDOMETRIOSIS, FIBROIDS AND GYNECOLOGY I

Floridian B

Robert N Taylor and Richard O Burney

4:00 O-013 **GATA6 Confers an Immunologic Phenotype in Endometriosis.**
Christia Angela M Sison, Matthew T Dyson, and Serdar Bulun. Chicago, IL, USA.

4:15 O-014 **Role of the Wnt Pathway in Endometriosis.**
Maik Obendorf, Juliane Hundt, Eva Simon, Ralf Lesche, Rene Wenzl, Lorenz Kuessel, and Thomas M Zollner. Berlin, Germany; and Vienna, Austria.

4:30 O-015 **Prostaglandin E2 Signaling, Estrogen-Dominance and Progesterone-Resistance in Endometriosis.**
Joe A Arosh, JeHoon Lee, Kaylon L Bruner-Tran, Kevin G Osteen, and Sakhila K Banu. College Station, TX, USA; and Nashville, TN, USA.

4:45 O-016 **Endometriosis Inherently Increases the Number of CD146/CD140b Double Positive Cells in the Eutopic Endometrium of Baboons with Induced Disease.**
Fatima Barragan, Michael R Strug, Ren-Wei Su, Amanda Patterson, and Asgerally Fazleabas. Grand Rapids, MI, USA.

5:00 O-017 **P2X3 - A Highly Innovative Target for the Non-Hormonal Treatment of Endometriosis.**
A Davenport, N Bräuer, A Rotgeri, A Rottmann, M Koch, TM Zollner, A Steinmeyer, J Nagel, F Machet, A Coelho, S Boyce, L Bone, M Gemkow, N Carty, M Herrmann, S Hess, I Neagoe, and OM Fischer. Abingdon, United Kingdom; Hamburg, Germany; and Berlin, Germany.

5:15 O-018 **Progesterone and KLF11 Mediate Sexually Dimorphic Fibrotic Responses.**
Chandra C Shenoy, Ye Zheng, Tiffanny L Jones, Zaraq Khan, and Gaurang S Daftary. Rochester, MN, USA.

5:30 O-019 **RPLP1 Is a Novel Target of *miR-451a* Whose Expression Is Elevated in Endometriotic Lesion Tissue and Correlates with Endometriotic Lesion Tissue and Cell Proliferation.**
Zahraa Alali, Tommaso Falcone, and Warren B Nothnick. Kansas City, KS, USA; and Cleveland, OH, USA.

5:45 O-020 **Expression Quantitative Trait Loci (eQTL) Approaches for Understanding the Genetics of Endometriosis.**
Peter AW Rogers, Sarah J Holdsworth-Carson, Jenny N Fung, Eliza M Colgrave, Premila Paiva, Jane E Girling, and Grant W Montgomery. Melbourne, VIC, Australia; and Brisbane, QLD, Australia.

Thursday, March 16, 2017 - Concurrent Session I

4:00 PM-6:00 PM **Concurrent Oral Session**

MATERNAL BIOLOGY AND HEALTH

Floridian C

Kirk P Conrad and Dean Myers

4:00 O-021 **Fetal Microchimerism by Mode of Delivery in Healthy Term Gestations.**
Raj Shree, JL Nelson, Sami B Kanaan, Alexandra Forsyth, Emma Cousin, and Hilary S Gammill. Seattle, WA, USA.

4:15 O-022 **Association Between the a2 Isoform of Vacuolar ATPase and Markers of Inflammation in Peripheral Blood Mononuclear Cells from Pregnant Women.**
Tomi T Kanninen, Giovanni Sisti, Aswathi Jayaram, Steven R Inglis, Ashwini Pandit, and Steven S Witkin. New York, NY, USA.

4:30 O-023 **Unique Innate Lymphoid Cells Revealed by Machine Learning/Dimensionality Reduction in Human Decidua.**
Jessica Vazquez, Yan Li, and Aleksandar K Stanic. Madison, WI, USA.

4:45 O-024 **Placental Growth Factor (Plgf) Blunts the Vascular Response to Angiotensin II: A Novel Mechanism for Vascular Regulation During Pregnancy.**
Jimmy Espinoza, Ancizar Betancourt, Karin Fox, Alireza Abdollah Shamshirsaz, and Chandra Yallampalli. Houston, TX, USA.

5:00 O-025 **Leptin Receptors During the Ovarian Cycle and Pregnancy: Angiogenesis in Uterine Artery Endothelial Cells.**
Vladimir E Vargas, Rosalina Villalon Landeros, Gladys E Lopez, Jing Zheng, and Ronald R Magness. Tampa, FL, USA; and Madison, WI, USA.

5:15 O-026 **Venoarterial Signaling (VAS) Modulates Shear Stress-Induced Gestational Uterine Artery Expansive Remodeling.**
Nga Ling Ko, Maurizio Mandalà, Liam V John, Adama Aja, and George J Osol. Burlington, VT, USA; and Cosenza, Italy.

5:30 O-027 **Pregnancy-Specific Estrogen Receptor-Mediated Upregulation of Endothelial AT_2 Receptor.**
Jay Mishra, Kathirvel Gopalakrishnan, Gary Hankins, and Sathish Kumar. Galveston, TX, USA.

5:45 O-028 **The Association Between the History of Hypertensive Disorders of Pregnancy, Obesity and Hypertension in Later Life by Age Group: A Cross-Sectional Analysis.**
Maiko Wagata, Naoki Nakaya, Naho Tsuchiya, Tomohiro Nakamura, Hirohito Metoki, Akimune Fukushima, Nobuo Yaegashi, Shigeo Kure, Shinichi Kuriyama, Atsushi Hozawa, and Junichi Sugawara. Sendai, Miyagi, Japan; and Morioka, Iwate, Japan.

4:00 PM-6:00 PM **Concurrent Oral Session**

PARTURITION I

Bonnet Creek XII

Roger Smith and Terry Morgan

4:00 O-029 **The Host Defence Peptide Cathelicidin Mediates Inflammatory Preterm Birth.**
Tina Baker, Heather MacPherson, Kirsten Wilson, Sara Rinaldi, Lorraine Frew, Adrian Thomson, Carmel Moran, Julia Dorin, Donald Davidson, and Sarah J Stock. Edinburgh, Scotland, United Kingdom.

4:15 O-030 **Protease Amplification of the Inflammatory Response Induced by *L. Iners:* Implications for Racial Disparities in Preterm Birth.**
Sheikh MK Alam, William H Nugent, Sonya L Washington, Kimberly K Jefferson, Jerome F Strauss, III, and Scott W Walsh. Richmond, VA, USA.

4:30 O-031 **Vaginal Dysbiosis Increases Risk of Preterm Membrane Rupture, Funisitis and Neonatal Sepsis.**
Richard G Brown, Yun S Lee, Ann Smith, Lyndsay Kindinger, Julian R Marchesi, Phillip R Bennett, and David A MacIntyre. London, United Kingdom; and Cardiff, Wales, United Kingdom.

4:45 O-032 **hCG Suppresses IP-10 in Human Decidua Through Histone Methylation.**
Michelle Silasi, Yang Yang-Hartwich, Gil Mor, Rosanna Ramhorst, and Esteban Grasso. New Haven, CT, USA; and Buenos Aires, Argentina.

5:00 O-033 **Relationship Between Yeast, Vaginal Microbiota Composition and Pregnancy Outcomes.**
Holly Lewis, Pamela Pruski, Lindsay Kindinger, Yun Lee, Phillip Bennett, Zoltan Takats, and David A MacIntyre. London, United Kingdom.

5:15 O-034 ***Nur77*, a Novel Player in Perinatal Neuroinflammation Associated with Preterm Labor in a Murine Model (*Mus Musculus*).**
Sarah Estrada, Andrew Thagard, Irina Burd, Peter Napolitano, and Nicholas Ieronimakis. Madigan Army Medical Center, WA, USA; and Baltimore, MD, USA.

5:30 O-035 **Effects of Receptor for Advanced Glycation End-Products (RAGE) on Inflammation Induced Preterm Birth and Neonatal Viability in a Genetically Engineered Mouse Model.**
Bethany T Stetson, Brian A Kellert, Hanaa Motawea, Megan Locke, Guomao Zhao, Antonette T Dulay, Catalin S Buhimschi, and Irina A Buhimschi. Columbus, OH, USA; and New Haven, CT, USA.

5:45 O-036 **T-Cell Activation-Induced Preterm Labor Involves Unique Innate and Adaptive Immune Responses That Differ from Those Observed in Inflammation- and Progesterone Withdrawal-Induced Preterm Labor.**
Marcia Arenas-Hernandez, Roberto Romero, Tara N Mial, Felipe Vadillo-Ortega, Sonia S Hassan, and Nardhy Gomez-Lopez. Detroit, MI, USA; and Mexico City, DF, Mexico.

Thursday, March 16, 2017 - Concurrent Session I

4:00 PM-6:00 PM **Concurrent Oral Session**

PREECLAMPSIA I

Bonnet Creek XI

Norman Gant and Justyna Dopierala

4:00 O-037 **Targeted Nanoparticle Delivery of Short Interfering RNAs to Treat Preeclampsia.**
Natalie J Hannan, Scott Pattison, Sally Beard, Natalie K Binder, Jennifer MacDiarmid, Himanshu Brahmbhatt, Tu'uhevaha J Kaitu'u-Lino, and Stephen Tong. Melbourne, VIC, Australia; and Sydney, NSW, Australia.

4:15 O-038 **Hydrogen Sulphide Ameliorates Preeclampsia-Like Phenotype Induced by Elevated sFlt-1 in Placenta Growth Factor Deficiency.**
Shakil Ahmad, Keqing Wang, Peter Hewett, and Asif Ahmed. Birmingham, West Midlands, United Kingdom.

4:30 O-039 **A Novel Conjugated Linoleic Acid Therapy for Preeclampsia Shows Protective Effects on Human Endothelial Cell Function In Vitro.**
Danielle M Berdahl, Dinesh M Shah, Ian M Bird, and Derek S Boeldt. Madison, WI, USA.

4:45 O-040 **Fetal Asymmetric Dimethylarginine Regulates Maternal Haemodynamics.**
Aikaterini Georgopoulou, James Leiper, and Mark R Johnson. London, United Kingdom.

5:00 O-041 **Molecular Evidence for Abnormal Differentiation of Invasive Trophoblast in Preeclampsia.**
Anna Natenzon, Sonia DaSilva-Arnold, Stacy Zamudio, Abdulla Al-Khan, and Nicholas P Illsley. Hackensack, NJ, USA.

5:15 O-042 **Role of Estrogen and Its Metabolites in Uterine Artery Endothelial Cells Migration from a Model of Unilateral Pregnant Sheep.**
Rosalina Villalon-Landeros, Chi Zhou, Jing Zheng, and Ronald R Magness. Madison, WI, USA; and Tampa, FL, USA.

5:30 O-043 **A Randomised Controlled Trial and Cost-effectiveness Analysis of Low Dose Aspirin with an Early Screening Test for Preeclampsia in Low Risk Women.**
F Mone, C Mulcahy, P McParland, J O'Mahony, E Tyrell, F Breathnach, C Normand, F Cody, J Morrison, S Daly, J Higgins, A Cotter, E Tully, P Dicker, Z Alfirevic, F Malone, and FM McAuliffe. Dublin, Ireland; and Liverpool, United Kingdom.

5:45 O-044 **Three Protein-Truncating Mutations That May Contribute to Developing Preeclampsia.**
HS Gammill, R Chettier, A Brewer, JM Roberts, R Shree, E Tsigas, and K Ward. Seattle, WA, USA; Salt Lake City, UT, USA; Melbourne, FL, USA; and Pittsburgh, PA, USA.

4:00 PM-6:00 PM **Concurrent Oral Session**

REPRODUCTIVE BIOLOGY I

Floridian A

Felice Petraglia and Zaher Merhi

4:00 O-045 **Maternal MiR-30d Deficiency Is Associated with Defects in Endometrial Receptivity, Embryonic Implantation and Fetal Development.**
Nuria Balaguer, Inmaculada Moreno, María Herrero, Marta González-Montfort, Carlos Simón, and Felipe Vilella. Paterna, VLC, Spain; Valencia, VLC, Spain; and Palo Alto, CA, USA.

4:15 O-046 **Double Conditional Knockout of SMAD2 and SMAD3 Results in Endometrial Dysfunction, Infertility, and Uterine Cancer.**
Maya Kriseman, Diana Monsivais, Julio Agno, Ramya Masand, William Gibbons, and Martin Matzuk. Houston, TX, USA.

4:30 O-047 **Non-Classical Progesterone Receptor (PGRMC1) and SERPINE1 mRNA Binding Protein (SERBP1) Interaction Influences the Human Decidualization Process.**
Stefania Salsano, Alicia Quiñonero, Silvia Pérez, Carlos Simón, and Francisco Domínguez. Paterna, Valencia, Spain.

4:45 O-048 **Hypoxia Inducible Factor (HIF) in the Endometrium: A Potential Therapeutic Target for Heavy Menstrual Bleeding (HMB).**
Jacqueline A Maybin, Alison Murray, Nik Hirani, Philippa TK Saunders, Peter Carmeliet, and Hilary OD Critchley. Edinburgh, Scotland, United Kingdom; and Leuven, Flanders, Belgium.

5:00 O-049 **Remodeling of Decidual Immune Landscape Across Murine Pregnancy.**
Yan Li, Jessica Vazquez, Melina Chavarria, and Aleksandar Stanic-Kostic. Madison, WI, USA.

5:15 O-050 ***In Vitro* Model of Bacterial Colonization for the Study of the Effect of the Endometrial Microbiota on the Reproductive Function.**
Inmaculada Moreno, Iolanda Garcia-Grau, Angela Silva, Felipe Vilella, Diana Valbuena, Daniel Ramon, and Carlos Simon. Valencia, Spain; and Palo Alto, CA, USA.

5:30 O-051 **Perivascular Expression of Vascular Adhesion Protein 1 (VAP-1) in the Endometrium Regulates Uterine Natural Killer (uNK) Cell Recruitment and Spiral Artery Remodeling in Pregnancy.**
Seley Gharanei, Ruban P Durairaj, Tianrong Jin, Kuo-Kang Liu, Christopher Weston, Marko Salmi, Pia Rantakari, Sirpa Jalkanen, Jan J Brosens, and Bee K Tan. Coventry, West Midlands, United Kingdom; Birmingham, West Midlands, United Kingdom; and Turku, Tykistökatu 6A, Finland.

5:45 O-052 **Mice Lacking Functional TRPV2 Show Intrauterine Growth Restriction.**
Katrien De Clercq, Charlotte Van den Eynde, Silvia Pinto, Voets Thomas, and Vriens Joris. Leuven, Vlaams-Brabant, Belgium.

Friday, March 17, 2017 - Concurrent Session II

9:15 AM-10:45 AM **Concurrent Oral Session**

DEVELOPMENTAL PROGRAMMING I

Floridian C

John Challis and Alina Maloyan

9:15 O-053 **The Mitochondria-Targeted Antioxidant MitoQ Prevents the Programming of Cardiovascular Dysfunction by Developmental Hypoxia in Sheep.**
KJ Botting, KL Skeffington, Y Niu, BJ Allison, KL Brain, N Itani, C Beck, A Logan, MP Murphy, and DA Giussani. Cambridge, United Kingdom.

9:30 O-054 **Adiponectin Supplementation During Late Pregnancy Normalises Offspring Cardiac Hypertrophic Gene Expression in a Mouse Model of Maternal Obesity.**
Owen R Vaughan, Fredrick J Rosario, Megan Gossling, Theresa Powell, and Thomas Jansson. Aurora, CO, USA.

9:45 O-055 **Chronic Fetal Hypoxaemia & Maternal Antioxidants: Identifying Mechanisms and Treatments to Improve Postnatal Lung Structure & Function in Growth Restricted Offspring.**
EV McGillick, S Orgeig, BJ Allison, KL Brain, Y Niu, N Itani, KL Skeffington, C Beck, KJ Botting, DA Giussani, and JL Morrison. Adelaide, Australia; and Cambridge, United Kingdom.

10:00 O-056 **Effects of Prenatal Hypoxia on Fetal Cardiomyocyte Proliferation.**
Laura M Reyes, Amin Shah, Anita Quon, and Sandra T Davidge. Edmonton, AB, Canada.

10:15 O-057 **Maternal Obesity (MO) Compromises Term Fetal Offspring (F1) Heart Mitochondrial Bioenergetic Profile.**
Qiurong Wang, Chaoqun Zhu, John F Odhiambo, Guadalupe L Rodríguez-González, Peter W Nathanielsz, Stephen P Ford, Jun Ren, and Wei Guo. Laramie, WY, USA; and Mexico City, Mexico.

10:30 O-058 **Fetal Growth Restriction Alters Chromatin Access in 1-Year-Old Rats with Metabolic Syndrome.**
Erin K Zinkhan, Baifeng Yu, Chris Callaway, and Robert McKnight. Salt Lake City, UT, USA.

9:15 AM-10:45 AM **Concurrent Oral Session**

FETUS I

Bonnet Creek X

Leslie Myatt and Emily J Su

9:15 O-059 **Oxygen and Glucose Supplementation Reduces Stress in Growth Restricted Sheep Fetuses.**
Leticia Camacho, Melissa Davis, Nathan Steffens, Amy Kelly, and Sean Limesand. Tucson, AZ, USA.

9:30 O-060 **Late-Onset Chronic Hypoxia Abolishes Adrenomedullary but Sensitises Adrenocortical Plasma Responses to Acute Stress in Fetal Sheep.**
N Itani, CS Shaw, BJ Allison, KL Brain, Y Niu, CC Lees, and DA Giussani. Cambridge, United Kingdom; and London, United Kingdom.

9:45 O-061 **Effect of Maternal Antioxidant MitoQ Treatment in a Rat Model of Intrauterine Growth Restriction (IUGR).**
Esha Ganguly, Jude S Morton, Christy L Cooke, and Sandra T Davidge. Edmonton, AB, Canada.

10:00 O-062 **Maternal Antioxidant Treatment Markedly Sensitizes Antioxidant Gene Expression in Peri-Renal Fat of Fetal Offspring of Hypoxic Pregnancy.**
A Martin, BJ Allison, KL Brain, C Ducsay, D Myers, and DA Giussani. Oklahoma City, OK, USA; Cambridge, United Kingdom; and Loma Linda, CA, USA.

10:15 O-063 **Elevated Hepatic Gluconeogenesis by H19-Mediated Epigenetic Regulation Underlies Altered Metabolism in Offspring Prenatally Exposed to Metformin.**
Jie Deng, Tingting Geng, Yuanyuan Shen, Liyong Zhu, Ya Liu, Hugh S Taylor, Michael Paidas, and Yingqun Huang. New Haven, CT, USA.

10:30 O-064 **In Utero Gene Therapy (IUGT) Using GLOBE Lentiviral Vector Phenotypically Corrects the Heterozygous Humanized Mouse Mode and Its Progress Can Be Monitored Using MRI Techniques.**
Panicos Shangaris, Stavros Loukogeorgakis, Laurence Jackson, Wei Wang, Mike Blundell, Shanrun Liu, Sindhu Subramaniam, Simon Eaton, Mike Antoniou, Daniel Stuckey, Manfred Schmidt, Adrian Thrasher, Thomas Ryan, Paolo De Coppi, and Anna David. London, United Kingdom; Birmingham, AL, USA; and Heidelberg, Germany.

Friday, March 17, 2017 - Concurrent Session II

9:15 AM-10:45 AM **Concurrent Oral Session**

ENDOMETRIOSIS, FIBROIDS AND GYNECOLOGY II

Floridian B

Sarah L Berga and Hiroshi Ishikawa

9:15 O-065 **Mechanisms of Dysregulated RANKL Gene Expression in Uterine Leiomyoma: Involvement of Epigenetic Modification and MED12 Gene Mutations.**
Shimeng Liu, Ping Yin, Stacy A Kujawa, and Serdar E Bulun. Chicago, IL, USA.

9:30 O-066 **Ulipristal Treatment Highlights the Link of MED12 and Fibrosis Regulation in Leiomyomas.**
Minnie Malik, Joy Britten, Lynnette Nieman, Matthew Wilkerson, Xijun Zhang, Jeris Cox, and William Catherino. Bethesda, MD, USA; and Fort Belvoir, VA, USA.

9:45 O-067 **Feedback Regulation Between TGF-β3 and miR-29c in Leiomyoma.**
Tsai-Der Chuang, and Omid Khorram. Torrance, CA, USA.

10:00 O-068 **Inflammatory and Immunological Processes Are Strongly Dysregulated in Uterine Fibroids Compared to Normal Myometrium and Are Shown to Offer Novel as well as Effective Treatment Options for Uterine Fibroids.**
Jörg Müller, Anette Sommer, Andrea Wagenfeld, Markus Koch, and Thomas M Zollner. Berlin, Germany.

10:15 O-069 **Rank-Fc Inhibits Growth of Leiomyoma Cells and Decreases Tumor Growth In Vivo.**
Deborah E Ikhena, Shimeng Liu, Stacy Kujawa, Serdar E Bulun, and Ping Yin. Chicago, IL, USA.

10:30 O-070 **Expression of Tumor Suppressor PCDH10 in Uterine Leiomyomas and Leiomyosarcomas.**
Joie Z Guner, Gyoung E Kim, Meaghan A Delaney, Triparna Ghosh-Choudhury1, Cecilia Valdes, William Gibbons, and Matthew L Anderson. Houston, TX, USA.

9:15 AM-10:45 AM **Concurrent Oral Session**

PARTURITION II

Bonnet Creek XII

K Joseph Hurt and Joy Vink

9:15 O-071 **Human Labour: A Joint Venture of PRA and ERα.**
Lubna Nadeem, Hedy Romero, Oksana Shynlova, Sam Mesiano, and Stephen Lye. Toronto, ON, Canada; and Cleveland, OH, USA.

9:30 O-072 **Thrombin-Induced Decidual CSF2 Induces Abruption-Related Preterm Birth by Weakening Fetal Membranes.**
Rachel Sinkey, Sefa Arlier, Robert Moore, Frederick Schatz, Nihan Semerci, Chinedu Nwabuobi, Kellie Larsen, Ozlem Guzeloglu-Kayisli, Deepak Kumar, John Moore, Umit Kayisli, and Charles Lockwood. Tampa, FL, USA; and Cleveland, OH, USA.

9:45 O-073 **Uterine Preconditioning Regulates Gestational Length.**
Judith Ingles, Jennifer Condon, and Pancharatnam Jeyasuria. Detroit, MI, USA.

10:00 O-074 **IL-1 Signaling Is Critical for Neutrophil Recruitment and Activation in a Rhesus Macaque Model of Intrauterine Inflammation.**
Pietro Presicce, Paranthaman Senthamaraikannan, Courtney Jackson, Cesar M Rueda, Lisa A Miller, Claire A Chougnet, Alan H Jobe, and Suhas G Kallapur. Cincinnati, OH, USA; and Davis, CA, USA.

10:15 O-075 **Platelet Activating Factor (PAF) Induces Preterm Birth in Mice Through TLR4-Dependant Induction of Pro-Inflammatory Cytokines.**
Hanan H Wahid, Lachlan M Moldenhauer, Kenner C Rice, Mark R Hutchison, and Sarah A Robertson. Adelaide, SA, Australia; and Washington, DC, USA.

10:30 O-076 **Oxidative Stress Induced p38MAPK Activation in Human Amnion Epithelial Cells Are Independent of ASK1-Signalosome.**
L Richardson, CL Dixon, and R Menon. Galveston, TX, USA.

Friday, March 17, 2017 - Concurrent Session II

9:15 AM-10:45 AM **Concurrent Oral Session**

PLACENTA I

Bonnet Creek XI

Loren P Thompson and Tania L Gonzalez

9:15 O-077 **The Detection of Placental Oxygenation by Photoacoustic Imaging and Ultrasound.**
Liliya M Yamaleyeva, Yao Sun, Tiffaney Bledsoe, and K Bridget Brosnihan. Winston-Salem, NC, USA.

9:30 O-078 **The Human Placental Proteome Secreted into the Maternal and Fetal Circulations.**
Trond M Michelsen, Tore Henriksen, Theresa L Powell, and Thomas Jansson. Aurora, CO, USA; and Oslo, Norway.

9:45 O-079 **Use of Circulating MicroRNAS to Predict Placental Dysfunction in Women at Risk of Stillbirth.**
Bernadette C Baker, Sylvia Lui, Alexander EP Heazell, Karen Forbes, and Rebecca L Jones. Manchester, United Kingdom; and Leeds, United Kingdom.

10:00 O-080 **Insertion of Human Corticotropin-Releasing Hormone and Retroviral Regulatory Element THE1B into the Mouse Genome Delays Birth Timing.**
Caitlin E Dunn-Fletcher, Lisa M Muglia, Elizabeth L Huffman, and Louis J Muglia. Cincinnati, OH, USA.

10:15 O-081 **Oxygen-Dependent JMJD6 Regulation of Fibronectin Synthesis and Assembly in the Human Placenta.**
Sruthi Alahari, and Isabella Caniggia. Toronto, ON, Canada.

10:30 O-082 **A Distinct Signature of ATP-Binding Cassete Transporter Expression in the Preterm Human Placenta with Chorioamnionitis.**
Guinever E Imperio, Enrrico Bloise, Mohsen Javan, Phetcharawan Lye, Andrea Constantinof, Caroline Dunk, Fernando M Reis, Stephen J Lye, William Gibb, Tania M Ortiga-Carvalho, and Stephen G Matthews. Toronto, ON, Canada; Rio de Janeiro, Brazil; Belo Horizonte, MG, Brazil; and Ottawa, OT, Canada.

9:15 AM-10:45 AM **Concurrent Oral Session**

REPRODUCTIVE ENDOCRINOLOGY AND INFERTILITY I

Floridian A

Lisa Halvorson and Satu Kuokkanen

9:15 O-083 **Cross-Sex Testosterone Therapy Is Not Sufficient for Bone Development in Female Mice: Implications for Treating Transgender Youth.**
Laura G Goetz, Ramanaiah Mamillapalli, Maureen J Devlin, Masoumeh Majidi-Zolbin, and Hugh S Taylor. New Haven, CT, USA; and Ann Arbor, MI, USA.

9:30 O-084 **Elevated Androgen Levels Impair Connexin43 Function Leading to Decreased EDHF-Mediated Relaxation and Hypertension in Adult Female Rats.**
Amar More, Jay Mishra, and Sathish Kumar. Galveston, TX, USA.

9:45 O-085 **Steroidogenic Factor 1 (*Nr5a1*) Is Necessary for Sertoli Cell Differentiation Post Sex Determination.**
Chandra S Miryala, Prashanth Anamthathmakula, Jennifer Ondon, Rebecca Moreci, and Jeyasuria Pancharatnam. Detroit, MI, USA; and Durham, NC, USA.

10:00 O-086 **Effects of Oxytocin on Atrophic Rat Vagina.**
Bernhard Lindenthal, Peter Muhn, Ulrike Fuhrmann, Ildiko Terebesi, Ralf Lesche, Qiong Lin, Reinhard Nubbemeyer, Thomas M Zollner, and Christina Bartnitzek. Berlin, Germany.

10:15 O-087 **Obesity Prevents Protective Down-Regulation of Mitogenic Insulin Receptor A in Uteri of Diet-Induced Obese Mice.**
Clare Flannery, Caitlin Radford, Farrah Saleh, Gina Choe, Jung Dae Kim, Sabrina Diano, and Hugh Taylor. New Haven, CT, USA.

10:30 O-088 **Altered Early Luteal Phase miRNA 483-3p Expression in Women with PCOS.**
Iris Eisenberg-Loebl, Debra Goldman-Wohl, Caryn Greenfield, Ronit Haimov-Kochman, Simcha Yagel, and Tal Imbar. Jerusalem, Israel.

Friday, March 17, 2017 - Concurrent Session III

2:15 PM-3:45 PM **Concurrent Oral Session**

CLINICAL PERINATOLOGY II

Bonnet Creek X

Marc Spaanderman and Levent Mutlu

2:15 O-089 **Differential Increases in First Trimester Maternal Weight (MW) by Maternal Age Over the Past Decade in 2.6 Million Pregnancies: Opportunity to Target Teenagers for Obesity Prevention.**
Shara M Evans, David A Krantz, Terrence W Hallahan, and Mark I Evans. New York, NY, USA; and Melville, NY, USA.

2:30 O-090 **Adiponectin Prevents Obesity and Hepatic Steatosis in Mouse Offspring Born to Obese Dams.**
Megan Gossling, Fredrick Rosario, Stephanie Wesolowski, Thomas Jansson, and Theresa Powell. Aurora, CO, USA.

2:45 O-091 **A Randomized Controlled Trial of an M-Health Behavioural Lifestyle Intervention to Prevent Gestational Diabetes in Overweight and Obese Pregnancy: PEARS.**
Maria A Kennelly, Kate M Ainscough, Elizabeth J O'Sullivan, Karen L Lindsay, and Fionnuala M McAuliffe. Dublin, Leinster, Ireland.

3:00 O-092 **Mild Intraventricular Hemorrhage Is Not Associated with Low Bayley Scores at Age 2.**
Emilie Vander Haar, Adina Goldberger, and Cynthia Gyamfi-Bannerman. New York, NY, USA.

3:15 O-093 **Adrenomedullin Is a New Modulator of Lipolysis in Human Adipocytes.**
Yuanlin Dong, and Chandra Yallampalli. Houston, TX, USA.

3:30 O-094 **The Impact of Altered IL-1 Signaling on Metabolic Dysfunction During Pregnancy.**
Jasmine Plows, Thashma Ganapathy, Philip Baker, Mark Vickers, Joanna Stanley, and Clare Reynolds. Auckland, New Zealand.

2:15 PM-3:45 PM **Concurrent Oral Session**

EPIDEMIOLOGY, POPULATION HEALTH AND GLOBAL HEALTH - FOCUS ON ZIKA

Bonnet Creek XII

Indira U Mysorekar and Irina Burd

2:15 O-095 **Short Interpregnancy Interval After Pregnancy Loss Is Associated with Decreased Risk of Subsequent Miscarriage in a Prospective Cohort.**
Alexandra C Sundermann, Katherine E Hartmann, Sarah H Jones, Eric S Torstenson, and Digna R Velez Edwards. Nashville, TN, USA.

2:30 O-096 **Evaluating the Clinical Burden of Preeclampsia (PEC) on a Tertiary Care Hospital in Harare, Zimbabwe.**
Lydia L Shook, Muchabayiwa F Gidiri, Kara M Rood, and Irina A Buhimschi. New Haven, CT, USA; Harare, Zimbabwe; and Columbus, OH, USA.

2:45 O-097 **Zika Virus Infects Human Endometrial Stromal Cells.**
Paola Panina-Bordignon, Isabel Pagani, Silvia Ghezzi, Adele Ulisse, Alicia Rubio, Elisabetta Garavaglia, Giuseppe Ippolito, Guido Poli, and Elisa Vicenzi. Milan, Italy; and Rome, Italy.

3:00 O-098 **Zika Virus Infection Damages the Testes in Mice.**
Jacques Halabi, Prabagaran Esakky, Suzanne Scheaffer, Andrea Drury, Michael S Diamond, and Kelle H Moley. St. Louis, MO, USA.

3:15 O-099 **Hyperemesis Gravidarum: Risk of Recurrence in Subsequent Pregnancies.**
Michael J Fassett, Morgan R Peltier, and Darios Getahun. Los Angeles, CA, USA; Mineola, NY, USA; and Pasadena, CA, USA.

3:30 O-100 **Zika Infection in Pregnant Rhesus Macaques Results in Placental Injury and Altered Brain Development Independent of Microcephaly.**
Peta L Grigsby, Victoria H Roberts, Alec J Hirsch, Matthias C Schabel, Chris D Kroenke, Jamie O Lo, Xiaojie Wang, Zheng Liu, Jessica Smith, Nicole Haese, Meredith Kelleher, Rebecca Broeckel, Craig N Kreklywich, Christopher J Parkins, Patricia Smith, Victor DeFillppis, William Messer, Jay A Nelson, Jon D Hennebold, Marjorie Grafe, Lois Colgin, Anne Lewis, Rhonda MacAllister, Terry K Morgan, Antonio E Frias, and Daniel N Streblow. Portland, OR, USA.

Friday, March 17, 2017 - Concurrent Session III

2:15 PM-3:45 PM **Concurrent Oral Session**

GYNECOLOGIC ONCOLOGY

Floridian B

Stefan M Gysler and Matthew L Anderson

2:15 O-101 **The Impact of the Cholesterol Metabolite 27-Hydroxycholesterol on Endometrial Proliferation.**
Douglas A Gibson, Frances Collins, Arantza Esnal, Alistair RW Williams, and Philippa TK Saunders. Edinburgh, United Kingdom.

2:30 O-102 **SYD985 Shows Antitumor Activity in Uterine and Ovarian Carcinosarcoma with HER2/Neu Expression.**
Gulden Menderes, Elena Bonazzoli, Jonathan D Black, Stefania Bellone, Francesca Pattinelli, Alice Masserdetti, Luca Zammataro, Gary Altwerger, Natalia Buza, Pei Hui, Serena Wong, Elena Ratner, Babak Litkouhi, Dan-Arin Silasi, Masoud Azodi, Peter E Schwartz, Peter Goedings, Patrick Beusker, Miranda van der Lee Marco, Timmers Wim Dokter, and Alessandro D Santin. New Haven, CT, USA; and Nijmegen, Netherlands.

2:45 O-103 **Serum MicroRNA Sequencing for Early Diagnosis of Invasive Ovarian Cancer.**
Kevin M Elias, Wojciech F Fendler, Konrad Stawiski, Allison Vitonis, Ross S Berkowitz, Daniel W Cramer, and Dipanjan Chowdhury. Boston, MA, USA; and Lodz, Poland.

3:00 O-104 **Exosomal Content in the Plasma of Patients with Ovarian Cancer Reflect Tumor State and Induce the Epithelial to Mesenchymal Transition in Target Cells.**
Shayna Sharma, Katherin Scholz-Romero, Richard Kline, Katrina Wade, Jacob Estes, Carlos Palma, Dominic Guanzon, Andrew Lai, John Hooper, Gregory E Rice, and Carlos Salomon. Brisbane, QLD, Australia; and New Orleans, LA, USA.

3:15 O-105 **Targeting Integrin αV/β1 Receptor Manifests Intriguing Anti-Tumor Effects in Sensitive and Chemoresistant Ovarian Cancer Cells: Potential Therapeutic Target.**
Ghassan M Saed, Nicole M Fletcher, Ira Memaj, Mohammed G Saed, Michael P Diamond, and Robert T Morris. Detroit, MI, USA; and Augusta, GA, USA.

3:30 O-106 **FDG-PET/CT Kinetic Modeling Provides Detailed Information of Glucose Metabolism in Ovarian Cancer.**
Xiaohua Yang, Kuan-Hao Su, Jung-Wen Kuo, Mustafa Tunc, Stefanie Avril, Analisa DiFeo, Raymond F Muzic Jr, and Norbert Avril. Cleveland, OH, USA.

2:15 PM-3:45 PM **Concurrent Oral Session**

ENDOMETRIOSIS, FIBROIDS AND GYNECOLOGY III

Floridian C

Micah J Hill and Joop Laven

2:15 O-107 **ATG4D Silencing Abrogates Autophagy and Induces a Fibroid-Like Transformation in Normal Human Myometrium Cells.**
Abdeljabar El Andaloussi, Nahed Ismail, and Ayman Al-Hendy. Augusta, GA, USA; and Pittsburgh, PA, USA.

2:30 O-108 **Can Preimplantation Genetic Screening (PGS) Be Applied to Previously Untested Cryopreserved Blastocysts?**
Jessica Rubin, Alfred Wun, Cecilia Valdes, and Randall Dunn. Houston, TX, USA.

2:45 O-109 **The Impact of Excisional Treatment for Cervical Intraepithelial Neoplasia on the Vaginal Microbiota.**
Anita Mitra, David MacIntyre, Jonathan Lai, Yun Lee, Ann Smith, Julian Marchesi, Deirdre Lyons, Phillip Bennett, and Maria Kyrgiou. London, United Kingdom; and Cardiff, United Kingdom.

3:00 O-110 **Progestin-Only Contraceptives Induce Decidualization by Enhancing ZBTB16 Expression: Implications for Abnormal Uterine Bleeding.**
Sefa Arlier, Ozlem Guzeloglu-Kayisli, Nihan Semerci, Kellie Larsen, Umit Kayisli, Frederick Schatz, and Charles Lockwood. Tampa, FL, USA.

3:15 O-111 **A Calcium Channel Blocker Used to Treat Hypertension Alters Contractility of the Uterosacral Ligament: Implications for Pelvic Organ Prolapse.**
Marsha K Guess, Joshua Johnson, Ritsuko Iwanaga, and Kathleen A Connell. Aurora, CO, USA.

3:30 O-112 **LGR5 Is Expressed by Human Endometrial Epithelial Cells and Regulated by Progesterone.**
Nicola Tempest, and Dharani Hapangama. Liverpool, Merseyside, United Kingdom.

Friday, March 17, 2017 - Concurrent Session III

2:15 PM-3:45 PM **Concurrent Oral Session**

PREECLAMPSIA II

Bonnet Creek XI

Chahinda Ghossein-Doha and Carlos Salomon

2:15 O-113 **VEGF Stimulates Macrophage Recruitment and M2-Polarization in the Decidua: Potential Relevance to the Pathogenesis of Preeclampsia.**
Karen C Wheeler, Manoj Jena, Bhola S Pradhan, Bo Pei, Neha Nayak, Subhendu Das, Sabita Dhal, Kang Chen, and Nihar R Nayak. Detroit, MI, USA.

2:30 O-114 **Syncytiotrophoblast Extracellular Vesicles Alter Angiotensin-II Induced Vasoconstriction in Mouse Uterine Arteries.**
Floor Spaans, Jude S Morton, Dionne S Tannetta, Ian L Sargent, and Sandra T Davidge. Edmonton, AB, Canada; and Oxford, United Kingdom.

2:45 O-115 **Severe Preeclampsia Is Associated with Resistance to Decidualization.**
Tamara Garrido-Gomez, Francisco Dominguez, Alicia Quiñonero, Patricia Diaz-Gimeno, Mirhan Kapidzic, Matthew Gormley, Katherine Ona, Pablo Padilla, Olga Genbacev, Alfredo Perales, Susan J Fisher, and Carlos Simon. Valencia, Spain; San Francisco, CA, USA; and Stanford, CA, USA.

3:00 O-116 **Placental Extracellular Vesicles Can Sequester VEGF to Induce Endothelial Cell Activation: Relevance for Preeclampsia.**
Mancy Tong, Qi Chen, Jo L James, Peter R Stone, and Larry W Chamley. Grafton, Auckland, New Zealand.

3:15 O-117 **Evidence for Partial Overlap of Molecular Etiology Between Preeclampsia and Decidualization Disorders.**
Maria B Rabaglino, Emiel D Post Uiterweer, and Kirk P Conrad. Córdoba, Argentina; Utrecht, Netherlands; and Gainesville, FL, USA.

3:30 O-118 **High Resolution Flow Cytometry Reveals Abnormal Distribution of Placental Extracellular Vesicles in Murine Placental Insufficiency Model.**
Nicole Marek, Mayu Morita, Pam Canaday, and Terry K Morgan. Portland, OR, USA.

2:15 PM-3:45 PM **Concurrent Oral Session**

REPRODUCTIVE BIOLOGY II

Floridian A

Linda C Giudice and Terrence D Lewis

2:15 O-119 **Granulocyte-Colony Stimulating Factor Reverses Detrimental Effects of High-Fat Diet on Ovarian Reserve.**
Delaney C Swindle, Alex J Polotsky, and Malgorzata E Skaznik-Wikiel. Aurora, CO, USA.

2:30 O-120 **High-Fat Diet and Aging Affect Ovarian RAGE Gene Expression.**
Erkan Buyuk, Maureen Charron, Kimberley Thornton, Obehi Asemota, and Zaher Merhi. Bronx, NY, USA; and New York, NY, USA.

2:45 O-121 **AKAP13-Deficient Oocytes Show Signs of Precocious Exit from Prophase I Arrest.**
Carter M Owen, Ophelia Yin, Sinnie Ng, Pola Olczak, Janice P Evans, and James H Segars. Bethesda, MD, USA; and Baltimore, MD, USA.

3:00 O-122 **Maternally Expressed NLRP2 Links the Subcortical Maternal Complex (SCMC) to Fertility, Embryogenesis and Epigenetic Reprogramming.**
Sangeetha Mahadevan, Varsha Sathappan, Budi Utama, Isabel Lorenzo, Khalied Kaskar, and Ignatia Van den Veyver. Houston, TX, USA.

3:15 O-123 **DMPS (Dimercapto-1-Propanesulfonic Acid), a Heavy Metal Chelator, Induces Oocyte Deterioration.**
Sarah R Aldhaheri, Roohi Jeelani, Mili Thakur, Marisa Hildebrandt, Farnoosh Qadri, and Husam M Abu-Soud. Detroit, MI, USA.

3:30 O-124 ***Med12* Is Critical in Reproductive Tract Development.**
Xinye Wang, Priya Mittal, and Aleksandar Rajkovic. Pittsburgh, PA, USA; Beijing, China; and Memphis, TN, USA.

Saturday, March 18, 2017 - Concurrent Session IV

10:30 AM-12:00 PM **Concurrent Oral Session**

DEVELOPMENTAL PROGRAMMING II

Floridian B

Sophie Petropoulos and Jorge P Figueroa

10:30 O-125 **Predictive Modelling of Stress-Related Behavior Through Gene Expression Following Prenatal Glucocorticoid Exposure.**
Andrea Constantinof, Vasilis Moisiadis, and Stephen Matthews. Toronto, ON, Canada.

10:45 O-126 **Treatment with Prenatal Glucocorticoids in Baboons Predisposes Male Offspring (F1) to Obesity in Adulthood.**
Hillary F Huber, Anderson H Kuo, Cun Li, Susan L Jenkins, and Peter W Nathanielsz. Laramie, WY, USA; and San Antonio, TX, USA.

11:00 O-127 **Maternal Obesity Is Associated with Decreased Dopamine Signaling in Juvenile Offspring: A Transgenerational Obesity Cycle.**
Larissa H Mattei, Chang Xue, Rachel Zeuner, Emmanuel N Pothos, and Andrea G Edlow. Boston, MA, USA.

11:15 O-128 **Accelerated Ovarian Ageing Induced by Chronic Fetal Hypoxia.**
CE Aiken, JL Tarry-Adkins, AM Spiroski, AM Nuzzo, SE Ozanne, and DA Giussani. Cambridge, Cambridgeshire, United Kingdom.

11:30 O-129 ***In Utero* Bisphenol-A Exposure Leads to Altered Uterine Stromal Cell Migration and Adenomyosis.**
Myles H Alderman III, Demetra Hufnagel, and Hugh S Taylor. New Haven, CT, USA.

11:45 O-130 **Nutrient Sensor-Epigenome Regulation of Adipogenesis Programs Obesity in Offspring of Obese Mothers.**
Mina Desai, Guang Han, Kavita Narwani, Elaheh Mossayebi, Marie H Beall, and Michael G Ross. Torrance, CA, USA; and Los Angeles, CA, USA.

10:30 AM-12:00 PM **Concurrent Oral Session**

FETUS II

Bonnet Creek X

Amy C Kelly and Dean Myers

10:30 O-131 **Cardiac Assessment by 4D Echocardiography of Fetal Guinea Pigs.**
Shifa Turan, Graham W Aberdeen, and Loren P Thompson. Baltimore, MD, USA.

10:45 O-132 **Neuronal Exosome Synaptopodin: An Early Predictor of Therapeutic Response to Controlled Hypothermia.**
Laura Goetzl, Diana Martirosyan, Nune Darbinian, Nana Merabova, Keri Fugarolas, and Ogechukwu Menkiti. Philadelphia, PA, USA.

11:00 O-133 **Volumetric and Vascular MRI Placental Changes with Exposure to Intrauterine Inflammation: Biomarker of Fetal Brain Injury.**
Jun Lei, Dan Wu, Solange Eloundou, Wael Alshehri, Jiangyang Zhang, and Irina Burd. Baltimore, MD, USA.

11:15 O-134 **Chronic Hypoxia Alters Fetal Cerebrovascular Responses to Endothelin-1.**
Jinjutha Silpanisong, Dahlim Kim, James M Williams, Olayemi O Adeoye, and William J Pearce. Loma Linda, CA, USA.

11:30 O-135 **Role of Uric Acid and GLUT9 in Pregnancy on Neonatal Development.**
Benjamin P Lüscher, Daniel V Surbek, Camilla Marini, and Marc U Baumann. Bern, Switzerland.

11:45 O-136 **Cardiac miRNA Expression in the Fetus and Six Month Old Sheep in Response to Myocardial Infarction.**
Mitchell Lock, Jia Yin Soo, Jack Darby, Doug Brooks, Enzo Porrello, Ross Tellam, and Janna Morrison. Adelaide, Australia; and Brisbane, Australia.

Saturday, March 18, 2017 - Concurrent Session IV

10:30 AM-12:00 PM **Concurrent Oral Session**

PARTURITION III

Bonnet Creek XII

Mala Mahendroo and Jennifer Herington

10:30 O-137 **Effect of Amnion Derived Exosomes on Feto-Maternal Gestational Cells: Novel Signalers in the Labor Cascade?**
Emily E Hadley, Samantha Sheller, Rheanna Urrabaz-Garza, Talar Kechichian, George Saade, Sam Mesiano, Robert Taylor, and Ramkumar Menon. Galveston, TX, USA; Cleveland, OH, USA; and Winston-Salem, NC, USA.

10:45 O-138 **Collagen Type 1 Gels Augment Healing of Ruptured Amnion in Mouse PROM.**
Haruta Mogami, Annvarapu H Kishore, and R Ann Word. Dallas, TX, USA.

11:00 O-139 **Mechanisms Underlying the Effects of Retosiban/GSK221149A on the Response to Mechanical Stretch in Human Myometrial Explants.**
Irving LMH Aye, Alex Moraitis, D Stephen Charnock-Jones, and Gordon CS Smith. Cambridge, Cambridgeshire, United Kingdom.

11:15 O-140 **Characterization of Peptides Against Neuromedin U Receptor 2 in Preterm Labor.**
Amarilys Boudreault, Christiane Quiniou, Xin Hou, Mathieu Nadeau-Vallée, and Sylvain Chemtob. Montreal, QC, Canada.

11:30 O-141 **Adiponectin Receptor Activation Mediates Myometrial Tocolysis: A Mechanism for Obesity Related Preterm Birth.**
Vibhuti Vyas, Nathan Anderson, Rachael Bok, Theresa Powell, Thomas Jansson, and Kenneth J Hurt. Aurora, CO, USA.

11:45 O-142 **Functional Pharmacology Coupled with Metabolomics Reveals Novel Pathways of Chlorophyll Compounds on Myometrial Activity.**
Enitome E Bafor, Edward G Rowan, and RuAngelie Edrada-Ebel. Benin, Edo State, Nigeria; and Glasgow, North Lanarkshire, United Kingdom.

10:30 AM-12:00 PM **Concurrent Oral Session**

PLACENTA II

Bonnet Creek XI

Vicki L Clifton and Susanne Lager

10:30 O-143 **Inhibition of the Auto-Inflammation Suppressor Protein ISG15 Triggers Preeclampsia by Blocking Trophoblast Migration and Invasion.**
Nihan Semerci, Ozlem Guzeloglu-Kayisli, Sefa Arlier, Kellie Larsen, Chinedu Nwabuobi, Frederick Schatz, Antony Odibo, Charles Lockwood, and Umit Kayisli. Tampa, FL, USA.

10:45 O-144 **Rosiglitazone Reduces Endotoxin Mediated Effects on Inflammation and Trophoblast Differentiation in First Trimester Human Placenta.**
Leena T Kadam, Brian Kilburn, Aalem Singh, Hamid Reza Kohan-Ghadr, and Sascha T Drewlo. Detroit, MI, USA; and , MI, USA.

11:00 O-145 **SDF2 Is a Novel Component of ER Stress-Induced Apoptosis Pathway in Trophoblast Cells via PERK-eIF2 Alpha-ATF4 Branch.**
Aline R Lorenzon-Ojea, Clarissa R Rocha, and Estela Bevilacqua. Sao Paulo, SP, Brazil.

11:15 O-146 **Human Placental Endothelial Cells Are Capable of Recovering from Failed Angiogenesis Secondary to Impaired Wnt Signaling.**
Toluwalope O Junaid, Paul Brownbill, Edward D Johnstone, and John D Aplin. Manchester, United Kingdom.

11:30 O-147 **mTOR Inhibition Down-Regulates Mitochondrial Function in Primary Human Trophoblast Cells and Is Associated with Decreased Expression of Electron Transport Chain Complexes in IUGR Placentas.**
FJ Rosario, MB Gupta, L Cox, TL Powell, and T Jansson. Aurora, CO, USA; London, ON, Canada; and San Antonio, TX, USA.

11:45 O-148 **Sexual Dimorphism in the Regulation of Placental Metabolism and Fetal Growth by miR-210.**
Yu Wang, Matthew S Bucher, Bailey L Simon, Alina Maloyan, and Leslie Myatt. Portland, OR, USA.

Saturday, March 18, 2017 - Concurrent Session IV

10:30 AM-12:00 PM **Concurrent Oral Session**

REPRODUCTIVE ENDOCRINOLOGY AND INFERTILITY II

Floridian A

Alan DeCherney and Reshef Tal

10:30 O-149 **Disruption of Mitochondrial Proteostasis Results in Impaired Mitochondrial Dynamics and Female Infertility.**
Tianren Wang, Tim Sanchez, Daniel Neddleman, Denny Sakkas, Tamas Horvath, and Emre Seli. New Haven, CT, USA; and Cambridge, MA, USA.

10:45 O-150 **Independent Serum Markers of Corpora Lutea Function After GnRH Agonist Trigger and Low Dose hCG in IVF.**
Leah A Kaye, Erica Anspach Will, Evelyn I Neuber, John C Nulsen, Claudio A Benadiva, and Lawrence Engmann. Farmington, CT, USA.

11:00 O-151 **Creating a Hormonally Active 3-Dimensional Ovarian Follicle via a Microfluidic System.**
Mae W Healy, Shelley N Dolitsky, Meera Raghavan, Alex Tillman, Maria Villancio-Wolter, Nicole Y Morgan, Alan H DeCherney, Erin F Wolff, and Solji Park. Bethesda, MD, USA; and New York, NY, USA.

11:15 O-152 **Discovery-Based Proteomic Profiling of Tubal Fluid in Hydrosalpinx Reveals Candidate Biomarkers.**
Morgan E Lindsay, Elizabeth H Yohannes, Avedis A Kazanjian, Ryan J Heitmann, and Richard O Burney. Tacoma, WA, USA.

11:30 O-153 **Oocyte/Embryo Utilization Rates and Disposition Decisions in Fertility Preservation Patients.**
Molly B Moravek, Rafael Confino, Angela K Lawson, Kristin N Smith, Susan C Klock, and Mary Ellen Pavone. Ann Arbor, MI, USA; and Chicago, IL, USA.

11:45 O-154 **Utility of PGS to Determine the Need for Repeat Embryo Cryopreservation Cycles and Improve Fertility Preservation Success in Cancer Patients.**
Ozgur Kan, and Kutluk Oktay. Valhalla, NY, USA.

10:30 AM-12:00 PM **Concurrent Oral Session**

STEM CELLS

Floridian C

Hugh Taylor and Panicos Shangaris

10:30 O-155 **Cytoskeletal Tension and YAP Regulation Modulate Mechanosensation in Oogonial Stem Cells.**
Julie A MacDonald, Dori C Woods, and Jonathan L Tilly. Boston, MA, USA.

10:45 O-156 **Identification of Novel Epigenetic Reprogrammed Genes in Myometrial Stem Cells Developmentally Exposed to Endocrine Disrupting Chemicals.**
Qiwei Yang, Lindsey S Treviño, Aymara Mas, Michael P Diamond, Cheryl Lyn Walker, and Ayman Al-Hendy. Augusta, GA, USA; and Houston, TX, USA.

11:00 O-157 **Maternal Mesenchymal Stem Cell Administration Alleviates Intrauterine Inflammation-Induced Perinatal Brain Injury Through $CD8^+$ T Cell Suppression in Placenta.**
Li Xie, Hongxi Zhao, Jun Lei, Lu Zong, Hattan Arif, Michael McLane, and Irina Burd. Baltimore, MD, USA; and Xi'an, Shaanxi, China.

11:15 O-158 **Trophoblast Spheroid Model Derived from hiPSCs to Study Trophoblast Functions Under Pathological-Like Conditions.**
Mehboob Ali, Mark Hester, Lisa Zhao, and Irina A Buhimschi. Columbus, OH, USA.

11:30 O-159 **High Throughput Screen (HTS) Using Viable Fluorescent ESC Reporters of Stressed-Forced Differentiation of the First Lineage.**
Erica D Louden, Elizabeth E Puscheck, Quanwen Li, Kang Chen, and Daniel A Rappolee. Detroit, MI, USA.

11:45 O-160 **Endothelial Progenitor Cells Contribute to Vasculogenesis of the Pregnant Mouse Uterus.**
Reshef Tal, Dong Dirong, Shafiq Shaikh, Ramanaiah Maimillapalli, and Hugh S Taylor. New Haven, CT, USA.

Thursday, March 16, 2017 - Poster Session I - Bonnet Creek I – IX

10:00 AM-11:30 AM **Poster Session**

BASIC PARTURITION

T-001 **Uterine Contraction Parameters Before and After Epidural Analgesia.**
Rebecca Benfield, Du Feng, Jan Salstrom, Melydia Edge, Denise Brigham, and Edward Newton. Las Vegas, NV, USA; Lebanon, NH, USA; and Greenville, NC, USA.

T-002 **Histologic Chorioamnionitis Induces Higher Lipid Oxidative Damage in Amniochorion Membranes from Pregnancies Complicated by Spontaneous Prematurity.**
Laura F Martin, Natália P Moço, Jossimara Polettini, Moisés D de Lima, Hélio A Miot, and Márcia G da Silva. Botucatu, São Paulo, Brazil; and Presidente Prudente, São Paulo, Brazil.

T-003 **Use of Mass Spectrometric Measurements to Determine Differential Expression of Prostaglandins and Prostamides in Amniotic Fluid of Women with Preterm Labor Delivering at Term and Women at Term in Labor.**
Hassendrini N Peiris, Robert J Romero, Kanchan Vaswani, Sarah Reed, Piya Chaemsaithong, Sonia Hassan, Eli Maymon, and Murray D Mitchell. Herston, QLD, Australia; and Detroit, MI, USA.

T-004 **Fetal Sex Differences in Prediction of Spontaneous Preterm Birth.**
Leonardo M Pereira, Kim A Boggess, George R Saade, Terry K Morgan, Ashoka D Polpitiya, ChienTing Hsu, Amir J Lueth, Angela C Fox, Tracey C Fleischer, J Jay Boniface, Durlin E Hickok, and Todd L Randolph. Portland, OR, USA; Chapel Hill, NC, USA; Galveston, TX, USA; and Salt Lake City, UT, USA.

T-005 **Biaxial Mechanical Properties of the Murine Uterus and Cervix.**
Cassandra Conway, Laurephile Desrosiers, Leise Knoepp, and Kristin Miller. New Orleans, LA, USA.

T-006 **Exosomal Profile in Amniotic Fluid Is Associated with Parturition Signal.**
Christopher L Dixon, Vyjayanthi Kinhal, Carlos Palma, Kechichian Talar, Rheanna Urrabaz-Garza, Poorna R Menon, Carlos Salomon, and Ramkumar Menon. Galveston, TX, USA; and Brisbane, Australia.

T-007 **Tumor Necrosis Factor-α and Interferon-γ Promote Preeclampsia-Related Decidual Inflammation by Synergistically Inducing Decidual Cell Expressed Inflammatory Cytokines via STAT5 Signaling.**
Ozlem Guzeloglu-Kayisli, Nicole Teal, Nihan Semerci, Kellie Larsen, Rachel Sinkey, Sefa Arlier, Frederick Schatz, Umit Kayisli, and Charles Lockwood. Tampa, FL, USA.

T-008 **Development of a Novel Co-Culture Model Studying Maternal/Fetal Interactions Driving Uterine Transformation for Labour.**
Kelycia B Leimert, Angela Messer, Theora Gray, Megan Malach, Xin Fang, and David M Olson. Edmonton, AB, Canada.

T-009 **Progesterone and the Repression of Myometrial Inflammation: The Roles of MKP-1 and the AP-1 System.**
Kaiyu Lei, Ektoras X Georgiou, Angela Yulia, Suren R Sooranna, Jan J Brosens, Phillip R Bennett, and Mark R Johnson. London, United Kingdom; and Coventry, United Kingdom.

T-010 **Pre-Maternal High-Fat Diet Consumption Initiates Preterm Birth by Potentiating the Actions of Lipopolysaccharide at Toll-Like Receptor 4 and Decreasing Utero-Placental Antioxidant Capacity.**
Clarence Manuel, and Sandra E Reznik. Queens, NY, USA; and Bronx, NY, USA.

T-011 **Progesterone Receptor B Blocks Inflammation by Increasing Expression of IL-1β Inhibitory Receptors, IL-1R2 and IL-1RN in Human Term Decidual Cells.**
Nihan Semerci, Vidya Krishan, Ozlem Guzeloglu-Kayisli, Kellie Larsen, Sefa Arlier, Frederick Schatz, Umit Kayisli, and Charles Lockwood. Tampa, FL, USA.

T-012 **Dysbiosis Leads to Cervical Remodeling *In Vivo*.**
Luz-Jeannette Sierra, Gillermo O Barila, Amy G Brown, Michael Humphrys, Jacques Ravel, and Michal A Elovitz. Philadelphia, PA, USA; and Baltimore, MD, USA.

T-013 **The Mid-Gestational Changes in Cervicovaginal RANTES and IL-1β Correlate with Fetal Fibronectin in Asymptomatic Pregnant Women and Are Predictive Markers of Inflammation-Associated Preterm Birth.**
Emmanuel Amabebe, Victoria Stern, David Chapman, and Dilly Anumba. Sheffield, United Kingdom.

T-014 **Cervicovaginal Levels of Human Beta-Defensin 1, 2, 3 and 4 of Reproductive-Aged Women with *Chlamydia trachomatis* Infection.**
Larissa B Bastos, Nathália M Noda-Nicolau, and Márcia G Silva. Botucatu, SP, Brazil.

T-015 **The Effect of TLR3 Receptor Priming on TLR 2,4 and 6 Agonist-Induced Inflammation in Placental Explants.**
Eberechi Anucha, Zahirrah Begam Mohamed Rasheed, Lee S Yun, David A MacIntyre, Phillip R Bennett, and Lynne Sykes. London, United Kingdom.

T-016 **An Anti-IL-6R Peptide as a Potential Therapeutic Agent in Inflammation- and Infection-Induced Preterm Birth.**
Estefania Marin Sierra, Christiane Quiniou, Mathieu Nadeau-Vallée, Xin Hou, Barbara Hales, and Sylvain Chemtob. Montreal, QC, Canada.

Thursday, March 16, 2017 - Poster Session I - Bonnet Creek I – IX

T-017 **Activation of the TLR3 Receptor: A Possible Mechanism for Virally Induced Preterm Labour.**
Zahirrah Begam Mohamed Rasheed, Yun S Lee, David A MacIntyre, Phillip R Bennett, and Sykes Lynne. London, United Kingdom.

T-018 **Simvastatin Treatment Reduces the Incidence of Preterm Birth in an Infection-Induced Mouse Model.**
Ashley K Boyle, Sara F Rinaldi, Adrian J Thomson, Adriano G Rossi, Philippa T Saunders, and Jane E Norman. Edinburgh, International, United Kingdom.

T-019 **Involvement of the Nicotinic Acetylcholine Receptor (nACHR) Pathway in RU486-Induced Preterm Delivery in Rats.**
Aihua Ye, Junjie Bao, Min Zhang, Yuanyuan Liu, Shao-Qing Shi, Robert E Garfield, and Huishu Liu. Guangzhou, China.

T-020 **The *Escherichia coli* Nissle 1917-Based Probiotic (EcN) Promotes Anti-Inflammation by Inhibiting Decidual Cell Expressed Pro-Inflammatory Cytokines.**
Kellie Larsen, Rachel L Hardison, Sheryl S Justice, Fred Schatz, Sefa Arlier, Nihan Semerci, Ozlem Guzeloglu-Kayisli, Charles J Lockwood, and Umit A Kayisli. Tampa, FL, USA; and Columbus, OH, USA.

T-021 **Pharmacological Inhibition of the Dimethylarginine-Dimethylaminohydrolase 1 (DDAH1) Enzyme Improves Survival and Haemodynamic Function in a Rodent Model of Severe Sepsis in Pregnancy.**
Julia Zöllner, Simon Lambden, Noor Mohd Nasri, Mark Johnson, and James Leiper. London, England, United Kingdom.

T-022 **A Light-Producing Mouse Model of Ascending Vaginal Infection-Related Preterm Birth.**
Natalie Suff, Rajvinder Karda, Suzanne MK Buckley, Mark Tangney, Simon N Waddington, Donald Peebles, and Donald Peebles. London, United Kingdom; and Cork, Ireland.

T-023 **Membranous Progestogen Receptors May Be Important in Controlling Fetal Membrane Weakening.**
Robert Moore, Deepak Kumar, Brian Mercer, Sam Mesiano, and John J Moore. Cleveland, OH, USA.

T-024 **Isolated Human Amnion Epithelial Cells Contain Multiple Cell Populations.**
Brittany L Sato, Anthony D Junker, Eric S Collier, and Claire E Kendal-Wright. Honolulu, HI, USA.

T-025 **Relationships of Cervical Collagen Content, as Determined by Light-Induced Fluorescence (LIF), During Normal Pregnancy, Preterm Birth and Association with Cervical Length.**
Zheng Zheng, Lele Wang, Weijuan Zhang, Shao-Qing Shi, Robert E Garfield, and Huishu Liu. Guangzhou, China.

T-026 **Progestins Inhibit IL1β Induced MMP9 Activity and GM-CSF Production from Primary Chorion Cells.**
TK Allen, L Feng, W Marinello, IA Buhimischi, and AP Murtha. Durham, NC, USA; and Columbus, OH, USA.

T-027 **Cervical Smooth Muscle Cells from Women with a History of Premature Cervical Remodeling Exhibit Altered Migrational Contractile Behavior.**
Victoria Yu, Sudip Dahal, James Lohner, Conrad SternAscher, Cande V Ananth, Kristin Myers, Ron Wapner, Jan Kitajewski, George Gallos, Michael Sheetz, and Joy Vink. New York, NY, USA; and Chicago, IL, USA.

T-028 **17α-Hydroxyprogesterone Caproate Is Not an Optimal Progestogen for Inhibition of *In-Vitro* Fetal Membrane Weakening.**
Deepak Kumar, Robert M Moore, Mercer M Brian, Sam Mesiano, and John J Moore. Cleveland, OH, USA.

T-029 **Alternative-Activated Macrophages from Amniotic Fluid Home to the Prematurely Ruptured Amnion.**
Haruta Mogami, Annavarapu Hari Kishore, Jesus Acevedo, and R Ann Word. Dallas, TX, USA.

T-030 **Evidence That MPRIP Targets Phosphatases and Kinases to Myosin to Regulate Relaxation and Contraction in the Human Myometrium.**
Trent Butler, Minoo Heidari Kani, Eng-Cheng Chan, Roger Smith, and Jonathan W Paul. Newcastle, NSW, Australia.

T-031 **HoxA Proteins Regulate the Expression of Contraction Associated Genes in Human Uterine Myometrium.**
Ning Xie, Yinan Li, Donna Slater, Stephen Lye, and Xuesen Dong. Vancouver, BC, Canada; Calgary, AB, Canada; and Toronto, ON, Canada.

T-032 **Characterizing Preterm Labor Through Muti-Sensor Electrical Activity Propagation.**
Hari Eswaran, Diana Escalona-Vargas, Sarah Theriot, Eric R Siegel, and Curtis L Lowery. Little Rock, AK, USA.

T-033 **Global Uterine Signaling During Labor Is Not Progressive Propagation.**
Lauren Miller, Neil Sligman, Eva Pressman, and Roger Young. Rochester, NY, USA; and Memphis, TN, USA.

T-034 **The Estrogen Receptor 1 (ESR1) Exon 7 Skip Isoform Functions by Blocking ESR1 Action Prior to Labor.**
Prashanth Anamthathmakula, Chandra S Miryala, Jennifer C Condon, and Pancharatnam Jeyasuria. Detroit, MI, USA.

CLINICAL PERINATOLOGY

T-035 **Placentally Derived Serotonin in Highly Seasonal Pregnant Women.**
Maria H Sqapi, Stephen G Matthews, and Robert Levitan. Toronto, ON, Canada.

Thursday, March 16, 2017 - Poster Session I - Bonnet Creek I – IX

T-036 **Evaluation of One or Both Umbilical Arteries in Fetal Growth Restriction.**
Teresa Harper, Mary Pinter, Diane Gumina, Allison Gillan, and John Hobbins. Aurora, CO, USA.

T-037 **Reducing Primary Cesarean Delivery: Adherence to National Guidelines for Management of Labor Arrest in a Single Center.**
Mesk Alrais, Nana-Ama E Ankumah, Farah H Amro, Rachel Landgren, Baha M Sibai, and Sean C Blackwell. Houston, TX, USA.

T-038 **Utility of Perinatal Autopsy for Stillbirth ≤ 20 Weeks.**
Karen J Gibbins, Robert M Siver, Yajing Xiong, and Jessica M Comstock. Salt Lake City, UT, USA.

T-039 **Maternal Plasma Hyperglycosylated hCG in Abnormally Invasive Placenta (AIP).**
Maegan Ford, Stacy Zamudio, Michael Sbarra, Sonia DaSilva-Arnold, Nicholas P Illsley, and Abdulla Al-Khan. Hackensack, NJ, USA.

T-040 **Single Dose Anti-D Prophylaxis in Pregnancy: Is It Time to Change?**
Craig E Pennell, Janice C Cheng, Blagica Penova-Veselinovic, Carol A Wang, Bernie Ingleby, Chris C Arnold, Andrew L Barr, Melanie K White, and Scott W White. Perth, Western Australia, Australia.

T-041 **A Retrospective Assessment of Periviable Outcomes Involving Vertex Presentations Depending on Delivery Method.**
Nicole R Albino, and Clark T Johnson. Baltimore, MD, USA.

T-042 **Novel Factors Associated with Spontaneous Onset of Preterm Labor.**
Elise N Erickson, Leonardo Pereira, Frances M Biel, and Jonathan M Snowden. Portland, OR, USA.

T-043 **Characteristics of Uterine Inertia in Uterine Electromyography at the Active Phase of Labor.**
Pin Li, Lele Wang, Xueya Qian, Abraham Morse, Robert E Garfield, and Huishu Liu. Guangzhou, Guangdong, China.

T-044 **Is a History of a Prior Term Birth Associated with a Reduction in the Risk of Recurrent Preterm Birth?**
Moeun Son, William A Grobman, Anna Palatnik, and Emily S Miller. Chicago, IL, USA.

T-045 **15-Hydroxy Prostaglandin Dehydrogenase Is a Target for Induction of Cervical Ripening and Labor.**
Annavarapu Hari Kishore, Bruce Posner, Joseph Ready, Sanford Markowitz, and R Ann Word. Dallas, TX, USA; and Cleveland, OH, USA.

T-046 **Antenatal Glucocorticoid Therapy Protects the Chronically Hypoxic Fetus from Programmed Endothelial Dysfunction and Hypertension in Adulthood.**
KJ Botting, Y Niu, KL Skeffington, BJ Allison, KL Brain, N Itani, C Beck, and DA Giussani. Cambridge, United Kingdom.

T-047 **Low Maternal BMI and Associated Pregnancy Outcomes.**
Kaitlin Hanmer, Ann Thomas, David Cantonwine, and Thomas McElrath. Boston, MA, USA.

T-048 **Maternal BMI Regulates the Exosomal Bioactivity on Cytokine Release from Endothelial Cells.**
Omar Elfeky, Sherri Longo, Andrew Lai, Gregory Duncombe, Gregory E Rice, and Carlos Salomon. Brisbane, QLD, Australia; and New Orleans, LA, USA.

T-049 **Gestational Diabetes Prevalence at Moderate & High Altitude.**
Anna G Euser, Andrew Hammes, Jared T Ahrendsen, Cassie Geremaia, Barbara Neistadt, David W Weitzenkamp, Colleen G Julian, and Lorna G Moore. Aurora, CO, USA.

T-050 **Pre-Pregnancy Obesity and Metabolomic and Transcriptomic Networks in Early-Mid Pregnancy.**
Alison G Paquette, Pandora L Wander, Vineet Sangar, Tanya K Sorensen, Michelle Williams, Nathan Price, and Daniel Enquobahrie. Seattle, WA, USA; and Boston, MA, USA.

T-051 **An Innovative Bioinformatics Approach to Identify New Potential Therapeutic Targets in Gestational Diabetes.**
Jeffery A Goldstein, Lisa A Bastarache, Joshua C Denny, and David M Aronoff. Nashville, TN, USA.

T-052 **Nonalcoholic Fatty Liver Disease in the First Trimester and Subsequent Development of Gestational Diabetes: A Prospective Cohort Study.**
SM Lee, JS Park, ER Norwitz, JN Koo, IH Oh, JE Kwon, BJ Kim, SM Kim, SY Kim, GM Kim, WKim, SK Joo, S Shin, CW Park, and JK Jun. Seoul, Republic of Korea; Boston, MA, USA; and Incheon, Republic of Korea.

T-053 **Early Maternal Nutrient Restriction in the Sheep Induces Collagen Accumulation in the Myocardium of Overfed Offspring (F1).**
Adel B Ghnenis, John F Odhiambo, Peter W Nathanielsz, and Stephen P Ford. Laramie, WY, USA.

T-054 **Prostaglandin Levels in Pregnant Women with and without Hyperemsis Gravidum.**
Avi Hameroff, Victor Mniarji, Ponjeli Talus, Vijaya Nacharaju, Cassandra Charles, Nicole Price, Mudar Dalloul, and Ozgul Muneyyirci-Delale. Brooklyn, NY, USA.

Thursday, March 16, 2017 - Poster Session I - Bonnet Creek I – IX

T-055 **Severe Vitamin K Deficiency in Pregnancy Presenting with Preterm Labor, Intrahepatic Cholestasis and Hematuria.**
Maria C Maldonado, Michael S Awadalla, Jay Idler, Welch Robert, and Alhousseini Ali. Detroit, MI, USA.

T-056 **Interventions for Uterine Atony Prior to Hysterectomy.**
Audrey A Merriam, Cande V Ananth, Yongmei Huang, Jason D Wright, Mary E D'Alton, and Alexander M Friedman. New York, NY, USA.

T-057 **The Efficacy of 3rd Generation Cephalosporin Plus Metronidazole versus 3rd Generation Cephalosporin Plus Clarithromycin in Perinatal Outcomes for Women with Preterm Premature Rupture of Membranes.**
Jong Woon Kim, Yoon Ha Kim, A Ra Cho, and Jong Ho Moon. Gwangju, Republic of Korea.

T-058 **Delivery at Academic Institutions May Improve Cesarean Delivery Rates in Patients with Gastroschisis.**
Jose R Duncan, Pranit N Chotai, Anna K Slaggle, Eunice Y Huang, Ajay J Talati, and Mauro H Schenone. Memphis, TN, USA.

T-059 **Variation in Endometritis Rates Following Cesarean Section.**
Joses A Jain, Cande V Ananth, Zainab Siddiq, Jason D Wright, Mary E D'Alton, and Alexander M Friedman. New York, NY, USA.

T-060 **Utilization of Inpatient Psychiatry Consults at an Urban Obstetric Hospital.**
Nicole R Hall, Emily C Rutledge, Susan M Ramin, Manju Monga, Mary K Shoemaker, and Lucy J Puryear. Houston, TX, USA.

T-061 **Management of Breech Presentation Beyond 40 Weeks of Gestation.**
Hanna Huerter, Isabel Voigt, and Frank Louwen. Frankfurt am Main, Hessen, Germany.

T-062 **High Pelvic Floor Muscle Stiffness Measured by Vaginal Elastometry Is a Risk Factor for Delayed Second Stage of Labour, Instrumental Vaginal Delivery and Pelvic Floor Damage.**
Dilly OC Anumba, Siobhan Gillespie, Swati Jha, Shahram Abdi, Jenny Kruger, and Xinshan Li. Sheffield, South Yorkshire, United Kingdom; and Auckland, New Zealand.

T-063 **Reduced Third Trimester Growth Velocity in Fetuses of a Normal Birthweight Is Associated with Uteroplacental Insufficiency.**
Teresa MacDonald, Alice Robinson, Lisa Hui, Stephen Tong, and Sue Walker. Melbourne, VIC, Australia.

T-064 **Pre-Conception Blood Pressure and Evidence of Placental Malperfusion.**
Jacqueline Atlass, Marie Menke, W Tony Parks, Karen Derzic, and Janet Catov. Pittsburgh, PA, USA; and Lebanon, NH, USA.

T-065 **Prenatal Stress and Gestational Weight Gain.**
MA Kominiarek, W Grobman, E Adam, C Buss, J Culhane, S Entringer, G Miller, H Simhan, P Wadhwa, D Williamson, KY Kim, L Keenan-Devlin, and A Borders. Chicago, IL, USA; Irvine, CA, USA; Berlin, Germany; Philadelphia, PA, USA; Pittsburgh, PA, USA; and Durham, NC, USA.

T-066 **Predictors of Antenatal Complications During Expectant Management of PPROM.**
Kelli Barbour, Christina Herrera, Robert Silver, Michael Varner, and Tracy Manuck. Salt Lake City, UT, USA; and Chapel Hill, NC, USA.

T-067 **Increased Proteinuria During Acute Pyelonephritis in Pregnancy.**
Cindy T Chau, Alex Fong, Rebecca Simon-Freeman, and Kenneth K Chan. Orange, CA, USA; and Long Beach, CA, USA.

T-068 **Is the Use of Prophylactic Antibiotics During Revision of the Uterine Cavity Really Necessary?**
Myriam Safrai, Yossef Ezra, Michal Lipschuetz, and Doron Kabiri. Jerusalem, Israel.

T-069 **Accuracy of Rapid Group B Streptococcus Polymerase Chain Reaction in Threatened Preterm Labor.**
Cindy T Chau, Jennifer Duffy, Craig V Towers, Callie Reeder, Kim Fortner, and Alex Fong. Orange, CA, USA; Knoxville, TN, USA; and Long Beach, CA, USA.

DEVELOPMENTAL PROGRAMMING

T-070 **A Scoping Review of Indigenous Longitudinal Studies of Both Pregnancy and Early Childhood.**
Julie Burrows, Gita Wahi, Sonia Anand, Peter Jones, Kirsty Pringle, and Kym M Rae. Tamworth, NSW, Australia; Hamilton, ON, Canada; Gold Coast, QLD, Australia; and Callaghan, NSW, Australia.

T-071 **Maternal Nutrition and Immune Developmental Programming, Role of the Microbiome.**
Ellen Kraig, Leslie Linehan, Eirleen Hyun, Lourdes Arteaga-Cortes, Peter Dube, Peter W Nathanielsz, Cun Li, Qunfeng Dong, Xiang Gao, and Mark J Nijland. San Antonio, TX, USA; Laramie, WY, USA; and Chicago, IL, USA.

T-072 **Effects of Constant Light During Development on Adult Metabolism.**
Keenan Bates, Omonseigho Talton, and Laura Schulz. Columbia, MO, USA.

T-073 **Cardiac-Specific *Akap13* Haploinsufficient Mice Exhibited Sex-Dependent Cardiomyopathy.**
K Maravet Baig-Ward, Stasia Anderson, Szu-Chi Su, and James H Segars. Baltimore, MD, USA; Richmond, VA, USA; and Bethesda, MD, USA.

T-074 **Transcriptomics of Fetal Skeletal Muscles in Response to Chronic Maternal Hypercortisolemia in Late Gestation.**
Serene Joseph, Elaine Richards, and Maureen Keller-Wood. Gainesville, FL, USA.

Thursday, March 16, 2017 - Poster Session I - Bonnet Creek I – IX

T-075 **Maternal Pre-Pregnancy Body Mass Index (BMI) Predicts Gene Expression in a Novel Human Model.**
Niraj R Chavan, Rebecca E Pollack, Leryn J Reynolds, Brett Dickens, John M O'Brien, and Kevin J Pearson. Lexington, KY, USA; and Charlotte, NC, USA.

T-076 **Ovarian Stimulation Increases the Risk of Fetal Cardiac Defects of Pups Exposed to Severe Maternal Hyperglycemia.**
Rolanda L Lister, Francine Hughes, Etoi Garrion, and Bin Zhou. Nashille, TN, USA; New York, NY, USA; and Bronx, NY, USA.

T-077 **Antenatal Glucocorticoid Exposure and Visceral Fat Effects on Epicardial Fat in Adult Sheep.**
G Angela Massmann, Won Joon Seong, Jie Zhang, and Jorge P Figueroa. Winston-Salem, NC, USA.

T-078 **Maternal Antioxidant Treatment May Improve Thermogenesis in Offspring of Hypoxic Pregnancy.**
A Martin, B Allison, K Brain, D Giussani, C Ducsay, and D Myers. Oklahoma City, OK, USA; Cambridge, United Kingdom; and Loma Linda, CA, USA.

T-079 **Developmental Programming of the Vasculature: Aortic Caliber (AC) and Distensibility (AD) Are Reduced in Adult IUGR Baboons Offspring (F1) and Show Signs of Earl Aging Changes.**
Anderson D Kuo, Cun Li, Peter W Nathanielsz, and Geoffrey D Clarke. San Antonio, TX, USA; and Laramie, TX, USA.

T-080 **Intrauterine Growth Restriction Enhances Hypertension and Markers of Vascular Remodeling in Adult Rat Offspring Fed a High Fat Diet.**
Blair Dodson, Tom Miller, Yueqin Yang, Baifeng Yu, and Erin Zinkhan. Aurora, CO, USA; and Salt Lake City, UT, USA.

T-081 **Changes in the M1/M2 Responses and Epigenetic Markers in Neonatal Monocyte-Derived Macrophages from Women with Pre-Gestational Obesity.**
Bernardo J Krause, Francisca Cifuentes-Zúñiga, Viviana Arroyo, Gustavo Soto-Carrasco, Ricardo Uauy, Paola Casanello, and Jose Castro-Rodríguez. Santiago, Metropolitana, Chile.

T-082 **Antenatal Magnesium Sulfate and Ponderal Index From Birth to Age 2 in Preterm Male and Female Infants.**
Tiffany E Deihl, and Hyagriv N Simhan. Pittsburgh, PA, USA.

T-083 **Chronic Pulsatile Hyperglycemia Does Not Increase Insulin Secretion in Growth Restricted Fetal Sheep.**
Brit H Boehmer, Laura D Brown, Stephanie R Wesolowski, William W Hay, and Paul J Rozance. Aurora, CO, USA.

T-084 **Outcomes in the Term Fetal Baboon Pancreas in Response to Challenges of Maternal Under Nutrition and Obesity.**
Cun Li, Ablat Tursun, JunFei Li, and Peter W Nathanielsz. San Antonio, TX, USA; Laramie, WY, USA; and Changsha, Hunan, China.

T-085 **Central Dopamine "Reward Pathway" Is Upregulated in Offspring of Obese Mothers.**
Daniela P Laureano, Elaheh Mossayebi, Kavita Narwani, Guang Han, Niyati Joshi, Mina Desai, and Michael G Ross. Porto Alegre, Rio Grande do Sul, Brazil; and Torrance, CA, USA.

T-086 **Ongoing Defects in Cerebellar Development in a Guinea Pig Model of Preterm Birth.**
Julia C Shaw, Hannah K Palliser, Rebecca M Dyson, Mary J Berry, and Jonathan J Hirst. Newcastle, Australia; and Wellington, New Zealand.

T-087 ***ZNHIT3*, a New Candidate Gene for Mayer-Rokitansky-Kuster-Hauser (MRKH) Syndrome.**
Lawrence C Layman, Lacey S Willaims, Lynn P Chorich, Megan E Sullivan, Hyung-Goo Kim, John A Phillips, III, Hugh S Taylor, Alka Chaubey, and Michael J Friez. Augusta, GA, USA; Nashville, TN, USA; New Haven, CT, USA; and Greenwood, SC, USA.

EPIDEMIOLOGY

T-088 **Are Preterm and Postterm Birth Related?**
Elise N Erickson, Frances M Biel, Jonathan M Snowden, and Leonardo Pereira. Portland, OR, USA.

T-089 **Prenatal Exposure to Maternal PCOS Associated with Increased Risk of Adult Body Mass Index in Children of Both Genders.**
Shruthi Mahalingaiah, Michael Winter, and Ann Aschengrau. Boston, MA, USA.

T-090 **Interdelivery Interval and Indicated Preterm Birth.**
Annie M Dude, and William Grobman. Chicago, IL, USA.

T-091 **Low-Frequency, Damaging Mutations in Hundreds of Genes Are Risk Factors for Endometriosis.**
Kenneth Ward, Kenneth Ward, and Kenneth Ward. Salt Lake City, UT, USA.

FETUS

T-092 **Effect of Maternal Binge Drinking on the Fetal Circulation.**
Ana Tobiasz, Jose Duncan, Ryan Sullivan, Danielle Tate, Alex Dopico, Anna Bukiya, and Giancarlo Mari. Memphis, TN, USA.

T-093 **Array Comparative Genomic Hybridization Yields Interpretable Results from Fetal Tissue Stored Up to 5 Days at Room Temperature.**
Neil S Seligman, Philip J Katzman, and Anwar Iqbal. Rochester, NY, USA.

Thursday, March 16, 2017 - Poster Session I - Bonnet Creek I – IX

T-094 **Impact of Delivery Route on Neonatal Morbidity and Mortality in Isolated Gastroschisis: A Systematic Review and Meta-Analysis.**
Ahizechukwu C Eke, Ashley Hesson, Conisha Holloman, and Anna Sfakianaki. Baltimore, MD, USA; Ann Arbor, MI, USA; Orlando, FL, USA; and New Haven, CT, USA.

T-095 **Prenatal Whole Exome Sequencing in Anomalous Fetuses: Improving Diagnosis, Expanding Mendelian Phenotypes, Identifying Novel Genes, and Identifying Counseling Challenges.**
Neeta L Vora, Bradford Powell, Emily Hardisty, Kelly Gilmore, Kate Foreman, Cindy Powell, Debra Skinner, Christine Rini, Karen Weck, Anne D Lyerly, Kim Boggess, Jonathan Berg, and James P Evans. Chapel Hill, NC, USA.

T-096 **Novel Three-Dimensional High-Frequency Ultrasonography for Early Detection and Characterization of Embryo Implantation Site Development in the Mouse.**
Mary Peavey, Corey Reynolds, William Gibbons, Cecilia Valdes, Francesco DeMayo, and John Lydon. Houston, TX, USA; and Research Triangle Park, NC, USA.

T-097 **Midtrimester Fetal Growth Restriction: Who Is at Risk of Remaining Small?**
Lorene A Temming, Fayola Fears, Roxane Rampersad, Methodius G Tuuli, George A Macones, and Alison G Cahill. St. Louis, MO, USA.

T-098 **Lipid Accumulation in the Primate Fetal Liver with Maternal Obesity (MO) May Be Regulated by Novel Epigenetic Mechanisms.**
Sobha Puppala, Cun Li, Jeremy P Glenn, Amy R Quinn, Jennifer J Palarczyk, Edward J Dick, Peter W Nathanielsz, and Laura A Cox. San Antonio, TX, USA; and Laramie, WY, USA.

T-099 **Left Ventricular Sphericity Index in Fetuses with Congenital Diaphragmatic Hernia.**
Rachel Rodel, Michael Zaretsky, Henry Galan, Nicholas Behrendt, Kenneth Liechty, Sonali Patel, and Bettina Cuneo. Aurora, CO, USA.

T-100 **Neonatal Lactic Acid and the Prediction of Severe Brain Injury and Death in Neurologically Depressed Neonates.**
Christopher Novak, Hattan Arif, and Ernest Graham. Baltimore, MD, USA.

T-101 **Modeling of Gene Expression in Newborn Heart Following Chronic Maternal Hypercortisolemia in Late Gestation.**
Andrew Antolic, Elaine Richards, and Maureen Keller-Wood. Gainesville, FL, USA.

T-102 **Atrial Natriuretic Peptide Regulates the Fetal Cardiomyocyte Cell Cycle.**
Eileen I Chang, Natasha N Chattergoon, Samantha Louey, Isa Lindgren, and Kent L Thornburg. Portland, OR, USA.

T-103 **A New Method of Predicting a Brain Hemorrhage Risk in Fetal Growth Restriction.**
Takahiro Minato, Takuya Ito, Naoaki Sato, Yoshitaka Kimura, and Nobuo Yaegashi. Sendai, Miyagi, Japan.

T-104 **Exposure to Intrauterine Inflammation Has a Sex-Specific Effect on Gene Expression in the Hippocampus of Exposed Offspring: Potential Mechanisms of Adverse Neurobehavioral Outcomes.**
Amy G Brown, Natalia M Tulina, Guillermo O Barila, and Michal A Elovitz. Philadelphia, PA, USA.

T-105 **In Utero Oxytocin (OXT) Exposure Alters Gene Expression Associated with Neurotransmitter Secretion and Metabolism in the Perinatal Mouse Brain.**
Frances Hsieh, Burton Rochelson, Gopal Kumar, Prodyot Chatterjee, Xiangying Xue, Ilya Kordunsky, and Christine Metz. Manhasset, NY, USA.

GLOBAL HEALTH

T-106 **Obstetrics Providers' Perceptions of the Barriers to Diagnosing Preeclampsia (PEC): A Clinical Needs Assessment in Two Low- and Middle-Income Countries (LMIC).**
Lydia L Shook, Muchabayiwa F Gidiri, Melanie Peña, Manuel Bousiéguez, and Irina A Buhimschi. New Haven, CT, USA; Harare, Zimbabwe; Mexico City, Mexico; and Columbus, OH, USA.

GYNECOLOGIC ONCOLOGY

T-107 **Paclitaxel Promotes Exosomal Expression of TLR8-Activating miR-146a-3p in Chemoresistant Epithelial Ovarian Cancer Cells.**
Stefan M Gysler, Mary C Pitruzzello, Melissa J Mulla, Julie A Potter, Ayesha B Alvero, Gil Mor, and Vikki M Abrahams. New Haven, CT, USA.

T-108 **Ovarian Cancer Cells Transfer Resistance to Chemotherapy to Other Cells via Exosomes.**
Mona Alharbi, Richard Kline, Katrina Wade, Jacob Estes, John Hooper, Gregory E Rice, and Carlos Salomon. Brisbane, QLD, Australia; and New Orleans, LA, USA.

T-109 **DNA Copy Number Alteration in Primary Fallopian Tube Carcinoma.**
Shoko Sakurada, Yoh Watanabe, Yusuke Shibuya, Hideki Tokunaga, Sakae Saito, Jun Yasuda, Hidekazu Yamada, Hitoshi Niikura, and Nobuo Yaegashi. Sendai, Miyagi, Japan; and Natori, Miyagi, Japan.

Thursday, March 16, 2017 - Poster Session I - Bonnet Creek I – IX

ENDOMETRIOSIS, FIBROIDS, AND GYNECOLOGY

T-110 **Gene Expression Patterns in Human Endometrium, Cervix, Sigmoid, and Ileum Suggest Distinct Mucosal-Associated Immune Environments with Potential Impact on Local Susceptibility to HIV Transmission.**
Shaina Balayan, Sahar Houshdaran, Karen Smith-McCune, Ruth M Greenblatt, Barbara L Shacklett, Juan C Irwin, and Linda C Giudice. San Francisco, CA, USA; and Davis, CA, USA.

T-111 **Side Effect Profile During Treatment of Symptomatic Endometriosis with Norethindrone or Leuprolide Treatment.**
Ozgul Muneyyirci-Delale, Cassandra Charles, Xiaobai Li, Ninet Sinaii, Mudar Dalloul, and Pamela Stratton. Brooklyn, NY, USA; and Bethesda, MD, USA.

T-112 **Invasive Growth of Endometrium in SHN Mice: Driven by Novel MMTV Integration Sites?**
Ralf Lesche, Djork-Arne Clevert, Thomas Zollner, and Martin Fritsch. Berlin, Germany.

T-113 **Novel EP4 Antagonist Demonstrated Significant Effects in Rat Model of Chronic Inflammatory Pain Employing a Dynamic Weight Bearing Readout.**
Anne-Marie Coelho, Stefan Baeurle, Daryl Walter, Olaf Peters, Markus Koch, Thomas M Zollner, Andreas Steinmeyer, Susan Boyce, Susan Boyce, and Jens Nagel. Berlin, Germany; Hamburg, Germany; Abingdon, United Kingdom; and Frankfurt/Main, Germany.

T-114 **Possible Role for Mast Cells and PAR-2 Receptor in the Hyperalgesic State of Women with Endometriosis.**
Bianca De Leo, Arantza M Esnal Zufiaurre, Hilary OD Critchley, Andrew W Horne, and Philippa TK Saunders. Edinburgh, Scotland, United Kingdom.

T-115 **Abstract Withdrawn**

T-116 **Dose-Dependent Suppression of Ovulation and Ovarian Activity by Elagolix in Healthy Premenopausal Women.**
David Archer, Juki Ng, Yi-Lin Chiu, Cheri Klein, and Kristof Chwalisz. Norfolk, VA, USA; and North Chicago, IL, USA.

T-117 **Rbfox2 Expression Is Upregulated in Stromal Cells of Endometriotic Lesions.**
Tal Saar, Debra Goldman-Wohl, Iris Eisenberg, Caryn Greenfield, Diana Pruss, Ronit Haimov-Kochman, Simcha Yagel, and Tal Imbar. Jerusalem, Israel.

T-118 **Aberrant Over-Expression of SIRT1 and K-Ras Reveals a Mechanism for Progesterone Resistance in Women with Endometriosis.**
Jae-Wook Jeong, Jung-Yoon Yoo, Tae Hoon Kim, Francesco J DeMayo, David P Schamme, Steven L Young, and Bruce A Lessey. Grand Rapids, MI, USA; Research Triangle Park, NC, USA; Greenville, SC, USA; Chapel Hill, NC, USA; and Greenville, NC, USA.

T-119 **A Familial History of Endometriosis Causes Developmental and Reproductive Anomalies in Male Offspring in an Animal Model.**
Emily K Secrist, Henda Nabli, Katherine Costello, Kelly Gissy, and Kathy L Sharpe-Timms. Columbia, MO, USA.

T-120 **TGM2 Is Highly Expressed and Active in Endometriosis Where It Mediates Pro-Fibrotic and Pro-Inflammatory Effects.**
Fernando Martinez Estrada, Maik Obendorf, Stefanie Mesch, Oliver M Fischer, Cemsel Bafligil, Manman Guo, Christian Becker, Krina Zondervan, Catherine Shang, Stephen Kennedy, Siamon Gordon, Thomas M Zollner, and Udo Oppermann. Oxford, United Kingdom; and Berlin, Germany.

T-121 **Endometriosis Alters Expression of Genes Modulating Anxiety, Depression and Pain in the Brain.**
Tian Li, Ramanaiah Mamillapalli, Sheng Deng, Hao Chang, Zhong-wu Lu, Xiao-Bing Gao, and Hugh S Taylor. New Haven, CT, USA.

T-122 **History of Pharmacologic and Surgical Interventions Among Canadian Women Presenting with Symptomatic Uterine Fibroids.**
Ally Murji, Philippe Y Laberge, Sukhbir S Singh, Nicholas Leyland, Joshua Polsky, Roy Jackson, Claude Fortin, Angelos Vilos, Barry Sanders, Aubrey Uretsky, John A Thiel, Diego Garzon, Alain Lamontagne, and George Vilos. Toronto, ON, Canada; Québec, QC, Canada; Ottawa, ON, Canada; Hamilton, ON, Canada; Windsor, ON, Canada; White Rock, BC, Canada; Montreal, QC, Canada; London, ON, Canada; Vancouver, BC, Canada; Edmonton, AB, Canada; Saskatoon, SK, Canada; and Markham, ON, Canada.

T-123 **Urinary Estrogen Metabolites and Antioxidant System Activity in Premenopausal Women with Uterine Fibroids.**
Larisa V Suturina, Leonid F Sholohov, Darya V Lizneva, and Lyubov I Kolesnikova. Irkutsk, Russian Federation; and Augusta, GA, USA.

T-124 **Effect of RhoA Pathway Inhibitors and Activators on the Interaction of a Kinase Anchoring Protein 13, AK**
Chantel I Washington, Paul H Driggers, Minnie Malik, and James H Segars. Baltimore, MD, USA; and Bethesda, MD, USA.

Thursday, March 16, 2017 - Poster Session I - Bonnet Creek I – IX

T-125 **Dimished DNA Repair Capacity in Stem Cells from Human Uterine Fibroids Compared to Adjacent Myometrium Leads to Compromised Genomic Integrity and Increased Tumorigenesis.**
Lauren Prusinski, Qiwei Yang, Michael Diamond, and Ayman Al-Hendy. Augusta, GA, USA.

T-126 **Abundance of Fungal Species in the Gravid Vaginal Microbiome.**
Brett Tortelli, Ping Liu, and Justin Fay. St. Louis, MO, USA.

T-127 **Effect of Gender on the Innate Immune Response in Septic Mice.**
Noor Mohd Nasri, Julia Zollner, James Leiper, and Mark Johnson. London, United Kingdom; and Kuala Lumpur, Malaysia.

MATERNAL BIOLOGY AND HEALTH

T-128 **Application of Thrombelastography to Monitor the Change of Coagulation Function in Patients of Recurrent Spontaneous Abortion with Different Times Miscarriages Before and After Pregnancy.**
Danyang Kang, Yue Hou, Qiaoni Yang, Qiushi Wang, and Chong Qiao. Shenyang, China.

T-129 **Elevated Maternal Testosteronemodulates Synthesis of Long-Chain Polyunsaturated Fatty Acids, Leading to Offspring Deficiency.**
Kathirvel Gopalakrishnan, and Sathish Kumar. Galveston, TX, USA.

T-130 **Mitogen-Activated Protein Kinases Mediate Leptin-Induced Proliferation of Ovine Uterine Artery Endothelial Cells During the Follicular phase of the Ovarian Cycle and Late Pregnancy in Sheep.**
Vladimir E Vargas, Maja Okuka, Rosalina Villalon Landeros, Gladys E Lopez, Jing Zheng, and Ronald R Magness. Tampa, FL, USA; and Madison, WI, USA.

T-131 **Echocardiography in Obese versus Non-Obese Pregnant Women.**
Jessica McPherson, Melissa Caughey, Patricia Chang, Nathan Howell, Zarina Sharalaya, and Thomas Ivester. Chapel Hill, NC, USA.

T-132 **Increased Fraction of Cardiac Output Toward Uterine Artery in Maternal Compromise in *Papio Spp.***
Natalia Schlabritz-Loutsevitch, Maria Chavez, Anand Cholia, Daniella Pino, Gary White, Marcel Chuecos, Saloni Cholia, and James Maher. Odessa, TX, USA; and Norman, OK, USA.

T-133 **Remodeling and Altered Biomechanics of the Mouse Abdominal Aorta During and After Pregnancy.**
Aaron Gelinne, Nga Ling Ko, Liam John, Lucia Brown, Stephen Brown, and George Osol. Burlington, VT, USA.

T-134 **Pre Pregnancy Hemodynamics and Changes During Pregnancy in Women Who Develop Recurrent Hypertensive Disease.**
Kylie Cooper, Carole McBride, Gary Badger, and Ira Bernstein. Burlington, VT, USA.

T-135 **Enriched H_2S Biosynthesis *via* Selective CBS Upregulation Is Associated with Endometrial Angiogenesis in Women.**
Thomas J Lechuga, Bansari A Patel, Nicole A Nguyen, Hong-hai Zhang, and Dong-bao Chen. Irvine, CA, USA.

T-136 **Patient and Provider Evaluation of a Postpartum Patient Navigation Program to Improve Postpartum Care Among Publicly Insured Women.**
Fengling Hu, Angelina M Strohbach, Noelle G Martinez, Nadia Hajjar, Melissa A Simon, and Lynn M Yee. Chicago, IL, USA.

T-137 **Increased Vaginal Gram-Negative Bacterial Diversity in Third Trimester of Pregnancy in NHP (Non-Human Primates).**
Natalia Schlabritz-Loutsevitch, Nithya Mudaliar, Abdul Hamood, James Maher, Gary White, and Gary Ventolini. Odessa, TX, USA; Lubbock, TX, USA; and Oklahoma, OK, USA.

PLACENTA

T-138 **Placental Vascular Endothelial Growth Factor165b Expression in Women with Uncomplicated Pregnancy.**
Jayasri Basu, Valmiki Seeraj, Samantha Gonzalez, Carolyn M Salafia, Aruna Mishra, Enyonam Agamasu, and Magdy Mikhail. Bronx, NY, USA.

T-139 **Temporal Expression of Genes Involved in Placental Tryptophan Metabolism in Chorionic Villus Tissues.**
Padma Murthi, Stacey Ellery, Hayley Dickinson, Miranda Davies-Tuck, Jan J Erwich, David Walker, Euan M Wallace, and Peter R Ebeling. Clayton, VIC, Australia; and Groningen, Netherlands.

T-140 **Could Gonadotrophin-Releasing Hormone Receptor Antagonists Be Repurposed to Treat Ectopic Pregnancy?**
Lisa L Campbell, Natalie J Hannan, Mohamed A Bedaiwy, Nicola Gray, Stephen Tong, and Andrew W Horne. Edinburgh, Scotland, United Kingdom; Melbourne, VIC, Australia; and Vancouver, BC, Canada.

T-141 **The NALP3 Inflammasome Mediates LPS Effects on IL-1β Secretion by Placental Hofbauer Cells (HBCs).**
Seth Guller, Zhonghua Tang, Vikki M Abrahams, and Gil Mor. New Haven, CT, USA.

Thursday, March 16, 2017 - Poster Session I - Bonnet Creek I – IX

T-142 **The Placental Microbiome in Intrauterine Growth Restricted Pregnancies.**
Men-Jean Lee, Michelle Wang, Yula Ma, Xiuliang Bao, Inga Peter, Luca Lambertini, and Jianzhong Hu. New York, NY, USA; and Honolulu, HI, USA.

T-143 **Trophoblasts Derived from Preeclamptic iPSCs Do Not Up-Regulate ITGA1 in Response to High Oxygen Over Time.**
Rowan M Karvas, Ying Yang, Toshihiko Ezashi, Schust Danny, R Michael Roberts, and Laura C Schulz. Columbia, MO, USA.

T-144 **Loss of Programmed Cell Death 4 Associates with the Progression of Gestational Trophoblastic Disease.**
Hui-Juan Zhang, Ya-Xin Wang, Jiu-Ru Zhao, Ramkumar Menon, and Yuan Liu. Shanghai, China; and Galveston, TX, USA.

T-145 **MicroRNA Signature in Progression of Gestational Trophoblastic Disease.**
Jiu-Ru Zhao, Hui-Juan Zhang, Ya-Xin Wang, Yue-Ying Xu, and Wei-Bin Wu. Shanghai, China.

T-146 **Redox-Sensitive Transcription Factor NRF2 Promotes Human Trophoblast Differentiation by Inducing miR-1246.**
Sribalasubashini Muralimanoharan, and Carole R Mendelson. Dallas, TX, USA.

T-147 **Acquisition of an Endothelial-like Fate in Differentiating Trophoblast Stem Cells and Vascular Mimicry at the Placentation Site.**
Masanaga Muto, Damayanti Chakraborty, Regan L Scott, and Michael J Soares. Kansas City, KS, USA.

T-148 **Trophoblast Dependent Secretion of Stannocalcin-1 and Interleukin-8 by Endothelial Cells and Their Role as Possible Mediators of Spiral Artery Remodeling.**
Arwa Esmail, Alexa Bishop, Judith E Cartwright, and Guy S Whitley. London, United Kingdom.

T-149 **Changes in the Expression of Calcium Channels in Placentas Complicated with Preeclampsia or Fetal Growth Restriction According to the Administration of MgSO4.**
Hyun-Hwa Cha, Jae Ryoung Hwang, Suk-Joo Choi, Soo-young Oh, and Cheong-Rae Roh. Daegu, Korea; and Seoul, Korea.

T-150 **The Effects of Periconceptional Maternal Under Nutrition on Mouse Placental Development.**
Gerialisa Caesar, Lauren Parmeley, and Laura Schulz. Columbia, MS, USA.

T-151 **Mechanisms Underlying Cell-Free DNA Release by Mouse Placental Explants.**
Mark Phillippe, and Sharareh Adeli. Boston, MA, USA.

T-152 **Computational Modeling of Murine Uteroplacental Blood Flow Using 3D Microct Imaging and Contrast-Enhanced Ultrasound Suggests Spiral Artery Number Is a Major Hemodynamic Regulator.**
Mabelle Lin, Jessica F Herbert, Terry K Morgan, and Alys R Clark. Auckland, New Zealand; and Portland, OR, USA.

T-153 **Placental-Specific Extracellular Vesicle Sorting by Multiparametric High-Resolution Flow Cytometry.**
Mayu Morita, Pam Canaday, Jessica Hebert, and Terry Morgan. Portland, OR, USA.

T-154 **Maintenance of Fatty Acid Oxidation in Placentas of Obese Women: A Role for Peroxisomes.**
Virtu Calabuig-Navarro, Judi Minium, and Perrie O'Tierney-Ginn. Cleveland, OH, USA.

T-155 **Baboon Placental Endocannabinoid Responses to Maternal High Fat Diet.**
Marcel Chuecos, Cun Li, Stacy Martinez, Kushal Gandhi, Cezary Skobowiat, Maira Carrillo, Moss Hampton, Suraparaju Raju, Gary Ventolini, Peter Nathanielsz, and Natalia Shlabritz-Loutsevitch. Odessa, TX, USA; Laramie, WY, USA; San Antonio, TX, USA; and Bydgoszcz, Poland.

T-156 **Role of Renin-Angiotensin System Activation in a Rat Model of Placental Insufficiency and Pregnancy-Induced Hypertension.**
Eugenia Mata-Greenwood, LeeAnna Sands, Daliao Xiao, Lubo Zhang, and Blood Arlin. Loma Linda, CA, USA.

T-157 **Effects of Tributyltin on Placental Cytokine Production.**
Yuko Arita, Michael Kirk, Neha Gupta, Ramkumar Menon, Darios Getahun, and Morgan R Peltier. Mineola, NY, USA; Galveston, TX, USA; and Pasadena, CA, USA.

T-158 **Elevated Biomarkers of Ageing in Placentas of Advanced Maternal Age Women.**
Katie J Stephens, Samantha C Lean, Mark R Dilworth, Alexander EP Heazell, and Rebecca L Jones. Manchester, United Kingdom.

POPULATION HEALTH

T-159 **Advanced Maternal Age as an Independent Risk Factor for Adverse Pregnancy Outcomes: A Systematic Review and Meta-Analysis.**
Samantha C Lean, Hayley Derricott, Rebecca L Jones, and Alexander EP Heazell. Manchester, United Kingdom.

T-160 **Testosterone Contributes to Angiotensin II-Induced Hypertension and Associated Pathophysiology.**
Amar More, Jay Mishra, Gary Hankins, and Sathish Kumar. Galveston, TX, USA.

Thursday, March 16, 2017 - Poster Session I - Bonnet Creek I – IX

PREECLAMPSIA

T-161 **Maternal and Fetal Fetuin-A Levels in Pregnancies Complicated by Preeclampsia.**
Ana Tobiasz, Jose Duncan, Laura Detti, and Luis Gomez. Memphis, TN, USA.

T-162 **The Circulating Levels of Estradiol-17b and Progesterone Are Reduced in Women with Preeclampsia.**
Jiayi Wan, Ke Zeng, Yongxiang Yin, Min Zhao, and Qi Chen. Wuxi, Jiangsu, China; and Shanghai, China.

T-163 **Risk Factors for Preterm and Term Pre-Eclamptic Pregnancies Complicated by an SGA Neonate- A Population Based Study.**
Dikla Akselrod, Neta Ben-Shalom Tirosh, Moshe Stavsky, Tal Refaeli-Yehudai, Paz Dorit, Majdi Imtirat, Shirley Greenbaum, Limor Besser, and Offer Erez. Beer Sheva, Israel.

T-164 **Biomarker Discovery for Preeclampsia Using Newly Established Global Metabolomic Analysis.**
Yasuhiro Kurosawa, Daisuke Saigusa, Maiko Wagata, Masatoshi Saito, Nobuo Yaegashi, and Junichi Sugawara. Sendai, Miyagi, Japan.

T-165 **Abnormal Angiogenic Gene Expression in the Decidua and Placenta in a Mouse Model of Preeclampsia.**
Angelina M Seffens, Carrie J Shawber, Xinjing Xu, Robin L Davisson, Jennifer L Sones, and Nataki C Douglas. New York, NY, USA; and Baton Rouge, LA, USA.

T-166 **Recurrence Rates of Preeclampsia After Postpartum Evaluation in the Past 20 Years.**
Eva G Mulder, Chahinda Ghossein-Doha, Fleur EM Froeling, and Marc EA Spaanderman. Maastricht, Netherlands.

T-167 **Placental Underperfusion and Its Clinical Associations.**
Carole A McBride, Brenda L Waters, Erin A Morris, Gary J Badger, and Ira M Bernstein. Burlington, VT, USA.

T-168 **Gender Imbalance Confounds Meta-Analysis of Pre-Eclampsia Microarray Studies of the Placental Transcriptome.**
Justyna Dopierala, Gordon CS Smith, and D Stephen Charnock-Jones. Cambridge, United Kingdom.

T-169 **The Impact of Low Dose Aspirin on Markers of Placental Disease – Results of the TEST Multicentre RCT.**
F Mone, C Mulcahy, P McParland, M Culliton, P Downey, O Maguire, P Clarke, A Stanton, F Breathnach, J Morrison, S Daly, J Higgins, A Cotter, E Tully, P Dicker, F Malone, and F McAuliffe. Dublin, Ireland.

T-170 **Amyloid Precursor Protein Products Are Associated with Vessel Stiffness and Hypertension in Subsequent Pregnancy.**
Carole A McBride, Erin A Morris, and Ira M Bernstein. Burlington, VT, USA.

T-171 **The Placental Expression of HLA-G, HLA-C, and HLAF in Severe Preeclampsia and Preterm Labor.**
Rinat Hackmon, Lakmini Pinnaduwage, Jianhong Zhang, Dan E Geraghty, Stephen J Lye, and Caroline E Dunk. Portland, OR, USA; Toronto, ON, Canada; Seattle, WA, USA; and Toronto, ON, USA.

T-172 **cAMP Rescues the Negative Regulatory Effects of TNF-α on Endothelial Cx43 Gap Junction Function and Protects Cell Permeability.**
Bryan C Ampey, Amanda C Hankes, Ian M Bird, and Ronald R Magness. Madison, WI, USA; and Tampa, FL, USA.

T-173 **Differences in Peripheral Guanylate-Binding Protein-1 Concentrations During Healthy and Preeclamptic Pregnancies.**
Joost HN Schuitemaker, Thomas IFH Cremers, Mariëlle G van Pampus, Sicco A Scherjon, and Marijke M Faas. Groningen, Netherlands; and Amsterdam, Netherlands.

T-174 **First Trimester T Helper Cell Subsets, Th1/Th2 and Th17/Treg Cell Ratio Levels May Predict Preeclampsia.**
Maria D Salazar Garcia, Yuvon Mobley, Jennifer Henson, Michael Davies, Nayoung Sung, Annie Skariah, Svetlana Dambaeva, Alice Gilman-Sachs, Kenneth Beaman, Charles Lampley, and Joanne Kwak-Kim. Vernon Hills, IL, USA; North Chicago, IL, USA; and Chicago, IL, USA.

T-175 **CD40 Inhibitor Is a Novel Translational Treatment for Inflammatory Modulation in Endometriosis.**
Alessandra J Ainsworth, Chandra C Shenoy, Ye Zheng, Abu Osman, Khashayarsha Khazaie, and Gaurang S Daftary. Rochester, MN, USA.

T-176 **Reduced CD200 Expression Contributes to Altered Th1/Th2 Cytokine Production in Placental Trophoblasts from Preeclampsia.**
Jie Xu, Yang Gu, David F Lewis, and Yuping Wang. Shreveport, LA, USA.

T-177 **A Case of Recurrent Posterior Reversible Encephalopathy Syndrome.**
Moayad Turkistani, Rana Alamoudi, Emad Alkhotani, and Abdulrahim Ali Rouzi. Jeddah, Makkah, Saudi Arabia.

T-178 **Preeclampsia Is an Independent Risk Factor for Surgical Site Infection (SSI) Following Cesarean Delivery After Labor.**
Kara M Rood, Mark A Klebanoff, Emily A Oliver, Mark B Landon, Irina A Buhimschi, and Catalin S Buhimschi. Columbus, OH, USA.

Thursday, March 16, 2017 - Poster Session I - Bonnet Creek I – IX

REPRODUCTIVE BIOLOGY

T-179 **2-Cell Embryos Are More Sensitive Than Blatocysts to AMPK-Dependent Suppression of Anabolism and Potency/Stemness by Commonly Used Fertility Drugs, a Diet Supplement and Stress.**
Alan Bolnick, Mohammed Abdulhasan, Brian Kilburn, Mindie Howard, Alexandra Shamir, Omar Pasalodos, Jing Dai, Elizabeth Puscheck, and Daniel Rappolee. Detroit, MI, USA; Haverhill, MA, USA; Salt Lake City, UT, USA; and Southfield, MI, USA.

T-180 **Early Endocrine Gene Expression in 8-Cell Human Embryos.**
Amy M Lee, Dimitri Loutradis, Peter Drakakis, Charalampos Theofanakis, Thomas L Toth, and Ann A Kiessling. Boston, MA, USA; Athens, Greece; and Bedford, MA, USA.

T-181 **Enhancement of Human Sperm Motility by Novel Recombinant Endo-β-Galactosidases.**
Toshiaki Shibata, Tomoya Akama, Kiyohiko Angata, Michiko Fukuda, Kazuhiro Sugihara, and Naohiro Kanayama. Hamamatsu, Shizuoka, Japan; Hirakata, Osaka, Japan; and Tsukuba, Ibaraki, Japan.

T-182 **Aberrant Expressions of Transmembrane Chloride Ion Channels in Endometriosis.**
Jeong Sook Kim, Ji Hyun Park, Jae Hoon Lee, Minkyung Kim, Bo Hyon Yun, Joo Hyun Park, Seok Kyo Seo, Young Sik Choi, SiHyun Cho, and Byung Seok Lee. Seoul, Republic of Korea.

T-183 **The Role of G-CSF Treatment in Recurrent Miscarriage on the Expression of FOXP3, VEGF, VEGF-R2 and C-KIT in First Trimester Pregnancy Specimens.**
Fabio Scarpellini, Marco Sbracia, and Avenir Balili. Rome, Italy; and Tirana, Albania.

T-184 **MicroRNA-27b Mimic Inhibits VEGF B and VEGF C in Human Endometrial Stromal Cells.**
Beverly G Reed, Bruce R Carr, Ruth A Word, and Patricia T Jimenez. Dallas, TX, USA.

T-185 **Network Biology of Menstrual Cycle to Understand the Key Drivers of Endometrial Receptivity.**
Patricia Sebastian-Leon, Ana Conesa, Vicente Arnau, Jose Remohí, Antonio Pellicer, Carlos Simon, and Patricia Diaz-Gimeno. Valencia, Spain.

T-186 **Oxytocin Activates Pro-Inflammatory Pathways in Decidualised Human Endometrial Stromal Cells.**
Camilla West, Sung Hye Kim, Shirin Khanjani, Aylin Hanyaloglu, Phillip Bennett, and Vasso Terzidou. London, United Kingdom.

T-187 **The Calcium-Permeable Mechanosensitive Piezo1 as Cellular Sensor in Human Endometrial Epithelial Cells.**
Aurélie Hennes, Katharina Held, Katrien De Clercq, Luc Meeuwis, Christel Meuleman, Thomas Voets, and Joris Vriens. Leuven, Belgium.

T-188 **Improvement of the Endometrial Receptivity Signature Reveals a Possible Maternal Origin of Biochemical Pregnancies.**
Patricia Diaz-Gimeno, María Ruiz-Alonso, Patricia Sebastián-León, Vineeta Singh, Antonio Pellicer, Diana Valbuena, and Carlos Simón. Valencia, Spain; and Stanford, CA, USA.

T-189 **Growth Differentiation Factor 9 Induces Granulosa Cell Proliferation via Inhibition of the Expression of AMH Type II Receptor.**
Akira Iwase, Satoko Osuka, Bayasula Bayasula, Sachiko Takikawa, Tomohiko Murase, Tomoko Nakamura, Maki Goto, and Fumitaka Kikkawa. Nagoya, Aichi, Japan.

T-190 **Melatonin Supplementation Improves Fetal Outcomes in a Mouse Model of Advanced Maternal.**
Samantha C Lean, Mark R Dilworth, Alexander EP Heazell, and Rebecca L Jones. Manchester, United Kingdom.

T-191 **Exercise Ameliorates the Oocyte Defects Associated with Impaired Fertility in Homozygous *PolG* Mitochondrial Mutator Mice.**
Christine E Faraci, Jonathan L Tilly, and Dori C Woods. Boston, MA, USA.

T-192 **Hormone-Dependent Chemotaxis and Homing of Innate Lymphoid Cells in the Context of Pregnancy.**
Christine Lamb, Damián O Muzzio, Kristina M Hilz, Laura N Castro, and Marek Zygmunt. Greifswald, Germany.

T-193 **Excess Glucose Induces Trophoblast Inflammation Through HMGB1 Activation of Toll-Like Receptor 4.**
Kathleen R Heim, Julie A Potter, Christina S Han, and Vikki M Abrahams. New Haven, CT, USA; and Los Angeles, CA, USA.

T-194 **Evaluation of B Cell Subsets in Women with Recurrent Pregnancy Losses and Implantation Failure.**
Annie M Skariah, Maria D Garcia, Wenmin Qin, Joanne Kwak-Kim, Alice G Sachs, and Alejandra Comins-Boo. North Chicago, IL, USA.

REPRODUCTIVE ENDOCRINOLOGY AND INFERTILITY

T-195 **Comparing Pain from Fertiloscopy and Laparoscopy for the Diagnosis of Infertility.**
Kathryn S Merriam, Lara Aboulhosn, Paul B Marshburn, Rebecca S Usadi, Michelle L Matthews, Megan Templin, and Bradley S Hurst. Charlotte, NC, USA.

T-196 **Hypochlorous Acid Reversibly Inhibits Caspase-3: A Potential Regulator of Apoptosis.**
Roohi Jeelani, Inga Sliskovic, Sasha Mikhael, Faten Shaeib, Mili Thakur, and Husam Abu-Soud. Detroit, MI, USA.

Thursday, March 16, 2017 - Poster Session I - Bonnet Creek I – IX

T-197 **Body Mass Index Modulates Anti-Mullerian Hormone Response After Ovarian Stimulation Treatment.**
Sanne B Overdijkink, Maria PH Koster, Esther B Baart, Fatima Hammiche, Joop SE Laven, and Regine PM Steegers-Theunissen. Rotterdam, Netherlands.

T-198 **The Impact of Race and Ethnicity on Infertility Diagnosis Among Haitians, African Americans, and Caucasians Seeking Infertility Care.**
Roxane Handal-Orefice, Melissa Pritchard, Joseph Politch, and Wendy Kuohung. Boston, MA, USA.

T-199 **An Updated Meta-Analysis Evaluating the Effect of Progesterone (P) Luteal Support on Live Birth After Ovulation Induction (OI) and Intrauterine Insemination (IUI).**
Katherine A Green, Jessica R Zolton, Sophia MV Schermerhorn, Alan H DeCherney, and Micah J Hill. Bethesda, MD, USA.

T-200 **Can Embryo Transfer Simulation Improve the Learning Curve for REI Fellow Training?**
Justin D Pilgrim, Micah J Hill, James H Segars, Alan H DeCherney, and Ryan J Heitman. Bethesda, MD, USA; Baltimore, MD, USA; and Tacoma, WA, USA.

T-201 **Ectopic Pregnancy Rate Does Not Correlate with the Number of Retrieved Oocytes or Estradiol Levels in Fresh Autologous IVF Cycles.**
Mohamad Irani, Vinay Gunnala, Zev Rosenwaks, and Steven D Spandorfer. New York, NY, USA.

T-202 **Characterization of Embryo-Derived Exosomal miRNAs: Implications on Endometrial Receptivity.**
Hayden Homer, Anusch Yazdani, Gregory E Rice, and Carlos Salomon. Brisbane, QLD, Australia; and New Orleans, LA, USA.

T-203 **Intra-Follicular C-Type Natriuretic Peptide (CNP) Levels: New Biomarker of Follicle Growth and Gamete Maturation in Humans.**
Julia A Dias, Cynthia Dela Cruz, Luiza C Lima, Maíra Casalechi, Maria T Pereira, Inês K Cavallo, Adelina M Reis, and Fernando M Reis. Belo Horizonte, MG, Brazil.

T-204 **Embryo Euploidy in Relation to Morphology, Embryo Sex, and Birth Outcomes.**
Ange Wang, Jonathan Kort, and Lynn Westphal. Stanford, CA, USA.

T-205 **No Increased Cardiovascular Disease Risk in Women with High Postmenopausal Androgen Levels: The Rotterdam Study.**
Cindy Meun, Oscar H Franco, Klodian Dhana, Loes Jaspers, Taulant Muka, Bart CJ Fauser, Maryam Kavousi, and Joop SE Laven. Rotterdam, Zuid-Holland, Netherlands; and Utrecht, Netherlands.

T-206 **Patient-Provider Communication Around Menopause-Related Symptoms and Quality of Life.**
Timothy DV Dye, Margaret Demment, Christopher Morley, Miriam Weber, Ollivier Hyrien, Ivelisse Rivera, Morgan Pratt, and James Woods. Rochester, NY, USA; and Syracuse, NY, USA.

T-207 **Ovarian Stimulation Is Safe and Effective in Many Patients with GYN Malignancies.**
Mary Ellen Pavone, Molly B Moravek, Rafael Confino, Susan C Klock, Angela K Lawson, and Kristin N Smith. Chicago, IL, USA; and Ann Arbor, MI, USA.

T-208 **Characteristics and Experiences of Women Who Have Undergone Oocyte Cryopreservation at an Academic Center.**
Sanaa H Suharwardy, Meera Shah, and Lynn M Westphal. Palo Alto, CA, USA.

STEM CELLS

T-209 **Mesenchymal Stem Cells Derived from the Human Placenta (PMSCs) Express Neuronal Stem/Progenitor Markers Nestin and SOX2, and Could Differentiate into Neuronal Cells In Vivo.**
Yuping Wang, Yang Gu, Xiaohong Lu, and David F Lewis. Shreveport, LA, USA.

T-210 **Novel p63-Expressing Epithelial Cells from Normal Human Endometrium.**
Shaina Balayan, Fatima Barragan, Sahar Houshdaran, Joseph Rabban, Juan C Irwin, and Linda C Giudice. San Francisco, CA, USA.

T-211 ***In Vitro* Derivation of Precursor Granulosa Cells from Human Pluripotent Stem Cells.**
Alisha M Truman, Jonathan Tilly, and Dori Woods. Boston, MA, USA.

T-212 **Intrauterine CXCL12 Therapy for Asherman's Syndrome.**
Gulcin Sahin Ersoy, Masoumeh Majidi Zolbin, Ramanaiah Mamillapalli, Irene Moridi, and Hugh Taylor. New Haven, CT, USA.

Friday, March 17, 2017 - Poster Session II - Bonnet Creek I – IX

10:45 AM-12:15 PM **Poster Session**

BASIC PARTURITION

F-001 **Comparison of Latency Antibiotic regimen for Preterm Premature Rupture of Membranes.**
Juliana Sung, Angela Rugino, Ann Lal, and Jean R Goodman. Maywood, IL, USA.

F-002 **Quantification of Exosomes in Cervico-Vaginal Fluid from Term and Preterm Pregnancies.**
Rachel M Tribe, Vikash Mistry, Vyjayanthi Kinhal, Gregory Rice, Carlos Palma, Natasha L Hezelgrave, Evonne C Chin-Smith, Andrew H Shennan, and Carlos Salomon. London, United Kingdom; Brisbane, QLD, Australia; and New Orleans, LA, USA.

F-003 **Expression of CPPED1 in Human Trophoblasts Is Associated with Timing of Term Birth.**
Antti M Haapalainen, Minna K Karjalainen, Steffen Ohlmeier, Julia Anttonen, Tomi A Määttä, Annamari Salminen, Mari Mahlman, Ulrich Bergmann, Kaarin Mäkikallio, Marja Ojaniemi, Mikko Hallman, and Mika Rämet. Oulu, Finland; Turku, Finland; and Tampere, Finland.

F-004 **Placenta-Derived Exosomes Profile During Term and Preterm Birth: Understanding the Signal of Human Parturition.**
Christopher L Dixon, Vyjayanthi Kinhal, Carlos Palma, Kechichian Talar, Rheanna Urrabaz-Garza, Carlos Salomon, and Ramkumar Menon. Galveston, TX, USA; and Brisbane, Australia.

F-005 **Uterine Tissue Orientation and Stiffness Influence Cervical Tissue Stretch.**
M Perez, AR Westervelt, J Vink, R Wapner, G Gallos, M House, and K Myers. New York, NY, USA; and Boston, MA, USA.

F-006 **Leukocyte Invasion of the Labouring Uterus Is Upregulated by Leukocyte and Uterine Activation.**
Han Lee, Xin Fang, and David M Olson. Edmonton, AB, Canada.

F-007 **A Novel Quantitative Framework for the Prioritization of sPTB Candidate Genes.**
Haley R Eidem, and Antonis Rokas. Nashville, TN, USA.

F-008 **Potential Role for Cytokines in Adverse Pregnancy Outcomes (APOs) in a Rat 2-Hit Stress Model.**
Barbara SE Verstraeten, J Keiko McCreary, Hans Verstraelen, Gerlinde AS Metz, and David M Olson. Edmonton, AB, Canada; Ghent, Belgium; and Lethbridge, AB, Canada.

F-009 **Comparative Exosomal Profile Analysis Between Maternal and Fetal Compartments During Term and Preterm Human Parturition.**
Ramkumar Menon, and Carlos Salomon. Galveston, TX, USA; and Brisbane, United Kingdom.

F-010 **Gestational Tissue Inflammatory Biomarker Phenotype at Term Labor: A Systematic Review.**
Emily E Hadley, Lauren Richardson, George Saade, Maria R Torloni, and Ramkumar Menon. Galveston, TX, USA; and Sao Paulo, Brazil.

F-011 **Risk Factors for Group B Streptococcal Colonization among Pregnant Women in West Virginia.**
Paul Dietz, Eric Coughlin, Dara Sebold, and Byron C Calhoun. Charleston, WV, USA.

F-012 **The Vaginal Microbiota Composition at First Admission in Korean Pregnancy Women.**
Young-Ah You, Eun Jin Kwon, Soo Yeon Park, Mi Hye Park, and Young Ju Kim. Seoul, Korea.

F-013 **Cytokine Profile in Women with Cervical Insufficiency.**
Stephany Monsanto, Silvia Daher, Erika Ono, Karen Pendeloski, Evelyn Trainá, Rosiane Mattar, and Chandra Tayade. Kingston, ON, Canada; and São Paulo, SP, Brazil.

F-014 **Racial Disparity in *Ureaplasma Parvum* Induced Inflammatory Responses.**
Liping Feng, Alex Antonia, Amy Murtha, and Dennis Ko. Durham, NC, USA.

F-015 **Colonization of the Cervicovaginal Space with *Gardnerella vaginalis* Leads to Inflammation and Cervical Remodeling *In Vivo*.**
Luz-Jeannette Sierra, Amy G Brown, Guillermo O Barila, and Michal A Elovitz. Philadelphia, PA, USA.

F-016 **Immunological Changes in the Choriodecidua, Placenta and Amnion in Preterm Deliveries Secondary to Chorioamnionitis.**
Sivatharjini P Sivarajasingam, Ananya Das, Bronwen R Herbert, Maria F Fais, Natasha Singh, Nesrina Imami, and Mark R Johnson. London, United Kingdom.

F-017 **Progesterone Prevents Preterm Birth by Suppressing the Enhancement of Uterine Contractility in Mice with Chronic Dental *Porphyromonas gingivalis* Infection.**
Haruhisa Konishi, Hiroshi Miyoshi, Yuko Teraoka, Satoshi Urabe, Hisako Furusho, Mutsumi Miyauchi, Takashi Takata, and Yoshiki Kudo. Hiroshima, Japan.

F-018 **Prognostic Capacity of Cervicovaginal Fluid Acetate-Glutamate Ratio for Risk of Preterm Delivery within Two Weeks of Presentation with Symptoms of Preterm Labor.**
Emmanuel Amabebe, Steven Reynolds, Victoria Stern, Graham Stafford, Martyn Paley, and Dilly Anumba. Sheffield, United Kingdom.

F-019 **Placental Clearance Modulates Circulating Levels of Fetal Pro-Inflammatory but Not Anti-Inflammatory Cytokines During Term Parturition and May Contribute to Histological Chorioamnionitis.**
Imran N Mir, Lina F Chalak, and Charles R Rosenfeld. Dallas, TX, USA.

Friday, March 17, 2017 - Poster Session II - Bonnet Creek I – IX

F-020 **A Role for IL-10 During Progesterone Mediated Prolongation of Gestation.**
Mark Phillippe, Ingrid Liff, and Sharareh Adeli. Boston, MA, USA.

F-021 **Amniotic Fluid Macrophage Activation Near Term Heralds the Initiation of Labor in Mice.**
Alina P Montalbano, and Carole R Mendelson. Dallas, TX, USA.

F-022 **Identification and Comparison of Bacteria in Brain Cortex and Placenta of Fetuses Exposed to Hypoxic Hypoxia.**
Miguel A Zarate, Michelle Rodriguez, Eileen I Chang, Thomas J Arndt, Maureen Keller-Wood, Eric W Triplett, and Charles E Wood. Gainesville, FL, USA.

F-023 **Treatment with Exendin-4 Reduces the Rate of Preterm Birth and Improves Adverse Neonatal Outcomes Induced by Systemic or Intra-Amniotic Inflammation.**
Valeria Garcia-Flores, Roberto Romero, Marcia Arenas-Hernandez, Chharitha Veerapaneni, Tara N Mial, George Schwenkel, Sonia S Hassan, and Nardhy Gomez-Lopez. Detroit, MI, USA.

F-024 **Cervical Length and Pregnancy Outcomes in Women with a History of Cervical Conization.**
Danielle M Panelli, Ann M Thomas, Sarah Feldman, and Thomas F McElrath. Boston, MA, USA.

F-025 **Exam-Indicated Cerclage with or without Prior Amniocentesis.**
Laura G Rodriguez Riesco, Jeannie Zuk, Zhaoxing Pan, Henry Galan, and Michael Zaretsky. Aurora, CO, USA.

F-026 **Extracellular Vesicle Release of Matrix Metalloproteinases by Amniotic Cells.**
Bethany Hart, Yasuko Yamamura, Wei-Ting Hung, Lane Christenson, and Jakub Tolar. Minneapolis, MN, USA; and Kansas City, KS, USA.

F-027 **Characterization of Fetal Membrane Microfractures in and Their Potential Significance in Pregnancy and Parturition.**
L Richardson, G Vargas, and R Menon. Galveston, TX, USA.

F-028 **Expression of Phospho-GSK3Beta Correlates with p38MAPK Activation in Human and Mouse Gestation.**
L Richardson, R Menon, and A Bonney. Galveston, TX, USA; and Burlington, VT, USA.

F-029 **A Novel Three-Dimensional Cell Culture Model for Human Amnion Mesenchymal Cells.**
Kimberly Foca, Eric S Collier, and Claire E Kendal-Wright. Honolulu, HI, USA.

F-030 **Progesterone Synergistically Augments Cytokine-Induced 11β-Hydroxysteroid Dehydrogenase-1 Expression in Cervical Stromal Fibroblasts.**
Douglas A Kniss, Taryn L Summerfield, and William E Ackerman IV. Columbus, OH, USA.

F-031 **A Dual Level of TLR4 Epigenetic Regulation Between Amnion and Choriodecidua at the Site of Rupture Prior to Labor.**
Corinne Belville, Flora Ponelle-Chachuat, Marion Rouzaire, Gaël Clairefond, Bruno Pereira, Denis Gallot, Vincent Sapin, and Loic Blanchon. Clermont-Fd, France.

F-032 **Measuring *In Vivo* Uterine Contractile Activity of Pregnant Mice via a Transcervical Intrauterine Pressure Catheter (IUPC).**
Michael Robuck, Christine O'Brien, Jeff Reese, and Jennifer Herington. Nashville, TN, USA.

F-033 **Expression Fingerprints of Human Primary Myometrial, hTERT and PHM Cells in Comparison to Term Myometrium for Myometrial Tissue Engineering.**
Minoo Heidari Kani, Jonathan W Paul, Roger C Young, Eng-Cheng Chan, and Roger Smith. Newcastle, NSW, Australia.

F-034 **Effects of Brief and Long Periods of Hypoxic Stress on Myometrial Contractility from Term Pregnant Women.**
Lele Wang, Huiping Hu, Junjie Bao, Shao-Qing Shi, Robert E Garfield, and Huishu Liu. Guangzhou, China.

F-035 **Circulating Markers of the Uterine Unfolded Protein Response Reflect Pregnancy Outcomes.**
Chandrashekara N Kyathanahalli, Offer Erez, Piya Chaemsaithong, Adi L Tarca, Roberto Romero, Sonia S Hassan, Pancharatnam Jeyasuria, and Jennifer C Condon. Detroit, MI, USA.

CLINICAL PERINATOLOGY

F-036 **The Association Between Intrahepatic Cholestasis of Pregnancy and Gestational Diabetes.**
Eli Rimon, Yael Raz, Michael Kupferminc, and Yariv Yogev. Tel Aviv, Israel.

F-037 **Novel Use of an Intra-Aortic Balloon May Limit Morbidity in Patients with Placenta Percreta.**
Elizabeth Blumenthal, Rashmi Rao, Aisling Murphy, Jeffrey Gornbein, Richard Hong, John M Moriarty, Daniel A Kahn, and Carla Janzen. Los Angeles, CA, USA.

F-038 **Is the Effect of Hyperemesis Gravidarum on Gestational Weight Gain Risk Modified by Prepregnancy Body Mass Index?**
Michael J Fassett, Darios Getahun, Vicki Y Chiu, Harpreet S Takhar, and Morgan R Peltier. Los Angeles, CA, USA; Pasadena, CA, USA; and Mineola, NY, USA.

F-039 **Labor Induction Outcomes with Prostaglandin Vaginal Inserts in Obese Women.**
Mary N Zaki, Megan L Stephenson, Kyle Raymond, Olaf Rugarn, Barbara Powers, and Deborah A Wing. Orange, CA, USA; Santa Clara, CA, USA; Copenhagen, Denmark; and Phoenixville, PA, USA.

Friday, March 17, 2017 - Poster Session II - Bonnet Creek I – IX

F-040 **Are the Genetics of Heme Oxygenase-1 Associated with Preeclampsia?**
Sarah Anderson, Elena Lobashevsky, Keith Do, Adrienne Wiggins, and Joseph Biggio. Birmingham, AL, USA.

F-041 **Preterm Fetal Growth Restriction with Acidemia Is Associated with Changes in mRNA Expression in Maternal Blood: The FOX Study.**
Owen Stock, Susan P Walker, Lavinia Gordon, Joanne Said, Natalie Hannan, Katie Groom, Scott Peterson, Sean Seeho, Amanda Henry, Stefan C Kane, Clare L Whitehead, and Stephen Tong. Melbourne, VIC, Australia; Auckland, New Zealand; Brisbane, QLD, Australia; and Sydney, NSW, Australia.

F-042 **Induction of Labor with the Recommended Two Hourly Oral Misoprostol Regimen.**
Abdulrahim A Rouzi, Nora Sahly, Nisma Mansouri, Nawal Alsenani, Rana Alamoudi, and Rayyan Rozzah. Jeddah, Makkah, Saudi Arabia.

F-043 **Risk Factors for Prolonged Interval from PROM to Delivery in Women with a Prior CS.**
Reem Elmikawy, Ruthy Beer-Weisel, Eric Kachko, Shirley Greenbaum, Majdi Imterat, Tal Rafaeli-Yehudai, Neta Benshalom-Tirosh, Limor Besser, and Offer Erez. Beer Sheva, Israel.

F-044 **Ultrasound-Indicated and Rescue Cervical Cerclage and Immediate Pregnancy Outcomes: A Retrospective Observational Study.**
V Andrews, M Meritahti, S Thomas, Angela Yulia, N Wales, and V Terzidou. London, United Kingdom.

F-045 **Predictive Values of ROM Plus® and Amnisure® for Diagnosing Rupture of Membranes by Pre-Test Probabilities.**
Lauren Theilen, Sean Esplin, and Matthew Hoffman. Salt Lake City, UT, USA; and Newark, DE, USA.

F-046 **Is Uterocervical Angle Associated with Gestational Latency After Physical Exam Indicated Cerclage?**
Kate Swanson, William A Grobman, and Emily S Miller. Chicago, IL, USA.

F-047 **Assoiciation of Urinary Flame Retardant Concentrations, Gestational Weight Gain and Gestational Diabetes.**
Rosemary J Froehlich, Phinnara Has, Megan Romano, Nicola Hawley, Joseph Braun, and Erika F Werner. Providence, RI, USA; and New Haven, CT, USA.

F-048 **Placental Lipid Metabolism in Obese Women with Gestational Diabetes Mellitus and Fetal Macrosomia.**
Haijun Gao, Jia Chen, and Chandra Yallampalli. Houston, TX, USA.

F-049 **Maternal BMI and Gestational Weight Gain Are Significantly Correlated with Markers of Metabolic Endotoxemia in Both Maternal and Neonatal Serum.**
Maike K Kahr, Min Hu, Kathleen M Antony, Kjersti M Aagaard, and Melissa A Suter. Houston, TX, USA.

F-050 **Association Between Interval Change in Body Mass Index and Subsequent Pregnancy Outcomes Among Women with Gestational Diabetes.**
Ashley N Battarbee, and Lynn M Yee. Chapel Hill, NC, USA; and Chicago, IL, USA.

F-051 **Association Between Serum Adipokine Levels and Insulin Resistance in Pregnant Women at High-Risk of Developing Gestational Diabetes Mellitus (GDM).**
Kym J Guelfi, John P Newnham, Shaofu Li, and Jeffrey A Keelan. Perth, WA, Australia.

F-052 **Nobiletin as a Therapeutic for Gestational Diabetes Mellitus (GDM).**
Stella Liong, Ratana Lim, Caitlyn Nguyen-Ngo, Stephanie Quak, Gillian Barker, and Martha Lappas. Heidelberg, VIC, Australia.

F-053 **Maternal Obesity Modulates Response to Omega-3 Fatty Acids Supplementation During Pregnancy.**
Carmen Monthé-Drèze, Annie Penfield-Cyr, Marcela Smid, and Sarbattama Sen. Boston, MA, USA; and Salt Lake City, UT, USA.

F-054 **Impact of an mHealth-Supported Behavioral Lifestyle Intervention on Behavioral Stage of Change and Physical Activity in Overweight and Obese Pregnancy: PEARs Randomized Controlled Trial.**
Kate M Ainscough, Maria A Kennelly, Elizabeth J O'Sullivan, Karen L Lindsay, and Fionnuala M McAuliffe. Dublin, Leinster, Ireland.

F-055 **Isolated Oligohydramnios Near Term: Should We Be Looking at Umbilical Artery Doppler?**
Natalie Porat, Zainab Al-Ibraheemi, Dyese Taylor, Meredith Kalberer, and Barak Rosenn. New York, NY, USA.

F-056 **Maternal and Fetal Outcomes in Pregnancy Complicated with Eisenmenger Syndrome.**
Shinji Katsuragi, Chizuko Kamiya, Reiko Neki, Takekazu Miyoshi, Jun Yoshimatsu, Koichiro Miwa, Yaemi Takagi, Takeshi Ogo, Norifumi Nakanishi, and Tomoaki Ikeda. Fuchu, Tokyo, Japan; Suita, Osaka, Japan; Tokyo, Japan; and Tsu, Mie, Japan.

F-057 **Intravenous Oxytocin Titration for Post-Dates Labor Induction Across Body Mass Index Groups.**
Angela B Maeder, Susan C Vonderheid, Chang G Park, Aleeca F Bell, Barbara L McFarlin, Catherine Vincent, and Sue Carter. Chicago, IL, USA; and Bloomington, IN, USA.

Friday, March 17, 2017 - Poster Session II - Bonnet Creek I – IX

F-058 **Umbilical Artery Cord Oxygen and Neonatal Morbidity at Term.**
Nandini Raghuraman, George A Macones, Alison G Cahill, and Methodius G Tuuli. St. Louis, MO, USA.

F-059 **Hypertensive Disorders of Pregnancy and Postpartum Readmission in the United States: National Surveillance of the Revolving Door.**
Mulubrhan F Mogos, Jason L Salemi, Kiara K Spooner, Barbara L McFarlin, and Hamisu H Salihu. Chicago, IL, USA; and Houston, TX, USA.

F-060 **Risk Factors for Maternal and Fetal Outcome in Pregnancy Complicated with Arteriovenous Malformation.**
Shinii Katsuragi, Tomoaki Ikeda, Hiroaki Tanaka, Kayo Tanaka, Masafumi Nii, Takekazu Miyoshi, Reiko Neki, Kazuko Minematsu, Kazunori Toyoda, Kazuyuki Nagatsuka, Eika Hamamo, Toru Sato, Susumu Miyamoto, Koji Iihara, and Jun Yoshimatsu. Fuchu, Tokyo, Japan; Tsu, Mie, Japan; and Suita, Osaka, Japan.

F-061 **Increased Obstetric Morbidity in a Hypertensive Haitian Population Compared to Hypertensive Non-Haitians.**
Conisha M Holloman, Neeraj Desai, Clifton Brock, Kesha Thomas, Priya Patel, Zoran Pavlovic, and Kathryne Kostamo. Orlando, FL, USA; and New York, NY, USA.

F-062 **Maternal Low Vitamin D Status and Risk of Small for Gestational Age: A Systematic Review.**
Shu Qin Wei, and Wei Guang Bi. Montreal, QC, Canada.

F-063 **Exposure to SSRI During Pregnancy and Postpartum Hemorrhage Risk.**
Silvia Corti, Paola Pileri, Martina Mazzocco, Ilenia di Bartolo, Chiara Mandò, and Irene Cetin. Milan, Italy.

F-064 **The Complex Relationship of Obesity and Spontaneous Preterm Birth.**
Abraham Tsur, Jonathan Mayo, Gary M Shaw, David K Stevenson, and Jeffrey B Gould. Stanford, CA, USA.

F-065 **Influence of SNPs in Immunoregulatory Genes in Morbidity of Preterm Newborns.**
Giovana F Bento, Bruna A Ramos, Hélio A Miot, and Márcia G Silva. Botucatu, Sao Paulo, Brazil.

F-066 **Longitudinal Pharmacokinetic and Psychiatric Analysis of Pregnant Women in Treatment with SSRI.**
Silvia Corti, Paola Pileri, Carlo Personeri, Anna Colombo, Caterina Viganò, Emilio Clementi, and Irene Cetin. Milan, Italy.

F-067 **Trends and Severe Morbidity Associated with Postpartum Admissions for Hypertensive Diseases of Pregnancy.**
Joses A Jain, Cande V Ananth, Zainab Siddiq, Jason D Wright, Mary E D'Alton, and Alexander M Friedman. New York, NY, USA.

F-068 **Maternal BMI, Cytokine Profiles and Risk of Early Infection in Pregnancy.**
Marcela C Smid, Carmen Monthe-Dreze, Kim Boggess, Karen Gibbins, Scott Commins, and Sarbattama Sen. Salt Lake City, UT, USA; Boston, MA, USA; and Chapel Hill, NC, USA.

F-069 **Acute Exposure to Lipopolysaccharide (LPS) Modifies Placental ABC Transporter Expression and Maternal Plasma Lipid Levels.**
Mila W Reginatto, Klaus N Fontes, Nathalia L Silva, Victoria RS Monteiro, Hannailly R Gomes, George Kluck, Flavia F Bloise, Guinever E Imperio, Atella Georgia, Enrrico Bloise, Stephen G Matthews, and Tania M Ortiga-Carvalho. Rio de Janeiro, RJ, Brazil; Belo Horizonte, MG, Brazil; and Toronto, OT, Canada.

F-070 **Early Pregnancy Infection as Risk Factor for PPROM < 37 weeks.**
Marcela C Smid, Carmen Monthe-Dreze, Kim Boggess, Alison Stuebe, Karen Gibbins, and Sarbattama Sen. Salt Lake City, UT, USA; Boston, MA, USA; and Chapel Hill, NC, USA.

DEVELOPMENTAL PROGRAMMING

F-071 **The Relationship between Maternal Nutrition, Obesity and Diabetes During Pregnancy and Maternal and Offspring's Kidney Structure and Function: A Systematic Review.**
Yu Qi Lee, Kirsty Pringle, Kym Rae, Clare E Collins, and Adrienne Gordon. Newcastle, NSW, Australia; and Sydney, NSW, Australia.

F-072 **Development of Placenta-Specific Glut1 Knockdown Mouse Strains to Model the Influence of Varying Glucose Transporter Levels on Fetal Overgrowth and Offspring Health.**
Marlee Elston, Joel Marh, Haide Razavy, Kainalu Matthews, Vivien Klein, and Johann Urschitz. Honolulu, HI, USA.

F-073 **Chronic Fetal Hypoxia Results in Significant Renal Tubule Pathology in Adulthood.**
MR Sutherland, KL Brain, KJ Botting, S Austin-Williams, EJ Camm, and DA Giussani. Cambridge, Cambridgeshire, United Kingdom.

F-074 **Postnatal Growth and Cardiovascular Phenotype Following Maternal Uterine Artery Adenoviral Vascular Endothelial Growth Factor-A_{165} Gene Therapy (Ad.VEGF) for Fetal Growth Restriction in Guinea Pigs.**
Owen R Vaughan, Carlo A Rossi, Yuval Ginsberg, Tara I Krishnan, Hannah Barker, Anthony White, and Anna L David. London, England, United Kingdom.

F-075 **Chronic Stress During Pregnancy Causes Sex-Specific Changes in Offspring Allergic Asthma Response by Influencing Fetal Immune Development.**
Arianna L Smith, Elizabeth Witte, Jack Harkema, Daven Jackson-Humbles, and Karen Racicot. East Lansing, MI, USA.

Friday, March 17, 2017 - Poster Session II - Bonnet Creek I – IX

F-076 **Exposure to Excess Maternal Cortisol in Late-Gestation Prevents the Normal Metabolic Transition of the Heart at Birth.**
Jacquelyn Walejko, Andrew Antolic, Maureen Keller-Wood, and Arthur Edison. Gainesville, FL, USA; and Athens, GA, USA.

F-077 **Effect of Maternal Antioxidant MitoQ Treatment on Offspring Vascular Function in a Rat Model of Intrauterine Growth Restriction (IUGR).**
Mais M Aljunaidy, Jude S Morton, Raven Kirschenman, Patrick Case, Christy-Lynn M Cooke, and Sandra T Davidge. Edmonton, AB, Canada; and Bristol, England, United Kingdom.

F-078 **Impaired Insulin Secretion in Pregnant Rats Fed a Low Protein Diet.**
Haijun Gao, Eric Ho, Meena Balakrishnan, and Chandra Yallampalli. Houston, TX, USA.

F-079 **Breath Analysis Reveals Molecular Signatures of Developmental Programming.**
Andrew C Bishop, Ahsan Choudary, Mark Libardoni, Biswapriya Misra, Kenneth Lange, John Bernal, Mark J Nijland, Cun Li, Michael Olivier, Peter W Nathanielsz, and Laura A Cox. San Antonio, TX, USA; and Laramie, WY, USA.

F-080 **Nutrient Sensor and De Novo Lipogenesis Mechanism for Programmed Fatty Liver in Offspring of Obese Mothers.**
Mina Desai, Kavita Narwani, Niyati Joshi, Guang Han, Elaheh Mossayebi, Jocelyn McGill, and Michael G Ross. Torrance, CA, USA.

F-081 **Folate Treatment Partially Reverses Gestational Low Protein Diet Induced Glucose Intolerance and the Magnitude of Reversal is Age and Sex Dependent.**
Chellakkan S Blesson, Amy Schutt, Pretty R Mathew, Daren Tanchico, Meena Balakrishnan, Uma Yallampalli, and Chandra Yallampalli. Houston, TX, USA.

F-082 **Developmental Programming of Pulmonary Hypertension by Isolated Chronic Prenatal Hypoxia.**
AM Spiroski, CJ Shaw, and DA Giussani. Cambridge, United Kingdom.

F-083 **Maternal Tobacco Smoke Exposure Alters Placental PPARγ Expression of Male and Female Rat Pups in a Sex-Divergent Manner.**
Claudia Weinheimer, Brent Locklear, Haimei Wang, Michelle Baack, and Lisa Joss-Moore. Salt Lake City, UT, USA; and Sioux Falls, SD, USA.

F-084 **Leucine Potentiates Glucose Stimulated Insulin Secretion in Fetal Sheep.**
Brit H Boehmer, Laura D Brown, Stephanie R Wesolowski, William W Hay, and Paul J Rozance. Aurora, CO, USA.

F-085 **Exposure to Maternal Nutrient Restriction in Development Increases Fructose Appetite in Juvenile Baboons.**
Laura A Cox, Kenneth G Gerow, Robert E Shade, Kenneth Lange, Shifra Birnbaum, Natalia Kuhn, Edward J Dick, Jr., John Bernal, Anthony G Comuzzie, Mark J Nijland, Cun Li, and Peter W Nathanielsz. San Antonio, TX, USA; and Laramie, WY, USA.

F-086 **Fetal Neuronal Exosome Morphine Receptor Levels and Maternal Opioid Use.**
Laura Goetzl, Laura Hart, Nana Merabova, Stephaniya Grebennikova, and Nune Darbinian. Philadelphia, PA, USA.

F-087 **A Single Course of Prenatal Glucocorticoid Programs the Stress Response and Pituitary Gene Expression Across Two Generations.**
Alexandros Mouratidis, Vasilis G Moisiadis, Alisa Kostaki, and Stephen G Matthews. Toronto, ON, Canada.

F-088 **Early Life Exposure to Environmental Estrogens Programs Uterine Signaling.**
Edwina P Kisanga, Shannon Whirledge, Robert H Oakley, and John A Cidlowski. New Haven, CT, USA; and Research Triangle Park, NC, USA.

EPIDEMIOLOGY

F-089 **Trends in Mode of Delivery in Intrauterine Fetal Demise in the United States Between 2003 and 2013.**
Emily A Oliver, Kara M Rood, Mark A Klebanoff, Kathryn Berryman, Michael Cackovic, Irina A Buhimschi, and Catalin S Buhimschi. Columbus, OH, USA.

F-090 **Congenital Malformation Risk in Obese Women of Advanced Maternal Age.**
Lauren Miller, Stefanie Hollenbach, Timothy Dye, Dongmei Li, and Loralei Thornburg. Rochester, NY, USA.

F-091 **Anti-Müllerian Hormone Levels in Female Rheumatoid Arthritis Patients Trying to Conceive – The Role of Ovarian Function in Time to Pregnancy in a Nationwide Cohort Study.**
Jenny Brouwer, Radboud JEM Dolhain, Johanna MW Hazes, Jenny A Visser, and Joop SE Laven. Rotterdam, Zuid-Holland, Netherlands.

F-092 **Validation of Electronic Algorithms Based on Abstracted Clinical Data for the Diagnosis of Hypertensive Pregnancy Disorders.**
Elisabeth Codsi, Yvonne S Butler Tobah, Wendy M White, Andrea G Kattah, Mie Saiki, Lisa E Vaughan, Amy L Weaver, Layan Alrahmani, Pavan Parikh, Kristi S Borowski, Norman P Davies, Carl H Rose, Michelle M Mielke, and Vesna D Garovic. Rochester, MN, USA.

Friday, March 17, 2017 - Poster Session II - Bonnet Creek I – IX

FETUS

F-093 **First Evidence of Intrinsic Fetal Heart Rate Variability Affected by Chronic Fetal Hypoxia.**
MG Frasch, CL Herry, Y Niu, and DA Giussani. Seattle, WA, USA; Ottawa, ON, Canada; and Cambridge, United Kingdom.

F-094 **Utility of Screening Fetal Echocardiogram for IVF Pregnancies.**
Ann Lal, and Nicole Sprawka. Maywood, IL, USA.

F-095 **Echogenic Bowel in Pregnant Women Taking Spatone as Iron Supplement.**
Sharon Maslovitz, and Avital Skornick-Rapaport. Tel Aviv, Israel.

F-096 **Fetal Hypothalamus-Pituitary-Adrenal Axis Alteration Through Late Gestational Low-Dose Dexamethasone Injection and Consequent Effects on ACTH and Cortisol Levels During Hypoglycemia in Pigs.**
Guadalupe L Rodríguez-González, Martin Schmidt, Florian Rakers, Peter W Nathanielsz, Sabine J Bischoff, Marius Nistor, and René Schiffner. Mexico City, Mexico; Jena, Germany; and Laramie, WY, USA.

F-097 **Race and Gender-Based Overestimation of Fetal Weight May Lead to Missed Diagnoses of Fetal Growth Restriction.**
Yasaswi Paruchuri, and Jacob Larkin. Pittsburgh, PA, USA.

F-098 **β-Oxidation Compensates for Impaired Glucose Metabolism in Skeletal Muscle from Intrauterine Growth Restricted Sheep Fetuses.**
Amy Kelly, Hailey Davenport, David Taska, Leticia Camacho, Melissa Davis, Christopher Bidwell, Ronald Allen, and Sean Limesand. Tucson, AZ, USA; and West Lafayette, IN, USA.

F-099 **Do Small for Gestational Age (SGA) Fetuses Also Exhibit Circadian Changes in Fetal Heart Rate Parameters as Do Appropriate for Gestational Age (AGA) Fetuses?**
Habiba Kapaya, Emma Dimelow, and Dilly Anumba. Sheffield, S. Yorkshire, United Kingdom.

F-100 **A Compromised Maternal Vitamin D Status Is Associated with an Increased Risk of Congenital Heart Defects in Offspring.**
Linette van Duijn, Maria PH Koster, Yvonne HM Krul-Poel, Joop S Laven, Willem A Helbing, Suat Simsek, and Régine PM Steegers-Theunissen. Rotterdam, Netherlands; and Alkmaar, Netherlands.

F-101 **The Interaction Between the Maternal Systemic and Uteroplacental Circulations in Pregnancies Resulting in Small for Gestational Age Newborns.**
Asma Khalil, Helen Perry, Sophie Bowe, Basky Thilaganathan, and Basky Thilaganathan. London, United Kingdom.

F-102 **Long-Term High Altitude Hypoxia During Gestation Represses Large Conductance Ca^{2+}-Activated K^+ Channel Expression *via* Upregulating DNA Methyltransferase in Ovine Uterine Arteries.**
Chiranjib Dasgupta, Xiang-Qun Hu, Man Chen, Daliao Xiao, Xiaohui Huang, and Lubo Zhang. Loma Linda, CA, USA.

F-103 **Fetal Syndrome of Endocannabinoid Deficiency (FSECD) in an Experimental Model of Maternal High Fat Diet.**
Natalia Schlabritz-Loutsevitch, Cun Li, Nadezhda German, Eneko Larumbe, James Maher, Peter Nathanielsz, and Gary Ventolini. Odessa, TX, USA; Laramie, WY, USA; Lubbock, TX, USA; Amarillo, TX, USA; and San Antonio, TX, USA.

F-104 **A Study of Three Risk Factors for Fetal Brain Injury Using a Mouse Model.**
Yupeng Dong, Yoshitaka Kimura, and Nobuo Yaegashi. Sendai, Miyagi, Japan.

F-105 **Cerebral Circulation in Fetal Growth Restriction.**
Shane Reeves, Diane Gumina, Mary Pinter, Allison Gillan, and John Hobbins. Aurora, CO, USA.

GYNECOLOGIC ONCOLOGY

F-106 **Hormonal Therapy for Low Grade Endometrial Stromal Sarcoma.**
Rachel Passarelli, Uma Deshmukh, Jonathan Black, Amanda Rostkowski, Javier Perez Irizarry, Pei Hui, Elena Ratner, Dan-Arin Silasi, Masoud Azodi, Alessandro D Santin, Thomas J Rutherford, and Peter E Schwartz. New Haven, CT, USA.

F-107 **The 17β-Hydroxysteroid Dehydrogenase Type 2 Expression Induced by the Androgen Signal in Endometrial Cancer.**
Chiaki Hashimoto, Yasuhiro Miki, Sota Tanaka, Kiyoshi Takagi, Misaki Fue, Zhulanqiqige Doe, Bin Li, Nobuo Yaegashi, Takashi Suzuki, and Kiyoshi Ito. Sendai, Miyagi, Japan.

F-108 **Neratinib Shows Efficacy in the Treatment of HER2/Neu Amplified Epithelial Ovarian Carcinoma In Vitro and In Vivo.**
Gulden Menderes, Stefania Bellone, Jonathan D Black, Salvatore Lopez, Elena Bonazzoli, Francesca Pettinella, Alice Masserdotti, Luca Zammataro, Dan-Arin Silasi, Babak Litkouhi, Elena Ratner, Masoud Azodi, Peter Schwartz, and Alessandro D Santin. New Haven, CT, USA; and Rome, Italy.

Friday, March 17, 2017 - Poster Session II - Bonnet Creek I – IX

F-109 **A Ten-Year Single Institution Experience Comparing Type 1 and Type 2 Endometrial Cancers.**
Jonathan Black, Rachel Passarelli, Margaret Whicker, Stefan Gysler, Benjamin Albright, Lingeng Lu, Gulden Menderes, Gary Altwerger, Babak Litkouhi, Elena Ratner, Dan-Arin Silasi, Masoud Azodi, Alessandro Santin, and Peter Schwartz. New Haven, CT, USA; and Philadelphia, PA, USA.

ENDOMETRIOSIS, FIBROIDS, AND GYNECOLOGY

F-110 **The Effect of Copper on Endometrial Receptivity and Induction of Apoptosis on Decidualizated Endometrial Stromal Cells.**
JA Horcajadas, JP Carrascosa, D Cotán, P Sánchez-Martín, and JA Sánchez-Alcázar. Seville, Spain.

F-111 **Surgical Outcomes of Minimally Invasive and Abdominal Hysterectomy for Benign Indications by Operative Time: An Analysis of the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP).**
Samantha L Margulies, Maria V Vargas, Kathryn Denny, Richard Amdur, and Cherie Marfori. New Haven, CT, USA; and Washington, DC, USA.

F-112 **Possible Role of Double Strand Break Repair Impairment in the Pathogenesis of Endometriosis and Decreased Ovarian Reserve.**
Jung Ho Shin, Jae Hoon Lee, JiHyun Park, JooHyun Park, Bo Hyun Yun, Seok Kyo Seo, SiHyun Cho, Young Sik Choi, and Byung Seok Lee. Seoul, Republic of Korea.

F-113 **Predictive Model for Endometriosis Diagnosis Based in Uterine Aspirates.**
Júlia Vallvé-Juanico, Elena Suárez-Salvador, Josep Castellví, Hugh S Taylor, Antonio Gil-Moreno, and Xavier Santamaria. Barcelona, Spain; Bellaterra, Spain; and New Haven, CT, USA.

F-114 **RNA Binding Protein, HuR/TTP Axis in Endometriosis.**
Kasra Khalaj, SooHyun Ahn, Mallikarjun Bidarimath, Yasmin Nasirzadeh, Steven L Young, Bruce A Lessey, Sukhbir S Singh, Madhuri Koti, and Chandrakant Tayade. Kingston, ON, Canada; Chapel Hill, NC, USA; Greenville, SC, USA; and Ottawa, ON, Canada.

F-115 **Tissue Specific Expression Analysis in Endometriosis by Laser Capture Microdissection (LCM).**
Lorenz Küssel, Eva Simon, Maik Obendorf, Ralf Lesche, Juliane Hundt, Arndt Schmitz, Agnes Jäger-Lansky, Reinhard Obwegeser, Thomas M Zollner, and Rene Wenzl. Vienna, Austria; and Berlin, Germany.

F-116 **IL-1β Disrupts Human Endometrial Stromal Cell Differentiation via Activation of the ERK 1/2 and p38 MAP Kinase Pathways: Potential Role in Endometriosis.**
Jie Yu, Sarah L Berga, Erika B Johnston-MacAnanny, Bansari Patel, and Robert N Taylor. Winston-Salem, NC, USA.

F-117 **Large-Scale Integrated Genome-Wide RNA Sequencing, miRNA Array, and Genomic Analyses to Unravel the Functionality of Genome-Wide Association Results in Endometriosis.**
Nilufer Rahmioglu, Helen Lockstone, Teresa Ferreira, Reedik Magi, Martijn Van De Bunt, Cecilia Lindgren, Andrew Morris, Christian Becker, and Krina Zondervan. Oxford, United Kingdom; Tartu, Estonia; and Liverpool, United Kingdom.

F-118 **Endometriosis Associated Risk of Ovarian Cancer Is Increased in Cases of Ovarian, but Not in Deep Infiltrating or Peritoneal Endometriosis.**
Liisu Saavalainen, Eero Pukkala, Anna But, Mika Gissler, Aila Tiitinen, Päivi Härkki, and Oskari Heikinheimo. Helsinki, Finland.

F-119 **Inflammation and Fibrosis Mediate Distinct Phenotypic Progression in Endometriosis.**
Tiffanny L Jones, Chandra C Senoy, Ye Zheng, Abdulrahman M Saadalla, Khashayarsha Khazaie, and Gaurang S Daftary. Rochester, MN, USA.

F-120 **Novel High-Risk Damaging Mutations Discovered in Familial Endometriosis.**
Kenneth Ward, Rakesh Chettier, and Hans Albertsen. Salt Lake City, UT, USA.

F-121 **The Predictive Potential of Peripheral Blood Basophils in Endometriosis.**
Jun Guan, Karin Hellner, Nilufer Rahmioglu, Carol Hubbard, Maryjane Dale, Kevin Paddon, Krina Zondervan, and Christian Becker. Oxford, United Kingdom.

F-122 **Novel PTGES Inhibitor BAY 1202229 Showed Significant Effects Against Inflammatory Pain and Vaginal Hyperalgesia and Proliferation in a Rat Model of Endometriosis.**
Anne-Marie Coelho, Marcus Koppitz, Daryl Walter, Nico Braeuer, Andrea Rotgeri, Susan Boyce, Markus Koch, Thomas M Zollner, Andreas Steinmeyer, and Michaele Peters. Berlin, Germany; Hamburg, Germany; and Abingdon, Oxfordshire, United Kingdom.

F-123 **The Effect of Operative Time on Outcomes in Minimally Invasive and Abdominal Myomectomy: An Analysis of the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP).**
Samantha L Margulies, Maria V Vargas, Kathryn Denny, Richard Amdur, and Cherie Marfori. New Haven, CT, USA; and Washington, DC, USA.

Friday, March 17, 2017 - Poster Session II - Bonnet Creek I – IX

F-124 **Oxidative Stress: A Key Regulator of Leiomyoma Cell Survival.**
Nicole M Fletcher, Ira Memaj, Mohammed S Abusamaan, Ayman Al-Hendy, Michael P Diamond, and Ghassan M Saed. Detroit, MI, USA; and Augusta, GA, USA.

F-125 **Ulipristal Directly Regulates Leiomyoma Fibrosis In Vivo and In Vitro.**
Minnie Malik, Jeris Cox, Joy Britten, Lynnette Nieman, and William H Catherino. Bethesda, MD, USA; and Fort Belvoir, VA, USA.

F-126 **Screening the Antiproliferative Effect of Seven Vitamin D Analogs in Human Uterine Fibroid Cells.**
Mohamed A Ali, Heba ElHusseini, Sunil K Halder, Archana Laknaur, and Ayman Al-Hendy. Augusta, GA, USA.

F-127 **Differential Susceptibility of Chlamydial Infection in the Gastrointestinal Tract to Doxycycline Treatment.**
Courtney Failor, Luying Wang, Robert Schenken, and Guangming Zhong. San Antonio, TX, USA.

MATERNAL BIOLOGY AND HEALTH

F-128 **Gestational Diabetes Results in Increased Energy Expenditure in a Mouse Model.**
Kathleen Pennington, and Nicola van der Walt. Houston, TX, USA.

F-129 **Optimal Non-Invasive Method of Measuring Cardiac Output During Pregnancy Reveals Marked Heterogeneity in the Magnitude of Responses Between Women.**
John W Petersen, Jing Liu, Yueh-Yun Chi, Melissa D Lingis, R Stan Williams, Alice Rhoton-Vlasak, Karen Hamilton, Mark S Segal, and Kirk Conrad. Gainesville, FL, USA.

F-130 **Pregnancy Upregulates Ten-Eleven Translocation (TET) Methylcytosine Dioxygenases and Increases Large Conductance Ca^{2+}-Activated K^+ Channel Expression in Ovine Uterine Arteries.**
Chiranjib Dasgupta, Xiang-Qun Hu, Man Chen, Xiaohui Huang, and Lubo Zhang. Loma Linda, CA, USA.

F-131 **Physiologic Adaptation of Endothelial Function to Pregnancy: A Systematic Review and Meta-Analysis.**
Tessa AG van Gansewinkel, Veronica A Lopes van Balen, Sander de Haas, Sander MJ van Kuijk, Joris van Drongelen, Chahinda Ghossein-Doha, and Marc EA Spaanderman. Maastricht, Limburg, Netherlands; and Nijmegen, Gelderland, Netherlands.

F-132 **Cardiac Remodeling During Physiologic and Complicated Pregnancies: A Systematic Review and Meta-Analysis.**
Chahinda Ghossein-Doha, Sander de Haas, Lauren Geerts, Joris Drongelen, and Marc Spaanderman. Maastricht, Limburg, Netherlands; and Nijmegen, Gelderland, Netherlands.

F-133 **Intrinsic Circadian Rhythms of Reproductive Tissues Over Pregnancy.**
Carmel Martin-Fairey, Beakal Gezahegn, Sarah Speck, Xioafang Ma, Ronald McCarthy, Sarah England, and Erik Herzog. Saint Louis, MS, USA.

F-134 **Role of DNA Demethylation in Pregnancy-Mediated Increase in BK_{Ca} Channel-Mediated Relaxations and Decrease in Myogenic Tone of Ovine Uterine Arteries.**
Daliao Xiao, Xiaohui Huang, Xiang-Qun Hu, and Lubo Zhang. Loma Linda, CA, USA.

F-135 **MicroRNA 210 Inhibits Large Conductance Ca^{2+}-Activated K^+ Channel Activity and Functions in Ovine Uterine Arteries.**
Xiang-Qun Hu, Daliao Xiao, Xiaohui Huang, and Lubo Zhang. Loma Linda, CA, USA.

F-136 **Navigating New Motherhood: Evaluating the Role of Patient-Navigator Communication on Postpartum Follow-Up in a Low-Income Community.**
Angelina M Strohbach, Fengling Hu, Noelle G Martinez, Nadia Hajjar, Melissa A Simon, and Lynn M Yee. Chicago, IL, USA.

PLACENTA

F-137 **Triclosan Exposure During Late Gestation Affects Placental Function in the Pregnant Ewe.**
Maria B Rabaglino, Maureen Keller-Wood, and Charlie E Wood. Córdoba, Argentina; and Gainesville, FL, USA.

F-138 **Placental Gene Expression Is Affected by Male Fetal Sex and Maternal Genotype in Fetal Growth Restriction Model.**
Jessica F Hebert, Jess Millar, Amie Romney, Rahul Raghavan, Jason Podrabsky, and Terry K Morgan. Portland, OR, USA.

F-139 **Exosomal Profile of Enzymes Involved in the Biosynthesis of Eicosanoids Generated by Human Gestational Tissues.**
Hassendrini N Peiris, Kanchan Vaswani, Sarah Reed, and Murray D Mitchell. Brisbane, QLD, Australia.

F-140 **Exposure to CrVI During Early Pregnancy Increases Oxidative Stress and Disrupts the Expression of Antioxidant Proteins in Placental Compartments.**
Sakhila K Banu, Jone A Stanley, Kirthiram K Sivakumar, and Joe A Arosh. College Station, TX, USA.

F-141 **Sex-Specific Differences in Placental Methylation That Are Associated with Transcript Abundance.**
MD Johnson, S Gong, U Sovio, J Dopierala, F Gaccioli, M Constância, DS Charnock-Jones, and GCS Smith. Cambridge, United Kingdom.

Friday, March 17, 2017 - Poster Session II - Bonnet Creek I – IX

F-142 **Sex-Specific Differences in Human Placenta Transcriptome.**
Justyna Dopierala, Sung Gong, Ulla Sovio, Gordon CS Smith, and D Stephen Charnock-Jones. Cambridge, Cambridgeshire, United Kingdom.

F-143 **Inter-Correlations Between Multiple Maternal Serum Placental Biomarkers in the First Trimester.**
Viola Seravalli, Dana Block-Abraham, Jena Miller, and Ahmet Baschat. Baltimore, MD, USA.

F-144 **Knockdown of GNA11 Decreases VEGFA- and FGF2-Stimulated Human Fetoplacental Endothelial Migration Under Physiological Chronic Normoxia.**
Qing-Yun Zou, Ying-Jie Zhao, Hua Li, Xiang-Zhen Wang, Chi Zhou, and Jing Zheng. Madison, WI, USA; Jinan, Shandong, China; Qingdao, Shandong, China; and Shenzhen, Guangdong, China.

F-145 **Autophagy Inhibition by Chloroquine Increased Invasion of HTR8/SVneo Trophoblast Cells.**
Juyoung Park, Ji-Hee Sung, Minji Choi, Jae Ryoung Hwang, Suk-Joo Choi, Soo-young Oh, Jong-Hwa Kim, and Cheong-Rae Roh. Seoul, Republic of Korea.

F-146 **Variable Effect of Docosahexaenoic Acid (DHA), Depending on Their Concentration, in the Trophoblast Function In Vitro.**
Jorge A Carvajal, Ana M Delpiano, and Gloria L Valdes. Santiago, RM, Chile.

F-147 **Chronic Hypoxia Disrupts Mitochondrial Function in the Guinea Pig Placenta.**
Hong Song, Bhanu P Telugu, and Loren P Thompson. Baltimore, MD, USA; and College Park, MD, USA.

F-148 **How Well Does Ultrasound Identify Abnormal Placental Cord Insertion?**
Amelia S McLennan, Victoria X Yu, Cande V Ananth, Russell S Miller, and Cynthia Gyamfi-Bannerman. New York, NY, USA.

F-149 **The Effectiveness of Tadalafil in Reversing Vasoconstriction in an *Ex Vivo* Human Placental Perfusion Model of Fetal Growth Restriction.**
Robert B Walton, Luckey C Reed, Sarah M Estrada, Peter G Napolitano, and Nicholas M Ieronimakis. Tacoma, WA, USA.

F-150 **Novel Localization of Hepcidin at the Human Maternal-Fetal Interface.**
Elizabeth Taglauer, Danielle Wuebbolt, Elizabeth Tully, Fionnuala Breathnach, Amir Khan, and Sarbattama Sen. Boston, MA, USA; and Dublin, Ireland.

F-151 **Unexplained Antepartum Stillbirth Is Associated with Biochemical Evidence of Placental Aging.**
Kaushik Maiti, Zakia Sultana, John Aitken, and Roger Smith. Newcastle, NSW, Australia.

F-152 **High Maternal Omega-3 Fatty Acid Levels in Hawaiian Women Impair Placental Lipid Storage.**
Fernanda L Alvarado, Virtu Calabuig-Navarro, Pai-Jong S Tsai, and Perrie O'Tierney-Ginn. Cleveland, OH, USA; and Buffalo, NY, USA.

F-153 **Next-Generation miRNA Sequencing Reveals That Exosomes Present in Maternal Circulation of Gestational Diabetes Pregnancies Regulate Glucose Metabolism in Placental Cells.**
Stefanie Adam, Dominic Guanzon, Katherin Scholz-Romero, Omar Elfeky, Sherri Longo, Andrew Lai, Gregory Duncombe, Gregory E Rice, Martha Lappas, and Carlos Salomon. Brisbane, QLD, Australia; New Orleans, LA, USA; and Melbourne, VIC, Australia.

F-154 **miR-210 Alters Mitochondrial Function in First Trimester Extravillous Trophoblast Cells.**
Lauren Anton, Ann DeVine, Amy G Brown, Erzsebet Polyak, Marni J Falk, and Michal A Elovtiz. Philadelphia, PA, USA.

F-155 ***Inhibin Alpha Chain* Gene Is Differentially Regulated by GATA-2, GATA-6 and WT1 in Human Cytotrophoblasts.**
Christophe L Depoix, Corinne Hubinont, and Frédéric Debiève. Brussels, Belgium.

F-156 **Effect of Tetrabromo-Bisphenol A (TBBPA) on Expression of Biomarkers for Inflammation, Oxidative Stress and Neurodevelopment by the Placenta.**
Yuko Arita, Michael Kirk, Matthew Pressman, Darios Getahun, Ramkumar Menon, and Morgan R Peltier. Mineola, NY, USA; Pasadena, CA, USA; and Galveston, TX, USA.

F-157 **Terminal Villi of the Human Placenta Have No Core Microbiome.**
Susanne Lager, Marcus de Goffau, Sharon J Peacock, Julian Parkhill, D Stephen Charnock-Jones, and Gordon CS Smith. Cambridge, United Kingdom; and Hinxton, United Kingdom.

POPULATION HEALTH

F-158 **State-by-State Trends in Labor and Delivery Costs: Association with Length of Stay and State-Specific Maternal Mortality Ratio.**
Mary C Tolcher, Amirhossein Moaddab, Catherine S Eppes, Alireza A Shamshirsaz, Gary A Dildy, Michael A Belfort, and Steven L Clark. Houston, TX, USA.

F-159 **How to Reduce Caesarean Section (CS) Rate: A Cultural and Organizational Issue.**
Denise E Rinaldo, Anna Zilioli, and Claudio Crescini. Treviglio, BG, Italy.

Friday, March 17, 2017 - Poster Session II - Bonnet Creek I – IX

PREECLAMPSIA

F-160 **The Effect of Low Molecular Weight Heparin on Antithrombin III in Patients with Recurrent Spontaneous Abortion Caused by Antiphospholipid Syndrome.**
Hailan Wang, Danyang Kang, and Chong Qiao. Shenyang, China.

F-161 **Effect of Altitude on Incidence of Hypertensive Complications of Pregnancy.**
Ibrahim Hammad, Jim VanDerslice, and Michael Varner. Salt Lake City, UT, USA.

F-162 **Prepregnancy Physiology Predicts Subsequent Preterm Preeclampsia.**
Ira Bernstein, Carole McBride, and Gary Badger. Burlington, VT, USA.

F-163 **Antenatal Blood Pressure Visit-to-Visit Variability and Risk of Pregnancy-Associated Hypertension.**
Christopher L Dixon, . Bethesda, MD, USA.

F-164 **Relaxin Reduces Vascular Sensitivity to Angiotensin II in Pregnant Relaxin-Deficient Mice and Prevents Onset of Vascular Dysfunction in Mouse and Human Arteries.**
Sarah A Marshall, Chen H Leo, Kelly O'Sullivan, Marianne Tare, Natalie J Hannan, Jane E Girling, and Laura J Parry. Parkville, VIC, Australia; Clayton, VIC, Australia; Churchill, VIC, Australia; and Heidelberg, VIC, Australia.

F-165 **Women with Prior Preterm Preeclampsia Have Elevated Inflammation and Endothelial Dysfunction Compared to Nulliparous Women.**
Carole A McBride, Erin A Morris, and Ira M Bernstein. Burlington, VT, USA.

F-166 **Identification of Novel Genetic Variants from Whole Exome Sequencing in Preeclampsia.**
HS Gammill, R Chettier, A Brewer, JM Roberts, R Shree, E Tsigas, and K Ward. Seattle, WA, USA; Salt Lake City, UT, USA; Melbourne, FL, USA; and Pittsburgh, PA, USA.

F-167 **Inhibition of the Auto-Inflammation Suppressor Protein ISG15 Blocks Proliferation and Induces Inflammatory Cytokine Expression in Trophoblasts: Implications for Preeclampsia.**
Sefa Arlier, Ozlem Guzeloglu-Kayisli, Nihan Semerci, Kellie Larsen, Selcuk Tabak, Frederick Schatz, Antony Odibo, Charles Lockwood, and Umit Kayisli. Tampa, FL, USA; and Adiyaman, Turkey.

F-168 **sFlt-1 Production Is Modulated Through the Activation of Angiotensin II Receptor Subtype 2 in Preeclampsia.**
Keiichi Matsubara, Yuko Matsubara, Yuka Uchikura, and Takashi Sugiyama. Toon, Ehime, Japan.

F-169 **Telomere Homeostasis and Senescence Markers Are Differently Expressed in Placentas from Pregnancies with Early Versus Late Onset Preeclampsia.**
Sivan Farladansky-Gershnabel, Hilah Gal, Dvora Kidron, Valery Krizhanovsky, and Tal Biron-Shental. Tel Aviv, Israel; and Rehovot, Israel.

F-170 **Pregnancy-Associated Exosomes Changes in Pregnancies Complicated by Small-for-Gestational-Age (SGA) Neonates and Intrauterine Growth Restriction (IUGR).**
Jezid Miranda, Cristina Paules, Fatima Crispi, Eduard Gratacos, Vyjayanthi Kinhal, Andrew Lai, Carlos Palma, and Carlos Salomon. Barcelona, Spain; Brisbane, QLD, Australia; and New Orleans, LA, USA.

F-171 **A Tissue-Based Proteomic Study of VEGFR2 in Human Term Placentas Revealed Its Association with Pyruvate Dehydrogenase and MDMX.**
John C Tsibris, Shannon Ho, Dale Chaput, Rachel Sinkey, Stanley Stevens, Maja Okuka, Angel Alsina, and Umit Kayisli. Tampa, FL, USA.

F-172 **Preeclampsia Down-Regulates MicroRNAs in Fetal Endothelial Cells: Roles of miR-29a/c-3p in Endothelial Function.**
Chi Zhou, Qing-Yun Zou, Ai-Xia Liu, Rui-Fang Wang, Ronald R Magness, and Jing Zheng. Madison, WI, USA; Hangzhou, Zhejiang, China; and Tampa, FL, USA.

F-173 **Pro-Inflammatory Cytokines in Lean and Obese Women with Preeclampsia.**
HW Hunt, H Gammill, E Schur, and S Chandrasekaran. Seattle, WA, USA.

F-174 **Early Pregnancy Chemokine C-C Motif Ligand 2 (CCL2), Not Leptin, Is Associated with Increased Risk of Preeclampsia in Obese Parturients.**
Sarah A Wernimont, Sabrina M Scroggins, Donna A Santillan, and Mark K Santillan. Iowa City, IA, USA.

F-175 **Comparative Characteristics of Myometrial and Decidual Chemokines Responsible for the Infiltration of Peripheral Leukocytes into Term Uterine Tissues.**
Tali Farine, Oksana Shynlova, and Stephen J Lye. Toronto, ON, Canada.

F-176 **Platelet Activation and Development of Preeclampsia.**
Heather Campbell, . Bethesda, MD, USA.

F-177 ***Is One Elevated Blood Pressure Enough?* A Retrospective Analysis of Preeclampsia Labs Sent from the Emergency Room.**
Martha B Kole, Phinnara Has, Samantha P DeAndrade, Sarah M Gaskell, Valery A Danilack, and Erika F Werner. Providence, RI, USA.

F-178 **Comparison of the fullPIERS Model to Physician Clinical Risk Assessment of Patients with Preeclampsia.**
Emily E Hadley, Luis Monsivais, Guiseppe Chiossi, Sangeeta Jain, Tony Wen, and Maged Costantine. Galveston, TX, USA.

Friday, March 17, 2017 - Poster Session II - Bonnet Creek I – IX

REPRODUCTIVE BIOLOGY

F-179 **Standardization of Sampling for Isolation of Exosomes from Peripheral Blood from Reproductive-Aged Women.**
Bruna Ribeiro de Andrade Ramos, Jéssica M Diehl, Natália Prearo Moço, Graziela G Romagnoli, and Márcia Guimarães da Silva. Botucatu, São Paulo, Brazil.

F-180 **Metabolic Hormonal Profiles of Follicular Fluid Are Abnormal in Obese Women Undergoing In-Vitro Fertilization.**
Laurice Bou Nemer, Haolin Shi, R Ann Word, Bruce R Carr, and Orhan Bukulmez. Dallas, TX, USA.

F-181 **Antimüllerian Hormone (AMH) Less Than 1 Is Associated with Increased Irregular Cell Cleavage in Women Less Than 35.**
I Okeigwe, JC Robins, J Zhang, and ME Pavone. Chicago, IL, USA.

F-182 **Differences in Serum and Ovarian Follicular Fluid Metabolites and Reproductive Outcomes of Obese Versus Non Obese Women.**
Mamie McLean, Wright Bates, Emily Gordon, Sara Cooper, and Lorie Harper. Birmingham, AL, USA; and Huntsville, AL, USA.

F-183 **An Unconventional Choice of Embryo Transfer Day.**
Stephanie Baum, Moti Gulersen, and Tomer Singer. New York, NY, USA.

F-184 **Interleukin-1ß Regulates Thymic Stromal Lymphopoietin (TSLP) Expression in Cultured Human First Trimester Decidua Cells.**
Felice Arcuri, Francesco Damiani, Lucia Funghi, Joseph Huang, and Felice Petraglia. Siena, Italy; Tampa, FL, USA; and Kaohsiung, Taiwan.

F-185 **Maternal Endometrial hsa-miR-30d Is Taken Up by the Human Blastocyst and Induces Transcriptional Modifications.**
Meera S Shah, Felipe Vilella, Barry Behr, Vikrant Reddy, Wanxin Wang, Roser Navarro, Jorge Jimenez, Steven Quake, and Carlos Simon. Palo Alto, CA, USA; Valencia, Spain; and Valencia, Paterna, Spain.

F-186 **Different Expression Pattern of Transient Receptor Potential Channels in Endometrial Epithelial and Stromal Cells of Mouse and Human.**
De Clercq Katrien, Hennes Aurélie, and Vriens Joris. Leuven, Vlaams-Brabant, Belgium.

F-187 **Reprogramming of the hCG Signaling Profile in Human Endometrial Stromal Cells from Recurrent Miscarriage Patients.**
Shirin Khanjani, Camilla West, Jan J Brosens, Stuart Lavery, Phillip R Bennett, and Aylin C Hanyaloglu. London, United Kingdom; and Warwick, Coventry, United Kingdom.

F-188 **Extracellular Vesicles Secreted by the Human Endometrium Contain Specific DNA Sequences That Are Uptaken by Murine Embryos.**
David Bolumar, Inmaculada Moreno, María Herrero, Sergio Cabanillas, Felipe Vilella, and Carlos Simon. Paterna, VLC, Spain; Valencia, VLC, Spain; and Palo Alto, CA, USA.

F-189 **Plural Murine Follicles Can Ovulate Simultaneously In Vitro with Angiotensin II Receptor Analogue Treatment.**
Seung-Yup Ku, Yoon Young Kim, Yong Jin Kim, Byeong-Cheol Kang, and Hung Ching Liu. Seoul, Korea; and New York, NY, USA.

F-190 **FOXO3 Expression in the Human Ovary.**
Helen P Swenson, Alice Rhoton, Dawn Beachy, Harry Nick, and Demaratta Rush. Gainesville, FL, USA.

F-191 **The lncRNA H19 Is Regulated by FSH and Estradiol, and H19 KD Results in Altered Follicular Dynamics and Enhanced Gonadotropin Response.**
Yanhong Fan, Chunrong Qin, Joshua Johnson, and Amanda Kallen. New Haven, CT, USA; and Aurora, CO, USA.

F-192 **Non-Invasive Imaging of Living Follicles in Human Ovarian Cortex with Reflectance Confocal Microscopy.**
Myra J Schleedoorn, Malou Peppelman, Willianne LDM Nelen, Kathrin Fleischer, and Ron Peek. Nijmegen, Gelderland, Netherlands.

F-193 **Inflammatory Monocytes Regulate Endometrial Repair and Remodeling.**
Phoebe M Kirkwood, Fiona L Cousins, Philippa TK Saunders, and Douglas A Gibson. Edinburgh, Midlothian, United Kingdom; and Clayton, VIC, Australia.

F-194 **First-Trimester Trophoblasts Promote Differentiation of IL-8 Expressing ILC3s.**
Kristina MT Hilz, Damián O Muzzio, Laura Núñez Castro, Christine Lamb, and Marek Zygmunt. Greifswald, Germany.

F-195 **Elevation of Reactive Oxidative Species in Uterine Myeloid Cells During Early Pregnancy.**
Hui Zhao, Flora Kalish, Ronald J Wong, and David K Stevenson. Stanford, CA, USA.

REPRODUCTIVE ENDOCRINOLOGY AND INFERTILITY

F-196 **Adherence to a "Healthy" Dietary Pattern Is Positively Associated with Semen Parameters Especially in Men with Poor Semen Quality.**
Eline C Oostingh, Régine PM Steegers - Theunissen, Jeanne HM de Vries, Joop SE Laven, and Maria PH Koster. Rotterdam, Netherlands; and Wageningen, Netherlands.

Friday, March 17, 2017 - Poster Session II - Bonnet Creek I – IX

F-197 **Genetic Variation Underlying the Clinical Heterogeneity of Endometriosis.**
Kenneth Ward, Rakesh Chettier, and Hans Albertsen. Salt Lake City, UT, USA.

F-198 **Recombinant Luteinizing Hormone (rLH) Can Reduce FSH Requirements in Normal Responding IVF Patients without Endogenous LH Activity.**
Alice J Shapiro, Emily Holden, and Peter McGovern. Newark, NJ, USA; and Hasbrouck Heights, NJ, USA.

F-199 **Racial and Ethnic Differences in Morphokinetic Cell Cleavage Patterns.**
I Okeigwe, ME Pavone, J Zhang, and JC Robins. Chicago, IL, USA.

F-200 **Impact of Assisted Reproductive Technologies on Pregnancy Outcomes Among Patients of Extremely Advanced Maternal Age.**
Stefanie J Hollenbach, Lauren A Miller, Courtney Olson-Chen, Dongmei Li, Timothy Dye, and Loralei Thornberg. Rochester, NY, USA.

F-201 **How Should the Threshold Value for Determining Elevated Progesterone in ART Cycles Be Determined?**
Toral P Parikh, Mae Healy, Kate Devine, Kevin Richter, Alan DeCherney, and Micah Hill. Bethesda, MD, USA; and Rockville, MD, USA.

F-202 **Neonatal Outcomes of Triplet Pregnancies Conceived via In-Vitro Fertilization.**
Danielle A Peress, Alan M Peaceman, and Lynn M Yee. Pennsylvania, PA, USA; and Chicago, IL, USA.

F-203 **ART Pregnancy Complications Are Significantly Associated with Endometriosis Severity Before Conception: A Retrospective Cohort Study.**
Tatsuya Fujii, Osamu Wada-Hiraike, Takeshi Nagamatsu, Miyuki Harada, Tetsuya Hirata, Kaori Koga, Tomoyuki Fujii, and Yutaka Osuga. Tokyo, Japan.

F-204 **ICSI Outcomes in Men Undergoing TESA for Azoospermia and Impact of Maternal Age.**
Silvina Bocca, Victor Brugh, Mahmood Morshedi, Laurel Stadtmauer, and Sergio Oehninger. Norfolk, VA, USA.

F-205 **Melatonin Treatment Is Able to Restore Menstrual Cyclicity in PCOS Women: A Pilot Study.**
Anna Tropea, Valeria Tagliaferri, Valentina Immediata, Simona De Cicco, Daniela Romualdi, Christian Di Florio, Elisa Scarinci, Antonio Lanzone, and Rosanna Apa. Rome, Italy.

F-206 **Elevated Testosterone Increases *Ins1* Transcription and Induces Pancreatic Beta Cell Proliferation and Glucose Intolerance in Female Rats.**
Jay Mishra, Amar More, and Sathish Kumar. Galveston, TX, USA.

F-207 **Effects of Estrogen on Proliferative Activity of Murine Female Bone Marrow Stromal Cells.**
Seung-Yup Ku, Yoon Young Kim, Hoon Kim, Chang Suk Suh, Seok Hyun Kim, and Young Min Choi. Seoul, Korea.

F-208 **Reproductive Aged Women Do Not View Employer Coverage of Egg Freezing as Coercive.**
Deborah E Ikhena, Rafael Confino, Angela K Lawson, Susan Klock, and MaryEllen G Pavone. Chicago, IL, USA.

STEM CELLS

F-209 **The Potential Oligodendroglial Fate Specification Capacity of Exosomes Derived from Stem Cells of the Umbilical Cord Tissue.**
Marianne S Joerger-Messerli, Marialuigia Spinelli, Byron Oppliger, Ivana Di Salvo, Martin Mueller, Daniel V Surbek, and Andreina Schoeberlein. Bern, Switzerland; and New Haven, CT, USA.

F-210 **Mitochondria Inhibition at Normoxia Is Sufficient to Emulate Hypoxic-Stress Induced Potency Loss and TGC Differentiation in mTSC.**
Yu Yang, Jing Dai, Elizabeth E Puscheck, and Daniel A Rappolee. Detroit, MI, USA.

F-211 **Lens Tissue Development from Mouse Embryonic and Induced Pluripotent Stem Cells.**
Emma R McGuirk, Nicholas Ng, Parveen Parasar, Samuel Hornstein, and Raymond M Anchan. Boston, MA, USA.

F-212 **The Role of TRF2 in Maintaining and Protecting Neural Cell Properties.**
Siti Aminah Muhammad Imran, and Wei Cui. London, United Kingdom.

Saturday, March 18, 2017 - Poster Session III - Bonnet Creek I – IX

9:00 AM-10:30 AM **Poster Session**

BASIC PARTURITION

S-001 **Impact of Hypoxia on PD-1/PD-L1 Interaction in the Immunosurveillance of Uterine Fibroid.**
Abdeljabar El Andaloussi, Nahed Ismail, and Ayman Al-Hendy. Augusta, GA, USA; and Pittsburgh, PA, USA.

S-002 **Effect of OBE022, an Oral and Selective Non-Prostanoid PGF2α Receptor Antagonist in Combination with Nifedipine for Preterm Labor: A Study on RU486-Induced Pregnant Mice.**
Oliver Pohl, Murielle Méen, Philippe Lluel, André Chollet, and Jean-Pierre Gotteland. Plan-les-Ouates, Switzerland; and Toulouse, France.

S-003 **History of Retained Placenta Is an Independent Risk Factor for Major Complications in Subsequent Pregnancies: Evidence from a Large Retrospective Cohort Study.**
Shirley Greenbaum, Tamar Wainstock, Doron Dukler, Elad Leron, and Offer Erez. Beer Sheva, Israel.

S-004 **Exosomes Analysis and Characterization of Human Umbilical Cord Blood from Normal and Preterm Pregnancies.**
Christopher L Dixon, Vyjayanthi Kinhal, Carlos Palma, Kechichian Talar, Rheanna Urrabaz-Garza, Carlos Salomon, and Ramkumar Menon. Galveston, TX, USA; and Brisbane, United Kingdom.

S-005 **Use of Mass Spectrometric Measurements to Determine Differential Expression of Prostaglandins and Prostamides in Amniotic Fluid of Women Delivering Preterm with and without Microbial Invasion of the Amniotic Cavity.**
Hassendrini N Peiris, Robert J Romero, Kanchan Vaswani, Sarah Reed, Piya Chaemsaithong, Sonia Hassan, Eli Maymon, and Murray D Mitchell. Brisbane, QLD, Australia; and Detroit, MI, USA.

S-006 **Mid-Trimester Changes in Cervicovaginal Fluid Cytokine Profile of Asymptomatic Women as Early Indicators of Preterm Birth.**
David Chapman, Emmanuel Amabebe, Victoria Stern, and Dilly OC Anumba. Sheffield, South Yorkshire, United Kingdom.

S-007 **Apoptosis in the Prepartum Cervix Increases at Term and Before Preterm Birth.**
Michael A Kirby, Julia Tapelband, Anne C Heuerman, and Steven M Yellon. Loma Linda, CA, USA.

S-008 **ATG16L1 and the Placental Response to Infection and Oxidative Stress via Exosomes.**
Bin Cao, Rheanna Urrabaz-Garza, Helen Feltovich, Ram Menon, and Indira Mysorekar. St. Louis, MO, USA; Galveston, TX, USA; and Salt Lake City, UT, USA.

S-009 **Granulocyte Macrophage-Colony Stimulating Factor (GM-CSF) Expression Is Increased in a Mouse Model of Preterm Birth.**
Christopher Nold, Julie Stone, Todd Jensen, and Anthony Vella. Hartford, CT, USA; and Farmington, CT, USA.

S-010 **Inflammation on the Amniotic Membrane Induces Preterm Delivery in Mice with Chronic Dental *Porphyromonas gingivalis* Infection.**
Yuko Teraoka, Hiroshi Miyoshi, Haruhisa Konishi, Satoshi Urabe, Mutsumi Miyauchi, Takashi Takata, and Yoshiki Kudo. Hiroshima, Japan.

S-011 **The Role of T Regulatory Cells in the Maternal-Fetal Rejection Phenotype of Preterm Birth.**
Jennifer B Gilner, Abigail Fulp, Rex Bentley, Joanne Kurtzberg, and Amy Murtha. Durham, NC, USA.

S-012 **Differential Expression of T Cell Receptor CXCR3 in Preterm Birth Placentas.**
Abigail Fulp, Tracy Truong, Yi-Ju Li, Rex Bentley, Amy Murtha, and Jennifer Gilner. Durham, NC, USA.

S-013 **A Comparison of Toll-Like Receptor 1-9 Induced Cytokine Responses in Whole Blood Collected in the First Trimester and at Term, and Matched Cord Blood.**
Denise CY Chan, Yun S Lee, TG Teoh, Phillip R Bennett, David A MacIntyre, and Lynne Sykes. London, United Kingdom.

S-014 **Autophagy May Predispose to *Chlamydia Trachomatis* Infection and Bad Outcome in Pregnancy.**
Aswathi Jayaram, Tomi Kanninen, Steven R Inglis, Ashwini Pandit, and Steven S Witkin. Jamaica, NY, USA; and New York, NY, USA.

S-015 **Differential Effects of Five Lactobacilli Bacteria Strains on Infection-Induced Cytokine Production by Human Myometrial Cell.**
Bona Kim, Oksana Shynlova, Alan Bocking, and Stephen Lye. Toronto, ON, Canada.

S-016 **Anti-Inflammatory Activity of N,N-Diethylacetamide (DEA) and N,N-Dipropylacetamide (DPA) in *In Vitro* and *Ex Vivo* Models of Inflammation-Induced Preterm Birth.**
Samir Gorasiya, Juliet Mushi, Sabesan Yoganathan, and Sandra E Reznik. Queens, NY, USA; and Bronx, NY, USA.

S-017 **Worse Outcomes in a Severe Sepsis Model in Pregnancy Were Not Associated with a TH1/Th2 Cytokine Bias or Immunosuppression.**
Julia Zöllner, Noor Mohd Nasri, James Leiper, and Mark Johnson. London, England, United Kingdom.

Saturday, March 18, 2017 - Poster Session III - Bonnet Creek I – IX

S-018 **Antenatal Suppression of Interleukin-1 Protects Against Inflammation-Induced Fetal Injury and Improves Neonatal and Developmental Outcomes in Mice.**
Mathieu Nadeau-Vallée, Peck-Yin Chin, Lydia Belarbi, Marie-Ève Brien, Sheetal Pundir, Alexandra Beaudry-Richard, David J Sharkey, Xin Hou, Christiane Quiniou, Jean-Sébastien Joyal, William D Lubell, David M Olson, Sarah A Robertson, Sylvie Girard, and Sylvain Chemtob. Montreal, QC, Canada; Adelaide, SA, Australia; Montréal, QC, Canada; and Edmonton, AB, Canada.

S-019 **Prior Pregnancy History Influences the Level of Autophagy and Immune Activation in Peripheral Blood Mononuclear Cells from Pregnant Women.**
Aswathi Jayaram, Tomi Kanninen, Giovanni Sisti, Steven R Inglis, Ashwini P Pandit, and Steven Witkin. Jamaica, NY, USA; and New York, NY, USA.

S-020 **D-Lactic Acid Inhibits Basal Inflammatory Pathways in Human Vaginal Epithelial Cells.**
Yun S Lee, Maria Marianoglou, Fabienne Hanton, Richard G Brown, Phillip R Bennett, and David A MacIntyre. London, United Kingdom.

S-021 **The Role of Antenatal Inflammation, Specifically Interleukin-1β, in Retinal and Sub-Retinal Vasculopathy of Offspring.**
Alexandra Beaudry-Richard, Mathieu Nadeau-Vallée, Ankush Madaan, Carlos Rivera, Sheetal Pundir, Xin Hou, Christiane Quiniou, Jean-Sébastien Joyal, and Sylvain Chemtob. Montreal, QC, Canada.

S-022 **Common Vaginal Bacterial Strains Regulate Cervical Epithelial Barrier Function Through Inflammation-Mediated Mechanisms.**
Lauren Anton, Ann DeVine, Amy G Brown, Luz-Jeannette Sierra, and Michal A Elovtiz. Philadelphia, PA, USA.

S-023 **An Objective Comparison of *In Vivo* Human Cervix Stiffness in Early and Late Pregnancy.**
Lindsey C Drehfal, Helen Feltovich, Ivan M Rosado-Mendez, Mark L Palmeri, and Timothy J Hall. Madison, WI, USA; Provo, UT, USA; and Durham, NC, USA.

S-024 **Monitoring Collagen Remodeling in the Cervix with Quantitative Ultrasound.**
Quinton W Guerrero, Lindsey C Drehfal, Ivan M Rosado-Mendez, Helen Feltovich, and Timothy J Hall. Madison, WI, USA; and Provo, UT, USA.

S-025 **Progesterone Modulates Cytokine-Induced Gene Expression in Human Cervical Stromal Fibroblasts.**
William E Ackerman IV, Taryn L Summerfield, and Douglas A Kniss. Columbus, OH, USA.

S-026 **Interleukin 8 Expression by Human Cervical Stromal Cells is Mediated by Increased Intracellular cAMP.**
Shweta J Bhatt, Emily C Holden, and Laura T Goldsmith. Newark, NJ, USA.

S-027 **Biomechanical Simulations of Pregnancy: Fetal Membrane Properties Influence Cervical Tissue Stretch at the Internal Os.**
AR Westervelt, M Fernandez, E Mazza, A Ehret, J Vink, CL Nhan-Chang, R Wapner, M House, and K Myers. New York, NY, USA; Zurich, Switzerland; and Boston, MA, USA.

S-028 **Transcriptomes of ER and PR Activation Reveal Unique Cross-Talk in Human Cervical Stromal Cells.**
Banupriya Mukundan, Patrick Keller, Tulip Nandu, and R Ann Word. Dallas, TX, USA.

S-029 **Distinct Effects of Simvastatin, Rosuvastatin and Progesterone on p38MAPK Mediated Senescence and Sterile Inflammation in Human Fetal Membranes.**
Martina T Ayad, Jayshil J Trivedi, Rheanna Urrabaz-Garza, Talar Kechichian, George Saade, Brandie Taylor, and Ramkumar Menon. Galveston, TX, USA; and College Station, TX, USA.

S-030 **Effects of Tension on cAMP-Driven Control of Contractility in Human Myometrial Tissue.**
Pei F Lai, Rachel M Tribe, and Mark R Johnson. London, England, United Kingdom.

S-031 **Both OTR Antagonists, Atosiban and Nolasiban, Inhibits PGE_2/$PGF_{2\alpha}$-Induced Contractions of Human Pregnant Myometrium *In Vitro*.**
Sung Hye Kim, Hauwa Ahmed, Lucia Riaposova, Oliver Pohl, Andre Chollet, Aylin Hanyaloglu, Phillip R Bennett, and Vasso Terzidou. London, United Kingdom; and Geneva, Switzerland.

S-032 **HSPA1A Is Abundantly Expressed in the Myometrium During Late Pregnancy and Labour and Regulated by Uterine Distension.**
Mckenzie F Russell, Ewa I Miskiewicz, and Daniel J MacPhee. Saskatoon, SK, Canada.

S-033 **Investigation of Human Myometrial Transcriptome and Progesterone Receptor Cistrome.**
San-Pin Wu, Matthew L Anderson, Tianyuan Wang, Xilong Li, and Francesco J DeMayo. Research Triangle Park, NC, USA; and Houston, TX, USA.

S-034 **Inhibition of GSNOR in the Management of Preterm Labor.**
Scott D Barnett, and Iain LO Buxton. Reno, NV, USA.

CLINICAL PERINATOLOGY

S-035 **Predictors of Neonatal Sepsis and Death Among Deliveries at <32 Weeks of Gestation.**
Anna Palatnik, Lilly Y Liu, Andy Lee, William A Grobman, and Lynn M Yee. Milwaukee, WI, USA; and Chicago, IL, USA.

Saturday, March 18, 2017 - Poster Session III - Bonnet Creek I – IX

S-036 **Implementation of Delayed Cord Clamping in Premature Neonates.**
Phoebe L Bacon, Clark T Johnson, Karen Frank, Johana Diaz, Janine E Bullard, and Angie C Jelin. Baltimore, MD, USA.

S-037 **Acute Fatty Liver of Pregnancy and Risk of Preterm Birth.**
Megan E Foeller, Jonathon Mayo, Amanda Yeaton-Massey, Anna Girsen, Samantha Do, Amen Ness, Gary Shaw, Yasser El-Sayed, and Maurice Druzin. Stanford, CA, USA.

S-038 **Improving Safety on Labor and Delivery Through Team Huddles and Teamwork Training.**
Elizabeth A Blumenthal, Myung Shin Sim, and Leslie Carranza. Los Angeles, CA, USA; and Sylmar, CA, USA.

S-039 **Low and Slow: Duration of Antenatal Steroid Exposure Determines Functional Maturation of the Preterm Ovine Lung.**
Matthew Kemp, Haruo Usuda, Peter Eddershaw, and Alan Jobe. Perth, WA, Australia; Stevenage, Herts, United Kingdom; and Cincinnati, OH, USA.

S-040 **Attitudes of Pregnant Women Towards Intrapartum Acupuncture Provision in a UK Maternity Unit.**
Melissa Rowe, and David J Carr. London, United Kingdom; and New York, NY, USA.

S-041 **Maternal and Neonatal Outcomes in Triplet Gestations by Trial of Labor Versus Planned Cesarean Delivery.**
Danielle A Peress, Alan M Peaceman, and Lynn M Yee. Philadelphia, PA, USA; and Chicago, IL, USA.

S-042 **Umbilical Cord Arterial pH and Birth Order in Twins: A Comparison Between Monochorionic and Dichorionic Pregnancies.**
Amelia S McLennan, Audrey A Merriam, Clifton O Brock, Russell S Miller, and Cynthia Gyamfi-Bannerman. New York, NY, USA.

S-043 **Assisted Reproductive Technology and Preterm Delivery in Twin Gestations.**
Clifton O Brock, and Cynthia Gyamfi-Bannerman. New York, NY, USA.

S-044 **Delivery Outcomes and Prostaglandin Use for Induction of Labor in Growth Restricted Fetuses Based on Umbilical Artery Velocimetry.**
Drew D Benac, Rebecca Pollack, Matthew Finneran, and William Anderson. Charlotte, NC, USA.

S-045 **A Human Clinically-Relevant Dose of Betamethasone Compared with Dexamethasone Has More Potent Direct Adverse Side-Effects on the Structure and Function of the Fetal Heart.**
KL Skeffington, FG Conlon, Y Niu, NEWD Teulings, SG Ford, KJ Botting, JB Derks, and DA Giussani. Cambridge, Cambridgeshire, United Kingdom; and , The Netherlands.

S-046 **Obesity and Periodontal Diseases In Pregnancy: miRNome in Saliva.**
C Mandò, S Abati, GM Anelli, L Dioni, C Novielli, C Favero, L Cantone, M Cardellicchio, I Cetin, and V Bollati. Milan, MI, Italy.

S-047 **Placental Lipid Metabolism in Obese Women with Fetal Macrosomia.**
Haijun Gao, Jia Chen, and Chandra Yallampalli. Houston, TX, USA.

S-048 **Abnormal MCA Dopplers in Diabetic Patients and the Association with Stillbirth.**
Allison Shannon, Sarah Crimmins, Jerome Kopelman, Chris Harman, and Ozhan Turan. Baltimore, MD, USA.

S-049 **Adrenomedullin Blockade Restores Expressions of Lipid Homeostasis Enzymes in Adipose Tissue from Gestational Diabetic Women.**
Yuanlin Dong, Ancizar Betancourt, Michael Belfort, and Chandra Yallampalli. Houston, TX, USA.

S-050 **Identifying Fetal Growth Disorders Using Ultrasound in Women with Diabetes.**
Annie M Dude, and Lynn M Yee. Chicago, IL, USA.

S-051 **Perinatal Outcomes of Twin Gestations with and without Gestational Diabetes Mellitus.**
Lynn M Yee, Aaron B Caughey, William A Grobman, and Yvonne W Cheng. Chicago, IL, USA; Portland, OR, USA; and San Francisco, CA, USA.

S-052 **Periconceptional Maternal Dietary Patterns Are Associated with Embryonic Growth: The Rotterdam Periconception Cohort.**
Melek Rousian, Francesca Parisi, Anton H Koning, Sten Willemsen, Irene Cetin, Eric A Steegers, and Régine P Steegers-Theunissen. Rotterdam, Zuid-Holland, Netherlands; and Milano, Italy.

S-053 **Pregestational Type 2 Diabetes Mellitus Induces Cardiac Hypertrophy in the Murine Embryo Through Cardiac Remodeling and Fibrosis.**
Penghua Yang, Xi Chen, E Albert Reece, and Peixin Yang. Baltimore, MD, USA.

S-054 **Unscheduled Cesarean Section: Interval to Delivery.**
Corrie P Anderson, Neil S Seligman, Lisa Gray, Loralei L Thornburg, and Richard Wissler. Rochester, NY, USA.

S-055 **Recurrent Intrauterine Growth Restriction (rIUGR): Is the Placenta Pathology the Key to the Conundrum?**
Keren Rotshenker-Olshinka, Sveta Terlezky, Letizia Shreiber, Rivka Farkash, Arnon Samueloff, and Sorina Grisaru Granovsky. Jerusalem, Israel; and TA, Israel.

Saturday, March 18, 2017 - Poster Session III - Bonnet Creek I – IX

S-056 **Interventions for Postpartum Hemorrhage Requiring Transfusion.**
Audrey A Merriam, Cande V Ananth, Yongmei Huang, Jason D Wright, and Alexander M Friedman. New York, NY, USA.

S-057 **Neonatal Outcomes of Newborns Exposed to SSRI During Pregnancy: A Pharmacokinetic and Pharmacogenetic Analysis.**
Silvia Corti, Paola Pileri, Chiara Mandò, Laura Pogliani, Emilio Clementi, Dario Cattaneo, and Irene Cetin. Milan, Italy.

S-058 **Recurrence of Extreme Serum Analytes in Subsequent Pregnancies and Obstetrical Outcomes.**
Shelly Soni, David Krantz, Meir Greenberg, Nidhi Vohra, and Burton Rochelson. Manhasset, NY, USA; and Melville, NY, USA.

S-059 **The Effect of Uterine Balloon Tamponade on the Cases of Postpartum Hemorrhage.**
Gen Ishikawa, Hanae Kawabata, Akihito Nakai, and Toshiyuki Takeshita. Bunkyo-ku, Tokyo, Japan.

S-060 **Universal MRSA Screening: Incidence in an Obstetric Population at an Academic Tertiary Care Center.**
Ann Lal, Thaddeus P Waters, and Jean R Goodman. Maywood, IL, USA.

S-061 **Risk Factors for Primary Cesarean in Women with Premature Rupture of Membranes.**
Sasha M Davidson, Sadia Sahabi, Catherine Wu, and Kafui A Demasio. Bronx, NY, USA.

S-062 **Re-Engineering the Interpretation of Electronic Fetal Monitoring (EFM): Using the Fetal Reserve Index (FRI) to Anticipate the Need for Emergent Operative Delivery (EOD).**
Robert D Eden, Mark I Evans, Shara M Evans, and Barry S Schifrin. New York, NY, USA.

S-063 **Preterm Birth and Arsenic Levels: A Pilot Study.**
Jasmine D Johnson, Shannon Robinson, Lisa Smeester, Rebecca Fry, and Neeta Vora. Chapel Hill, NC, USA.

S-064 **Evaluating Hospitals' Comparative Effectiveness in Managing Shoulder Dystocia Using Data Envelopment Analysis.**
Chester Chambers, Maqbool Dada, and Edith D Gurewitsch Allen. Baltimore, MD, USA.

S-065 **Disparities in Trial of Labor Among Women with Twin Gestations in the United States.**
Lynn M Yee, Aaron B Caughey, William A Grobman, and Yvonne W Cheng. Chicago, IL, USA; Portland, OR, USA; and San Francisco, CA, USA.

S-066 **Serum Procalcitonin Levels as a Marker for Discontinuation of Antibiotics in Acute Pyelonephritis in Pregnancy.**
Manuel E Rivera-Alsina, Jessica Prussa, Gabbrielle C Rivera, Diana M Martinez, and Christine C Rivera. Dallas, TX, USA; Boston, MA, USA; and San Juan, Puerto Rico, United States Minor Outlying Islands.

S-067 **Reverse Syphilis Testing Compared to Traditional Testing in Pregnancy for Diagnosis of Syphilis in Pregnancy in High Burden Regions: A Cost Effectiveness and Decision Analysis.**
Ahizechukwu C Eke, Israel T Agaku, Uzoamaka A Eke, and Jeanne Sheffield. Baltimore, MD, USA; Atlanta, GA, USA; and Detroit, MI, USA.

S-068 **Antepartum Rubella Infection and Pregnancy Outcomes.**
Courtney Olson-Chen, Dongmei Li, Timothy Dye, and Dzhamala Gilmandyar. Rochester, NY, USA.

DEVELOPMENTAL PROGRAMMING

S-069 **Fetal Nicotine Exposure Increases Brain Hypoxic-Ischemic Injury in Neonatal Rats: The Role of miRNA-210.**
Lei Wang, Jun Ke, Yong Li, Qinyi Ma, Chiranjib Dasgupta, Xiaohui Huang, Lubo Zhang, and DaLiao Xiao. Loma Linda, CA, USA.

S-070 **Life-Course Differences in Liver Transcriptome Programming in Offspring of Obese (MO) Rats.**
Consuelo Lomas, Claudia J Bautista, Luis A Reyes-Castro, Guadalupe L Rodríguez-González, Laura Cox, Peter W Nathanielsz, and Elena Zambrano. Mexico City, Mexico; San Antonio, TX, USA; and Laramie, WY, USA.

S-071 **Maternal Obesity (MO) Accelerates Male (M) Offspring (F1) Aging in Proteasome, Proteolysis and Autophagy Signaling Pathways.**
Consuelo Lomas, Luis A Reyes-Castro, Lilia Vargas, Carlos A Ibañez-Chavez, Laura A Cox, Peter W Nathanielsz, and Elena Zambrano. Mexico City, Mexico; San Antonio, TX, USA; and Laramie, WY, USA.

S-072 **Gestational Diabetes Programs Offspring Adiposity.**
Omonseigho Talton, Keenan Bates, Kylie Hohensee, and Laura Schulz. Columbia, MS, USA.

S-073 **Antenatal Steroids Do Not Affect Splicing or DNA Methylation of the Glucocorticoid Receptor Gene in Cord Blood T-Cells.**
J Carpenter, K Jablonski, J Koncinsky, M Varner, and L Joss-Moore. Salt Lake City, UT, USA; and Washington, DC, USA.

S-074 **Simulated Shift Work in the Pregnant Sheep Disrupts Maternal Rhythms and Metabolism.**
Tamara J Varcoe, Kathryn L Gatford, Hong Liu, Timothy R Kuchel, and David J Kennaway. Adelaide, SA, Australia; and Gilles Plains, SA, Australia.

Saturday, March 18, 2017 - Poster Session III - Bonnet Creek I – IX

S-075 **Neonatal Heat-Shock Proteins in Pregnancies Complicated by Gestational Diabetes and Preeclampsia.**
Ana Mrkaic, Barak Rosenn, Ivana Stojanovic, and Samir Tivari. New York, NY, USA; Nis, Serbia; and Newark, NJ, USA.

S-076 **POMC, MC4R and HNF4A Methylation Are Associated with Metabolic Components in Obese Children.**
Eun Jin Kwon, Young Ah You, Hae Soon Kim, Eun Ae Park, Su Jin Cho, and Young Ju Kim. Seoul, Korea.

S-077 **Impaired Ischemia Reperfusion Responses in Adult Male and Female Hearts of Offspring (F1) of Obese Rats.**
Carlos Ibáñez, Francisco Correa, Gabriela Lira-León, Luis A Reyes-Castro, Francisco J Roldan, Alejandro Silva-Palacios, Mabel Buelna, Cecilia Zazueta, Peter W Nathanielsz, and Elena Zambrano. Mexico City, Mexico; Laramie, WY, USA; and San Antonio, TX, USA.

S-078 **Antenatal Glucocorticoids Exposure Induces Left Ventricular Hypertrophy in the Adult Offspring in Sheep.**
Won Joon Seong, Angela G Massmann, Jie Zhang, and Jorge P Figueroa. Winston-Salem, NC, USA.

S-079 **A Potential Mechanism for Developmental Programming of Adult Cardiac Disease: Increased Apical Pericardial Fat (PCF) in 5.7 Year (Yr: Human Equivalent 20 Yr) Old Male but Not Female IUGR Baboon.**
Anderson H Kuo, Cun Li, Peter W Nathanielsz, and Geoffrey D Clarke. San Antonio, TX, USA; and Laramie, WY, USA.

S-080 **Developmental Programming: Ectopic Lipid Accumulation in Liver and Muscle Likely Contributes to Insulin Resistance in Prenatal Testosterone-Treated Female Sheep.**
Vasantha Padmanabhan, and Muraly Puttabyatappa. Ann Arbor, MI, USA.

S-081 **Rescue of the Developmental Programming of Cardiovascular Dysfunction with the Mitochondria-Targeted Antioxidant MitoQ.**
AM Spiroski, Y Niu, KL Skeffington, MP Murphy, and DA Giussani. Cambridge, United Kingdom.

S-082 **Embryonic Development Is Associated with Periconceptional Maternal One-Carbon Metabolism and Fetal Size: The Rotterdam Periconception Cohort.**
Francesca Parisi, Melek Rousian, Anton K Koning, Sten P Willemsen, Eric A Steegers, and Règine P Steegers-Theunissen. Rotterdam, Netherlands.

S-083 **Characterisation and Identification of the Placental Androgen Receptor Isoforms and Its Relationship to Fetal Growth.**
Vicki L Clifton, Ashley Meakin, and Zarqa Saif. Brisbane, QLD, Australia.

S-084 **Maternal Obesity (MO) Up-Regulates 11β-Hydroxysteroid Dehydrogenase Type 1(11βHSD1) and the Mineralocorticoid Receptor (MR) in the Late Gestation Baboon Fetal Frontal Cortex (FC).**
Shanshan Yang, Diana Castro-Rodriguez, Peter W Nathanielsz, and Cun Li. Harbin, Heilongjiang, China; San Antonio, TX, USA; and Laramie, WY, USA.

S-085 **Behavioral Changes in Adult Male Baboons Exposed to Synthetic Glucocorticoids (sGC) in Fetal Life Indicate Increased Stress and Accelerated Aging.**
Hillary F Huber, Thad Q Bartlett, Cun Li, Susan L Jenkins, Kenneth G Gerow, and Peter W Nathanielsz. Laramie, WY, USA; and San Antonio, TX, USA.

S-086 **Offspring Sex and Maternal Diet Impact the Effects of Maternal Obesity on Offspring Neurobehavior.**
Larissa H Mattei, Rachel Zeuner, Ingy Khattaby, Diana W Bianchi, and Andrea G Edlow. Boston, MA, USA; and Queens, NY, USA.

S-087 **Maternal Protein Restriction (MPR) in Pregnancy and/or Lactation Impacts Sperm Aging without Affecting Fertility in Male Rat Offspring (F1).**
Guadalupe L Rodríguez-González, Claudia C Vega, Luis A Reyes-Castro, Lourdes Boeck, Carlos Ibáñez, Peter W Nathanielsz, Fernando Larrea, and Elena Zambrano. Mexico City, Mexico; Laramie, WY, USA; and San Antonio, TX, USA.

EPIDEMIOLOGY

S-088 **Effect of Very Advanced Maternal Age on Early Neonatal Outcomes After Assisted Reproductive Technology.**
Amir Shamshirsaz, Amirhossein Moaddab, Haleh Sangi-Haghpeykar, Sara Arian, Susan Ramin, Zhoobin Heidari-Bateni, Hadi Erfani, Karin Fox, Steven Clark, Michael Belfort, Gary Dildy, Laurence McCullough, Frank Chervenak, and Alireza Shamshirsaz. Houston, TX, USA; and New York, NY, USA.

S-089 **Ten-Year Trend in Hypertensive Disorders in Pregnancy in the United States.**
Amir Shamshirsaz, Amirhossein Moaddab, Alireza Shamshirsaz, Christina Davidson, Gary Dildy, Michael Belfort, and Steven Clark. Houston, TX, USA.

S-090 **Effect of Very Advanced Maternal Age on Maternal Outcomes After Assisted Reproductive Technology.**
Amir Shamshirsaz, Amirhossein Moaddab, Haleh Sangi-Haghpeykar, Sara Arian, Hadi Erfani, Zhoobin Heidari-Bateni, Susan Ramin, Karin Fox, Frank Chervenak, Laurence McCullough, Steven Clark, Michael Belfort, Gary Dildy, and Alireza Shamshirsaz. Houston, TX, USA; and New York, NY, USA.

Saturday, March 18, 2017 - Poster Session III - Bonnet Creek I – IX

FETUS

S-091 **Use of a Novel Decision Aid for Prenatal Aneuploidy Screening: A Pilot Study.**
Laura Carlson, Sally Harris, Emily Hardisty, and Neeta L Vora. Chapel Hill, NC, USA.

S-092 **Cell-Free Fetal DNA Screening: How It Has Affected the Choices of Women with Advanced Maternal Age.**
Zainab Al-Ibraheemi, Barak Rosenn, Natalie Porat, Dyese Taylor, Heather Fisher, and Meredith Kalberer. New York, NY, USA.

S-093 **Umbilical Vein Flow Calculation Methods: Correlation with Each Other and Umbilical Artery Pulsatility Index.**
Diane Gumina, Nicholas Behrendt, Mary Pinter, Allison Gillan, Henry Galan, and John Hobbins. Aurora, CO, USA.

S-094 **Sex Specific Weight Elevation in Adult Progeny of Mothers with Pregestational Diabetes.**
Rolanda L Lister, Francine Hughes, Etoi Garrison, and Bin Zhou. Nashville, TN, USA; New York, NY, USA; and Bronx, NY, USA.

S-095 **Effects of Pregnancy and Obesity on Vitamin D (D) Status and Metabolism in a Baboon Model.**
Eugenia Mata-Greenwood, Hillary F Huber, Cun Li, and Peter W Nathanielsz. Loma Linda, CA, USA; and Laramie, WY, USA.

S-096 **Targeting Interventions to Prevent Adult Consequences of Impaired Fetal Growth.**
Carol A Wang, Wei Ang, Scott White, Melanie K White, David Mackey, Stephen J Lye, and Craig E Pennell. Perth, Western Australia, Australia; and Toronto, ON, Canada.

S-097 **Risk Factors for Neonatal Hypoxic-Ischemic Encephalopathy of Unknown Origin.**
Christopher Novak, Hattan Arif, and Ernest Graham. Baltimore, MD, USA.

S-098 **Assessment of the Global Sphericity Index and Cardiac Area as Indirect Indicators of Cardiac Dysfunction in Fetal Growth Restriction.**
Michael Zaretsky, Greggory DeVore, Diane Gumina, Mary Pinter, and John Hobbins. Aurora, CO, USA; and Los Angeles, CA, USA.

S-099 **Impact of Late-Onset Hypoxemia During the Final Third of Gestation on Adrenocortical Expression of Steroidogenic Genes in the Ovine Fetus.**
A Martin, D Myers, BJ Allison, KL Brain, DA Giussani, and C Ducsay. Oklahoma City, OK, USA; Cambridge, United Kingdom; and Loma Linda, CA, USA.

S-100 **Use of Doppler Ultrasound (US) in Evaluating Uterine and Umbilical Artery Blood Flow in the Hypoxic (HPX) Pregnant Guinea Pig.**
Shifa Turan, Graham W Aberdeen, and Loren P Thompson. Baltimore, MD, USA.

S-101 **Variability of MRI Based Volumetric Measurements of Fetal Brain.**
Anat Lavie, Maya Dvir, Daphna Link, Dafna Ben Bashat, Gustavo Malinger, Liat Ben-Sira, and Ariel Many. Tel Aviv, Israel.

S-102 **Prophylactic Maternal Creatine Supplementation in a NHP Model of Birth Asphyxia.**
Meredith A Kelleher, Stacey Ellery, David W Walker, Hayley Dickinson, and Peta L Grigsby. Beaverton, OR, USA; and Melbourne, VIC, Australia.

S-103 **An Innovative Fetoscopic Technique for Closure of Large Non-Cystic Meningomyelocele/ Myeloschisis Lesions.**
Michael A Belfort, William E Whitehead, Alireza A Shamshirsaz, Olutoyin A Olutoye, Zhoobin Bateni, Sundeep Keswani, Timothy Lee, Jimmy Espinoza, Oluyinka O Olutoye, Magdalena Sanz Cortes, and Darrell L Cass. Houston, TX, USA.

GLOBAL HEALTH

S-104 **Time Series Analysis of Electroencephalogram Signal Using Simple Device for Getting EEG and Fluctuation of Hormone Levels with a Menstrual Cycle.**
Eri Okuzumi, and Yasue Mitsukura. 3-14-1, Hiyoshi, Kohokuku, Yokohama, Kanagawa, Japan.

GYNECOLOGIC ONCOLOGY

S-105 **Regulation of Innate Lymphoid Cells by Human Papillomavirus' Oncoproteins.**
Laura F Núñez Castro, Damián O Muzzio, Kristina MT Hilz, Christine Lamb, and Marek Zygmunt. Greifswald, Mecklenburg-Vorpommern, Germany.

S-106 **Identification of Somatic Genetic Alterations in Ovarian Clear Cell Carcinomas with Next Generation Sequencing.**
Yusuke Shibuya, Sakae Saito, Kaname Kojima, Bin Li, Hideki Tokunaga, Masao Nagasaki, Jun Yasuda, and Nobuo Yaegashi. Sendai, Miyagi, Japan.

S-107 **Bartholin's Gland Carcinoma, a Retrospective Review.**
Gary Altwerger, Samantha Margulies, Gulden Menderes, Jon Black, Babak Litkouhi, Dan-Arin Silasi, Masoud Azodi, Alessandro Santin, Peter E Schwartz, and Elena Ratner. New Haven, CT, USA.

S-108 **The Impact of Tumor Fragments in the Lumen of Fallopian Tubes on Recurrence and Survival in Type I and Type II Endometrial Cancers.**
Jonathan D Black, Rachel Passarelli, Margaret Whicker, Benjamin Albright, Stefan Gysler, Lingen Lu, Gulden Menderes, Gary Altwerger, Babak Litkouhi, Elena Ratner, Dan-Arin Silasi, Masoud Azodi, Alessandro Santin, and Schwartz Peter. New Haven, CT, USA; and Philadelphia, PA, USA.

Saturday, March 18, 2017 - Poster Session III - Bonnet Creek I – IX

ENDOMETRIOSIS, FIBROIDS, AND GYNECOLOGY

S-109 **New Medical Therapeutics for Ectopic Pregnancy.**
Roxanne Hastie, Natalie Hannan, Louie Ye, Tu'uhevaha J Kaitu'u-Lino, Stephen Tong, and The University of Melbourne. Heidelberg, VIC, Australia.

S-110 **Uterine Gene Expression in a Murine Model of Menstruation Largely Mimics Human Endometrial Gene Expression in Women with Abnormal Uterine Bleeding.**
Jörg Müller, Ralf Lesche, Andrea Wagenfeld, Alison Murray, Moira Nicol, Lucy Whitaker, Jackie Maybin, Thomas M Zollner, and Hilary OD Critchley. Berlin, Germany; and Edinburgh, United Kingdom.

S-111 **ID4 Allelic Variant Is Associated with Endometriosis and May Affect Mesothelial Epithelial to Mesenchymal Transition.**
Colin Bergstrom, and Terry K Morgan. Portland, OR, USA.

S-112 **PreImplantation Factor* in Endometriosis: A Potential Role in Inducing Immune Privilege for Ectopic Endometrium.**
Martin Mueller, Marco Sbracia, Brett McKinnon, Fabio Scarpellini, Daniela Marconi, Gabriele Rossi, Cedric Simmilion, Michael Mueller, and Eytan R Barnea. Rome, Italy; Bern, Switzerland; Cherry Hill, NJ, USA; and New Haven, CT, USA.

S-113 **Pro-Inflammatory Effects of IL-33 In Endometriosis.**
Jessica E Miller, Stephany P Monsanto, SooHyn Ahn, Kasra Khalaj, Bruce A Lessey, Steven Young, Asgi T Fazleabas, and Chandrakant Tayade. Kingston, ON, Canada; Greenville, SC, USA; Chapel Hill, NC, USA; and Lansing, MI, USA.

S-114 **Elucidating the Polarization of THP-1 Cells by Interleukin-17A Induced Cytokines from Peritoneal Endometriotic Epithelial Cells.**
Soo Hyun Ahn, Kasra Khalaj, Asgerally T Fazleabas, and Chandrakant Tayade. Kingston, ON, Canada; and East Lansing, MI, USA.

S-115 **The Baboon Model for Investigation of Endometriosis-Associated Pain.**
Arne Vanhie, Stan Kivai, Daniel Chai, Erik Omolo, Galo Mary, Nicholas Kiulia, Atunga Nyachieo, Cleophas Kyama, Jason Mwenda, and Thomas D'Hooghe. Leuven, Vlaams-Brabant, Belgium; and Karen, Nairobi, Kenya.

S-116 **Treatment with Icon, Results in Regression of Red Lesions in a Non-Human Primate Model of Endometriosis.**
Graciela Krikun, Demetra Hufnagel, Laura G Goetz, Zhiwei Hu, Atunga Nyachieo, Thomas D'Hoogie, Antoni Duleba, Hugh S Taylor, and Charles J Lockwood. New Haven, CT, USA; Columbus, OH, USA; Nairobi, Kenya; Leuven, Belgium; La Jolla, CA, USA; and Tampa, FL, USA.

S-117 **External Technical Confirmation of Panels of Plasma Biomarkers for Endometriosis.**
O Dorien, Yousef El Aalamat, Arne Vanhie, Daniëlle Peterse, Bart De Moor, Christel Meuleman, Etienne Waelkens, Amelie Fassbender, and Thomas D'Hooghe. Leuven, Belgium.

S-118 **DNA Methylation Profiling in Endometriosis – RRBS Based Analyses in LCM Separated Endometrial Samples.**
Maik Obendorf, Ralf Lesche, Eva Simon, Joern Toedling, Kati Hasenbein, Anne Kroker, Arndt Schmitz, Rene Wenzl, Lorenz Kuessel, and Thomas M Zollner. Berlin, Germany; and Vienna, Austria.

S-119 **Dysregulated Lipid Mediator Profile in the Peritoneal Fluid of Endometriosis Patients.**
Matthias Keck, Thomas M Zollner, and Frank Sacher. Berlin, Germany.

S-120 **Endometriosis and Ovarian Cancer: Shared Genetic Risk and Common Mechanisms.**
Grant W Montgomery, Jenny N Fung, Sarah J Holdsworth-Carson, Jane E Girling, Juliet D Franch, Stacey L Edwards, Joseph E Powell, and Peter AW Rogers. Brisbane, QLD, Australia; and Melbourne, VIC, Australia.

S-121 **MRI Assessment Is Not Predictive of Patient Symptoms from Uterine Fibroids.**
Alessandra J Ainsworth, Shannon K Laughlin-Tommaso, Lisa E Vaughan, Amy L Weaver, Elizabeth A Stewart, and Gina K Hesley. Rochester, MN, USA.

S-122 **Clinical Limitations of the International Federation of Gynecology and Obstetrics (FIGO) Classification of Uterine Fibroids.**
Shannon K Laughlin-Tommaso, Elizabeth A Stewart, Matthew R Hopkins, Kathleen R Brandt, and Gina K Hesley. Rochester, MN, USA.

S-123 **Silibinin Inhibits Progesterone Induced Rankl Expression, Cell Proliferation and Extracellular Matrix Deposition in Human Uterine Leiomyoma Cells.**
Deborah E Ikhena, Shimeng Liu, Stacy Kujawa, Serdar Bulun, and Ping E Yin. Chicago, IL, USA.

S-124 **African Genetic Ancestry and Body Mass Index Interact to Modify Risk for Uterine Fibroids.**
Ayush Giri, Todd Edwards, Katherine Hartmann, Melissa Wellons, Pamela Schreiner, and Digna Velez Edwards. Nashville, TN, USA; Nasvhille, TN, USA; and Minneapolis, MN, USA.

S-125 **The Effect of Local Estrogen Therapy on Extracellular Matrix Biogenesis and Remodeling in Vaginal Tissue of Postmenopausal Women with Severe Pelvic Organ Prolapse.**
Tanya Tyagi, May Alarab, Harold Drutz, Stephen Lye, and Oksana Shynlova. Toronto, ON, Canada.

Saturday, March 18, 2017 - Poster Session III - Bonnet Creek I – IX

S-126 **Koch's Experimental Postulate Applied to Bacterial Vaginosis: Identification of a Single Organism as Sufficient to Elicit Clinical Features and Health Complications Associated with BV.**
Nicole Gilbert, and Amanda Lewis. St. Louis, MO, USA.

MATERNAL BIOLOGY AND HEALTH

S-127 **Longitudinal Lifestyle Monitoring in "Maternity Log Study" to Predict Preterm Birth.**
Daisuke Ochi, Takafumi Yamauchi, Yoshiki Tsunemoto, Yuki Harada, Riu Yamashita, Takahiro Mimori, Maiko Wagata, Osamu Tanabe, Hirohito Metoki, Nobuo Yaegashi, Maternity Log Project Team, Satoshi Hiyama, Masao Nagasaki, and Junichi Sugawara. Yokosuka, Kanagawa, Japan; and Sendai, Miyagi, Japan.

S-128 **Inhibition of DNA Methylation Rescues Chronic Hypoxia-Mediated Decrease in BK_{Ca} Channel Activity and Increase in Myogenic Contractility in Uterine Arteries of Pregnant Sheep.**
Xiang-Qun Hu, Chiranjib Dasgupta, Daliao Xiao, Xiaohui Huang, Shumei Yang, and Lubo Zhang. Loma Linda, CA, USA; and San Bernardino, CA, USA.

S-129 **Inhibition of DNA Demethylation Blocks Pregnancy-Mediated Increase in Large Conductance Ca^{2+}-Activated K^+ Channel Activity in Ovine Uterine Arteries.**
Xiang-Qun Hu, Limin Han, and Lubo Zhang. Loma Linda, CA, USA.

S-130 **Validation of Microparticle Proteomics as a Means to Stratify the Risk of Spontaneous Preterm Birth.**
David Cantonwine, Zhen Zhang, Kevin Rosenblatt, Brian Brohman, Robert Doss, and Thomas McElrath. Boston, MA, USA; Baltimore, MD, USA; Houston, TX, USA; and Louisville, KY, USA.

S-131 **Does Gestational Diabetes Increase the Risk of Pregnancy Induced Hypertension in Twin Gestations?**
Mirella Mourad, Gloria Too, Cynthia Gyamfi-Bannerman, and Noelia Zork. New York, NY, USA.

S-132 **Relationship of Fat Distribution to Pre Pregnancy Uterine Artery Hemodynamics and Fetal Growth.**
Kylie Cooper, Carole McBride, Gary Badger, and Ira Bernstein. Burlington, VT, USA.

S-133 **Greater Adenosine Monophosphate Kinase (AMPK) Activation During High-Altitude (HA) Pregnancy.**
Colleen G Julian, Haemin Park, Gabriel Wolfson, and Lorna G Moore. Denver, CO, USA.

S-134 **Soluble Fms-Like Tyrosine Kinase-1 (Sflt-1) Adversely Impacts CGRP Family Peptide System in Omental Artery Smooth Muscle Cells.**
Madhu Chauhan, Uma Yallampalli, Yuanlin Dong, and Chandra Yallampalli. Houston, TX, USA.

S-135 **Association of Interpregnancy Interval with Subsequent Perinatal Outcomes Following Pregnancies Complicated by Gestational Diabetes.**
Ashley N Battarbee, and Lynn M Yee. Chapel Hill, NC, USA; and Chicago, IL, USA.

PLACENTA

S-136 **Sphingosine 1-Phosphate Receptor Characterization in Term Diabetic and Normal Human Placentas.**
Luckey C Reed, Diana Villazana-Kretzer, Robert Walton, Sarah Estrada, Peter G Napolitano, and Nicholas Ieronimakis. Tacoma, WA, USA.

S-137 **Differential Effects of TNF-α on the Production of Prostaglandins and Prostamides by Human Amnion Explants.**
Hassendrini N Peiris, Kanchan Vaswani, Sarah Reed, and Murray D Mitchell. Brisbane, QLD, Australia.

S-138 **The Effect of Melatonin on Antioxidant Enzymes in Trophoblasts of Lean and Obese Women.**
Kayla E Ireland, and Leslie Myatt. San Antonio, TX, USA.

S-139 **First Trimester Placenta Transcriptome and Variation Among the Sexes.**
Tania L Gonzalez, Alexander F Koeppel, Bora Lee, Tianyanxin Sun, Erica Wang, Lindsay Kroener, Charles R Farber, Stephen S Rich, Yii-Der Ida Chen, Jerome I Rotter, Stephen D Turner, John Williams III, and Margareta D Pisarska. Los Angeles, CA, USA; Charlottesville, VA, USA; and Torrance, CA, USA.

S-140 **Time Course Analysis of RNA Quality From Human Placenta and Decidua Biospecimens Preserved By RNA*later* or Flash Freezing.**
Nicole M Martin, Katherine M Cooke, Caitlin C Radford, Lauren E Perley, Michelle Silasi, and Clare A Flannery. New Haven, CT, USA.

S-141 **Role of High-Mobility Group A1 Protein in Preeclampsia.**
Yuka Uchikura, Keiichi Matsubara, Yuko Matsubara, and Takashi Sugiyama. Toon, Ehime, Japan.

S-142 **Systems Biology Identifies Key Molecular Networks and Hub Factors in Placental Pathways of Preeclampsia.**
Nandor Than, Roberto Romero, Adi Tarca, Katalin Kekesi, Yi Xu, Kata Juhasz, Hamutal Meiri, Sonia Hassan, Tinnakorn Chaiworapongsa, Offer Erez, Manuel Krispin, Graham Burton, Chong Kim, Gabor Juhasz, and Zoltan Papp. Detroit, MI, USA; Budapest, Hungary; Tel Aviv, Israel; Irvine, CA, USA; and Cambridge, United Kingdom.

Saturday, March 18, 2017 - Poster Session III - Bonnet Creek I – IX

S-143 **VEGFR-1 Is the Predominant Vascular Endothelial Growth Factor Receptor Mediating Human Fetoplacental Endothelial Cell Angiogenesis.**
Shuhan Ji, Hong Xin, and Emily J Su. Aurora, CO, USA.

S-144 **Preconceptional and First-Trimester Utero(Placental) Vascularization Using Three-Dimensional Power Doppler Virtual Reality Ultrasound.**
Igna F Reijnders, Annemarie G Mulders, Wendy P Koster, Anton H Koning, Régine P Steegers-Theunissen, and Eric A Steegers. Rotterdam, ZH, Netherlands.

S-145 **Mechanisms Implicated in the Development of Acute Atherosis: A Role for Intravascular Inflammation and Lipid Metabolic Disturbances.**
Yeon Mee Kim, Roberto Romero, Chong Jai Kim, Piya Chaemsaithong, Yi Xu, Nardhy Gomez-Lopez, Gaurav Bhatti, Bo Hyun Yoon, Offer Erez, Sonia S Hassan, and Young-Ran Yoon. Busan, Republic of Korea; Daegu, Republic of Korea; Detroit, MI, USA; Ann Arbor, MI, USA; East Lansing, MI, USA; Seoul, Republic of Korea; and Shatin, Hong Kong.

S-146 **Increased Lipid Deposition in the Spiral Arteries and Villous Trophoblast of Patients with Acute Atherosis: A Potential Explanation for the Increased Risk of Subsequent Cardiovascular Death of Mothers with Preeclampsia and Preterm Birth.**
Yeon Mee Kim, Roberto Romero, Bomi Kim, Joo-Yeon Kim, Chong Jai Kim, Jung-Sun Kim, Sonia S Hassan, Young-Ran Yoon, and Offer Erez. Busan, Republic of Korea; Daegu, Republic of Korea; Detroit, MI, USA; Ann Arbor, MI, USA; East Lansing, MI, USA; and Seoul, Republic of Korea.

S-147 **Alterations in Metabolomic Profiles of Human Placental Tissue Among Male and Female Fetuses.**
Anushka M Chelliah, Jacquelyn Walejko, Cheyenna Espinoza, Gustavo Vilchez, Arthur Edison, and Anthony R Gregg. Gainesville, FL, USA; and Athens, GA, USA.

S-148 **Placental Fatty Acid Translocase (FAT/CD36) and Tranport Protein-4 (FATP-4) Are Less Expressed in the Human Preterm Than Term Placenta.**
AnnieBelle J Sassine, Gavin R Sooranna, Natasha Singh, Bronwen R Herbert, Suren R Sooranna, Michael A Crawford, and Mark R Johnson. London, United Kingdom.

S-149 **Metabolomic Differences Between Maternal and Fetal Surfaces of Human Placenta.**
Anushka Chelliah, Jacquelyn Walejko, Alexa Avecilla, Maureen Keller-Wood, Arthur Edison, and Anthony R Gregg. Gainesville, FL, USA; and Athens, GA, USA.

S-150 **Phthalate Exposure Alters First Trimester Placental Gene Methylation in Women.**
N Grindler, I Yang, L Vanderlinden, K Rajendiran, K Kannan, D Schwartz, S Teal, A Polotsky, T Powell, and T Jansson. , CO, USA; , NY, USA; Albany, NY, USA; and Aurora, CO, USA.

S-151 **Unraveling the Obesity Epidemic: Is the Early and Persistent Disruption of Placental Vascularity Playing a Major Role?**
Kathleen O'Neill, Tami Stuart, David Condon, Kyoung Won, and Rebecca Simmons. Philadelphia, PA, USA.

S-152 **Studies of Lipid Transport and Metabolism in Primary Human Trophoblast Cells Using ^{13}C-Fatty Acids.**
Veronique Ferchaud-Roucher, Thomas Jansson, and Theresa L Powell. Denver, CO, USA.

S-153 **Folate Deficiency Alters Expression of Placental MicroRNAs In Vivo and In Vitro.**
Bernadette C Baker, Susan L Greenwood, Alexander EP Heazell, Karen Forbes, and Rebecca L Jones. Manchester, United Kingdom; and Leeds, United Kingdom.

S-154 **A Novel Marker of Neonatal Respiratory Disorders: Umbilical 25-Hydroxyvitamin D (25(OH)D).**
Yumiko Ito, Hiroyuki Tsuda, Kenji Imai, Tomoko Nakano, Tomomi Kotani, and Fumitaka Kikkawa. Nagoya, Aichi, Japan.

S-155 **Can the Anti-Inflammatory Effect of Progesterone Be Enhanced in Stretched IL-1β Stimulated Human Amnion Cells?**
Ananya Das, Suren Sooranna, and Mark R Johnson. London, United Kingdom.

S-156 **Pre-Eclampsia, Fetal Growth Restriction and Pre-Term Birth Are Not Associated with Placental Infection with Eukaryotic Microbiota.**
Susanne Lager, Marcus de Goffau, Sharon J Peacock, Julian Parkhill, D Stephen Charnock-Jones, and Gordon CS Smith. Cambridge, United Kingdom; and Hinxton, United Kingdom.

POPULATION HEALTH

S-157 **Agreement Conform Current Operational Rules and Directives (ACCORD): A Novel Method to Reach Multidisciplinary Agreement.**
Stephanie MP Lemmens, Veronica A Lopes van Balen, Hubertina CJ Scheepers, Raymond G De Vries, Yvonne CM Roselaers, and Marc EA Spaanderman. Maastricht, Limburg, Netherlands; and Eindhoven, Noord-Brabant, Netherlands.

S-158 **Testosterone Supplementation Impairs Glucose Tolerance Mechanism in High Fat but Not Standard Diet Fed Male Rats.**
Amar More, Jay Mishra, and Sathish Kumar. Galveston, TX, USA.

Saturday, March 18, 2017 - Poster Session III - Bonnet Creek I – IX

PREECLAMPSIA

S-159 **Effect of LMWH in the Treatment of Recurrent Spontaneous Abortion on Liver Function.**
Yuan Gao, and Chong Qiao. Shenyang, Liaoning, China.

S-160 **Basal Plate Myometrial Fibers and Hypertensive Disorders of Pregnancy: A Case-Control Study.**
Ann A Wang, Emily S Miller, and Linda Ernst. Chicago, IL, USA.

S-161 **Adipokine Profiles in Preeclampsia and Visceral Fat Distribution.**
S Chandrasekaran, H Hunt, HS Gammill, and EA Schur. Seattle, WA, USA.

S-162 **Characterization of HO1, CPR, and BVR in the Serum and Placenta of Patients with Preeclampsia with Severe Features.**
Warren J Huber III, Paula Krueger, Phinnara Has, James Padbury, Surendra Sharma, and Brenna Hughes. Providence, RI, USA; and Durham, NC, USA.

S-163 **CORM-A1 Treatment Leads to Increased Blood Carboxyhemoglobin in Pregnant CD-1 Mice.**
Karalyn E McRae, Nichole Peterson, and Graeme N Smith. Kingston, ON, Canada.

S-164 **Sphingosine 1-Phosphate and Increased Vasodilation in Pregnancy.**
Joren Manz, and Denise G Hemmings. Edmonton, AB, Canada.

S-165 **Cardiac Remodeling and Preeclampsia: An Overview of Overlapping Circulating miRNAs.**
Chahinda Ghossein-Doha, Zenab Mohseni, Leon de Windt, and Marc EA Spaanderman. Maastricht, Limburg, Netherlands.

S-166 **miRNAs Associated with Small for Gestational Age in Placenta and Maternal Plasma at Term.**
F Gaccioli, S Gong, U Sovio, DS Charnock-Jones, and GCS Smith. Cambridge, United Kingdom.

S-167 **Cardiomyopathy and Preeclampsia: Shared genetics?**
HS Gammill, R Ch, A Brewer, JM Roberts, R Shree, E Tsigas, and K Ward. Seattle, WA, USA; Salt Lake City, UT, USA; Melbourne, FL, USA; and Pittsburgh, PA, USA.

S-168 **Bone Mineral Density Is Decreased in Women Who Develop Preeclampsia.**
Carole A McBride, Erin A Morris, and Ira M Bernstein. Burlington, VT, USA.

S-169 **Performance of the Fetal Medicine Foundation Preeclampsia Screening Test in Nulliparous Women: Results of the TEST Multicenter RCT.**
F Mone, C Mulcahy, P McParland, F Breathnach, J Morrison, S Daly, J Higgins, A Cotter, A Hunter, E Tully, P Dicker, F Malone, and F McAuliffe. Dublin, Ireland.

S-170 **Abnormal Lymphatic Vessel Development and Difference of Lymphangiogenesis-Related Gene Expression Are Associated with Preeclampsia.**
Yun Ji Jung, Yejin Park, Da Hee Yoon, Yong-sun Maeng, Yoo-na Kim, Joon Ho Lee, Young-Han Kim, and Ja-Young Kwon. Seoul, Republic of Korea.

S-171 **Human Myometrial H_2S Biosynthesis Increases to Stimulate Myometrial Mcrovascular Endothelial Cell Angiogenesisduring Pregnancy.**
Honghai Zhang, Jennifer C Chen, Thomas J Lechuga, and Dong-bao Chen. Irvine, CA, USA.

S-172 **Decidual Cell Regulation of CX3CL1: Implications for the Pathogenesis of Preeclampsia.**
Joseph Huang, Chie-Pein Chen, Longzhu Piao, Frederick Schatz, Ozlem Guzeloglu-Kayisli, Umit Kayisli, Li-Yen Shiu, Chun-Yen Huang, Nihan Semerci, and Charles J Lockwood. Tampa, FL, USA; Kaohsiung, Taiwan; Taipei, Taiwan; and Columbus, OH, USA.

S-173 **The Impact of Hyperglycemia and Antiphospholipid Syndrome on Trophoblast Function.**
Daisy Leon-Martinez, Melissa J Mulla, Christina S Han, Lawrence W Chamley, and Vikki M Abrahams. New Haven, CT, USA; Los Angeles, CA, USA; and Auckland, New Zealand.

S-174 **Low Dose VEGF Protects, While IL-6 Amplifies TNFα-Induced Damage to Pregnancy-Derived UAEC Monolayers.**
Amanda C Hankes, Mary A Grummer, and Ian M Bird. Madison, WI, USA.

S-175 **Elevated Complement Deposition and Altered CD46 Isoform Profiles in Preterm Delivery and Preeclampsia Placentas.**
Manu Banadakoppa, Meena Balakrishnan, Kjersti Aagaard, and Chandra Yallampalli. Houston, TX, USA.

S-176 **Is Home Blood Pressure Monitoring in Hypertensive Disorders of Pregnancy Consistent with Clinic Recordings?**
Helen Perry, Elaine Sheehan, Basky Thilaganathan, and Asma Khalil. London, United Kingdom.

REPRODUCTIVE BIOLOGY

S-177 **Oocyte Cryopreservation in Transgender Men: A Case Series.**
Terrence D Lewis, Mae Wu Healyt, Alan H DeCherney, Kimberly Moon, Kate Devine, and Belinda J Yauger. Bethesda, MD, USA; and Rockville, MD, USA.

S-178 **Cyclophosphamide and Its Metabolite Impact on Fertilization Through Mitochondrial Dysfunction.**
Roohi Jeelani, Mili Thakur, Sara Aldaheri, Hamid-Reza Kohan-Ghadr, Robert Morris, and Husam Abu-Soud. Detroit, MI, USA.

Saturday, March 18, 2017 - Poster Session III - Bonnet Creek I – IX

S-179 **ZP1 and CD9 Play a Synergistic Role in Zona Pellucida Formation.**
Nicole Banks, Yangu Zhao, Boris Baibakov, and Jurrien Dean. Bethesda, MD, USA.

S-180 **Galactose and Its Metabolites Interfere with Normal Maturation and Function of Metaphase II Mouse Oocytes.**
Mili Thakur, Roohi Jeelani, Sarah Aldahaheri, Bernard Gonik, and Husam Abu-Soud. Detroit, MI, USA.

S-181 **Glucocorticoids in Assisted Reproduction-Should the Uterine Environment Dictate Use?**
Sarah Moustafa, Edwina Kisanga, Robert N Taylor, and Shannon D Whirledge. New Haven, CT, USA; and Winston-Salem, NC, USA.

S-182 **Vitamin D Does Not Enhance Endometrial Stromal Cell Decidualization in Immortalized Human Endometrial Stromal Cells.**
Kathleen Jaeger, Arin Kettle-Oestreich, Maureen Schulte, Andrew Cusumano, and Kelle Moley. St. Louis, MS, USA.

S-183 **A Novel Approach to Optimizing Implantation in Young Patients Undergoing IVF-ICSI-PGS.**
Stephanie Baum, Moti Gulersen, Avner Hershlag, Christine Mullin, Matthew Cohen, and Tomer Singer. New York, NY, USA; and Manhasset, NY, USA.

S-184 **Organoid Cultures of Human Endometrial Glands: A Model for Investigating Early Pregnancy.**
Margherita Y Turco, Lucy Gardner, Tereza Cindrova-Davies, Jan J Brosens, Hilary O Critchley, Benjamin D Simons, Myriam Hemberger, Bon-Kyoung Koo, Ashley Moffett, and Graham J Burton. Cambridge, Cambridgeshire, United Kingdom; Edinburgh, Scotland, United Kingdom; and Coventry, Warwickshire, United Kingdom.

S-185 **Uterine Natural Killer Cell Subpopulations and Their Proximity to Endometrial Arterioles Are Not Altered in Women with Recurrent Implantation Failure Following In Vitro Fertilisation.**
Premila Paiva, Wan Tinn Teh, Leonie M Cann, Cameron Nowell, Jacqueline Donoghue, Judith N Bulmer, Catharyn Stern, John McBain, and Peter A Rogers. Melbourne, VIC, Australia; East Melbourne, VIC, Australia; Parkville, VIC, Australia; and Newcastle upon Tyne, United Kingdom.

S-186 **Development of an Endometrial Classifier for the Early Detection of Ectopic Pregnancy.**
Jessica Lentscher, Logan Peterson, Tim Clem, Richard O Burney, and Greg E Chow. Tacoma, WA, USA.

S-187 **Analysis of Follicular Growth and Oocyte Maturation in Cultured Murine Ovarian Tissue.**
Tomohiko Murase, Akira Iwase, Phuoc Xuan Nguyen, Umida Ganieva, Ying Qin, Natsuki Nakanishi, Yukiyo Kasahara, Takashi Nagai, Ken Shimizu, Chiharu Ishida, Nao Kato, Satoko Osuka, Tomoko Nakamura, Sachiko Takikawa, Maki Goto, and Fumitaka Kikkawa. Nagoya, Japan.

S-188 **Altered Gene Expression Indicative of Precocious Granulosa Cell Differentiation in the Fragile X Premutation Mouse.**
Xin Chen, Carola Conca Dioguardi, Monique Haynes, and Joshua Johnson. Guangzhou, China; Milan, Italy; New Haven, CT, USA; and Aurora, CO, USA.

S-189 **Mass Spectrometry Analysis of Ovarian Autoimmunity in Spontaneous Primary Ovarian Insufficiency (POI) Patients.**
Satoko Osuka, Akira Iwase, Yukiyo Kasahara, Tomohiko Murase, and Fumitaka Kikkawa. Nagoya, Aichi, Japan.

S-190 **Transcriptomic Analysis of Laser Captured Human Primordial Follicles by RNA Sequencing: Bird's Eye View into Oocyte Aging.**
Shiny Titus, Biran Musul, Sumanta Goswami, and Kutluk Oktay. Valhalla, NY, USA; and New York, NY, USA.

S-191 **ILCs Adopt a Tolerogenic Phenotype During Normal Pregnancies.**
Damián O Muzzio, Jens Ehrhardt, Krüger Diana, and Zygmunt Marek. Greifswald, Mecklenburg-Vorpommern, Germany.

S-192 **Umbilical Cord CD71+ Erythroid Cells from Neonates Born to Women Who Undergo Spontaneous Term or Preterm Labor Do Not Exhibit Immunosuppressive Functions but Enhance T-Cell Activation and Suppress CD8+ Regulatory T Cell Proliferation.**
Derek Miller, Roberto Romero, Ronald Unkel, Yi Xu, Sonia S Hassan, and Nardhy Gomez-Lopez. Detroit, MI, USA.

S-193 **Altered CD4 and NK Cell Profile with Inverse IFNγ and IL-10 Antiviral Response in HIV-1$^+$ Pregnancies.**
Alexander Cocker, Sarah Dermont, Waheed Khan, Nesrina Imami, and Mark Johnson. London, United Kingdom.

REPRODUCTIVE ENDOCRINOLOGY AND INFERTILITY

S-194 **Hydroxychloroquine as Empiric Treatment for Recurrent Pregnancy Loss.**
Elizabeth Constance, Angela Kelly, Neil Kamdar, Emily Kobernik, Kristian Seiler, John Randolph, Cosmas Van De Ven, and Molly Moravek. Ann Arbor, MI, USA.

Saturday, March 18, 2017 - Poster Session III - Bonnet Creek I – IX

S-195 **Metformin Improves Endometrial Responsivity to Progesterone in Women with PCOS.**
Tugba Ensari, Harvey J Kliman, and Lubna Pal. Ankara, Turkey; and New Haven, CT, USA.

S-196 **Does Preimplantation Genetic Screening (PGS) Improve Blastocyst Implantation Rates (IR)?**
Jessica Rubin, Khalied Kaskar, Terri Woodard, and William Gibbons. Houston, TX, USA.

S-197 **Are Embryos That Reach Blastocyst on Day 5 or Day 6 More Likely to Be Euploid?**
Jessica Rubin, Khalied Kaskar, Paul Zarutskie, and William Gibbons. Houston, TX, USA.

S-198 **The Bottom Line of Fresh versus Frozen ART Cycles in PCOS Patients: Cost Analysis of an RCT.**
Jessica R Zolton, Mae W Healy, Alan H DeCherney, and Micah J Hill. Bethesda, MD, USA.

S-199 **Low BMI Is Associated with Poorer Infertility Treatment Outcomes: Analysis of 249,436 Treatment Cycles from 13 US Fertility Clinics.**
Anthony Santistevan, Karen Hunter Cohn, Keri H Kalmbach, Elizabeth Amador, Polaris Data Network, Erin F Wolff, and Piraye Yurttas Beim. New York, NY, USA.

S-200 **Risk Factors Associated with Complete Failure to Fertilize in IVF with Conventional Insemination.**
Andrew R Fisher, Maureen M Schulte, Stephanie Tsai, Joan K Riley, and Emily Jungheim. Saint Louis, MS, USA.

S-201 **Elevated Progesterone Impacts Embryo Development During IVF.**
Amanda Kohlmeier, John Zhang, and Jared Robins. Chicago, IL, USA.

S-202 **Serum hCG Levels and Prediction of Live Birth in IVF Pregnancies.**
Lia A Bernardi, Angela K Lawson, John X Zhang, and Randall B Barnes. Chicago, IL, USA.

S-203 **Melatonin in Assisted Reproductive Technology (MIART) – Oral Melatonin Treatment During Ovarian Stimulation Does Not Affect Sleep – A Double-Blind Randomized Placebo Controlled Trial.**
Shavi Fernando, Euan Wallace, Sarah Biggs, Rosemary Horne, and Luk Rombauts. Melbourne, VIC, Australia; and Clayton, VIC, Australia.

S-204 **Role of mTOR (Mammalian Target of Rapamycin) Signal Mechanism in the Treatment of Polycystic Ovary Syndrome (PCOS).**
Aylin Yaba Uçar, Mehmet Serif Aydin, Sami Agus, Elif Günalan, Ecem Yildirim, and Bayram Yilmaz. Istanbul, Turkey.

S-205 **The Effect of Semen Parameters on Intrauterine Insemination (IUI) Success.**
Emily C Holden, Ashley Papapetrou, Sara S Morelli, and Peter McGovern. Hasbrouck Heights, NJ, USA; Newark, NJ, USA; and Paterson, NJ, USA.

S-206 **Melatonin and Women Quality of Life at a Climacteric Syndrome.**
Elena Usoltseva, . Chelyabinsk, Russian Federation.

S-207 **CoQ10 Increases ATP and Oct4 While AMPK Activity and Oocyte Death Decrease During IVM.**
Mohammed Abdulhasan, Quanwen Li, Jing Dai, Elizabeth E Puscheck, and Daniel A Rappolee. Detroit, MI, USA.

STEM CELLS

S-208 **Testing of a New Tyramine-Substituted Hyaluronan Gel for the Culture of Embryonic Stem Cells.**
Nina Desai, Arsela Gishto, and Pavinder Gill. Beachwood, OH, USA.

S-209 **Human Endometrial Reconstitution Using W5C5^{+}, ICAM1^{+} Cells and Side Population Cell Lines in a Xenograft Model.**
Nuria López-Pérez, Claudia Gil-Sanchis, Amparo Faus, Ana Díaz, Hannes Campo, Antonio Pellicer, Irene Cervelló, and Carlos Simón. Paterna, Valencia, Spain; Valencia, Spain; and Stanford, CA, USA.

S-210 **Syncytiotrophoblast Derived from Induced Pluripotent Stem Cells (iPS) of Patients with Preeclampsia Display Increased Sensitivity to External Stressors.**
Jie Zhou, Megan A Hollenbeck, Aihua Dai, Yuchen Tian, Toshihiko Ezashi, and Danny J Schust. Columbia, MO, USA.

S-211 **Effects of Single or Repeated Intranasal Administration of Umbilical Cord Stem Cells in Neonatal Rats with Hypoxic-Ischemic Brain Lesions.**
Byron Oppliger, Marianne Joerger-Messerli, Martin Mueller, Ursula Reinhart, Philipp Schneider, Daniel V Surbek, and Andreina Schoeberlein. Bern, Switzerland; and New Haven, CT, USA.

Abstracts

Figures will be available only online

Underline represents presenting author; Asterisk represents senior author; Dagger represents an in-training author.

O-001

MiR-200b Mediates the Teratogenic Effect of Maternal Diabetes Leading to Neural Tube Defects by Suppressing Autophagy and Inducing Endoplasmic Reticulum Stress. Daoyin Dong†, Wei-Bin Shen, Peixin Yang*. *University of Maryland Baltimore, Baltimore, MD, USA.*

INTRODUCTION: Pregestational maternal diabetes mellitus (DM) disrupts neurulation leading to neural tube defects (NTDs) in the offspring. Our previous study has shown DM increases miR-200b expression. In the present study, we investigated the role of miR-200b in DM-induced NTDs.

METHODS: Diabetes in female mouse was induced by intravenous injection of 75 mg/kg streptozotocin over 2 days. Diabetes was defined as 12-hour fasting blood glucose level ≥ 14 mM. The male and female miR-200b$^{+/-}$ mice were paired to produce embryos. Neuroepithelial specific miR-200b transgenic (TG) mice were used to determine if miR-200b overexpression impacts neurulation. MiR-200b$^{+/-}$ females were paired with the compound miR-200b$^{+/-}$;miR-200b TG males in restoring miR-200b levels to determine the specific miR-200b function in neural tube closure.

RESULTS: Full or heterozygous deletion of the miR-200b gene did affect embryonic development. The NTD incidence in miR-200b null embryos from diabetic dams was 3.7%, which was significantly lower than that in wild-type (WT) embryos (25.0%) from diabetic dams. The NTD incidence of miR-200b$^{+/-}$ embryos of diabetic dams (21.7%) was comparable to that of WT embryos of diabetic dams. Although there was no NTD in miR-200b TG embryos under nondiabetic conditions, miR-200b overexpression in the neuroepithelium enhanced DM-induced NTDs from 22.2% to 60.0%. MiR-200b overexpression in the neuroepithelium overrode the preventive effect of miR-200b deletion on DM-induced NTDs because under diabetic conditions, the NTD incidence in compound miR-200b$^{-/-}$;miR-200b TG embryos (37.5%) slightly higher than that of WT embryos. Further study showed that miR-200b participated in DM-induced autophagy impairment and endoplasm reticulum (ER) stress through silencing of its target genes, Ambra1 and Cited2, respectively. MiR-200b deletion restored the conversion of LC3 from I to II suppressed by diabetes, and blocked the ER stress signaling pathways: IRE1α phosphorylation, PERK phosphorylation and XBP1 splicing and eIF2α phosphorylation.

CONCLUSIONS: This study demonstrates that miR-200b deletion ameliorates DM-induced NTDs. MiR-200b overexpression in the neuroepithelium abolishes the preventive effect of miR-200b deletion and enhances DM-induced NTDs. MiR-200b mediates the teratogenic effect of DM leading to NTDs by inhibiting autophagy and activating ER stress in the developing neuroepithelium.

O-002

SOX17 Governs the Indian Hedgehog to Promote Female Fertility via Uterine Epithelial-Stromal Interactions. Xiaoqiu Wang†,[1] Xilong Li,[2] Nyssa R Adams,[3] San-Pin Wu,[4] Rainer B Lanz,[5] John P Lydon,[6] Jae-Wook Jeong,[7] Francesco J DeMayo.[8] *[1]National Institute of Environmental Health Sciences (NIEHS), RTP, NC, USA; [2]Baylor College of Medicine, Houston, TX, USA; [3]NIEHS, RTP, NC, USA; [4]NIEHS, RTP, NC, USA; [5]Baylor College of Medicine, Houston, TX, USA; [6]Baylor College of Medicine, Houston, TX, USA; [7]Michigan State University, Grand Rapids, MI, USA; [8]NIEHS, RTP, NC, USA.*

INTRODUCTION: Recent studies have identified the *Sox17* gene as a novel target for progesterone receptor (PGR), and haploinsufficiency and ablation of *Sox17* affects female fertility. We hypothesize that SOX17 regulates female fertility via signaling cascade between uterine epithelial-stromal interactions during the window of receptivity.

METHODS: Using Cre-lox and CRISPR/Cas9 approaches, combined with analyses of immunohistochemistry (IHC), immunofluorescence, quantitative PCR (qPCR), microarray and ChIP-seq, we investigated the loss-of-function of SOX17 in the uterus.

RESULTS: SOX17 is expressed in uterine luminal (LE) and glandular epithelia (GE) and in endothelial cells in the stroma. The *Sox17* -KO mouse models were created by crossing the *Sox17$^{f/f}$* mouse to uterine *Pgr^{Cre}* and *Ltf^{iCre}* mice. Both models resulted in female infertility due to a failure of embryo implantation and decidualization. Neonatal ablation using the *Pgr^{Cre}* mouse resulted in inhibition of adenogenesis whereas post-pubertal deletion using the *Ltf^{iCre}* mouse delayed gland loss. Microarray, ChIP-seq and validation by IHC and qPCR showed that ablation of *Sox17* resulted in loss of the IHH-COUPTFII-HAND2-FGF signal transduction cascade between LE and stroma, with activation of estrogen receptor (ESR) signaling pathways, and therefore, altered proliferation in uterine epithelia. Further, *Sox17* ablation eliminated FOXA2 expression in structurally normal uterine glands. ChIP-seq analysis revealed that SOX17 bound to two putative enhancer region located -11 and -19 kb upstream of the *Ihh* locus. Mice have been generated with deletion of these putative enhancers using CRISPR/Cas9 approaches; these mice lost the *Ihh* response to progesterone stimulation.

CONCLUSIONS: SOX17 has a critical role in maintaining epithelial quiescence from proliferation during the window of implantation via IHH-mediated epithelial-stromal interactions.

O-003

Cervical Gene Delivery of Human Beta-Defensin-3(HBD-3) Prevents Ascending Bacterial Infection in Pregnant Mice. Natalie Suff†,[1] Rajvinder Karda,[1] Mona Bajaj-Elliott,[1] Suzanne MK Buckley,[1] Mark Tangney,[2] Simon N Waddington,[1] Donald Peebles.[1] *[1]IFWH, UCL, London, United Kingdom; [2]UCC, Cork, Ireland.*

INTRODUCTION: Approximately 40% of preterm births are preceded by microbial invasion of the intrauterine space, with ascent from the vagina thought to be the most common pathway. Antimicrobial peptides (AMPs), in combination with mucin and immune cells, constitute a barrier within the cervical canal to prevent ascending infection. We investigated whether overexpression of HBD-3, a potent AMP, in cervical mucosa prevents bacterial ascent from the vagina into the uterine cavity of pregnant mice.

METHODS: An adeno-associated virus vector (AAV8) containing the HBD-3 transgene was synthesised (AAV8-HBD3). 10µl of 1x10^{12} genomic copies/mL of vector (AAV8-HBD3 or AAV8-GFP control) was administered intravaginally into E13.5 pregnant mice (C57BL/6$^{J\text{-}Tyrc\text{-}2J}$). Immunohistochemistry, ELISAs and bacterial killing assays were used to determine HBD-3 expression and function. Mice received 1x10^{9} CFU of *E.coli* (K12 with integrated luxABCDE operon) intra-vaginally at E16.5 and bacterial ascension was monitored by live whole body bioluminescence imaging.

RESULTS: Intravaginal application of AAV8-HBD3 resulted in cervical epithelial expression of HBD-3 72 hours after application and secreted HBD-3 was detected in vaginal lavage 96 hours after application (n=3/group, $p=0.02$). The secreted HBD-3 was functional resulting in significant *E.coli* killing *in vitro* (n=3/group, $p=0.003$) and recruitment of neutrophils to the cervical epithelium (n=3/group, $p=0.01$), compared with AAV8-GFP transduced controls.

Following vaginal infection in the AAV8-GFP controls, bioluminescence imaging showed bacterial ascent into the uterine cavity and colonisation of the placental and fetal membranes. There was significantly less uterine bioluminescence in the AAV8-HBD3 transduced mice at 24 and 48 hours after infection compared with the AAV8-GFP controls (n=12/group, $p<0.05$ *repeated measures ANOVA*). This signifies reduced bacterial ascent in the AAV8-HBD3 treated mice. There was no difference in the pregnancy length or number of born pups per litter between the two groups ($p=0.28$ and $p=0.26$, respectively).

CONCLUSIONS: AAV 8 can target the cervical epithelium to locally overexpress HBD-3. This expression reduces bacterial ascent into the pregnant mouse uterine cavity and may be a promising candidate for augmenting the cervical innate immune response to prevent ascending infection.

O-004

Maternal Lifestyle Impairs Embryonic Growth: A Prospective Periconception Cohort Study. Matthijs R Van Dijk†, Nicole V Borggreven, Sten P Willemsen, Anton HJ Koning, Regine PM Steegers-Theunissen, Maria PH Koster*. *Erasmus MC, University Medical Centre, Rotterdam, Zuid-Holland, Netherlands.*

INTRODUCTION: The evidence is overwhelming that healthy maternal lifestyle, including nutrition, improves fertility, pregnancy course and outcome. Therefore, we developed the successful m-Health program

'Smarter Pregnancy' (English version: www.smarterpregnancy.co.uk) to empower couples to improve intakes of folic acid, fruits and vegetables and to quit smoking and alcohol consumption (Van Dijk et al. JMIR Mhealth Uhealth, 2016). In the current study, we investigated whether the same maternal lifestyles are associated with embryonic growth.

METHODS: Pregnant women entered the Rotterdam periconception cohort before 8 weeks of pregnancy and filled out a questionnaire regarding demographic and medical data, and a validated food frequency questionnaire. Serial three-dimensional ultrasound scans (3D-US) were performed from study entry up to 12 weeks of pregnancy. Associations between maternal lifestyles and embryonic growth were assessed by linear mixed models adjusted for potential confounders. Embryonic growth was assessed by longitudinal crown-rump length (CRL) and embryonic volume (EV) measurements using the Barco I-Space and V-Scope software.

RESULTS: On a total of 342 pregnancies, 1,255(86.8%) CRLs and 1,116(77.2%) EVs were measured. No or post-conception initiation of folic acid supplement use (inadequate) compared to preconception initiation (adequate) was significantly associated with a 0.76 mm (-7.8%) and 1.63 mm (-3.7%) smaller CRL (effect estimate:-0.124, 95%CI: -0.22;-0.03), and a 0.01 cm^3 (-19.5%) and 0.86 cm^3 (-12.2%) smaller EV (effect estimate:-0.06, 95%CI: -0.11;-0.01). Smoking, alcohol consumption, and inadequate fruit and vegetable intake showed weaker associations with embryonic growth

**Figure(s) will be available online.*

CONCLUSIONS: This study demonstrates the positive influence of periconception folic acid supplement use on embryonic growth trajectories, whereas fruit and vegetable intake, smoking and alcohol consumption also suggest associations with embryonic growth, but these should be confirmed in a larger study.

O-005

Non-Invasive Assessment of Fetal CMV Infection and Injury via Fetal Neuronal Exosomes: A Non-Human Primate Model. Laura Goetzl,[1] Nune Darbinian,[1] Nana Merabova,[1] Kinari Patel,[1] Alice F Tarantal,[2] Peter A Barry*.[3] *[1]Temple University, Philadelphia, PA, USA; [2]University of California Davis, Davis, CA, USA; [3]University of California Davis, Davis, CA, USA.*

INTRODUCTION: Approximately 1 in every 150 neonates is born with congenital cytomegalovirus (CMV) infection, yet clinical outcomes range from unaffected to severe disability. Limited prenatal diagnostic tools constrain the accuracy of prognostic counseling, especially in the absence of significant sonographic pathology.

METHODS: Rhesus macaque fetuses were inoculated intraperitoneally under ultrasound guidance with rhesus CMV (RhCMV) in the late 1st/early 2nd trimester. Fetal tissues were harvested in the late 3rd trimester. Maternal blood samples were collected at both time points. Fetal neuronal exosomes (FNEs) were isolated from maternal serum using previously published methods. RhCMV viral copy number was quantified in FNEs and fetal brain using standard PCR protocols. RE1-Silencing Transcription Factor (REST), neurogranin and synaptophysin were quantified using commercial ELISA kits and normalized to CD81. Pre-Post infection levels of exosomal proteins were compared (paired Student's t-test).

RESULTS: Ten mother-infant pairs were studied. One fetal demise was found at harvest. CMV could be detected in 6 of 10 fetal brains. No gross pathology or ultrasound changes were noted. When comparisons were restricted to cases with detectable brain CMV, infection did not alter FNE neurogranin or synaptophysin. However FNE REST decreased significantly following infection (1697.2±40.4 vs. 1369.0±58.9 pg/mL, p=0.02). There was a strong negative correlation between FNE neurogranin and parietal lobe CMV viral copy number that did not reach statistical significance (r=-0.826, p=0.085). FNE REST and neurogranin appeared positively correlated (r=0.772, p=0.07). FNE CMV viral copy number was low but not undetectable.

CONCLUSIONS: REST is an essential modulator of neuronal differentiation and plasticity and serves a critical role in repressing pro-apoptotic genes. In this non-human primate model of mild congenital disease, neural CMV infection was associated with decreased FNE REST. Larger studies are needed to explore the potential that FNE REST could be developed into a clinically useful, non-invasive, prenatal diagnostic tool. Non-infected comparateurs are required to control for unknown gestational age changes in REST.

O-006

The New Triple I Classification Scheme and Outcomes Among Term Infants. Christina A Herrera†,[1] Julie Shakib,[2] Erin AS Clark,[1] Michael W Varner,[1] Bob Silver*.[1] *[1]University of Utah and Intermountain Healthcare, Salt Lake City, UT, USA; [2]University of Utah, Salt Lake City, UT, USA.*

INTRODUCTION: We sought to determine the association between the new Triple I (intrauterine inflammation, infection, or both) classification scheme and outcomes in term infants.

METHODS: Retrospective cohort study of women with chorioamnionitis, 2009-2016. Women with chorioamnionitis or intrapartum fever at term were included. Women with a non-viable pregnancy (<23 weeks), fetal demise, or preterm birth were excluded. Maternal and neonatal morbidity were compared according to isolated maternal fever versus suspected Triple I. The primary outcome was a composite of: neonatal clinical sepsis, broad spectrum antimicrobial therapy >72 hours, or death.

RESULTS: 419 women were included, from 37-42 weeks gestation. 196 had isolated fever and 223 had suspected Triple I. Of women with suspected Triple I, 91 (43%) had a WBC >15,000, 167 (75%) had fetal tachycardia, and 2 (0.01%) had purulent amniotic fluid. Among women with histopathologic placental examination, 9 (53%) women with isolated fever and 13 (72%) women with suspected Triple I, had confirmed Triple I (OR 1.36, 95%CI 0.58-3.19). Intrapartum antibiotics were administered to 114 (59%) women with isolated fever and 139 (62%) women with suspected Triple I (p=0.53). Antibiotics were administered to 57% of infants born to mothers with isolated fever and 62% of infants born to mothers with suspected Triple I. There was no difference in the composite outcome (Table). There were no cases of culture-positive neonatal sepsis. Despite intrapartum antibiotic use, 9.3% of infants born to mothers with isolated fever received ≥4 days of antimicrobial therapy, indicating concern for actual infection. Postpartum endometritis was more common in the suspected Triple I group.

CONCLUSIONS: Women with suspected Triple I are at increased risk for postpartum endometritis. Isolated maternal fever and suspected Triple I similarly predict neonatal infection risk. Of infants born to women with isolated fever, 9.3% were treated for clinical sepsis, underscoring the need for better prediction of neonatal infection.

**Figure(s) will be available online.*

O-007

Network Analysis of Maternal Genes Implicated in Preterm Birth. Maria Schmoll†,[1] Ravindu Gunatilake,[2] Avinash Patil,[2] Annabeth Barnard.[1] *[1]Indiana University School of Medicine, Indianapolis, IN, USA; [2]Valley Perinatal Services, Phoenix, AZ, USA.*

INTRODUCTION: Maternal genomic studies have previously identified a wide range of single nucleotide polymorphisms (SNPs) associated with preterm birth (PTB) within specific thematic areas. Our aim was to consolidate previously identified target genes into functional networks in order to prioritize PTB pathways.

METHODS: A systematic review of maternal SNPs associated with PTB was performed using pre-defined criteria. Genes found to have a statistically significantly association with PTB from literature review were compiled into a database for network analysis using NetworkAnalyst. Networks of interacting genes were developed using the initial database supplemented with first-order neighbors identified through the STRING Database v.10. Pathways with potential biologic significance within the genetic network were identified based on relatedness and further characterized by function (KEGG analysis) to determine the most important contributors to PTB. Statistical significance was set at 0.00017 to correct for multiple comparisons.

RESULTS: Systematic review of the literature yielded 236 SNPs associated with PTB from 114 individual maternal genes. Based on network analysis, an additional 244 genes were identified as first-order neighbors with direct interactions and potential significance for PTB. Seven pathways of genes met statistical significance for relatedness

**Figure(s) will be available online.*

Genes within these pathways were implicated in a diverse range of functions by KEGG analysis, including chemokine signaling, angiogenesis, and growth factor signaling.
CONCLUSIONS: Network analysis identified unique genetic pathways implicated in PTB. Future research correlating aberrations in these pathways to clinical outcomes may lead to novel biomarkers for the prediction of PTB.

O-008

***Futurebirth*™- Prediction by 12w of Future Preterm Birth (PTB)<33w Using a Novel Test of Cell Free Plasma (cfp) RNA.** Carl Weiner*,[1] Helen Zhou,[1] Howard Cuckle,[2] Argyro Syngelaki,[3] Kypros Nicolaides,[3] Yafeng Dong.[1] *[1]University Kansas School of Medicine, Kansas City, KS, USA; [2]Tel Aviv University, Tel Aviv, Israel; [3]Fetal Medicine Foundation, London, United Kingdom.*
INTRODUCTION: *Futurebirth*™ is a new diagnostic panel of 5 maternal cfpRNAs predictive of PTB<33w and early onset preeclampsia. In a 2017 abstract (SMFM #321), we reported the 1st prospective test of *Futurebirth*™ in a CDC sponsored prospectively collected cohort of 305 women sampled 16-18w. The AUC for PTB<33w for the markers alone was 0.76, rising to 0.85 after including maternal demographics and history (detection rate 79% with a 20% false positive rate (FPR)). Here we report the 1st validation study of *Futurebirth*™ in samples collected at 12w.
METHODS: 60 women at 12w were randomly selected from the prospective Fetal Medicine Foundation Biobank (London) after excluding women who developed preeclampsia or a history of prior PTB. 20 had an uncomplicated term birth. The remaining 40 experienced PTB<33w. *Futurebirth*™ RNA marker expression was quantified by RT PCR and normalized with control RNAs. Gaussian modeling was not possible with this sample size, and expression was log transformed for modeling. AUC analyses was used since it is unaffected by prevalence. It was calculated after adjusting for weight and race if indicated. Detection rates for a 10, 20 & 30% FPR were determined.
RESULTS: Table 1.

		AUC	Detection Rates (%)		
	FPR		10%	20%	30%
Marker 3 + Maternal Weight / Race		0.79	53	69	70
Markers 1 & 3 + Maternal Weight / Race		0.78	50	64	74

CONCLUSIONS: This 1st validation of *Futurebirth*™ cfpRNA markers at 12w reveals test accuracy matches the cohort study at 16-18w, suggesting *Futurebirth*™ is a good test for PTB<33w when performed 12-18w. The results provide new insights into PTB. We previously showed the 5 markers originate from and are over expressed in placentas of women who suffer PTB. Abnormal expression by 12w suggests PTB is essentially programmed before placentation is completed. We also reported that *in vitro*, the cfpRNA markers increase pregnant myometrial cell contraction suggesting high levels may interfere with quiescence. Lastly, we reported that marker triggered contractions could be pharmacologically blocked by targeting putative downstream marker targets suggesting *Futurebirth*™ levels may provide a basis for therapy selection. Funded in part by CDC-DP000187, Burroughs Welcome Fund planning award and angel supporters.

O-009

Altered Acylcarnitine Metabolism in the Placenta in Spontaneous Preterm Birth. Summer Elshenawy†,[1] Paschalis T Doulias,[1] Samuel Parry,[2] Michael Bennett,[1] Harry Ischiropolous,[1] Rebecca A Simmons*.[2] *[1]The Children's Hospital of Philadelphia, Philadelphia, PA, USA; [2]University of Pennsylvania, Philadelphia, PA, USA.*
INTRODUCTION: The placenta is an active metabolic organ involved in energy production. Thus, it is likely that deficits in the capacity of the placenta to maintain bioenergetic and metabolic stability during the course of pregnancy could result in spontaneous preterm birth (SPTB). Acylcarnitines (AC) are responsible for transporting long-chain fatty acids into the mitochondria and play an important role in energy production in the placenta. Previous studies showed increased static levels of AC metabolites suggesting that AC metabolism is altered in the setting of SPTB. The aim of this study is to compare AC metabolism and fatty acid oxidation (FAO) in the placenta in term control birth to SPTB, as an indicator of metabolic dysfunction in the placenta in SPTB.
METHODS: *Human*placental biopsies obtained at the time of delivery were derived from a nested case (SPTB <36 weeks)-control (delivery >38 weeks) study as part of the prospective MOD Preterm Birth Study cohort. To determine if metabolic changes were simply due to gestational age effects, placentas were obtained from control rhesus monkey pregnancies at preterm (105 days) and term (150 days). AC quantification was performed on homogenized placenta tissue using LC-MS/MS, and normalized to protein concentration. FAO rates were measured on homogenized placenta tissue using radiolabeled 9,10- ^{3}H-palmitoyl-CoA. In vitro conversion of 9,10- ^{3}H-palmitoyl-CoA to $^{3}H_2O$ was measured.
RESULTS:
AC quantification performed on 9 SPTB cases and 9 term controls demonstrated significantly elevated levels of several ACs in placentas of SPTB which was consistent with previous findings ($p<0.05$ vs. controls). AC levels did not differ between gestational ages in placenta of rhesus monkeys, indicating that the findings are associated with pathological metabolic alterations in SPTB. Rates of FAO measured in 6 cases and 6 controls showed significantly lower rates of FAO in the SPTB placenta compared to the term control placentas ($p<0.05$ vs. controls).
CONCLUSIONS: Elevated levels of AC metabolites and decreased rates of FAO in the SPTB placenta suggest a buildup of substrate as a result of dysfunctional pathways in lipid metabolism. This altered metabolism may reflect potential energy failure that is associated with SPTB.
Funded by MOD Prematurity research center at UPENN.

O-010

PreImplantation Factor (PIF*) Prevents Fetal Loss by Modulating LPS Induced Inflammatory Response. Martin Mueller*,[3,5] Nicoletta Di Simone,[1] Fiorella Di Nicuolo,[1] Riccardo Marana,[1] Roberta Castellani,[1] Francesco Ria,[2] Manuela Veglia,[1] Giovanni Scambia,[1] Daniel Surbek,[3] Eytan Barnea.[4] *[1]Università Cattolica Del Sacro Cuore, Rome, Italy; [2]Università Cattolica Del Sacro Cuore, Rome, Italy; [3]University Hospital Bern, Bern, Switzerland; [4]BioIncept LLC (*PIF proprietary), Cherry Hill, NJ, USA; [5]Yale University School of Medicine, New Haven, CT, USA.*
INTRODUCTION: In pregnancy exaggerated inflammatory response may result in fetal loss. TLRs initiate this response resulting in NALP-3 mediated assembly of ASC and caspase-1 into the inflammasome and production of pro-inflammatory cytokines. PreImplantation Factor (PIF) modulates Inflammation in pregnancy. Synthetic PIF (sPIF) protects against multiple immune disorders.
METHODS: We used a pregnant mouse model (n=36) of fetal loss (Fig. 1A). We used LPS or PBS to induce inflammation and sPIF or PBS as treatment. We investigated fetuses and placentae using IHC (anti-PIF), Western blot (anti-NALP-3 and -ASC), ELISA (caspase-1), and multiplex array (22 cyto/chemokines). The data were analyzed using ANOVA followed by a Bonferroni test. $p<0.05$ was statisticaly significant.
RESULTS: LPS increased fetal loss and sPIF reduced this loss significantly (Fig. 1B). sPIF increased fetal weight (Fig. 1D).
**Figure(s) will be available online.*
LPS increased PIF expression and this was not amplified by sPIF (Fig. 2A). sPIF abolished LPS induced pro-inflammatory cytokines (placental and serum) increase including inflammasome signaling: TNF-α, IL-18, and GM-CSF. LPS increased NALP-3, ASC, and caspase-1 (Fig. 2B). sPIF reduced this activation significantly.
**Figure(s) will be available online.*
CONCLUSIONS: sPIF is a candidate to treat inflammatory induced pregnancy loss.

O-011

Genetic Deficiency in IL-6 Modifies Sex-Related Differences in Neonatal Mouse Mortality in Response to Influenza Infection. Elizabeth A Bonney*,[1] Jenna E McQuesten,[1] Kendall Krebs,[1] Mercedes Rincon.[2] *[1]University of Vermont, Burlington, VT, USA; [2]University of Vermont, Burlington, VT, USA.*

INTRODUCTION: Evidence in human viral infections suggests sexual dimorphism, with incidence of infection higher in males and severity higher in infected females. This can occur in the very old or young and supports the idea that, beyond sex hormones, the sex chromosomes produce an "environment" in the gene-environment interactions governing infection. Influenza causes significant disease, particularly in infants. Mortality occurs due to lung inflammation, tissue damage, and secondary bacterial infection. The sexual dimorphism observed in influenza infection is complex, and unique factors governing the neonatal immune response are not yet determined. Interleukin 6 (IL-6) is a pro-inflammatory cytokine that is protective in an adult mouse model of influenza infection. It is not clear if this is true in neonates.

METHODS: C57BL/6 (B6) or IL-6 deficient (KO) infants (age 14-16 days) or juveniles (age 33-45 days) received an intranasal infection of a mouse-adapted influenza strain (Pr8). Infants received 35 EIU/g in 15ul of saline. Juveniles received 400 EIU/g in 20ul saline. Mice were weighed daily and were euthanized per our institution's Animal Care and Use Committee or died spontaneously when they lost more than 30% body weight. Univariate analysis of survival (over >10 experiments) of mice by age, strain or sex was performed by Fisher's exact test. Significance was set at probability <0.05.

RESULTS: Survival of infected B6 and KO infants was similar (54 of 86 vs 33 of 49 p=0.6). This was also true for juveniles (B6, 22 of 31 vs KO, 14 of 26 p=0.18). However, analysis of the data by sex revealed that survival of B6 females was lower than males in both infants (15 of 33 vs. 39 of 53, p=0.012) and juveniles (10 of 19 vs 12 of 12, p=0.005). This was not true of infant KO mice (survival females 13 of 19 vs males 20 of 33, p=1) or of juveniles (p=0.5).

CONCLUSIONS: We cannot reject the null hypothesis that survival is the same in young B6 and KO mice. Future studies are needed. Sex may be a more important predictor than IL-6 in influenza. Ongoing work will determine if sex is an independent risk factor when controlling for environmental and nutritional factors as well further delineate any possible interaction between IL-6 and sex in influenza-mediated neonatal mortality. *Supported by NIH P30 GM118228 and NIH R21 AI115458.*

O-012

Healthy, Infection-Free Growth of Preterm Lambs Maintained with Ex-Vivo Uterine Environment (EVE) Therapy for One Week. Haruo Usuda,[1,2] Shimpei Watanabe,[2] Eleanor Woodward,[1] Masatoshi Saito,[2] Gabrielle C Musk,[3] Suhas G Kallapur,[1,4] Judith Rittenschober-Böhm,[1] Hideyuki Ikeda,[2] Shinichi Sato,[2] Takushi Hanita,[2] Tadashi Matsuda,[2] John P Newnham,[1] Matthew W Kemp*.[1] *[1]UWA, Perth, WA, Australia; [2]TUH, Sendai, Miyagi, Japan; [3]UWA, Perth, WA, Australia; [4]CCHMC, Cincinnati, OH, USA.*

INTRODUCTION: Extremely preterm infants are at significant risk of morbidity and mortality, suggesting a need for alternative life-support strategies. *Ex-vivo* uterine environment (EVE) therapy is an experimental neonatal intensive care strategy. Gas exchange is provided by parallel membranous oxygenators connected to the umbilical vessels, with the infant submerged in protective artificial amniotic fluid. Herein, we aimed to achieve one week of healthy, infection-free growth in preterm lambs using our EVE therapy platform.

METHODS: Six ewes with singleton pregnancies underwent surgical delivery at 114d gestation (term is 150d). Fetuses were adapted to EVE therapy and maintained for one week with constant monitoring of key physiological parameters. Antibiotics and nutrients were provided by continuous venous infusion. Humerus and femur lengths were measured daily with ultrasound. Umbilical artery samples were regularly collected to assess blood gas data and white corpuscle counts. Blood cultures were performed daily to exclude infection. Six pregnant control animals were euthanized at 121d gestation to allow comparative post-mortem analyses. Data were tested for group differences with ANOVA.

RESULTS: Five of six fetuses completed one week of EVE therapy with stable vital signs and had no significant differences ($p>0.05$) in arterial spO2, lactate or weight at euthanasia compared to control. White blood corpuscle and differential leukocyte counts were not significantly changed ($p>0.05$) and blood cultures were negative for infection throughout the whole period. Humerus ($p<0.05$) and femur ($p<0.001$) lengths were significantly increased at euthanasia, relative to length at EVE therapy day one.

CONCLUSIONS: Preterm lambs were maintained in a stable condition for one week using EVE therapy. Significant growth was obtained without clinically significant bacteremia. A refined *ex-vivo* uterine environment therapy platform may thus provide an avenue to improve outcomes for extremely preterm infants.

O-013

GATA6 Confers an Immunologic Phenotype in Endometriosis. Christia Angela M Sison†, Matthew T Dyson, Serdar Bulun*. *Northwestern University Feinberg School of Medicine, Chicago, IL, USA.*

INTRODUCTION: Endometriosis affects 5–10% of reproductive-age women. The mechanism through which normally-located eutopic endometrial cells (NoEM) are associated with endometriotic cells (OSIS) remains unknown. Recent genome-wide methylation analyses from our lab have pinpointed a unique epigenetic fingerprint in endometriosis, suggesting DNA methylation is an integral component of the disease. We observed significant differences between NoEM and OSIS in DNA methylation of the GATA family of transcription factors, suggesting a novel role for the GATA family as key regulators of uterine physiology. When GATA6 is expressed in NoEM, there is a lack of developmental plasticity and an induction of endometriosis markers. Our study aims to investigate the role of GATA6 in the progression of endometriosis.

METHODS: Both normal endometrial and endometriotic tissue were taken from patients undergoing uterine surgery at Northwestern Memorial Prentice Women's Hospital. We digested the tissue and isolated NoEM and OSIS for primary cell culture. We developed two groups for ChIP-Seq analyses: 1) NoEM overexpressing GATA6 via adenoviral vector and 2) OSIS control. For RNA-Seq analyses, our two groups consisted of 1) NoEM control and 2) NoEM overexpressing GATA6 via adenoviral vector. By conducting ChIP-Seq and RNA-Seq, we can determine which genes and pathways are modulated by GATA6 in endometriosis.

RESULTS: We found that many key genes affected by GATA6 in endometriosis were immune-related. We observed GATA6 was highly enriched at the promoters of immunomodulatory genes via ChIP-Seq. Concurrently, our RNA-Seq results indicated differential expression of many immune-related genes. Examples of these genes include chemokines (e.g., RANTES and CCL2) and interleukins (e.g., IL6). This coincides with several observations of inflammation and pain in patients with endometriosis and apoptotic resistance in OSIS.

CONCLUSIONS: Endometriotic cells possess a unique immunoregulatory, anti-apoptotic, and steroidogenic phenotype that directly contributes to the survival and persistence of diseased tissue. Our data suggest that differential DNA methylation directing the expression of GATA6 contribute to this phenotype. This study uncovers a potential epigenetic and immunologic basis for GATA6 action in endometriosis, proposing a usefulness for the development of targeted and effective therapies for this disease.

O-014

Role of the Wnt Pathway in Endometriosis. Maik Obendorf,[1] Juliane Hundt,[1] Eva Simon,[1] Ralf Lesche,[1] Rene Wenzl,[2] Lorenz Kuessel,[2] Thomas M Zollner*.[1] *[1]Bayer AG, Berlin, Germany; [2]Medical University of Vienna, Vienna, Austria.*

INTRODUCTION: Endometriosis is defined by the presence of endometrial tissue outside the uterine cavity causing among other symptoms chronic pelvic pain and subfertility. Sampson's theory of retrograde menstruation is widely accepted to explain peritoneal lesions. However the theory does not sufficiently explain why endometriosis develops only in some women. Endometrium has a high potential for healing, suggesting pathological self-renewal at ectopic sites. The WNT

pathway has important functions in self-renewal of stem cells and has been implicated in growth pathologies, such as cancer. In a Laser Capture Microscopy (LCM) based analysis of clinical samples (from EMMA – Endometriosis Marker Austria) we have previously observed deregulated WNT signaling. In this study, we have analyzed the role of WNT signaling in more detail *in vitro* and *in vivo*.

METHODS: IHC was done on FFPE tissue from informed and consenting endometriosis patients and controls. An immortalized endometrial stromal cell line (ESC) was used for knockdown and overexpression of WNT pathway members. WNT activity was measured by Cignal TCF/LEF Reporter Assay Kit (Qiagen), viability by CellTiter-Glo®, cell death & caspase activity by ApoTox-Glo™ (Promega), and migration assays were done in Boyden chambers. The WNT pathway inhibitor LGK974 was used in a vehicle controlled 14d retrograde menstruation mouse model of endometriosis.

RESULTS: We confirmed overexpression of several Wnt pathway genes (WNT2B, WNT7A, LGR5, RSPO1, FZD7) in ectopic stromal or epithelial compartments compared to eutopic samples by IHC. Overexpression of LGR5 in ESC led to increased WNT activity, viability, migration and decreased cell death. Reduced LGR5 mRNA levels exhibited reverse results. To explore the function of Wnt signaling *in vivo*, we applied the porcupine inhibitor (LGK974) in a retrograde menstruation model in mice. We observed down-regulation of several Wnt pathway genes and a significant reduction of disease burden in terms of total lesion size (-71%) and lesion number (-47%).

CONCLUSIONS: Our data suggest that the WNT pathway is implicated in the pathogenesis of endometriosis.

O-015

Prostaglandin E2 Signaling, Estrogen-Dominance and Progesterone-Resistance in Endometriosis. Joe A Arosh,[1] JeHoon Lee,[1] Kaylon L Bruner-Tran,[2] Kevin G Osteen,[2] Sakhila K Banu.[1] *[1]Texas A&M University, College Station, TX, USA; [2]Vanderbilt University School of Medicine, Nashville, TN, USA.*

INTRODUCTION: Endometriosis is an estrogen-dependent and progesterone-resistant inflammatory gynecological disease of reproductive age women. Prostaglandin E2 (PGE2) plays important roles in the pathogenesis of endometriosis. PGE2 brings forth its actions through EP1, EP2, EP3, and EP4 receptors. Objective is to evaluate the therapeutic use of EP2 and EP4 inhibitors on estrogen-dominance and progesterone-resistance and to understand the underlying molecular mechanisms in endometriosis.

METHODS: Mixed population of human endometriotic epithelial cells (12Z-GFP) and stromal cells (22B-RFP) were xenografted into the peritoneal cavity of eight-week old Rag2g(c) intact mice. Group-1 mice were treated with vehicle and served as control and Group-2 mice were treated with EP2 and EP4 inhibitors.

RESULTS: Results indicated that inhibition of EP2 and EP4: (i) decreased growth, survival, and dissemination of endometriotic lesions; (ii) decreased expression of p450 aromatase protein and estrogen receptors ERa and ERb proteins, and restored expression of PR-B protein; and (iii) did not modulate expression of SF1 protein in epithelial and stromal cells of the induced endometriotic lesions and endometrium in a cell and tissue-specific pattern. In addition, in vitro results indicated the inhibition of EP2 and EP4 restored PR-B expression in human endometriotic stromal cells 22B through multiple histone modification and DNA methylation mechanisms.

CONCLUSIONS: These results together indicate that selective inhibition of EP2 and EP4 decreases growth of endometriotic lesions, estrogen-dominance, and progesterone-resistance in both endometriotic lesions and endometrium in experimental endometriosis. Further, our results suggest that inhibition of EP2 and EP4 restores the progesterone-responsive microenvironment in both endometriotic lesions and endometrium. Our novel results provide molecular and preclinical basis to formulate long-term nonsteroidal therapy through inhibition of EP2 and EP4 for endometriosis.

O-016

Endometriosis Inherently Increases the Number of CD146/CD140b Double Positive Cells in the Eutopic Endometrium of Baboons with Induced Disease. Fatima Barragan†, Michael R Strug†, Ren-Wei Su†, Amanda Patterson†, Asgerally Fazleabas*. *Michigan State University, Grand Rapids, MI, USA.*

INTRODUCTION: Endometriosis affects up to 10% of reproductive aged women. Studies investigating the initiation and progression of endometriosis have been facilitated by the use of the baboon model that closely phenocopies the disease in women. Endometrial mesenchymal stem cells (eMSC) may contribute to endometriotic lesion propagation if shed in a retrograde fashion. Co-expression of CD146 and CD140b has been used to identify eMSC. We hypothesized that an increase in the number of eMSC may be seen in the endometrium of baboons after the induction of endometriosis.

METHODS: Endometriosis was experimentally induced in female baboons by intraperitoneal inoculation with menstrual endometrium on two consecutive menstrual cycles. Eutopic endometrium was collected prior to inoculation and functioned as control. The progression of disease was monitored in animals over a period of 15 months after inoculation. At 15 months ectopic endometriotic lesions and eutopic endometrium were subsequently harvested for immunohistochemical analysis. Immunofluorescent staining of collected samples was performed for co-localization of CD146 and CD140b. Percentage of double-positive cells were compared using a one-way ANOVA with post-hoc Tukey HSD to determine significant differences among groups.

RESULTS: Results demonstrated that the percentage of CD146/CD140b double-positive cells was significantly increased ($F(2,9) = 14.4$ $p<0.05$ SS=345.04 MSE=11.99, n=4/gp) in eutopic endometrium following the induction of endometriosis when compared to controls. No difference was seen between the comparison of control endometrium to ectopic lesions ($p>0.05$, n=3/gp).

CONCLUSIONS: Our data suggests there may be a link between increased stem cell number in eutopic endometrium in response to endometriosis, which may subsequently contribute to lesion development during retrograde menstruation. When control endometrium was compared to ectopic lesions we noted no increase in percentage of eMSC, which may suggest that a different repertoire of stem cells or small number of eMSC may contribute to lesion development or persistence. To our knowledge, this is the first time that these stem cells have been identified in the ectopic endometrium of baboons following the induction of endometriosis (NIH HD 082453 to AF).

O-017

P2X3 - A Highly Innovative Target for the Non-Hormonal Treatment of Endometriosis. A Davenport,[1] N Bräuer,[3] A Rotgeri,[3] A Rottmann,[3] M Koch,[3] TM Zollner,[3] A Steinmeyer,[3] J Nagel,[3] F Machet,[2] A Coelho,[2] S Boyce,[2] L Bone,[1] M Gemkow,[2] N Carty,[1] M Herrmann,[2] S Hess,[2] I Neagoe,[2] OM Fischer*.[3] *[1]Evotec Ltd, Abingdon, United Kingdom; [2]Evotec AG, Hamburg, Germany; [3]Bayer AG, Berlin, Germany.*

INTRODUCTION: P2X3 is a purinergic ion channel mainly expressed in nociceptive sensory neurons where it plays a prominent role in pain processing. Under inflammatory conditions P2X3 expression is increased in dorsal root ganglia (DRG) and is thought to contribute to the development of central sensitization. In this work, we aimed to characterize the anti-nociceptive properties of our selective potent P2X3 antagonist and to assess its potential as an innovative non-hormonal treatment option for endometriosis.

METHODS: P2X3 expression was assessed using immunohistochemistry on human endometriotic tissue. Human and rodent P2X3 and P2X2/3 compound activity and human selectivity were measured in recombinant cell lines in FLIPR and patch-clamp assays. Compound activity was confirmed in rodent native tissue by manual patch-clamp. *In vivo* characterization was performed in models of inflammatory pain using CFA-induced paw inflammation, as well as neurogenic inflammation and dyspareunia rat models.

RESULTS: P2X3 expression on nerve fibers in human endometriotic lesions was shown by immunohistochemistry. Medicinal chemistry efforts

led to the discovery of a potent lead P2X3 antagonist with, however, high metabolic clearance in primates. Optimisation resulted in BAY 1817080, exhibiting high selectivity versus the P2X family and off-targets. *In vivo* characterization showed desirable pharmacokinetics and efficacy in rodent CFA-induced inflammatory pain models. Robust efficacy of a P2X3 antagonist was shown for the first time in a rat neurogenic inflammation model indicating the potential to interfere with the vicious circle between the nervous and the immune system. Finally, in a rat endometriosis-induced dyspareunia model BAY 1817080 demonstrated significant reduction of vaginal hyperalgesia. The effect was maintained 1 week after treatment cessation. Together with the effect on neurogenic inflammation this result underlines the disease-modifying potential of BAY 1817080 beyond rapid and robust analgesic efficacy.
CONCLUSIONS: P2X3 is a prominent mediator of acute and chronic pain and is expressed in human endometriotic lesion nerve fibers. Based on the robust *in vivo* pharmacology of the potent P2X3-selective antagonist, this approach provides the potential for an innovative, non-hormonal treatment of endometriosis.

O-018

Progesterone and KLF11 Mediate Sexually Dimorphic Fibrotic Responses. Chandra C Shenoy†, Ye Zheng, Tiffanny L Jones, Zaraq Khan, Gaurang S Daftary*. *Mayo Clinic, Rochester, MN, USA.*
INTRODUCTION: Fibrosis is a common, morbid consequence of endometriosis, chronic diseases and surgery. We showed that fibrosis is sexually dimorphic with female predilection, and is mediated by gene dysregulation from loss of Klf11, a transcription factor implicated in the endometriosis. Here we use a translationally relevant approach to investigate in vitro and in vivo the role of sex steroids in the sexually dimorphic fibrotic response.
METHODS: We used a peritoneal sclerosis rather than an endometriosis model as it is applicable to both sexes (N=7 for each subgroup). Fibrosis was induced in 8-week wt and Klf11-/- mice by daily IP injection of chlorhexidine gluconate (CHX). Additional subgroups of wt and Klf11-/- females underwent ovariectomy or sham surgery followed by SC injections of Estradiol (E2), Progesterone (P4), Dihydrotestosterone (DHT) or placebo (C) in addition to daily IP CHX for 3 weeks. Fibrosis was objectively scored and peritoneal biopsies evaluated by histology and gene expression. Translational relevance was evaluated in Klf11-/- female mice treated by daily SC placebo or P4 antagonists: Mifepristone or Ulipristal and IP CHX. Human relevance was evaluated in a peritoneal cell line treated with sex steroids and KLF11shRNA.
RESULTS: Significant fibrosis was noted only in Klf11-/- but not wt females, males or Klf11-/- males. Ovariectomy in Klf11-/- females abrogated fibrosis. Ovariectomized Klf11-/- mice developed fibrosis only with replacement of P4 but not E2 or DHT. (p=0.014, Kruskal-Wallis test), corroborated by histology (p=.0117, paired t-test). Correspondingly, the fibrosis score and peritoneal histology were significantly diminished in Klf11-/- mice treated with either P4 antagonists compared to placebo (p=.0092, wilcoxon; p=.0242 t-test). Significant up-regulation of TGFbeta signaling as well as MMP3, 9 was observed in P4 and in P4+KLF11shRNA treated human stromal and peritoneal cells.
CONCLUSIONS: Inflammation and scarring commonly cause morbidity in endometriosis and surgery. We show for the first time that this response is sexually dimorphic and dependent on progesterone. Progesterone acts synergistically with the disease relevant gene KLF11 to promote fibrosis via dysregulation of MMP and Collagen signaling. These novel mechanisms can be targeted at several levels with P4 antagonists and previously shown epigenetic inhibitors to offer novel individualized treatment options.

O-019

RPLP1 Is a Novel Target of *miR-451a* Whose Expression Is Elevated in Endometriotic Lesion Tissue and Correlates with Endometriotic Lesion Tissue and Cell Proliferation. Zahraa Alali†,[1] Tommaso Falcone,[2] Warren B Nothnick*.[1] *[1]University of Kansas Medical Center, Kansas City, KS, USA; [2]Cleveland Clinic, Cleveland, OH, USA.*
INTRODUCTION: Endometriosis is a disease common in women of reproductive age where endometrial tissue establishes and survives in ectopic locations. However, how these lesions establish and survive is unknown. We have recently identified ribosomal protein large P1 (RPLP1; which is a modulator of cell proliferation) as a potential target of *miR-451a* expressed in endometriotic epithelial 12Z cells. The objective of the current study was to determine the expression of RPLP1 in human endometriotic lesion tissue, examine the function of RPLP1 in modulating cell survival/proliferation and *miR-451a* regulation of RPLP1.
METHODS: RPLP1 mRNA and protein levels were examined in paired endometriotic lesion tissue and eutopic endometrium from women with stage III/IV endometriosis (N=35) as well as tissue from women without symptoms of endometriosis (controls; N=20 for localization studies).
RESULTS: Net expression of RPLP1 mRNA was significantly higher in ectopic lesion tissue compared to paired eutopic endometrium (3.72 fold increase; P<0.01) and immunohistochemical localization revealed predominant localization to epithelial cells (lesion > endometriosis eutopic > control eutopic; P<0.05). As RPLP1 is proposed to drive cellular proliferation, we assessed the correlation between lesion RPLP1 mRNA expression and that of cyclinE1 and observed a positive correlation between both markers (Pearson r = 0.571; P<0.01; N=35). To further demonstrate functionality, we generated a stable 12Z cell line in which RPLP1 was deleted and found that loss of RPLP1 expression was associated with a 90% reduction in cell number/survival (P<0.001; N=3). We further demonstrated that over-expression of *miR-451a* via transient transfection of 12Z cells resulted in a significant (P<0.05; N=3) reduction in RPLP1 expression as well as that of cylcinE1.
CONCLUSIONS: These studies reveal that RPLP1 is a novel target of *miR-451a* and that RPLP1 expression and its regulation by *miR-451a* are associated with cell proliferation and survival. These results, as well as our previous and ongoing studies, continue to support a role for *miR-451a* in modulation of endometriotic lesion tissue/cell survival which may prove useful as a non-hormonal therapeutic agent for endometriosis treatment.
Supported by HD069043.

O-020

Expression Quantitative Trait Loci (eQTL) Approaches for Understanding the Genetics of Endometriosis. Peter AW Rogers*,[1] Sarah J Holdsworth-Carson,[1] Jenny N Fung,[2] Eliza M Colgrave,[1] Premila Paiva,[1] Jane E Girling,[1] Grant W Montgomery.[2] *[1]University of Melbourne and Royal Women's Hospital, Melbourne, VIC, Australia; [2]University of Queensland, Brisbane, QLD, Australia.*
INTRODUCTION: Endometriosis is a complex gynaecological disease affecting up to 10% of women, causing chronic pelvic pain and infertility. It is influenced by both environmental and genetic factors. Genome-wide association studies (GWAS) have identified several single nucleotide polymorphisms (SNPs) associated with endometriosis. However, identification of SNPs alone cannot determine which gene(s) are responsible for endometriosis. Therefore, we need to determine if individual SNPs have downstream effects on gene expression. SNPs that influence gene expression are termed expression quantitative trait loci (eQTL).
METHODS: Blood and endometrium were collected from women at the Royal Women's Hospital (n=591). Blood samples were genotyped using Human CoreExome chips. Endometrial gene expression was generated using Illumina Human HT-12 v4.0 Beadchips. eQTL analysis was performed on tissues with recoded SNP genotypes based on minor allele dosage and fitted linear regression models, with menstrual cycle phases included as a covariate. eQTL gene lists were analysed by Ingenuity Pathways Analysis (IPA) for functional pathway studies.
RESULTS: GWAS have identified seven genomic regions with multiple target genes in each region. *LINC00339* is the most significant endometrial

eQTL, with decreased expression associated with increased endometriosis risk. *Vezatin* was also identified as a significant eQTL; increased endometrial expression associated with increased endometriosis risk. Some significant eQTLs have been investigated at the protein level (eg. GREB1, WNT4 and VEZT). Interestingly, several SNPs have multiple significant eQTLs. IPA analysis on eQTLs reveal plausible gene pathways for endometriosis (eg. inflammation) and some novel pathways (eg. transcription and haemoglobin pathways).

CONCLUSIONS: eQTL analyses are important for improving understanding of complex diseases, including endometriosis. Ongoing studies are examining the roles and pathways of these eQTLs in endometriosis pathophysiology; studies are underway to identify additional eQTLs to help explain how genetic variants linked to increased endometriosis-risk, cause disease.

Fung et al., Hum Reprod.2015;30(5):1263-75.
Holdworth-Carson et al., Hum Reprod.2016;31(5):999-1013.

O-021

Fetal Microchimerism by Mode of Delivery in Healthy Term Gestations. Raj Shree†,[1] JL Nelson,[2] Sami B Kanaan,[2] Alexandra Forsyth,[2] Emma Cousin,[2] Hilary S Gammill.[1,2] *[1]U of Washington, Seattle, WA, USA; [2]Fred Hutch Research Center, Seattle, WA, USA.*

INTRODUCTION: During pregnancy, bidirectional transplacental exchange of cells and subcellular material occurs between mother and fetus, establishing microchimerism (Mc). Fetal microchimerism (FMc) is detected more readily and at higher concentrations in women undergoing a surgical procedure for early pregnancy loss or termination. Here we sought to evaluate peripartum transfer of cellular FMc in normal term gestations by mode of delivery (MOD).

METHODS: Maternal blood (n=68 samples from 34 subjects) was collected pre-labor in the third trimester and postpartum within 2 hours of placental delivery, along with cord blood. Medical record review confirmed uncomplicated antenatal and delivery course. DNA was isolated from Ficoll-purified mononuclear cells from maternal and cord blood. Maternal and fetal DNA was genotyped and FMc was quantified by quantitative polymerase chain reaction assays targeting fetal-specific non-shared polymorphisms. Detection and concentration of FMc was compared between pre- and post-delivery, and between VD and CD in post-delivery samples.

RESULTS: 22 patients delivered via VD and 12 via CD. There were no demographic differences between the groups, except for MOD. FMc detection was significantly higher post-delivery in the CD group (Table 1). After controlling for the number of cell equivalents tested, the likelihood of post-delivery FMc detection was ten-fold higher with CD vs VD (OR 10.2, 95% CI 1.7-62.4). Due to trends toward higher detection (29.4% vs 14.7%, p=0.14) and concentration (3.6 vs 0.17 Mc cell equivalents per 10^5 total cells, p=0.08) of FMc post- vs pre-delivery, we analyzed quantitative differences in FMc concentration via the change from pre- to post-delivery. The median change in FMc concentration was higher in CD, though the range was broader with VD (Table 1).

CONCLUSIONS: Our data demonstrate that post-delivery FMc detection and concentration are significantly higher after CD vs VD. This difference may be from an abrupt disruption of the placental interface resulting in showering of fetal cells into the maternal circulation. Studies are warranted in a larger population to confirm these findings and further characterize factors that influence fetal-maternal transfer.

	VD	CS	*p-value*
Post-delivery FMc Detection, n (%)	3 (14%)	7 (58%)	0.01
Absolute Change in FMc Concentration in Mc Cell Equivalents per 10^5, median (range)	0 (-0.9-100.9)	0.4 (0-6.8)	0.02

O-022

Association Between the a2 Isoform of Vacuolar ATPase and Markers of Inflammation in Peripheral Blood Mononuclear Cells from Pregnant Women. Tomi T Kanninen†,[1] Giovanni Sisti,[2] Aswathi Jayaram,[1] Steven R Inglis,[1] Ashwini Pandit,[1] Steven S Witkin*.[2] *[1]Jamaica Hospital Medical Center, New York, NY, USA; [2]Weill Cornell Medicine, New York, NY, USA.*

INTRODUCTION: Down-regulation of the pro-inflammatory immune response by the a2 isoform of vacuolar ATPase (a2V) has been implicated in the promotion of successful implantation and placentation in animal models. We evaluated associations between the concentration of a2V and markers of inflammation in peripheral blood mononuclear cells (PBMCs) of pregnant women and their association with outcome.

METHODS: PBMCs were isolated from 120 women with ongoing pregnancies. Cells were lysed in the presence of protease inhibitors and the intracellular concentration of a2V, as well as the stress inducible 70kDa heat shock protein (hsp70), the cytokines tumor necrosis factor-alpha (TNF) and interleukin-10 (IL-10) and the immune activator spermidine/spermine acetyltransferase (SSAT) were measured by ELISA. Clinical data was obtained after completion of all lab experiments. Correlations were analyzed by Spearman rank correlation test.

RESULTS: The a2V concentration was inversely proportional to the concentration of hsp70 (p=0.0128), IL-10 (p=0.0007), TNF (p=0.0227) and SSAT (p = 0.0159). The a2V level increased with gestational age at blood collection (p=0.0015) and was marginally associated with body mass index (p=0.0535). A preterm birth occurred in 16.7% of our subjects, in 6.7% prior to 32 weeks gestation. The a2V concentration was not associated with gestational age at delivery, history of spontaneous abortions, race, maternal age or neonatal birthweight.

CONCLUSIONS: In our population of women with ongoing gestations, the a2V concentration in PBMCs was associated with the extent of immune quiescence as shown by reduced intracellular levels of hsp70, TNF, IL-10 and SSAT. The a2V level in PBMCs increased with gestational age, but there was no relationship between a2V concentration and pregnancy outcome in this population.

O-023

Unique Innate Lymphoid Cells Revealed by Machine Learning/Dimensionality Reduction in Human Decidua. Jessica Vazquez†, Yan Li†, Aleksandar K Stanic*. *University of Wisconsin-Madison, Madison, WI, USA.*

INTRODUCTION: Immune cells at the maternal-fetal interface play a complex role in regulation of vascular remodeling, fetal tolerance and protection from infection. We have previously presented an experimental workflow novel to reproductive biology for unbiased identification of decidual immune subsets by dimensionality reduction of highly-polychromatic flow cytometry. Canonical ILC transcription factors (T-bet, Eomes, RORgt) were examined within gated machine-learning identified ILC subsets, revealing novel tissue-specific subsets.

METHODS: Decidual specimens were dissected from term placentas and mononuclear cells (MCs) were isolated by mechanical (GentleMACS) and enzymatic (**Collagenase, DNAse**) disruption. MCs labeled by flurochrome-conjugate antibodies against surface CD3, 14, 16, 19, 34, 45, 49a, 56, 94, 117, 127, 335 and intracellular Eomes, RORgt, and T-bet. Data acquisition was performed using BD Fortessa flow cytometer in a 5 laser, 18 detector configuration. Manual data analysis was performed using FlowJo 10.2. Dimensionality reduction by Barnes Hut-modified t-distributed Stochastic Neighbor Embedding (t-SNE) and machine-learning aided density-based clustering (DenseVM) was performed using the R Cytofkit package (ver 1.4).

RESULTS: tSNE-DenseVM analysis mapped innate lymphoid cell subsets onto 2-dimensional scaffolds. This revealed the presence of NK cell groups ($CD56^{high}16^{Neg}$, $CD56^{int}16^{+}$) and confirmed the presence of group 3 innate lymphoid cells ($CD3^{Neg}14^{Neg}19^{Neg}34^{Neg}45^{+}56^{+}94^{Neg}117^{+}127^{+}ROR\gamma t^{+}$). Furthermore, mapping also revealed two unique $CD56^{high}$ NK cells based on Eomes expression ($Eomes^{lo/hi}$) in human decidua. Further manual analysis showed that T-bet expression also distinguished decidual and PBMC $CD56^{high}$ NK cells.

CONCLUSIONS: Dimensionality reduction with machine learning-based clustering of highly polychromatic flow cytometry data proved to be a powerful tool for the identification of novel innate lymphoid cell subsets in human term decidua. Further gene expression analysis will reveal if these novel subsets represent terminally differentiated groups or developmental intermediates, enhancing our knowledge of the immune network at the maternal-fetal interface.

O-024

Placental Growth Factor (Plgf) Blunts the Vascular Response to Angiotensin II: A Novel Mechanism for Vascular Regulation During Pregnancy. Jimmy Espinoza, Ancizar Betancourt, Karin Fox, Alireza Abdollah Shamshirsaz, Chandra Yallampalli. *Baylor College of Medicine, Houston, TX, USA.*

INTRODUCTION: Gant NF et al reported that normal pregnancy was associated with blunted vascular responses to intravenous administration of Angiotensin II (Ang II); however, pregnant women who later developed hypertension remained sensitive to Ang II (JCI, 1973). Changes in maternal serum concentration of PlGF during normal pregnancy mimic changes in maternal vascular response to exogenous administration of Ang II during normotensive gestations. This study was designed to 1) determine effects of PlGF and soluble vascular endothelial growth factor receptor-1 (sFlt-1) on responses of human uterine arteries (UA) to Ang II; and 2) to explore mechanisms of PlGF blunting Ang II actions during pregnancy.

METHODS: UA (n=12) samples were obtained from hysterectomy specimens from normotensive women undergoing cesarean hysterectomy at ≥ 32 weeks due to placenta accreta. 2 mm UA rings were incubated for 24 hrs, with 1) Krebs (controls); 2) PlGF, 0.1 nM (concentrations seen at ≥ 32 weeks of gestation), or 3) sFlt-1 and PlGF at 2 concentration ratios. UA rings were mounted onto wire myographs and dose-contraction response to Ang II (relative to KCl) were determined. To assess the mechanisms of PlGF actions, responses were measured in presence of inhibitor of nitric oxide (NO) synthase (L-NAME), or inhibitors of Endothelium-Derived Hyperpolarizing Factor (EDHF): Apamine (APA) + Charybdotoxin (CHX). UA responses to bradykinin were also evaluated to confirm endothelial integrity. Paired t-test was used and $p<0.05$ was considered significant.

RESULTS: 1) PlGF blunted UA contractility and maximum responses to Ang II (Emax: control: 91.9 ± 27.4; p=0.037) 2) sFlt-1 (at both sFlt-1/PlGF ratios) attenuated PlGF effects on uterine artery responses to Ang II, in a dose-dependent manner ($p<0.05$); 3) L-NAME , and EDHF inhibitors, APA and CHX reversed the relaxation effects of PlGF on UA rings responses to Ang II (Emax: PlGF: 28.2 ± 7.2; L-NAME: 98.5 ± 10.2; APA+ CHX: 90.9 ± 15.9; $p<0.05$).

CONCLUSIONS: 1) PlGF contributes to the blunted vascular response to Ang II during normotensive pregnancies; 2) sFlt-1 appears to modulate this effect; 3) The influence of PlGF on vascular responses to Ang II appears to involve both NO synthesis and EDHF from endothelial cells; 4) PlGF and sFlt-1 may contribute to the regulation of vascular tone during pregnancy by altering the vascular response to Ang II.

O-025

Leptin Receptors During the Ovarian Cycle and Pregnancy: Angiogenesis in Uterine Artery Endothelial Cells. Vladimir E Vargas†,[1,2] Rosalina Villalon Landeros†,[2] Gladys E Lopez,[2] Jing Zheng,[2] Ronald R Magness*.[1,2] *[1]Univ. South Florida, Tampa, FL, USA; [2]Univ. of Wisconsin, Madison, WI, USA.*

INTRODUCTION: Leptin regulates reproductive processes, vascular function, and angiogenesis. The follicular phase and pregnancy are physiological states of elevated estrogen, angiogenesis, and uterine blood flow. Little is known concerning leptin and its receptor (OB-R) in regulating uterine artery (UA) angiogenesis. We **hypothesized**: 1) *Ex vivo* expression of OB-R in UA endothelium (UAendo) and UA vascular smooth muscle (UAvsm) is elevated in pregnant vs. nonpregnant (Luteal and Follicular) sheep; 2) *In vitro* leptin treatments differentially modulate cell proliferation in uterine artery endothelial cells from pregnant (P-UAECs) greater than nonpregnant (NP-UAECs) ewes and; 3) *In vitro* OB-R is also upregulated in P-UAECs vs.NP-UAECs in association with leptin activation of intracellular p-STAT3.

METHODS: *Ex vivo* OB-R protein expression was determined on UAendo/UAvsm by immunohistochemistry (IHC), and Western analysis; *in vitro* OB-Ra, OB-Rb, and phospho-STAT3 were also evaluated in NP-UAECs and P-UAECs. To evaluate angiogenesis, UAECs obtained from NP-UAECs (n=4/group)and P-UAECs (n=4) sheep were treated with vehicle (control), or 7 doses of leptin (0.001-1000 ng/ml; 24 and 48 hr). The effect of leptin on UAEC proliferation was evaluated using the 5-ethynyl-2-deoxyuridine (EdU-labeled) assay technique.

RESULTS: IHC revealed expression of OB-R in UAendo/UAvsm from nonpregnant and pregnant sheep. For *ex vivo* expression studies, we utilized a unilateral pregnant (120-130d, term=147d) sheep model where pre-breeding uterine horn isolation (nongravid) restricted pregnancy to one horn (gravid). Contrary to our hypothesis, western analysis revealed that compared to follicular UAendo/UAvsm, OB-Rs were reduced ($P<0.05$) in UAendo/UAvsm from luteal, nongravid, gravid, and control pregnant groups. Leptin treatment significantly increased *in vitro* cell proliferation in NP-UAECs from follicular (1.70±0.18-fold;$P<0.05$), and P-UAECs (1.50±0.12-fold;$P<0.05$), but not luteal (0.80±0.20-fold) phase. Although leptin receptors in UAECs were expressed at similar levels between groups, leptin treatment only activated p-STAT3 in the follicular phase and P-UAECs.

CONCLUSIONS: Leptin may play an angiogenic role particularly in preparation for the increase UBF during the periovulatory period and subsequently to meet the demands of the growing fetus.

O-026

Venoarterial Signaling (VAS) Modulates Shear Stress-Induced Gestational Uterine Artery Expansive Remodeling. Nga Ling Ko†,[1] Maurizio Mandalà,[2] Liam V John,[1] Adama Aja,[1] George J Osol*.[1] *[1]University of Vermont, Burlington, VT, USA; [2]University of Calabria, Cosenza, Italy.*

INTRODUCTION: Although significant growth of the maternal uterine arterial vasculature is essential for increasing uteroplacental blood flow (UPBF) during pregnancy, the physiological mechanisms that regulate this process are ill-defined. We hypothesized that the transfer of placentally-derived signals from vein to adjacent artery (venoarterial signaling, VAS) actively modulates the shear stress-induced process of gestational arterial enlargement, thereby revealing an active role of the fetus in UPBF regulation.

METHODS: Unilateral ligation of the main uterine artery (MUA) and vein (MUV) at similar vs. opposite (cervical vs. ovarian) locations was carried out in Sprague Dawley rats on day 10 of pregnancy (n=16) to produce counter- vs. concurrent arteriovenous flow as the former is a more efficient method for signal transfer. In some cases, VAS was eliminated by the ligation and removal of a venous segment adjacent to an artery. The effects of surgical interventions on arterial remodeling were evaluated 10 days later, during late pregnancy (day 20/22 of gestation).

RESULTS: Cervical end arterial ligation induced significant expansive remodeling of the MUA at the ovarian end, as evidenced by a 46 ± 7% increase in lumen diameter ($p<0.01$). This effect was augmented under countercurrent flow conditions secondary to cervical end MUA+MUV ligation, and significantly diminished (~ 40%; $p<0.05$) by the removal of an adjacent vein.

CONCLUSIONS: To our knowledge, this is the first study to conclusively demonstrate a role for VAS in maternal uterine arterial remodeling. Attenuation of this pathway in preeclampsia could help explain why this disease generally manifests in the second half of pregnancy, long after the completion of spiral artery endovascular trophoblast invasion.

O-027

Pregnancy-Specific Estrogen Receptor-Mediated Upregulation of Endothelial AT_2 Receptor. Jay Mishra†, Kathirvel Gopalakrishnan†, Gary Hankins, Sathish Kumar. *University of Texas Medical Branch, Galveston, TX, USA.*

INTRODUCTION: During pregnancy, blood pressure (BP) is decreased despite increase in circulating angiotensin II levels, a potent vasoconstrictor. This paradoxical gestational decrease in BP in spite of increased angiotensin II levels is attributed to the parallel increase (~[thinsp]6–8-fold) in expression of vasodilatory angiotensin type 2 receptor (AT_2R) because AT_2R knockout or blockade in pregnant rat/mice prevents gestational BP decrease and increases uterine arterial resistance index. While it is known that AT_2R is critical for gestational vascular adaptations, it is not known how this critically important receptor is transcriptionally upregulated during pregnancy.

METHODS: Pregnant female Sprague Dawley rats were sacrificed on different days of pregnancy to assess temporal changes in plasma estradiol (E_2) and uterine arterial AT_2R expression. Aorta and primary uterine artery endothelial cells (hUAECs) isolated from nonpregnant and pregnant rats and women were used for in vitro studies.

RESULTS: Pregnancy induced progressive increase in plasma E_2 levels and this was associated with a parallel increase in vascular AT_2R expression. In isolated aorta from pregnant ratsand hUAECs from pregnant women, E_2 induced a dose-dependent increase in AT_2R expression that was blockaded by estrogen receptor (ER) antagonist ICI182,780. In nonpregnant rat aorta and hUAECs, E_2 treatment did not alter AT_2R expression suggesting that E_2 induces *AT_2R* upregulation only in pregnant vessels. Cycloheximide (protein synthesis inhibitor) did not alter E_2 induced upregulation of *AT_2R* transcription suggesting that the E_2 effect is probably direct, rather than involving an E_2-induced intermediary. Analysis of *AT_2R* promoter revealed 11 estrogen response elements (ERE, 7 for ERα and 4 for ERβ). Chromatin immunoprecipitation showed that E_2 stimulation induced greater ERα binding to EREs in non-pregnancy while ERβ binding was higher in pregnancy. Furthermore, luciferase reporter assays showed that ERα binding to ERE did not alter reporter activity while ERβ binding to ERE significantly induced reporter activity.

CONCLUSIONS: Our studies identified that ER differentially binds to ERE in pregnant and nonpregnant endothelial cells and E_2ERβ positively regulates *AT_2R* transcription through a functional ERE in the *AT_2R* promoter, in a pregnancy-specific manner.

O-028

The Association Between the History of Hypertensive Disorders of Pregnancy, Obesity and Hypertension in Later Life by Age Group: A Cross-Sectional Analysis. Maiko Wagata†,[1] Naoki Nakaya,[1] Naho Tsuchiya,[1] Tomohiro Nakamura,[1] Hirohito Metoki,[1] Akimune Fukushima,[2] Nobuo Yaegashi,[1] Shigeo Kure,[1] Shinichi Kuriyama,[1] Atsushi Hozawa,[1] Junichi Sugawara.[1] *[1]Tohoku University, Sendai, Miyagi, Japan; [2]Iwate Medical University, Morioka, Iwate, Japan.*

INTRODUCTION: To clarify the association between hypertensive disorders of pregnancy (HDP) and hypertension(HT) in later life, and to determine which is the higher risk factor, a history of HDP or obesity, by age group analysis.

METHODS: A cross-sectional population based study was conducted in Miyagi from May 2013 to March 2016. Of the 24,518 women, 19,470 parous women aged between 20 and 75(mean 59.5±11.0) were included in this study of age group analysis. First, we analyzed the association between a history of HDP and HT using chi-square test. Second, multivariate logistic regression analysis was also performed adjusting for age, body mass index (BMI) and drinking status. At last, we constructed a composite variable that combined a history of HDP (+/-) and obesity (BMI≥25kg/m^2) (+/-), providing four categories, and analyzed the risks of each categories by multivariate logistic regression analysis adjusting for age and drinking status.

RESULTS: 889 (4.6%) women had a history of HDP. The prevalence of HT in women with and without HDP was 49.0% and 33.8%, respectively ($p<0.01$). Women with HDP had a higher prevalence of HT in all age groups. The adjusted odds ratio(OR) for HT in women with HDP and 95% confidence interval(CI) in 30s, 40s, 50s, 60s, and 70s were 3.83(2.04-7.18), 2.29(1.57-3.35), 2.35(1.85-3.00), 1.64(1.40-1.92) and 2.05(1.53-2.74), respectively. In the analysis of four categories, the combination of a history of HDP and obesity had the highest OR for HT. Obesity without HDP participants had higher risk than non-obesed participants with HDP in all age groups except for 70s.

	30s	40s	50s	60s	70s
HDP(-) Obesity(-)	1.00	1.00	1.00	1.00	1.00
HDP(+) Obesity(-)	3.05*	3.07*	2.38*	1.60*	2.52*
HDP(-) Obesity(+)	4.06*	4.39*	2.83*	3.21*	2.52*
HDP(+) Obesity(+)	27.42*	7.82*	9.49*	4.52*	5.87*

(*$p<0.05$)

CONCLUSIONS: Women with a history of HDP had higher risk of HT in later life. But obesity is a higher risk factor than the history of HDP, then weight control is effective to prevent HT in later life even for women with a history of HDP.

O-029

The Host Defence Peptide Cathelicidin Mediates Inflammatory Preterm Birth. Tina Baker,[1] Heather MacPherson,[2] Kirsten Wilson,[2] Sara Rinaldi,[2] Lorraine Frew,[2] Adrian Thomson,[3] Carmel Moran,[3] Julia Dorin,[1] Donald Davidson,[1] Sarah J Stock*.[2] *[1]University of Edinburgh, Edinburgh, Scotland, United Kingdom; [2]University of Edinburgh, Edinburgh, Scotland, United Kingdom; [3]University of Edinburgh, Edinburgh, Scotland, United Kingdom.*

INTRODUCTION: Cathelicidin is a host defence peptide with immunomodulatory functions, expressed in inflammatory and epithelial cells. We hypothesise it has a role in modulating intrauterine inflammation that can cause preterm labour and delivery.

METHODS: Human myometrium was collected from women undergoing cesarean section in labor or prelabor, at term and preterm (<34 weeks) gestations (n=5-7 each group) and examined with immunofluorescence. Pregnant wild-type (C57/BL6) or cathelicidin knock out (*Camp* -/-) mice were injected with intrauterine lipopolysaccharide (LPS; 1μg) or saline under ultrasound guidance at E17, and time to delivery monitored by camera. In a separate cohort of mice (n=3 each group) tissues and serum were collected 6 hours post injection, and analysed by immunofluorescence, Taqman PCR and ELISA.

RESULTS: Human cathelicidin (LL-37) was increased in myometrium in labor, compared to non-labor controls ($p<0.05$). It was mainly localised in neutrophils. In wild-type mice, mouse cathelicidin (CRAMP) was increased in the myometrium 6 hours after intrauterine LPS injection, compared to saline controls ($p<0.05$), and was predominantly found in neutrophils, mirroring the findings in human preterm labor. CRAMP was not expressed in *Camp-/-* mice. Preterm birth (delivery of first pup within 24 hr) following intrauterine LPS occurred more frequently in wild-type mice than in *Camp* -/- mice (10/12 [83.3%] wild-type vs 4/10 [40%] *Camp* -/-; $p=0.048$) and there was increased pup survival in *Camp* -/- mice ($p=0.02$). Preterm birth was rare in saline treated animals of either genotype (1/6 [17%] wild-type vs 0/4 [0%] *Camp* -/-; $p=0.38$). Placental RNA expression of *Ptgs2* and *Cxcl1* was lower in *Camp* -/- mice than in wild-type mice after LPS treatment ($p<0.05$). Compared to saline controls, IL-6 and TNF were increased in maternal serum following intrauterine LPS in wild-type mice ($p<0.05$) but not in *Camp*-/- mice.

CONCLUSIONS: Cathelicidin has a role in mediating inflammatory preterm birth. Mice lacking the cathelicidin gene are protected from preterm delivery, and have an altered inflammatory response to LPS. Targeting cathelicidin may lead to new treatments to prevent preterm birth.

O-030

Protease Amplification of the Inflammatory Response Induced by *L. Iners:* Implications for Racial Disparities in Preterm Birth. Sheikh MK Alam†,[1] William H Nugent,[1] Sonya L Washington,[1] Kimberly K Jefferson,[2] Jerome F Strauss, III,[1] Scott W Walsh*.[1] [1]*Virginia Commonwealth University, Richmond, VA, USA;* [2]*Virginia Commonwealth University, Richmond, VA, USA.*

INTRODUCTION: The vaginal microbiome of African American women is significantly more diverse than that of women of European ancestry, with a prevalence of bacterial taxa that are associated with microbial invasion, and *Lactobacillus* species that are not protective of vaginal health, which may contribute to the racial disparity in preterm birth. Hypothesis: *Lactobacillus* species more prevalent in African Americans induce a robust inflammatory response, amplified by macrophage release of proteases, that activate adjacent macrophages via proteinase-activated receptor 1 (PAR-1).

METHODS: Decidual tissue was collected from fetal membranes after delivery from women at term-not-in-labor (TNL), term labor (TL), spontaneous preterm labor (sPTL), infected preterm labor (iPTL). Mononuclear cells of pregnant women and THP-1 cells were exposed to *Lactobacilli* characteristic of the vaginal microbiome of women of European (*L. crispatus*) or African (*L. iners*) ancestry, *Fusobacterium nucleatum* (pathologic, invasive), and PAR-1 and RhoA kinase (ROCK) inhibitors. The inflammatory response was monitored by confocal microscopy of the subcellular location of the p65 subunit of NF-κB and IL-8 production determined by ELISA.

RESULTS: Decidual areas of immunohistochemical staining for PAR-1 and CD14, a macrophage marker, increased TNL<TL<sPTL< iPTL ($p<0.001$). % cells with nuclear localization of p65 was low for control (8±3%) and *L. crispatus* (19± 3%), but significantly increased for *L. iners* (62±7%) and *F. nucleatum* (97±3%) ($P<0.001$). Inhibition of PAR-1 or ROCK prevented nuclear localization of p65 demonstrating amplification of the inflammatory response was mediated by proteases. *L. iners* and *F. nucleatum*, but not *L. crispatus*, caused dose response increases in IL-8 ($P<0.001$).

CONCLUSIONS: *Lactobacillus* species prevalent in African American women initiate a more robust inflammatory response than *Lactobacillus* species prevalent in European ancestry women. The response is amplified by protease activation of PAR-1 and phosphorylation of NF-κB by ROCK, causing its nuclear localization. The presence of *Lactobacillus* species that are not protective of vaginal health may contribute to the higher incidence of preterm birth in African Americans. HL069851, P60MD002256.

O-031

Vaginal Dysbiosis Increases Risk of Preterm Membrane Rupture, Funisitis and Neonatal Sepsis. Richard G Brown†,[1] Yun S Lee,[1] Ann Smith,[2] Lyndsay Kindinger,[1] Julian R Marchesi,[2] Phillip R Bennett,[1] David A MacIntyre*.[1] [1]*Imperial College, London, United Kingdom;* [2]*Cardiff University, Cardiff, Wales, United Kingdom.*

INTRODUCTION: Preterm prelabour rupture of the membranes(PPROM) precedes 30% of preterm births(PTB) and is a significant risk factor for chorioamnionitis, funisitis and early onset neonatal sepsis. Detailed understanding of the qualitative and quantitative composition of the vaginal microbiome before and after PPROM is pivotal for the development of predictive, preventive and therapeutic strategies.

METHODS: Vaginal swabs were taken antenatally from pregnant women(n=250). We analysed a representative subset of women who delivered at term(n=20) and women who subsequently experienced PPROM(n=15). We recruited women upon diagnosis of PPROM before(n=36) and after(n=42) Erythromycin treatment. Bacterial species composition was examined by sequencing of 16SrRNA gene amplicons(V1-V2) and quantitative RT-PCR to calculate total bacterial load. Histological examination of the placental was performed in 51 PPROM cases and neonatal metadata collected.

RESULTS: The vaginal microbiome in uncomplicated pregnancies was characterised by low diversity and *Lactobacillus* spp. dominance. In comparison, women who subsequently experienced PPROM showed increased *L.iners* dominance(35 vs 53%) and the emergence of a community state low in *Lactobacillus* spp. abundance and high diversity(dysbiotic, 0 vs 34%). Following PPROM(before Erythromycin) diversity rose significantly becoming the predominant feature in 53% of cases with reduced bacterial load. Erythromycin treatment was associated with increased prevalence of dysbiosis(70%) with unaltered bacterial load. Histological chorioamnionitis and funisitis was associated with vaginal dysbiosis(70%), elevated maternal CRP and the emergence of *Sneathia* spp*., Ureaplasma parvum, Atopobium vaginae* and *Fusobacterium nucleatum* when compared to women with normal placental histology who were more likely to harbour *Lactobacillus* spp.(69%). Vaginal colonization with *L.crispatus* following PPROM was associated with reduced incidence of early onset neonatal sepsis.

CONCLUSIONS: *L.iners* and dysbiosis represent antenatal risk factors for PPROM which could be used for risk stratification and targeting of microbial modulatory therapies. PPROM and Erythromycin treatment are both associated with persistent vaginal dysbiosis a significant risk factor for chorioamnionitis, funisitis and the emergence of pathogens implicated in neonatal sepsis.

O-032

hCG Suppresses IP-10 in Human Decidua Through Histone Methylation. Michelle Silasi,[1] Yang Yang-Hartwich,[1] Gil Mor*,[1] Rosanna Ramhorst,[2] Esteban Grasso.[2] [1]*Yale University, New Haven, CT, USA;* [2]*University of Buenos Aires School of Sciences, IQUIBICEN-CONICET National Research Council, Buenos Aires, Argentina.*

INTRODUCTION: hCG is an immune regulator preventing T- cell migration. The decidua plays a major role in immune cell migration, especially T- cell migration. During infection, elevated levels of IP-10, a major T- cell chemoattractant, are associated with adverse pregnancy outcomes. But, the mechanism regulating chemokine expression and immune cell migration in the decidua is unknown. The PRC2 complex, the main protein complex silencing target genes by methylated histone binding to DNA. We hypothesize that hCG immune suppression occurs in the decidua. Here we demonstrate that hCG, enhances histone methylation binding to the IP-10 promoter, repressing IP-10 expression. Changing histone methylation leads to IP-10 expression and pregnancy loss.

METHODS: In vitro studies were done using the human endometrial stromal cell line (hESC). IP-10 and EZH2 expression were determined by quantitative PCR. T-cell migration assays were performed using the two-chamber migration assay comparing conditioned media from stromal cells and decidualized stromal cells. Chromatin immunoprecipitation was performed to determine the binding region of H3K27me3 by PCR. Organ cultures were prepared from freshly isolated human decidua tissue (non labor). Expression and secretion of IP-10 in decidua tissue was determined by quantitative PCR and ELISA.

RESULTS: hCG-inhibits IP-10 expression by inducing H3K27me3 histone methylation, which binds to Region 4 (505-601bp upstream) of the IP-10 promoter, thereby suppressing IP-10 expression. hCG-induced histone methylation is through EZH2, the enzyme of the PRC2 complex. T- cell migration is decreased towards conditioned media from decidualized stromal cells compared to non-decidualized stromal cells. LPS treatment reverses hCG suppression increasing IP-10 expression/ secretion and enhancing CD8+ T cells. These findings were validated with organ culture of freshly isolated human decidua tissue.

CONCLUSIONS: We describe a novel mechanism by which hCG suppresses immune cell recruitment in the decidua. Our data demonstrates an active cross talk between the placenta (hCG) and the decidua (IP-10) to control immune cell recruitment. Infection disrupting the immune regulatory function of hCG and PRC2 complex interactions, may have detrimental effects on pregnancy success and may lead to pregnancy loss.

O-033

Relationship Between Yeast, Vaginal Microbiota Composition and Pregnancy Outcomes. Holly Lewis†, Pamela Pruski†, Lindsay Kindinger†, Yun Lee, Phillip Bennett, Zoltan Takats, David A MacIntyre*. *Imperial College London, London, United Kingdom.*

INTRODUCTION: Vaginal microbiota-maternal host interactions influence pregnancy outcomes. While the bacterial component of the microbiome has been extensively investigated, the impact of yeast presence on vaginal microbiota and pregnancy outcome is poorly defined. The aim of this study was to examine the relationship between vaginal yeast, microbiota and the metabolome in pregnancy.

METHODS: Vaginal swabs (n=590) were collected from asymptomatic women at specific time points in pregnancy. Culture methods were used to identify samples with normal flora (blood agar) or yeast (Sabouraud). Microbiota profiling was performed using MiSeq-based sequencing of the bacterial 16S rRNA gene. Results were clustered at species level according to ward linkage into community state types (CST). Desorption electrospray ionization mass spectroscopy was used to assess the vaginal metabolome in matched swabs.

RESULTS: A total of 250 samples (42%) were classified as normal flora (3+ score, n=169; 68%) or yeast presence (3+ score, n=81; 32%). Presence of yeast was higher in term (68/193; 35%) compared to preterm delivery <37 weeks gestation (13/57; 23%). Yeast was positively associated with *L. iners* dominated (CST III) vaginal microbial communities (47% vs. 24%; P<0.001; Fisher's exact) and negatively associated with CST I (*L. crispatus*); (32% vs. 50%; P<0.001; Fisher's exact). No relationship was observed between yeast or normal flora and prevalence of CST II (*L. gasseri*), CST V (*L. jensenii*) or CST IV (dysbiotic). CST III was associated with increased risk of preterm birth (33% vs. 23%, P<0.001, Fisher's exact). Women with CST III and yeast presence had significantly reduced rates of preterm birth (9% vs. 24%; Odds Ratio: 0.26 [95% CI=0.09-0.73]). Yeast presence substantially altered the mucosal metabolic profile of CST III-dominated communities.

CONCLUSIONS: Our results indicate that yeast presence is associated with differences in both the vaginal microbiome community structure and metabolome in pregnancy. Women with presence of yeast are more likely to have CST III and less likely to have CST I. In our cohort, preterm birth is significantly associated with CST III. However yeast presence in CST III dominated communities is associated with reduced preterm birth risk.

O-034

***Nur77*, a Novel Player in Perinatal Neuroinflammation Associated with Preterm Labor in a Murine Model (*Mus Musculus*).** Sarah Estrada†,[1] Andrew Thagard,[1] Irina Burd,[2] Peter Napolitano,[1] Nicholas Ieronimakis*.[1] *[1]Madigan Army Medical Center, Madigan Army Medical Center, WA, USA; [2]Johns Hopkins University, Baltimore, MD, USA; [3]Madigan Army Medical Center, Madigan Army Medical Center, WA, USA.*

INTRODUCTION: The current understanding of perinatal neuroinflammation in preterm labor remains incomplete. Using an established murine model of preterm birth and perinatal brain injury, we examined changes of gene expression in embryonic brain resulting from lipopolysaccharide (LPS) mediated neuroinflammation. Through microarray analysis we have previously identified the upregulation of *Nur77* in embryonic brains exposed to intrauterine LPS. *Nur77* is an orphan nuclear receptor that is not normally expressed in embryonic brains but has been implicated in adult neuroinflammation and apoptosis. To understand the role of *Nur77* in perinatal brain injury, we evaluated the response of *Nur77* knockout (KO) versus wild type (wt) mice to LPS and hypothesized that its absence in KO mice would reduce neuroinflammation.

METHODS: *Nur77* KO and wt dams were randomized to receive an intrauterine injection of PBS or LPS on day 15 of the 19-21 day embryonic gestation. E15 brains were collected 6 hours post surgeries for mRNA expression analysis of inflammatory genes by qRT-PCR. Expression levels were normalized to *18s* rRNA and compared by student's *t*-test for significance.

RESULTS: In wt embryo brains, the relative expression of key inflammatory cytokines Il1b, Il6 and Tnfa was significantly elevated with LPS. In contrast, *Nur77* KO brains exposed to LPS showed significantly lower expression or near the level of controls for these same genes. **Figure(s) will be available online.*

CONCLUSIONS: The absence of *Nur77* in KO mice diminished the inflammatory response in embryonic brains. This provides a basis for the role of *Nur77* in intrauterine perinatal neuroinflammation. Whether *Nur77* signaling directly or indirectly influences the neuroinflammatory response still remains in question. Future studies will be aimed at looking at the cellular expression and signaling of *Nur77*.

O-035

Effects of Receptor for Advanced Glycation End-Products (RAGE) on Inflammation Induced Preterm Birth and Neonatal Viability in a Genetically Engineered Mouse Model. Bethany T Stetson†,[1] Brian A Kellert†,[1] Hanaa Motawea,[2] Megan Locke,[2] Guomao Zhao,[2] Antonette T Dulay,[3] Catalin S Buhimschi,[1] Irina A Buhimschi*.[2] *[1]The Ohio State College of Medicine, Columbus, OH, USA; [2]Nationwide Children's Hospital, Columbus, OH, USA; [3]Yale School of Medicine, New Haven, CT, USA.*

INTRODUCTION: RAGE is a multi-ligand pattern recognition receptor with key roles in inflammation and irreversible tissue damage. We hypothesized that maternal endotoxin-induced RAGE activation shortens the length of gestation and decreases neonatal viability.

METHODS: Intra-peritoneal maternal administration of lipopolysaccharide (LPS) was performed on day 15 of gestation (d0 = sperm plug) in mice randomly assigned to the following groups: **1)** C57BL6 RAGE knockout (BL6 RAGE-/-); **2)** C57BL6 wild-type (BL6+/+); **3)** CD1 humanized overexpressing RAGE transgenic mice (CD1 RAGE-Tg); **4)** CD1 wild-type (CD1+/+); (n=5-15 animals/group). Due to known strain variance in sensitivity to LPS, BL6 and CD1 mice received 2.5 or 25 μg of LPS respectively with saline controls. A continuously operated infrared video monitoring system was used to record the length of gestation and viability of each neonate at birth. Based on study findings and to assess translational potential, real-time PCR was performed to assess human myometrial expression of RAGE.

RESULTS: After administration of LPS, BL6 RAGE-/- mice had significantly longer gestations compared to BL6+/+ mice (P<0.001).

Injection	Strain and Genotype	Latency (h), mean ± SEM	Liveborn pups (%), mean ± SEM
LPS 2.5 μg	BL6 RAGE -/-	137.1 ± 4.4	96.8 ± 1.2
	C57BL6 +/+	61.0 ± 10.4	51.2 ± 7.0
Saline	BL6 RAGE -/-	86.3 ± 4.4	100 ± 0
	C57BL6 +/+	84.7 ± 1.5	100 ± 0
LPS 25 μg	CD1 RAGE-Tg	10.8 ± 2.7	23.5 ± 0.8
	CDI +/+	87.3 ± 21.4	74.4 ± 0.8
Saline	CD1 RAGE-Tg	108.8 ± 4.7	77.4 ± 0.6
	CDI +/+	117.5 ± 5.6	80.3 ± 0.1

Conversely, LPS-treated CD1 RAGE-Tg mice had shorter gestations compared to CD1+/+ dams (P=0.022). More neonates were born alive by BL6 RAGE-/- mice, when compared to BL6+/+ controls (P<0.001). LPS increased the rate of stillbirth in CD1 RAGE-Tg mice when compared to BL6 RAGE-/- and CD1+/+ mice (all, P<0.001). Real-time PCR confirmed human myometrial expression of RAGE.

CONCLUSIONS: Maternal RAGE expression impacts neonatal viability and susceptibility to inflammation-induced preterm birth.

O-036

T-Cell Activation-Induced Preterm Labor Involves Unique Innate and Adaptive Immune Responses That Differ from Those Observed in Inflammation- and Progesterone Withdrawal-Induced Preterm Labor. Marcia Arenas-Hernandez†,[1,2] Roberto Romero,[2] Tara N Mial,[1,2] Felipe Vadillo-Ortega,[3] Sonia S Hassan,[1,2] Nardhy Gomez-Lopez.[1,2] *[1]Wayne State University, Detroit, MI, USA; [2]NICHD, Detroit, MI, USA; [3]UNAM, Mexico City, DF, Mexico.*

INTRODUCTION: Preterm labor is a syndrome of multiple mechanisms of disease, including microbial-induced inflammation and progesterone withdrawal. T-cell activation has emerged as a new mechanism of disease for preterm labor. Herein, we investigated the innate and adaptive immune responses induced by a microbial product (lipopolysaccharide or LPS), progesterone withdrawal (RU486 administration), and T-cell activation (injection of a monoclonal αCD3ε antibody).

METHODS: C57BL/6 mice were injected with 10μg of αCD3ε antibody (n=10), 10μg of IgG1κ isotype (controls, n=13), 15μg of LPS (n=8), or 200μL of 1X PBS (controls, n=8) on 16.5 days *post coitum* (dpc). Another group of mice was injected with either 150μg of RU486 (n=10) or 1:13 DMSO (controls, n=10) on 15.5 dpc. Peripheral blood as well as the myometrium and decidua were collected 13-16 hours post-injection. Leukocyte suspensions were prepared and the activation of innate and adaptive immune cells was determined by immunophenotyping.

RESULTS: 1) administration of αCD3ε, but not LPS or RU486, enhanced the expression of IL2 and IL4 by CD4+ T cells (i.e. T-cell activation) in the maternal circulation, decidua and myometrium; 2) administration of αCD3ε, but not LPS or RU486, enhanced the expression of IFNγ by myometrial CD8+ T cells (i.e. T-cell activation); 3) administration of αCD3ε, but not LPS or RU486, increased the expression of IFNγ by decidual B cells (i.e. B-cell activation); 4) administration of αCD3ε, but not LPS or RU486, enhanced the expression of iNOS, Arg1 and IL10 by decidual and myometrial macrophages (i.e. macrophage activation); and 5) administration of LPS, but not αCD3ε or RU486, increased the proportion of decidual and myometrial neutrophils (i.e. innate immune activation).

CONCLUSIONS: T-cell activation-induced preterm labor involves unique innate and adaptive immune responses that differ from those observed in inflammation- and progesterone withdrawal-induced preterm labor.

O-037

Targeted Nanoparticle Delivery of Short Interfering RNAs to Treat Preeclampsia. Natalie J Hannan,[1] Scott Pattison,[2] Sally Beard,[1] Natalie K Binder,[1] Jennifer MacDiarmid,[2] Himanshu Brahmbhatt,[2] Tu'uhevaha J Kaitu'u-Lino,[1] Stephen Tong.[1] *[1]The University of Melbourne, Melbourne, VIC, Australia; [2]EnGeneIC Ltd, Sydney, NSW, Australia.*

INTRODUCTION: Preeclampsia is a serious complication of pregnancy. Claiming over 60,000 mothers worldwide and far more babies. Central to its pathogenesis is soluble Flt1 (sFlt1): produced in excess and released from the preeclamptic placenta, it spreads throughout the maternal bloodstream, causing endothelial dysfunction and major organ injury. There are currently no treatments other than delivery. Thus a treatment that can quench disease severity would allow an extension of the pregnancy. EnGeneIC Delivery Vehicles (EDVs) are nanocells able to deliver agents specifically to target tissues. This study aimed to determine whether EDVs targeted to the placenta via the epidermal growth factor receptor (EGFR), loaded with short interfering RNAs to block sFlt1 production (si-sFlt1) could reduce expression and secretion of sFlt1 by the placenta.

METHODS: Human primary trophoblasts were isolated, si-sFlt1 was added and cultured for 24 hours. Placental explant tissue was dissected and suspended in hanging drops of media, EDVs loaded with either si-sFlt1 or negative control siRNA were added and the explants were cultured for 48 hours. Cells, tissue and media were collected. RNA was extracted to examine sFlt1 expression by qPCR and sFlt1 secretion was assessed in the media. Pregnant mice received intravenous injection of si-sFlt1 loaded EDVs either 1) placental targeted (via EGFR), or 2) non-targeted on E12.5 of pregnancy, placentas were collected on E14.5 and assessed si-sFlt1 accumulation.

RESULTS: Treatment of trophoblast with si-sFlt1 significantly reduced sFlt1 mRNA expression and sFlt1 protein secretion, compared to scrambled si-sFlt1 siRNA. There was a significant reduction in both sFlt1 mRNA and protein secretion in the placental explant tissue treated with EDVs loaded with si-sFlt1, compared to scrambled si-sFlt1. Abundant si-sFlt1 was detected in mouse placentas that received placental targeted EDVs loaded with si-sFlt1, where as minimal si-sFlt1 was found in placentas that received control non-targeted EDVs.

CONCLUSIONS: These data provide proof of principle for targeted delivery of siRNA to the placenta and provide a novel platform for the development of placenta-specific therapeutics as a treatment strategy for preeclampsia. We are currently testing their ability to rescue the preeclamptic phenotype in a mouse model of disease.

O-038

Hydrogen Sulphide Ameliorates Preeclampsia-Like Phenotype Induced by Elevated sFlt-1 in Placenta Growth Factor Deficiency. Shakil Ahmad,[1] Keqing Wang,[1] Peter Hewett,[2] Asif Ahmed.[1] *[1]Aston University, Birmingham, West Midlands, United Kingdom; [2]University of Birmingham, Birmingham, West Midlands, United Kingdom.*

INTRODUCTION: Low circulating placenta growth factor (PlGF) is a strong predictor of preeclampsia (PE), a life threatening condition in pregnancy characterized by widespread endothelial damage leading to maternal hypertension, proteinuria and fetal growth restriction. Equally, high soluble Flt-1 (sFlt-1) and low PlGF give rise to poor maternal and infant outcomes in women diagnosed with PE. However, the functional significance of PlGF in the pathogenesis of PE phenotype remains unknown. We investigated whether the decreased levels of PlGF in pregnancy, exacerbate the fetal growth restriction associated with preeclampsia in the presence of high sFlt-1 and the potential of hydrogen sulfide to ameliorate these effects.

METHODS: Pregnant $PlGF^{-/-}$ mice were injected with adenovirus encoding sFlt-1 (Ad-sFlt-1) at $1x10^9$ pfu/ml at E10.5 and mean arterial blood pressure (MAP), biochemical and histological analysis of maternal kidney, placenta and embryos were assessed at the end of pregnancy.

RESULTS: Ad-sFlt-1 significantly increased MAP and induced severe glomerular endotheliosis in $PlGF^{-/-}$ mice compared to wild-type animals. Soluble Flt-1 also significantly elevated albumin-creatinine ratio and increased levels of urinary kidney injury molecule-1, a marker for proximal tubule injury.Furthermore, sFlt-1 overexpression increased fetal resorption rate in the $PlGF^{-/-}$ mice and promoted abnormal placental vascularization. To determine whether placental PlGF is critical for preventing fetal growth restriction associated with preeclampsia, we generated haploinsufficient $PlGF^{+/-}$ placentas and embryos in dams and exposed to high sFlt-1 environment. These mothers showed reduced fetal resorption, gestational hypertension and proteinuria when compared to pregnant $PlGF^{-/-}$ mice. Furthermore, treatment with hydrogen sulfide-releasing agent, GYY4137, significantly reduced resorption, hypertension and proteinuria observed in Ad-sFlt-1 treated pregnant $PlGF^{-/-}$ mice.

CONCLUSIONS: Placental derived PlGF is a protective factor against the damaging effects of elevated sFlt-1 associated with pregnancies complicated with preeclampsia and activation of the hydrogen sulphide pathway may rescue preeclampsia phenotype even under low PlGF environment.

O-039

A Novel Conjugated Linoleic Acid Therapy for Preeclampsia Shows Protective Effects on Human Endothelial Cell Function In Vitro. Danielle M Berdahl†, Dinesh M Shah, Ian M Bird, Derek S Boeldt*. *Univ Wisconsin-Madison, Madison, WI, USA.*

INTRODUCTION: A hallmark of preeclampsia (PE) is endothelial dysfunction. Changes in circulating growth factors (GF) and cytokines (Cyt) are implicated in PE-related endothelial dysfunction. Multiple factors reduce endothelial vasodilator production capacity through inhibition of sustained Ca2+ responses via Src kinase activation. The t10,c12 isomer of conjugated linoleic acid (CLA) at 50uM inhibits Src signaling and restores Ca2+ signaling in endothelial cells exposed to GF and Cyt. Commercially available and dietary CLA therapies include both

t10,c12 and c9,t11 isomers of CLA, but doses of 50uM are unrealistic in vivo. Thus, we tested a physiologically achievable dose of 10uM t10,c12 and c9,t11 CLA combination on GF and Cyt known to inhibit sustained Ca2+ bursts in human endothelial cells, for therapeutic efficacy.
METHODS: Human umbilical vein endothelial cells (HUVEC) from normal pregnancies were grown on 35mm glass bottom dishes to >90% confluence. HUVEC were loaded with Ca2+ sensitive Fura-2 AM dye and mounted on an inverted fluorescent microscope. A control stimulation of 100uM ATP was recorded for 30min and Ca2+ bursts counted. The cells were washed and pretreated with the 10uM CLA combination or the Src inhibitor PP2 for 30min while retaining focus on the previously stimulated cells. Cells were then treated with 10ng/ml VEGF165, bFGF, TNFa, or IL-6 for 30min before re-stimulation with ATP. Ca2+ bursts in response to ATP were counted again and compared to initial ATP control treatment.
RESULTS: Significant improvement in ATP-stimulated Ca2+ burst function was achieved with PP2 pretreatment for VEGF165 ($p<.001$), bFGF ($p<.001$), and TNFa ($p<.05$) only. Pretreatment with 10uM t10,c12 CLA and 10uM c9,t11 CLA combination significantly rescued Ca2+ burst inhibition due to VEGF165 ($p<.001$), bFGF ($p<.001$), TNFa ($p<.001$), and IL-6 ($p<.05$). All comparisons were analyzed by Rank Sum test on the distribution of relative change in ATP-stimulated Ca2+ bursts before and after treatment.
CONCLUSIONS: The results of this study confirm that Src kinase activation plays an important role in promoting endothelial dysfunction in states of aberrant GF and Cyt profiles such as in PE. Novel therapies targeting endothelial Src signaling such as CLA administration through pharmacological or dietary intervention may be a viable strategy to combat symptoms of PE related to endothelial dysfunction. *NIH HD079865, HD38843, HD41921.*

O-040

Fetal Asymmetric Dimethylarginine Regulates Maternal Haemodynamics. Aikaterini Georgopoulou†,[1] James Leiper,[2] Mark R Johnson*.[1] *[1]Imperial College London, London, United Kingdom; [2]Imperial College London, London, United Kingdom.*
INTRODUCTION: Circulating levels of Asymmetric Dimethylarginine (ADMA) are increased in women with preeclampsia and have been linked to a higher disease incidence. Studies have also suggested a paternal contribution to the disease. ADMA is mainly cleared from the body through the action of the enzyme called dimethylarginine diaminohydrolase 1 (DDAH1). The activity and expression of this enzyme is lower in placentas from preeclamptic pregnancies. We have developed a mouse model of embryonic DDAH1 insufficiency, in order to assess the impact of DDAH1 absence from the fetoplacental unit upon circulating ADMA levels and haemodynamics of a normotensive female during pregnancy.
METHODS: *ddah1fl/flCre-/-* (WT) females were mated to *ddah1fl/flCre+/+* (KO) males to generate *ddah1fl/flCre+/-* (KO) embryos. As control matings, *ddah1fl/flCre-/-* females were mated with the same genotype of males to generate WT embryos. Plasma was collected from the two groups of pregnant females in early (E6.5), mid (E12.5) and late pregnancy (E18.5). ADMA was measured in these samples by Liquid Chromatography Mass spectrometry (LCMS). Systemic blood pressure was monitored during pregnancy using radiotelemetry probes.
RESULTS: Females who bred KO fetuses had almost 1.5-fold higher ADMA in their circulation in late pregnancy compared to females who bred WT foetuses (2.49uM±0.17 and 1.75 uM±0.13 respectively) suggesting that excessive ADMA produced in the fetoplacental unit can raise maternal circulating ADMA levels. Systemic blood pressure was found to be elevated at late pregnancy in the mothers who bred KO fetuses compared to those who bred WT fetuses ($p<0.05$).
CONCLUSIONS: Fetal DDAH1 seems to play an important role in regulating maternal circulating ADMA and haemodynamics during mouse pregnancy. This is an interesting observation, if we take into account the fact that polymorphisms within the *ddah1* gene, which affect DDAH1 activity, have been linked to a higher risk of preeclampsia. This finding also suggests a fetal (paternally-derived) contribution to the disease.

O-041

Molecular Evidence for Abnormal Differentiation of Invasive Trophoblast in Preeclampsia. Anna Natenzon, Sonia DaSilva-Arnold†, Stacy Zamudio, Abdulla Al-Khan, Nicholas P Illsley. *Hackensack University Medical Center, Hackensack, NJ, USA.*
INTRODUCTION: Preeclampsia (PE) is associated with impaired remodeling of maternal spiral arteries by extravillous trophoblast (EVT), which has been ascribed to defective trophoblastic invasion. Cytotrophoblast differentiation to the invasive phenotype involves an epithelial-mesenchymal transition (EMT), which includes loss of cell-cell adhesion and apical-basal polarity, and increased cell motility and invasive activity. We hypothesized that molecular markers of EMT would be diminished in EVT from PE placentae, consistent with more limited invasion.
METHODS: EVT isolated from early-onset PE (n=3, GA 31.6±0.2 wks) were compared with preterm controls (placenta previa; n=8, GA 35.3±1.3 wks). We included only nulliparous PE patients without significant maternal comorbidities. We evaluated PE and control transcripts using a PCR array specific for EMT-associated genes. Results were analyzed using the $\Delta\Delta C_T$ method. Results below are significant at $p<0.05$, and are reported as the fold change in PE relative to control.
RESULTS: PE was characterized by reduction in MMP9 (-17.5) and TIMP1 (-3.2), genes involved in ECM degradation. VCAN, which increases cell motility and decreases cell adhesion, was reduced 8.2-fold. There were reductions in VIM (-18.0), SPARC (-2.4), and SPP1 (-8.6), markers of the mesenchymal phenotype and in the regulatory inducers of EMT, including IGFBP4 (-16.1), JAG1 (-2.4), and WNT5A (-13.6). Most notable was the decrease in the ZEB2 transcription factor (-23.2), a master regulator of the EMT that is profoundly increased in normal trophoblast EMT.
CONCLUSIONS: Our results suggest that EMT is impaired in EVT from subjects with severe preeclampsia. There is under-expression of transcriptional, regulatory, and structural components of the EMT. These data do not permit us to ascertain whether the gene expression changes are intrinsic to EVT or due to external factors at the maternal-fetal interface. The gestational age difference between PE and control placentae is a limitation that will be addressed by adding alternate controls more closely matched in GA. Our prior work in the over-invasion pathology, abnormally invasive placenta (AIP), shows over-expression of EMT genes in the EVT. These data support that the EVT in PE and AIP pregnancies have opposing molecular profiles consistent with under- versus over-invasion due to altered EMT.

O-042

Role of Estrogen and Its Metabolites in Uterine Artery Endothelial Cells Migration from a Model of Unilateral Pregnant Sheep. Rosalina Villalon-Landeros,[1] Chi Zhou†,[1] Jing Zheng,[1] Ronald R Magness*.[2] *[1]University of Wisconsin-Madison, Madison, WI, USA; [2]University of South Florida, Tampa, FL, USA.*
INTRODUCTION: Uterine artery endothelial cells (UAECs) play a central role in the regulation of uterine vascular adaptations, including angiogenesis, which increase uterine blood flow during normal pregnancy. Using an ovine surgically-induced unilateral pregnancy model to study the local uterine vascular adaptations to pregnancy, we demonstrated that compared to contralateral uterine arteries (UA), vessels ipsilateral to the gravid horn show increased blood flow and larger diameters. Moreover, endothelial cell proliferation in response to estrogen ($E_2\beta$) and its metabolites is up regulated in UAECs isolated from UAs ipsilateral to the gravid horn compared to UAs contralateral to the gravid horn. However, it is unknown if endothelial cell migration (another major step of angiogenesis) stimulated by $E_2\beta$ and its metabolites is also differentially regulated by the gravid versus non-gravid environment. We **hypothesize** that UAECs from UAs ipsilateral to the gravid horn [(Gravid)P-UAECs] will exhibit increased migration in response to $E_2\beta$, 2-hydroxyestradiol ($2OHE_2$) and 2-methoxyestradiol ($2ME_2$), as compared with UAECs isolated from UAs contralateral to the gravid horn [(NonGravid)P-UAECs].

METHODS: (Gravid)P-UAECs and (NonGravid)P-UAECs were isolated and validated from ewes (n=4) with unilateral uterine surgical isolation. Endothelial cell migration was measured using a scratch wound-healing assay. After serum starvation, cells were treated with vehicle, $E_2\beta$, $2OHE_2$, $2ME_2$ (0.1 and 100nM) or complete growth media. Images of wound area were taken at 0 and 12 hr of treatment and quantified using ImageJ software.
RESULTS: $E_2\beta$ and $2OHE_2$, but not $2ME_2$ induced more migration of (Gravid)P-UAECs ($P<0.01$) compared to (Non-Gravid)P-UAECs at both 0.1 and 100nM. We also observed that (Non-Gravid)P-UAECs migrated about 40% slower than (Gravid)P-UAECs ($P<0.05$) when treated with complete growth media.
CONCLUSIONS: These results demonstrate that endothelial cell programming during pregnancy regulates angiogenesis; which is highly dependent on the local environment ipsilateral to the feto-placental unit. In addition, basic endothelial cell function appears to be altered in response to the local gravid environment since endothelial cell migration was significantly different between the (Gravid)P-UAECs and (Non-Gravid)P-UAECs when treated with complete growth media alone.
F31HD088096.

O-043

A Randomised Controlled Trial and Cost-effectiveness Analysis of Low Dose Aspirin with an Early Screening Test for Preeclampsia in Low Risk Women. F Mone,[1] C Mulcahy,[2] P McParland,[1] J O'Mahony,[3] E Tyrell,[3] F Breathnach,[2] C Normand,[3] F Cody,[2] J Morrison,[2] S Daly,[2] J Higgins,[2] A Cotter,[2] E Tully,[2] P Dicker,[2] Z Alfirevic,[4] F Malone,[2] FM McAuliffe*.[1] *[1]National Maternity Hospital, Dublin, Ireland; [2]Rotunda Hospital, Dublin, Ireland; [3]Trinity College, Dublin, Ireland; [4]University of Liverpool, Liverpool, United Kingdom.*
INTRODUCTION: The objectives were;(i) determine feasibility and acceptability of routine daily 75mg aspirin versus screening test indicated aspirin from 11-weeks in low risk nulliparous women and (ii) assess cost-effectiveness of each approach.
METHODS: Low risk nulliparous women were randomised to; (i) routine aspirin, (ii) no aspirin, (iii) aspirin based on a Fetal Medicine Foundation preeclampsia screening test. Outcome measures included acceptability and feasibility of each approach. A health economic decision model was devised to estimate net health and cost outcomes.
RESULTS: In terms of acceptability, 546/1054 (51.8%) approached took part in an RCT involving routine aspirin. Adherence was 95% amongst the aspirin arm, and 92.3% (489/530) of women asked were willing to take aspirin in a subsequent pregnancy. The feasibility of performing the screening test was limited by time taken to obtain laboratory analysed PAPP-A and PLGF results; 7.6 (0-26) days. There was no difference in rates of preeclampsia (4.5% vs 4% vs 4%) or fetal growth restriction (8% vs 10% vs 14%). For cost-effectiveness, universal aspirin was the preferred strategy with 12.4 life years gained compared to 6.7 for screen and treat. Universal aspirin would result in an estimated cost saving of $215 million based on a population of four million.
**Figure(s) will be available online.*
CONCLUSIONS: This is the first RCT using routine aspirin in low-risk women. Such women were willing to take aspirin in pregnancy and were compliant. Universal aspirin is an optimal preventative strategy to prevent preeclampsia in nulliparous women with the largest health gain and cost saving. A universal aspirin approach for preeclampsia prevention should be considered.

O-044

Three Protein-Truncating Mutations That May Contribute to Developing Preeclampsia. HS Gammill,[1,2] R Chettier,[3] A Brewer,[3,4] JM Roberts,[5] R Shree,[1] E Tsigas,[4] K Ward*.[3] *[1]Univ Washington, Seattle, WA, USA; [2]Fred Hutch, Seattle, WA, USA; [3]Affiliated Genetics, Salt Lake City, UT, USA; [4]Preeclampsia Foundation, Melbourne, FL, USA; [5]Univ Pittsburgh, Pittsburgh, PA, USA.*
INTRODUCTION: As protein truncating variants (PTVs) often cause complete loss of function of a gene, finding PTVs associated with a disease can efficiently uncover novel pathophysiologic factors. We conducted a genome-wide search for PTVs associated with preeclampsia (PE).
METHODS: 190 subjects with PE were identified from The Preeclampsia Registry and Biobank. Subjects reporting a history of PE completed a detailed questionnaire and provided medical records for diagnostic confirmation. Saliva samples were collected for DNA isolation. Whole exome sequencing (WES) was performed using Ion Proton Instrument and AmpliSeq Exome Capture Kit. Only PTVs were considered in the initial analysis (variants introducing a stop codon, frame-shift, or the disruption of an essential splice site). Results were compared with data from 530 unrelated women with endometriosis who underwent WES by the same methods (EndoC) and 33,000 subjects in the Exome Aggregation Consortium (ExAC). PE was not excluded in these population controls.
RESULTS: Of 190 subjects with PE (170 confirmed and 20 probable/awaiting additional records), 165 (87%) were Caucasian. 136 (72%) had 1 or more preterm PE delivery prior to 37 weeks. Truncating variants in genes encoding for three proteins [trichohyalin like 1 (TCHHL1), epithelial cell transforming sequence 2 oncogene-like (ECT2L) FGFR1 oncogene partner (FGFR1OP)], were detected in the PE cohort (7.9% of affected women) that were virtually absent in the controls.

Gene	PTV Type	Nucleotide Change	PE subjects with PTV, n(%)	# haplotypes observed (freq. of haplotype)	PTV freq (EndoC)	PTV freq (ExAC)
TCHHL1	Stop gain	c.C1966T	6 (3.2)	One (37%)	1 (0.2%)	0.0004
ECT2L	Splicing	exon15: c.2028 +1G>T	5 (2.6)	One (8%)	0	0
FGFR1OP	Stop gain	c.T806A	4 (2.1)	Two (15%, 6%)	0	0

As further evidence of these genes' role, rare damaging missense variants were also found in FGFR1OP(2 variants) and ECT2L (6 variants).
CONCLUSIONS: 13% of PE subjects have likely pathogenic or protein-truncating mutations in the three genes implicated. As these genes have not been reported to have any association with or implication in PE, these findings may provide insights into novel pathophysiologic processes contributing to the development of PE.

O-045

Maternal MiR-30d Deficiency Is Associated with Defects in Endometrial Receptivity, Embryonic Implantation and Fetal Development. Nuria Balaguer†,[1,3] Inmaculada Moreno,[1,2,4] María Herrero,[2] Marta González-Montfort,[2] Carlos Simón,[1,2,3,4] Felipe Vilella*.[2,4] *[1]Igenomix, Paterna, VLC, Spain; [2]IVI/Incliva, Valencia, VLC, Spain; [3]Valencia University School of medicine, Valencia, VLC, Spain; [4]Standford University Medical School, Palo Alto, CA, USA.*
INTRODUCTION: We have previously demonstrated that maternal endometrial miRNAs acted as transcriptomic modifiers of the pre-implantation embryo (Development, 2015). Maternal miR-30d favored an increase of embryo adhesion in vitro. Here, we aim to prove this finding with a miR-30d KO model to determine if a maternal or embryonic defect of this miRNA leads to a phenotype during embryonic implantation and fetal development.
METHODS: KO mice were produced from the strain MirC26tm1Mtm/Mmjax. Ovulation and fertilization were studied on day 2 of pregnancy, and embryonic implantation at day 4 and 5. Implantation markers (COX-2, LIF, BMP-2, MSX-1, MSX-2, ER, PR) were analyzed by

immunofluorescence in both, pregnant and pseudopregnant mice (n=12). To investigate the impact of the bi-directional maternal-embryo transfer of miR-30d, several embryo transfer combinations (n= 6) were tested in both WT and KO recipient mice (n=42) in six biological replicates. Finally, feto-placental development was analyzed on pregnant dams on days 5,6 and 12.

RESULTS: Transfer of miR-30d KO embryos in WT recipients was associated with decreased implantation rates when compared to the transfer of WT embryos (48.93% ± 7.00 vs 80.56% ± 3.38 vs p=0.015). Similarly, the transfer of miR-30d KO embryos in KO recipients lead to lower implantation rates compared to the transfer of WT embryos in KO recipients (30.17% ± 5.22 vs 46.07% ± 2.27, p=0.04). Pretreatment of KO embryos with a synthetic miR-30d partially restored implantation rates, although it was not statistically significant. Implantation markers were reduced in KO pseudopregnant dams but their level of expression was reverted in KO pregnant females, suggesting the relevance of the embryonic miR-30d also as a transcriptomic modifier of the maternal site. Finally, the study of pregnancy outcome showed the existence of smaller implantation sites and fetuses in KO mice compared to WT dams.

CONCLUSIONS: The absence of miR-30d in the maternal endometrium is associated with defects in endometrial receptivity, embryonic implantation and fetal development. Therefore, this study demonstrates that not only key genes are mandatory for the onset and course of gestation, but also their regulatory elements. CS&FV con. eq.

O-046

Double Conditional Knockout of SMAD2 and SMAD3 Results in Endometrial Dysfunction, Infertility, and Uterine Cancer. Maya Kriseman†,[1,2] Diana Monsivais†,[2] Julio Agno,[2] Ramya Masand,[2] William Gibbons,[1] Martin Matzuk.[2] *[1]Baylor College of Medicine/Texas Children's Hospital Pavilion for Women, Houston, TX, USA; [2]Baylor College of Medicine, Houston, TX, USA.*

INTRODUCTION: TGFβ family signaling is involved in many reproductive processes including oocyte competence, implantation, and placental development. Ligands in the TGFβ family control key processes in the ovary, such as follicular development and cumulus expansion. Ligands such as activins and GDF9 signal intracellularly through SMAD2 and SMAD3, which translocate to the nucleus, bind DNA and regulate expression of target genes. While we know SMAD2/3 play important and redundant roles in the ovary, we do not know the role of SMAD2/3 in the uterus.

METHODS: SMAD2 and SMAD3 conditional knockout (cKO) mice were generated using the Cre-LoxP system. Smad2- and Smad3-flox/flox females were mated to males expressing the progesterone receptor-cre knock-in allele to obtain tissue-specific deletion in PR-expressing tissues. Smad2flox/-; Smad3flox/-; PRcre/+ (Smad2/3 cKO) mice were produced. Fertility studies and histology analyses of the reproductive tract were used to determine the roles of SMAD2 and SMAD3 in female reproductive function. Fertility studies were conducted by mating SMAD2/3 double cKO females with wild type C57/129 males.

RESULTS: Hyperproliferation of the endometrial lining was observed as early as 6 weeks of life. Endometrial hyperproliferation worsened with age, and all cKO mice went on to develop bulky endometrioid-type uterine tumors with a 100% mortality rate by 8 months of age. The tumors showed a significant increase in glandular tissue. We also observed that SMAD2/3 cKO mice were infertile. Implantation sites were on average smaller and fewer in the cKO mice as compared to the control group.

CONCLUSIONS: SMAD2/3 serve important roles in the regulation of the endometrium. Hyperproliferation of the endometrium affected both implantation of pregnancy as well as sustaining pregnancy. Endometrial hyperproliferation resulted in tumor formation incompatible with life. We are currently looking at the mechanism responsible for the dysfunction and hyperproliferation of the endometrium in the absence of SMAD2/3.

Research supported by the Eunice Kennedy Shriver National Institute of Child Health and Human Development grant R01-HD033438 (to M.M.M.) and by the Postdoctoral Enrichment Program Award from the Burroughs Wellcome Fund (to D.M).

O-047

Non-Classical Progesterone Receptor (PGRMC1) and SERPINE1 mRNA Binding Protein (SERBP1) Interaction Influences the Human Decidualization Process. Stefania Salsano†,[1] Alicia Quiñonero,[1] Silvia Pérez†,[1] Carlos Simón,[2] Francisco Domínguez*.[1] *[1]Fundación IVI, Paterna, Valencia, Spain; [2]Igenomix, Paterna, Valencia, Spain.*

INTRODUCTION: PGRMC1's mechanism of action in the human endometrium remains unclear.This protein is down-regulated in receptive endometrium but its expression is higher in stroma compared to epithelial cells(1).It interacts with SERBP1 in granulosa cells(2). We hypothesized that low levels of PGRMC1 and its interaction with SERBP1 in endometrial stromal cells(ESC)are needed for a correct decidualization process.

METHODS: We studied PGRMC1 and SERBP1 *in vivo* expression in endometrial biopsies throughout the menstrual cycle by IHC(n=5/each phase).To assess the functional effect of PGRMC1 in the decidualization process we performed *in vitro* PGRMC1 inhibition/overexpression studies with primary ESC.We transfected ESC cultures with small interfering PGRMC1(n=4)/PGRMC1 overexpression plasmid(n=25)or scramble/empty vector(n=4)and we induced in vitro decidualization. Decidualization was checked by measuring secreted Prolactin and IGFBP1 by ELISA and cytoskeleton reorganization by F-actin staining.We also checked abundance of both proteins by Western Blot in the subcellular fractions.Last,we focused on the specific PGRMC1/SERBP1 interaction in the decidualization process analyzing their co-localization in non decidualized(nDESC)and decidualized ESC(DESC)by immunofluoresce and co-immunoprecipitation.

RESULTS: *In vivo* analysis showed higher PGRMC1 expression in stroma compartment compared to SERBP1 throughout the menstrual cycle. PGRMC1 signal strongly decreased in late-secretory phase while SERBP1 was slowly increased across the menstrual cycle in stroma.PGRMC1 overexpression significantly inhibited *in vitro* decidualization,while its inhibition did not affect the process.Additionally,we showed a higher amount of PGRMC1 and SERBP1 in cytoplasmic fractions of nDESC and DESC.Although PGRMC1 was barely detected in the nucleus,it was found higher in DESC compared to nDESC.Finally,co-localization of PGRMC1 and SERBP1 was observed in the cytoplasm of nDESC and DESC.

CONCLUSIONS: Low PGRMC1 in human ESC is crucial for a correct decidualization.Furthermore,PGRMC1 interacts with SERBP1 in the cytoplasm of these ESC.Further studies may clarify the functional role of PGRMC1 in progesterone signaling during the decidualization process in humans.

Supported by Miguel Servet Program(CP13/00075)co-founded by FEDER

(1)T.Garrido-Gómez et al.,Hum.Reprod 29(9)2014
(2)J.J.Peluso et al.,Biol.Reprod 88(1)2013.

O-048

Hypoxia Inducible Factor (HIF) in the Endometrium: A Potential Therapeutic Target for Heavy Menstrual Bleeding (HMB). Jacqueline A Maybin†,[1] Alison Murray,[1] Nik Hirani,[2] Philippa TK Saunders,[2] Peter Carmeliet,[3] Hilary OD Critchley.[1] *[1]University of Edinburgh, Edinburgh, Scotland, United Kingdom; [2]University of Edinburgh, Edinburgh, Scotland, United Kingdom; [3]KU, Leuven, Flanders, Belgium.*

INTRODUCTION: HMB is a common, debilitating condition requiring new medical therapies. Progesterone-withdrawal in the late secretory phase causes vasoconstriction of endometrial spiral arterioles. The presence and role of subsequent hypoxia has been intensely debated.

Hypotheses: (1) hypoxia and hypoxia inducible factor (HIF-1) are necessary for efficient endometrial repair at menstruation (2) delayed endometrial repair may be corrected by pharmacologically increasing HIF-1 at menses.

METHODS: Endometrial biopsies were collected from healthy women and menstrual blood loss objectively measured (modified alkaline-haematin method: HMB>80ml). HIF-1α was detected by Western blot and downstream targets by PCR (n≥4 per group/cycle stage). Ovariectomy, administration of estradiol/progesterone and decidualization induction enabled modelling of endometrial shedding/repair in mice, allowing manipulation of hypoxia and HIF *in vivo* (n≥6/group). Histological grading quantified endometrial repair.

RESULTS: HIF-1α was present in nuclear extracts from human endometrium exclusively during the perimenstrual phase. Women with HMB had decreased endometrial HIF-1α and downstream targets (*CXCL4/VEGF*) at menstruation versus those with normal loss (P<0.05, P<0.001). Women with HMB bled for 2 days longer than those with normal loss (P<0.01).

We genetically (HIF-1α heterozygotes vs wild type) or pharmacologically (i.p. echinomycin vs vehicle) reduced endometrial HIF-1α during menstruation in our mouse model. This resulted in significantly delayed endometrial repair (P<0.05).

We detected a transient hypoxic episode in murine endometrium during menses using pimonidazole (marker of O2 <10mmHg). We prevented endometrial hypoxia during menses using a hyperoxic chamber (75% O2). This non-hypoxic menses model demonstrated menstrual hypoxia is necessary for (1) sufficient endometrial HIF-1α induction and (2) efficient endometrial repair. Delayed endometrial repair on prevention of physiological menstrual hypoxia was partially rescued by i.p. DMOG (HIF stabiliser) at menses.

CONCLUSIONS: Hypoxia and HIF-1 are necessary for efficient endometrial repair at menses. Absence of menstrual hypoxia delays repair but this can be abrogated by pharmacological stabilisation of HIF-1α, providing a potential non-hormonal treatment for women with HMB.

O-049

Remodeling of Decidual Immune Landscape Across Murine Pregnancy. Yan Li†, Jessica Vazquez†, Melina Chavarria†, Aleksandar Stanic-Kostic. *University of Wisconsin-Madison, Madison, WI, USA.*

INTRODUCTION: Decidual immune cells play an essential role at the maternal-fetal interface, contributing to vascular remodeling, fetal tolerance and protection against infection. Recent discovery of novel innate immune subsets (Innate lymphoid cells - ILCs) in mucosal tissues warrants a comprehensive re-examination of immune cell dynamics across pregnancy. To map the decidual cellular "immunome", we have employed highly polychromatic flow cytometry to examine murine virgin uterus, decidua from 3 gestational ages (GAs), and placenta. Conventional multivariate statistical analysis and novel dimensionality reduction/machine learning algorithms were used to abstract immune cell dynamics from this high-content dataset.

METHODS: Microscopically-dissected murine (C57BL/6) uterine tissue (V-virgin), timed-gestation decidua (D) and placenta (P) at timed GAs of 6-8; 12-14; 16-18 days were dissociated and labeled by 3 panels of fluorochrome-conjugated monoclonal antibodies, corresponding to ILCs (16 parameters), antigen presenting cells (Dendritic cells-DCs, macrophages, and others – 17 parameters), and T cells (15 parameters). Data acquisition and manual analysis were performed using BD Fortessa flow cytometer in a 20 parameters, 5-laser configuration and Flowjo10.2, respectively. ANOVA with Tukey post-test was employed for statistical analysis of manually gated immune cells. Dimensionality reduction was performed by Barnes Hut-modified t-distributed Stochastic Neighbor Embedding (t-SNE) and machine-learning aided density-based clustering (DenseVM) using the Cytofkit package in R v3.2.4.

RESULTS: Analysis revealed the presence and divergent patterns of multiple ILC-, DC-, and T-cell subsets in uterus of virgin mice, decidua and placenta of pregnant mice across pregnancy. Highlights of the dataset revealed increase in Lti-like ILC3s (p=0.0243) and similar trend for NKp46+ ILC3s (p=0.0715) from the virgin uterus through mid-pregnancy with subsequent decline. DCs displayed altered dynamics, with sharp rise in early pregnancy (GA6-8 vs V, p=0.0028), with subsequent decline from GA6-8 to 12-14 and 16-18 (p=0.0423 and 0.0153, respectively).

CONCLUSIONS: High-content analysis of murine decidual immunome reveals novel cell dynamics of ILC subsets. These results provide a novel framework for understanding pregnancy immunology and suggest areas for targeted disruption and analysis in models of pregnancy pathology.

O-050

***In Vitro* Model of Bacterial Colonization for the Study of the Effect of the Endometrial Microbiota on the Reproductive Function.** Inmaculada Moreno,[1] Iolanda Garcia-Grau,[1] Angela Silva,[2] Felipe Vilella,[3,4] Diana Valbuena,[1] Daniel Ramon,[2] Carlos Simon*.[1,3,4,5] *[1]Igenomix, Valencia, Spain; [2]Biopolis, Valencia, Spain; [3]INCLIVA, Valencia, Spain; [4]Stanford University, Palo Alto, CA, USA; [5]University of Valencia, Valencia, Spain.*

INTRODUCTION: The investigation of bacterial communities in the reproductive tract has revealed the existence of an endometrial microbiota mainly represented by *Lactobacillus* spp., followed by *Gardnerella*, *Bifidobacterium*, *Streptococcus* and *Prevotella*, among others (AJOG, 2016). The endometrial microbiota can be defined as *Lactobacillus* dominated (LD) or non-*Lactobacillus* dominated (NLD) according to the abundance of *Lactobacilli*. An NLD microbiota is associated with poor reproductive outcome in IVF patients. The aim of this work was to investigate the possible mechanisms responsible for adverse reproductive outcome in infertile patients with NLD microbiota.

METHODS: To mimic the effect of LD vs NLD endometrial microbiota, primary cultures of human endometrial epithelial cells (hEECs) were colonized with *Lactobacilli* (10e6 CFU), alone or in combination with NLD bacteria (10e4 CFU) as *Gardnerella*, *Atopobium*, *Streptococcus* or *Propionibacterium*, for 16h under anaerobic conditions. Then, cell morphology, bacterial growth measured by qPCR, pH, inflammatory cytokines (IL-6, IL-8, MCP-1, IL-1b, IL-1 ra, IL-1 RI, RANTES, GM-CSF) and production of bacterial short chain fatty acids (SCFA) were assessed by HPLC in the co-cultures.

RESULTS: The biochemical study of our *in vitro* model showed that colonization of hEECs with NLD bacteria produced a sharp increase of pro-inflammatory cytokines IL-8 and MCP-1 (12- and 30-fold, respectively), accompanied by production of SCFA, mainly acetic and succinic acids, when compared to hEECs only colonized with *Lactobacillus* spp. These effects were reverted by adding back *Lactobacilli* to the hEEC-NLD co-culture, which not only reduced the growth rate of NLD bacteria, but also resulted in decreased levels of pro-inflammatory cytokines (1 pg/mL of IL-8 and 0.02 pg/mL of MCP-1), increased levels of IL-1 ra, and high production of lactic acid to the detriment of other SCFA.

CONCLUSIONS: Our results demonstrated that NLD microbiota might trigger an inflammatory response in the endometrium characterized by increased pro-inflammatory cytokines IL-8 and MCP-1 concomitant with decreased inhibition of IL-1 by IL-1 ra receptor, together with SCFA production that induce cellular pathways that impairs embryo implantation.

O-051

Perivascular Expression of Vascular Adhesion Protein 1 (VAP-1) in the Endometrium Regulates Uterine Natural Killer (uNK) Cell Recruitment and Spiral Artery Remodeling in Pregnancy. Seley Gharanei,[1] Ruban P Durairaj,[1] Tianrong Jin,[2] Kuo-Kang Liu,[2] Christopher Weston,[3] Marko Salmi,[4] Pia Rantakari,[4] Sirpa Jalkanen,[4] Jan J Brosens,[1] Bee K Tan*.[1] *[1]University of Warwick, Coventry, West Midlands, United Kingdom; [2]University of Warwick, Coventry, West Midlands, United Kingdom; [3]University of Birmingham, Birmingham, West Midlands, United Kingdom; [4]University of Turku, Turku, Tykistökatu 6A, Finland.*

INTRODUCTION: During pregnancy, uNK cells are recruited to the feto-maternal interface, where they mediate decidual angiogenesis and spiral artery remodelling, processes that underpin the formation of a functional hemochorial placenta. VAP-1 (AOC3) is an adhesion protein, involved in leukocyte recruitment, and an ectoenzyme that deaminates primary amines. It is highly expressed in perivascular endometrial stromal cells, although its function is unknown.

METHODS: RNA sequencing, qRT-PCR, western blotting and immunohistochemistry analyses were used to measure AOC3/VAP-1 levels in mid-luteal endometrial biopsies. Perivascular endometrial ($W5C5^+$) cells were purified from mid-luteal endometrial biopsies by magnetic bead separation. The function of VAP-1, and its interaction with uNK cells, was investigated with the Stamper-Woodruff adhesion

assay, collagen gel contraction assay, migration, and proliferation assays. uNK cells and litter size were examined in *Aoc3*$^{-/-}$(C57BL/6) and wild-type dams.

RESULTS: RNA sequencing showed that AOC3 is highly expressed in perivascular stromal cells. Spearman's rank analysis showed a strong correlation ($r = 0.431$, $P < 0.001$) between the abundance of uNK cells and *AOC3* mRNA expression in 145 mid-luteal endometrial biopsies, suggesting a role for this adhesion protein in regulating immune cell trafficking at the feto-maternal interface. Functional analyses also indicated that AOC3/VAP-1 is essential for migration and contractility of perivascular stromal cells. Animal studies substantiated the *in vitro* findings. uNK cells [detected by Dolichos Biflorus Agglutinin staining] were completely absent in frozen sections of implantation chambers of *Aoc3*$^{-/-}$(C57BL/6) dams at embryonic days 6.5, 8.5 and 10.5. The decidua basalis of *Aoc3*$^{-/-}$dams also exhibited hypocellularity. Litter size in knockout animals was reduced by 50%.

CONCLUSIONS: Uterine VAP1 plays a pivotal role in uNK cell recruitment and spiral artery remodelling during pregnancy.

O-052

Mice Lacking Functional TRPV2 Show Intrauterine Growth Restriction. Katrien De Clercq†,[1] Charlotte Van den Eynde†,[1] Silvia Pinto,[2] Voets Thomas,[2] Vriens Joris*.[1] *[1]KU Leuven, Leuven, Vlaams-Brabant, Belgium; [2]KU Leuven, Leuven, Vlaams-Brabant, Belgium.*

INTRODUCTION: Transient Receptor Potential (TRP) channels are known to be involved in a myriad of physiological functions and serve as an important role as cellular sensors. TRPV2, a calcium permeable non-selective channel, has been shown to play pivotal roles in various cellular functions. Recently, its functional expression was found particularly in endometrial stromal cells isolated from human and mouse uteri. However, the function of TRPV2 in reproduction remains unknown. Interestingly, TRPV2$^{-/-}$ mice showed a reduced body weight and are susceptible to perinatal death, suggesting intrauterine growth restriction (IUGR). Intrauterine growth restriction is known to lead to stillbirth and cause long-term growth problems.

METHODS: Using TRPV2$^{-/-}$ mice, we investigated the role of TRPV2 in female reproduction in non-pregnant and pregnant mice at day 18.5 of gestation.

RESULTS: TRPV2$^{-/-}$ mice have a later onset of cyclicity and have a more irregular estrus cycle compared to wild type mice, which was correlated with the overall lower body weight. Moreover, TRPV2$^{-/-}$ mice have smaller litter size and circa 80% of homozygous (-/- x -/-) breeding pairs fail to produce six litters. Interestingly, residual tissue was found in 50% of TRPV2$^{-/-}$ mice after 6 litters or after failure to produce a litter for 3 months. When sacrificing pregnant females at day 18.5 of pregnancy, we found that TRPV2$^{-/-}$ have significantly more abnormal implantation sites compared to wild type. Furthermore, the body weight and placental weight from TRPV2$^{-/-}$ pups at E18.5 was significantly reduced compared to wild type mice. Since placental insufficiency is a known cause for IUGR, we assessed the placental expression of TRPV2 at different gestational days.

CONCLUSIONS: These data suggest that TRPV2 might be an important regulator in the establishment of successful pregnancy. The absence of functional TRPV2 will result in IUGR in mice.

O-053

The Mitochondria-Targeted Antioxidant MitoQ Prevents the Programming of Cardiovascular Dysfunction by Developmental Hypoxia in Sheep. KJ Botting†,[1] KL Skeffington,[1] Y Niu,[1] BJ Allison,[1] KL Brain,[1] N Itani,[1] C Beck,[1] A Logan,[2] MP Murphy,[2] DA Giussani*.[2] *[1]University of Cambridge, Cambridge, United Kingdom; [2]MRC, Cambridge, United Kingdom.*

INTRODUCTION: Chronic fetal hypoxia programmes cardiovascular dysfunction via oxidative stress. In rodents, maternal treatment of hypoxic pregnancies with the antioxidant vitamin C is protective, however, only at concentration incompatible with human clinical translation (see Giussani & Davidge. *J DOHaD* **4(5)**:328, 2013). Here, we show in sheep that MitoQ is a suitable alternative therapeutic candidate.

METHODS: Pregnant ewes were exposed to normoxia (N) or hypoxia (H; 10% O_2) +/- MitoQ treatment (Q; 1.2mg/kg/day i.v. in saline) during the last third of gestation (105-138 d; *n*= N:10, H:10, HQ:6, NQ:8). After natural delivery, offspring were maintained until 9 months, then chronically instrumented under anaesthesia with vascular catheters and a femoral flow probe to determine *in vivo* cardiovascular function followed by *ex vivo* peripheral vascular function (wire myography). Data were analysed by 2-way ANOVA with or without RM.

RESULTS: MitoQ crossed the placenta, reaching therapeutic concentrations (Adlam et al. *FASEB J.* **19(9)**:1088, 2005) in the fetus (A). Offspring of H pregnancy were smaller at birth (B) and hypertensive at adulthood (N: 90±2; H: 98±2; HQ: 91±2; NQ: 89±3mmHg, P<0.05). Maternal MitoQ in H pregnancy restored the programmed hypertension including diastolic blood pressure in adulthood (C). Adult offspring from NQ and HQ pregnancies had increased NO sensitivity [greater increase in femoral vascular conductance (FVC) during *SNP* (2.5mg/kg/min i.a.; D] and bioavailability [greater fall in FVC during LNAME (100mg/kg i.a.; E]. Similarly, maternal MitoQ in H pregnancy restored femoral artery dilator sensitivity to SNP *in vitro* in adult offspring (F).

CONCLUSIONS: Maternal MitoQ treatment in pregnancy complicated by chronic fetal hypoxia protects against cardiovascular dysfunction in adulthood. The mechanism underlying this protection involves programmed increases in cardiovascular NO sensitivity and bioavailability in adulthood.

Supported by the *British Heart Foundation*

**Figure(s) will be available online.*

O-054

Adiponectin Supplementation During Late Pregnancy Normalises Offspring Cardiac Hypertrophic Gene Expression in a Mouse Model of Maternal Obesity. Owen R Vaughan†,[1] Fredrick J Rosario,[1] Megan Gossling,[2] Theresa Powell,[2] Thomas Jansson.[1] *[1]University of Colorado, Aurora, CO, USA; [2]University of Colorado, Aurora, CO, USA.*

INTRODUCTION: Maternal obesity increases the risk of cardiovascular disease, including cardiac hypertrophy, in the adult offspring. Pathological hypertrophy is associated with re-expression of fetal cardiac genes e.g. *Nppb, Acta1, Myh7*. Recent studies show that adiponectin supplementation in late pregnancy reverses the effects of maternal obesity on placental nutrient transport and fetal growth. We tested the hypothesis that adiponectin supplementation during pregnancy normalises cardiac hypertrophic gene expression in the offspring of obese pregnant mice.

METHODS: Obese (OB) and control (C) pregnant female C57BL6/J mice were infused with either PBS or recombinant full-length adiponectin (ADN, 0.62μg.g^{-1}.d^{-1}, s.c.) from day 14.5-18.5 of pregnancy. Dams littered at term (~day 19.5) and nursed their own pups. Weaned offspring were group housed and maintained on standard chow. Males were killed at 3 months of age, their hearts excised and ventricular gene expression determined by qRT-PCR (n=12-15 per group). Effects of maternal obesity and ADN were assessed by two-way ANOVA with Fisher LSD test.

RESULTS: OB/PBS, but not OB/ADN, offspring gained weight more quickly and were glucose intolerant and hyperinsulinaemic in adulthood, compared to their respective controls (P<0.05). Maternal obesity increased cardiac *Nppb* (+83%, P=0.03, Fig. A) and tended to increase *Acta1* (+420%, P=0.08, Fig. B) and *Myh7* expression (+70%, P=0.11, Fig C). ADN supplementation normalised expression of all hypertrophic genes in OB offspring and did not affect expression in C offspring hearts. Expression of the adult cardiac gene, *Myh6,* was not affected by either maternal obesity or ADN supplementation (Fig D).

CONCLUSIONS: These preliminary observations indicate that adiponectin supplementation in late pregnancy ameliorates the effect of maternal obesity on expression of the cardiac hypertrophic gene *Nppb* in adulthood.

**Figure(s) will be available online.*

Mean±SEM relative gene expression in 3 month male offspring hearts. *, effect of obesity, †, effect of ADN.

O-055

Chronic Fetal Hypoxaemia & Maternal Antioxidants: Identifying Mechanisms and Treatments to Improve Postnatal Lung Structure & Function in Growth Restricted Offspring. EV McGillick†,[1] S Orgeig,[1] BJ Allison,[2] KL Brain,[2] Y Niu,[2] N Itani,[2] KL Skeffington,[2] C Beck,[2] KJ Botting,[2] DA Giussani,[2] JL Morrison*.[1] *[1]University of South Australia, Adelaide, Australia; [2]University of Cambridge, Cambridge, United Kingdom.*

INTRODUCTION: Chronic fetal hypoxaemia is a common pregnancy complication associated with intrauterine growth restriction and respiratory disease at birth and in later life. However, the underlying mechanisms remain unclear. Chronic fetal hypoxaemia programmes cardiovascular dysfunction and maternal antenatal antioxidant administration is protective. Here, we determined the effect of chronic fetal hypoxaemia with and without maternal antioxidant administration on molecular regulation of lung structure and function in early adulthood.

METHODS: Chronically catheterised pregnant sheep carrying female singletons were exposed to normoxia (N; n=20) or hypoxia (H; n=18; 10% O_2) +/- saline (NS=11; HS=8) or Vitamin C (NVC=9; HVC=10; maternal 200mg/kg i.v. daily) from 105-138d (term, ~145d). Lungs were collected from lambs 9 months after birth (early adulthood). Lung expression of genes regulating oxidative stress, airway remodelling & surfactant maturation were quantified by qRT-PCR. Numerical density of surfactant protein-B positive cells was determined by point counting. Data were analysed by two-way ANOVA (P<0.05).

RESULTS: H induced fetal growth restriction (Fig 1) but there was no effect of H or VC on body weight or relative lung weight at 9 months of age. H increased expression of pro-oxidant & airway remodelling markers (Fig 1) in lung tissue in early adulthood, and this was ameliorated by VC. There was no effect of H or VC on surfactant proteins or number of surfactant producing cells in lung tissue (Fig 1).

CONCLUSIONS: Here we show effects of chronic fetal hypoxaemia on molecular programming of oxidative stress and airway remodelling in the lung in early adulthood and that maternal antenatal antioxidant treatment is protective, offering insight into mechanism and possible treatment.

Support: British Heart Foundation & NHMRC of Australia.

**Figure(s) will be available online.*

O-056

Effects of Prenatal Hypoxia on Fetal Cardiomyocyte Proliferation. Laura M Reyes†,[1,2,3] Amin Shah†,[1,2,3] Anita Quon,[2,3] Sandra T Davidge*.[1,2,3] *[1]University of Alberta, Edmonton, AB, Canada; [2]University of Alberta, Edmonton, AB, Canada; [3]University of Alberta, Edmonton, AB, Canada.*

INTRODUCTION: Intrauterine growth restriction (IUGR) is known to decrease fetal cardiomyocyte proliferation. TNF-related weak inducer of apoptosis (TWEAK) induces cardiomyocyte proliferation through activation of the fibroblast growth factor-inducible molecule 14 (Fn-14) receptor. The TWEAK/Fn-14 pathway has not being studied in offspring born growth restricted after a hypoxic insult. We hypothesized that IUGR offspring will exhibit reduced cardiomyocyte proliferation due to reduced Fn-14 expression. Moreover, compared to controls, cardiomyocytes from IUGR offspring exposed to recombinant TWEAK (r-TWEAK) will proliferate less.

METHODS: Pregnant Sprague Dawley rats were exposed to control (21% oxygen) or hypoxic (11% oxygen, IUGR) conditions from gestational day 15 to 21. Ventricular cardiomyocytes were isolated from female and male, control and IUGR offspring at postnatal day 1 (PND 1). Proliferation and protein expression of Fn-14 were determined. Cardiomyocyte proliferation was also assessed in the presence or absence of r-TWEAK (72-hours, 100 ng/mL) and the Fn-14 receptor antibody (100µg/mL).

RESULTS: Being born growth restricted was not associated with differences in the Fn-14 protein expression or cardiomyocyte proliferation at PND 1 in either male or female offspring. After being in culture for 72-hours, cardiomyocytes from IUGR male offspring had a decreased proliferation compared to controls. The addition of r-TWEAK increased proliferation in both groups. Moreover, Fn-14 receptor antibody decreased cardiomyocyte proliferation in control (164.4% vs. 47.1%; p=0.04), and IUGR (208.5% vs. 70.03%; p=0.02) male offspring. Interestingly, in female offspring, being born growth restricted was not associated with decreased proliferation. The addition of r-TWEAK increased proliferation in both control and IUGR offspring. The Fn-14 receptor antibody decreased cardiomyocyte proliferation in control (175.9% vs. 76.8%; p=0.007), and IUGR (224.4 % vs. 39.9%; p=0.02) female offspring.

CONCLUSIONS: Only male IUGR offspring had a decreased cardiomyocyte proliferation compared to controls, but this was not due to changes in the Fn-14 pathway. Thus proliferation is altered in a sexual dimorphic manner in IUGR offspring and studies addressing other mechanisms of proliferation that may be compromised in growth restricted offspring should be addressed.

O-057

Maternal Obesity (MO) Compromises Term Fetal Offspring (F1) Heart Mitochondrial Bioenergetic Profile. Qiurong Wang†,[1,2] Chaoqun Zhu†,[1] John F Odhiambo†,[1,2] Guadalupe L Rodríguez-González†,[3] Peter W Nathanielsz,[1,2] Stephen P Ford,[1,2] Jun Ren,[4] Wei Guo*.[1] *[1]University of Wyoming, Laramie, WY, USA; [2]University of Wyoming, Laramie, WY, USA; [3]Instituto Nacional de Ciencias Medicas y Nutricion SZ, Mexico City, Mexico; [4]University of Wyoming, Laramie, WY, USA.*

INTRODUCTION: Epidemiological studies indicate that MO negatively impacts F1 fetal heart development and later-life cardiac health. Our published data show t MO and maternal overfeeding from before pregnancy elevates fetal blood cortisol levels and increases ventricular weights, left and right ventricular (LV and RV) free wall sizes and LV wall thickness in fetal sheep. MO also results in greater fetal heart fibrosis with an up-regulated TGFβ/p38 signaling pathway in late gestation. However, the underlying mechanism(s) remain unclear. We hypothesize that decreased mitochondrial function plays a role in MO compromised cardiac development. Here we test fetal cardiomyocyte (CM) cellular bioenergetics in MO vs. control fetuses at gestation day 135 with the Seahorse extracellular flux analyzer (XF96).

METHODS: From 60 days before and through pregnancy, ewes were fed either 100% of National Research Council (NRC) recommendations (control, n=5) or 150% of NRC's recommendations (MO, n=4). At 135-day gestation (Term 150 days), the fetal heart was quickly removed under general anesthesia, and CM isolated and bioenergetics and glycolysis measured. Analysis by Student's t-test: $*p < 0.05$.

RESULTS: MO reduced LV and RV CM maximal and spare respiration capacity ($p < 0.05$). LV cardiomyocytes in MO ewes showed suppressed ATP production ($p < 0.05$). MO depressed fetal CM glycolysis, evidenced by decreased glycolytic capacity in LV fetal CM ($p < 0.05$) in MO vs. control.

**Figure(s) will be available online.*

CONCLUSIONS: MO attenuates fetal CM mitochondrial bioenergetics by decreasing ATP production, maximal and spare respiration capacity. MO negatively impacts glycolysis in fetal CM by suppressing glycolytic capacity. These data suggest that MO compromises fetal CM metabolism by iimpairing glycolysis and mitochondrial oxidative phosphorylation.

O-058

Fetal Growth Restriction Alters Chromatin Access in 1-Year-Old Rats with Metabolic Syndrome. Erin K Zinkhan, Baifeng Yu, Chris Callaway, Robert McKnight*. *University of Utah, Salt Lake City, UT, USA.*

INTRODUCTION: Fetal growth restriction (FGR) and a high fat diet (HFD) program metabolic syndrome. Physiologic changes resulting in metabolic syndrome occur by alteration in gene expression of numerous metabolic pathways in multiple tissues including visceral adipose tissue (VAT) and liver. Chromatin access determines gene expression; increased chromatin access allows for increased gene expression. A recently described genome-wide assay, called assay for transposase-accessible chromatin using sequencing (ATAC-Seq), directly measures chromatin access to provide a mechanism through which alterations in gene expression can occur. We previously reported FGR-induced increases in visceral adiposity, serum lipids, and serum glucoses on glucose tolerance testing in a rat model of FGR combined with a HFD. We hypothesized that FGR combined with a HFD would alter chromatic access around genes for lipid and glucose metabolism more than a HFD alone.

METHODS: Adult female rats were fed a HFD prior to mating and through gestation and lactation. FGR was induced by uterine artery ligation at E19.5 of a 21 day gestation. At postnatal day (PND) 21 all offspring were weaned to a HFD through 1 year of age. At 1 year of age, genome-wide ATAC-Seq was performed on n=3 fasting female rat liver and visceral adipose tissues and data queried for chromatin access around genes involved in glucose and lipid metabolism.
RESULTS: Compared to non-growth restricted female rats, FGR female rats had increased VAT chromatin access of lipid transcription factors Srebf1 and Srebf2, the low density lipoprotein receptor (Ldlr), fatty acid synthase (Fas), insulin receptor (Ir), and glucose transporters Glut4 and Glut2. Conversely, FGR decreased hepatic chromatin access of Srebf1, Ldlr, Fas, Ir, Glut4, and Glut2. Data analyzed by pairwise analysis with log2 ratios with a cutoff of greater than +/- 0.5-fold log2 change. An unexpected finding was that by 10 months of age, FGR increased mortality 2.5-fold over non-FGR rats consuming the same amount of the HFD (p=0.01).
CONCLUSIONS: FGR altered tissue-specific chromatin access in genes involved in glucose and lipid metabolism in a model of metabolic syndrome with increased premature mortality. Increased VAT chromatin access suggests enhanced lipid biosynthesis and increased glucose and lipid uptake into the adipose tissue of FGR rats with metabolic syndrome.

O-059

Oxygen and Glucose Supplementation Reduces Stress in Growth Restricted Sheep Fetuses. Leticia Camacho†, Melissa Davis, Nathan Steffens, Amy Kelly, Sean Limesand. *University of Arizona, Tucson, AZ, USA.*
INTRODUCTION: Placental insufficiency (PI) lowers fetal oxygen and glucose concentration, which increase catecholamine (CA) and cortisol concentrations. Maternal oxygen supplementation increases fetal oxygen content. However, previous interventions have not simultaneously administered oxygen and glucose, which may be required to alleviate fetal stress. Our objective was to determine if increasing oxygen and glucose concentrations in the intrauterine growth restricted (IUGR) sheep fetus for 5-days lowers plasma CA and cortisol concentrations.
METHODS: PI-IUGR was created by exposing pregnant ewes to high ambient temperatures in mid gestation. At 123±2 days fetal catheters were surgically placed and ewes were fitted with a trachea catheter. At 128±2 days tracheal insufflation of oxygen and an intravenous dextrose infusion were started and routinely adjusted to maintain arterial PO2 at 20mmHg and plasma glucose to 1.1mmol/L for 5 days in IUGR+O2 fetuses (n=5). IUGR+Air controls received air and saline (n=4). Arterial blood gases and glucose were measured for 3 days prior to treatment and daily during treatment. Plasma cortisol and CA were measured and log transformed for analysis. Comparisons were made for pretreatment and post-treatment averages.
RESULTS: There was a treatment by time point interaction ($P \leq 0.05$) for glucose, PO2, and oxygen content. Glucose concentrations were not different pretreatment (IUGR+O2=0.83±0.09mmol/L vs. IUGR+O2=0.80 ±0.11mmol/L) but increased in IUGR+O2 (1.06±0.09mmol/L) compared to IUGR+Air fetuses (0.89±0.10mmol/L). In IUGR+O2 fetuses, PO2 was increased ($P<0.05$) from pretreatment levels. Oxygen content was not different prior to treatment (IUGR+O2=2.6±0.2mmol/L vs. IUGR+Air=2.5±0.2mmol/L) but increased in IUGR+O2 (3.4±0.1mmol/L) vs. IUGR+Air fetuses (2.4±0.2mmol/L). Epinephrine (Epi) and cortisol were lower ($P<0.02$) in IUGR+O2 (Epi=33.4±1.3pg/mL, cortisol=8.3±1.2pg/mL) than IUGR+Air fetuses (Epi=90.3±1.3pg/mL, cortisol=22.6±1.2pg/mL). There was a treatment by time point interaction ($P=0.05$) for norepinephrine where fetuses were similar on day 0 (2300±1.1pg/mL) but by day 5 IUGR+O2 (1582±1pg/mL) had lower norepinephrine concentrations than IUGR+Air (2513±1pg/mL) fetuses.
CONCLUSIONS: Simultaneous supplementation of oxygen and glucose to PI-IUGR fetuses for 5 days lowered CA and cortisol concentrations. These data establish interventions to reduce fetal stress caused by PI-IUGR. (Supported by NIH DK084842).

O-060

Late-Onset Chronic Hypoxia Abolishes Adrenomedullary but Sensitises Adrenocortical Plasma Responses to Acute Stress in Fetal Sheep. N Itani†,[1] CS Shaw,[2] BJ Allison,[1] KL Brain,[1] Y Niu,[1] CC Lees,[2] DA Giussani*.[1] [1]*University of Cambridge, Cambridge, United Kingdom;* [2]*Imperial College London, London, United Kingdom.*
INTRODUCTION: Elegant studies exploiting the natural chronic hypobaric hypoxia of high altitude have established in sheep that early-onset chronic fetal hypoxia from 40 days gestation (dG) through to term has marked effects on the physiology of the fetal adrenal gland, designed to prevent the induction of preterm birth and maintain normal fetal growth and development (Myers & Ducsay. *Adv Exp Med Biol*. **814**:147, 2014). However, the effect late-onset chronic hypoxia on the physiology of the fetal adrenal gland remains unknown. Here, we show in sheep marked differential effects of late-onset chronic hypoxia on fetal adrenal cortical versus medullary responses to acute hypoxic stress.
METHODS: Chronically-catheterised fetal sheep (n=12) were subjected to an acute episode of hypoxia (30 min, fetal PaO2 20±0.5 to 10±1 mmHg, $P<0.05$) at 124 dG. The day after, half of the animals (n=6) were subjected to chronic hypoxia (fetal PaO2 21±1 to 12±1 mmHg, $P<0.05$) for 10 days, from 125 to 135 dG in bespoke isobaric hypoxic chambers, and then returned to normoxia, as previously described (Allison et al. *J Physiol*. **594(5)**:1247, 2016) . The other half (n=6) remained in normoxia. At 136 days, the acute episode of hypoxia (30 min, PaO2 20±1 to 10±0.5 mmHg, $P<0.05$) was repeated in all animals. Fetal blood was collected during all acute hypoxic episodes and processed for plasma catecholamine and cortisol analyses (ELISA).
RESULTS: Late-onset chronic hypoxia did not affect basal fetal plasma noradrenaline, adrenaline or cortisol. However, fetal sheep exposed to chronic hypoxia had blunted plasma catecholamine but significantly enhanced plasma cortisol responses to acute hypoxia (Fig).
CONCLUSIONS: Late-onset chronic fetal hypoxia has marked differential effects on fetal adrenal medullary versus cortical responses to acute hypoxic stress. These effects have major implications for the programmed outcome of an individual's response to stress after birth.
Supported by *The British Heart Foundation*
**Figure(s) will be available online.*

O-061

Effect of Maternal Antioxidant MitoQ Treatment in a Rat Model of Intrauterine Growth Restriction (IUGR). Esha Ganguly†,[1,2,3] Jude S Morton,[1,3] Christy L Cooke,[1,3] Sandra T Davidge*.[1,2,3] [1]*University of Alberta, Edmonton, AB, Canada;* [2]*University of Alberta, Edmonton, AB, Canada;* [3]*University of Alberta, Edmonton, AB, Canada.*
INTRODUCTION: Chronic hypoxia during pregnancy, associated with IUGR, has been linked to fetal programming of cardiovascular disease. A prenatal hypoxic insult reduces placental perfusion, increases placental oxidative stress, and alters gene expression in growth restricted fetuses. Placental factors released due to a stressed placenta have been known to affect fetal development of key organ systems. MitoQ is an antioxidant which, when attached to nanoparticles (nMitoQ), can be used to target maternal and placental oxidative stress without crossing the placenta. We hypothesized that treatment with nMitoQ will reduce hypoxia associated placental oxidative stress thus programming the placenta and fetal heart by altering DNA methylation patterns in a sexually dimorphic manner, ultimately leading to better pregnancy outcomes.
METHODS: Pregnant rats were exposed to either hypoxia (11% O_2) or normoxia (21% O_2) from gestational day (GD) 15-21. On GD15, rats were intravenously injected with saline or nMitoQ. Placentae and fetal tissues were collected from both sexes on GD21. Reactive oxygen species (ROS) in placenta and fetal cardiac tissues were assessed by dihydrorhodamine staining. Whole tissue DNA methylation was determined by ELISA.
RESULTS: Prenatal hypoxia increased ROS levels in placentae of female (normoxia-0.02±0.001a.u. vs. hypoxia 0.12±0.03a.u. $p<0.05$) but not male offspring. nMitoQ reduced the generation of ROS in prenatally hypoxic female placentas. Evidence of cardiac oxidative stress was greater in both male (normoxia 0.02±0.001a.u. vs. hypoxia 0.13±0.03a.u. $p<0.05$) and female (normoxia 0.04±0.01a.u. vs. hypoxia 0.08±0.01a.u. $p<0.05$)

hypoxic exposed offspring. nMitoQ treatment reduced cardiac ROS in both sexes. DNA methylation profile tended to be increased in hearts of male offspring from nMitoQ-treated dams.
CONCLUSIONS: Prenatal hypoxia was associated with an increased ROS production in female but not male placentae and fetal hearts of both sexes. nMitoQ reduced ROS in female placentae. Interestingly, without crossing the placenta, nMitoQ reduced ROS in prenatally hypoxic hearts of both sexes. In addition, DNA methylation was altered in a sexually dimorphic manner in fetal hearts. Treatment targeted to the placenta could lead to improved cardiovascular outcomes in offspring.

O-062

Maternal Antioxidant Treatment Markedly Sensitizes Antioxidant Gene Expression in Peri-Renal Fat of Fetal Offspring of Hypoxic Pregnancy. A Martin†,[1] BJ Allison,[3] KL Brain,[3] C Ducsay,[4] D Myers,[2] DA Giussani*.[3] [1]*University of Oklahoma HSC, Oklahoma City, OK, USA;* [2]*University of Oklahoma HSC, Oklahoma City, OK, USA;* [3]*University of Cambridge, Cambridge, United Kingdom;* [4]*Loma Linda Univ, Loma Linda, CA, USA.*
INTRODUCTION: In newborns, perirenal fat (PRF) functions as brown adipose (BA), essential for non-shivering thermogenesis. We reported (PMID:25504105) that gestational hypoxemia (H) increases expression of key genes governing mitochondrial function in ovine fetal PRF. Enhanced mitochondrial endowment could increase oxidative stress in PRF. Here, we show that maternal antioxidant treatment markedly enhances mRNA for antioxidant genes in PRF in the fetus of H pregnancy.
METHODS: Chronically catheterized pregnant sheep carrying male singletons were exposed to normoxia (N) or hypoxia (H, 10% maternal inspired O_2) +/- saline (NS=9; HS=8) or Vitamin C (NC=9; HC=7; maternal 200mg/kg i.v. daily) from 105-138d (term, ~145d), as described (PMID: 26660546). Quantitative real time PCR (qRT-PCR) was used to measure superoxide dismutase 1 (SOD1), SOD2, glutathione synthetase (GSS) and glutaredoxin (GLRX). Cyclophilin was the housekeeping gene. All data are expressed as mean±SEM and compared using ANOVA with the Tukey's post-hoc test.
RESULTS: Maternal PaO_2 was similarly reduced in HS or HC pregnancy (HS=47±1 and HC 46±1 mmHg). This level of maternal H yields fetal PaO_2 values of 11.5±0.6 relative to controls of 20.9±0.5 mmHg (PMID: 26926316). GSS mRNA was reduced in the HS PRF. In response to vitamin C, SOD1, SOD2, GSS and GLRX mRNA increased in fetal PRF of H but not N pregnancy.
CONCLUSIONS: Hypoxic pregnancy decreased the expression of the potent antioxidant glutathione synthetase (GSS) in fetal PRF. Maternal treatment with the antioxidant vitamin C sensitized PRF to increase antioxidant capacity in fetal offspring of hypoxic but not normoxic pregnancy. Thus, maternal treatment with vitamin C may greatly enhance fetal PRF to limit oxidative stress in pregnancy complicated by gestational hypoxia.
Supported by the British Heart Foundation and NIH grant HD083132.
**Figure(s) will be available online.*

O-063

Elevated Hepatic Gluconeogenesis by H19-Mediated Epigenetic Regulation Underlies Altered Metabolism in Offspring Prenatally Exposed to Metformin. Jie Deng†, Tingting Geng†, Yuanyuan Shen, Liyong Zhu, Ya Liu, Hugh S Taylor, Michael Paidas, Yingqun Huang*. *Yale School of Medicine, New Haven, CT, USA.*
INTRODUCTION: Pregnant women are increasingly being exposed to metformin for conditions including ovulation induction, polycystic ovary syndrome and gestational diabetes mellitus. Animal studies showed that prenatal exposure to metformin in the absence of maternal diabetes increases the risk of developing glucose intolerance and insulin resistance in the offspring during adulthood. Here we investigated the molecular mechanism underlying the metabolic phenotype programming in offspring from prenatal metformin exposure in mice, and asked whether metformin-induced programming effect is mediated by H19 long noncoding RNA.
METHODS: Metformin (250 mg/kg/day) or vehicle was administrated in drinking water to female mice on regular diet from embryonic day E0.5 to E17.5. Expression of genes that are associated with glucose metabolism in liver were analyzed from 1-day old offspring by RT-qPCR. Mouse hepatic cell line AML12 was transfected with H19-expressing plasmid and the regulatory effect of H19 on hepatic gluconeogenesis was assessed by RT-qPCR, Western blotting, and hepatic glucose output assays. Quantitative methylation-specific PCR (QMSP) was used to determine methylation status of key gluconeogenic genes in neonatal liver and in AML12 cells.
RESULTS: Prenatal metformin exposed neonatal liver had increased expression of key gluconeogenic genes G6PC, PEPCK, and Foxa2, concomitant with an elevated expression of H19. This was phenocopied in AML12 cells when H19 was overexpressed. H19 was previously shown to induce hypomethylation of Foxa2 in mouse skeletal muscle cells through the H19/SAHH regulatory pathway. Consistently, G6PC and Foxa2 were found to be hypomethylated (which was correlated with enhanced gene expression) both in the neonatal liver of offspring from prenatal metformin exposed mice and from H19 overexpressed AML12 cells. Finally, H19 overexpression increased glucose output from AML12 cells.
CONCLUSIONS: Prenatal metformin exposure leads to an elevated hepatic gluconeogenesis programming in the neonate, which has been previously linked to a higher risk of developing type 2 diabetes in adulthood in animal models. Our results also identify H19 as a novel epigenetic regulator in hepatic gluconeogenesis.

O-064

In Utero Gene Therapy (IUGT) Using GLOBE Lentiviral Vector Phenotypically Corrects the Heterozygous Humanized Mouse Mode and Its Progress Can Be Monitored Using MRI Techniques. Panicos Shangaris†,[2] Stavros Loukogeorgakis,[1] Laurence Jackson,[6] Wei Wang,[5] Mike Blundell,[1] Shanrun Liu,[3] Sindhu Subramaniam,[1] Simon Eaton,[1] Mike Antoniou,[4] Daniel Stuckey,[6] Manfred Schmidt,[5] Adrian Thrasher,[1] Thomas Ryan,[3] Paolo De Coppi,[1] Anna David*.[2] [1]*UCL, London, United Kingdom;* [2]*UCL, London, United Kingdom;* [3]*UAB, Birmingham, AL, USA;* [4]*KCL, London, United Kingdom;* [5]*National Centre for Tumour Diseases, Heidelberg, Germany;* [6]*UCL, London, United Kingdom.*
INTRODUCTION: In utero gene therapy (IUGT) to the fetal hematopoietic compartment is a promising approach to treat congenital blood disorders such as thalassemia. Monitoring efficacy can be challenging. We hypothesized that magnetic resonance imaging (MRI) could be a useful tool.
METHODS: A humanized mouse model of thalassemia was used in which heterozygous animals are anemic with splenomegaly and extramedullary hematopoiesis.We injected a "GLOBE" vector(20ul of 10^6 viral particles) into the liver of each fetus, in utero, at E13.5.At 32 weeks of age we analyzed blood, liver, spleen and bone marrow for complete blood count, blood film, and DNA for integration site analysis. Using MRI we assessed relaxation times T2*****.Results were compared to those from uninjected heterozygous thalassemia and normal humanized mice,expressed as mean±SEM.Statistical analysis used one-way ANOVA with Holm-Sidak's multiple comparisons test.
RESULTS: Compared to noninjected heterozygous pups, IUGT increased hemoglobin levels at 32 weeks postnatal(9.13±0.35vs8.42±0.16,n=7 ,p=0.005) and decreased spleen weight(0.2±0.030vs0.31±0.017,n=7 ,p=0.067). Spleen volume over mass was reduced in treated heterozygous compared to untreated heterozygous thalassemia pups(1.99±1.02vs5.1 2±1.04,n=7,p=0.006).There was no difference in iron accumulation in the heart expressed as MRI relaxation times T2*(n=7,p=0.98). The left ventricular injection fraction in treated heterozygous pups was similar to that of normal non-thalassemia mice, but significantly higher than untreated heterozygous thalassemia pups(n=7,p=0.009), suggesting that IUGR ameliorated poor cardiac function. Integration site analysis showed no homogeneous integration sites.
CONCLUSIONS: IUGT using the GLOBE vector corrects the phenotype in a heterozygous humanized model of beta-thalassemia as monitored by MRI *in vivo*.

O-065

Mechanisms of Dysregulated RANKL Gene Expression in Uterine Leiomyoma: Involvement of Epigenetic Modification and MED12 Gene Mutations. Shimeng Liu†, Ping Yin, Stacy A Kujawa, Serdar E Bulun*. *Northwestern University Feinberg School of Medicine, Chicago, IL, USA.*

INTRODUCTION: Uterine leiomyomas (LM) represent the most common tumor in women. Although LM growth requires ovarian steroid hormones, the underlying mechanisms remain unclear. We previously demonstrated that RANKL expression (a progesterone (P) receptor (PR) target) was dramatically higher and was more robustly induced by P in LM compared to adjacent myometrial (MM) tissue. Here, we aim to investigate the mechanisms by which RANKL is differentially expressed and regulated by P in LM vs MM.

METHODS: MM and LM tissues were collected from premenopausal women undergoing hysterectomies. MED12 mutation was screened using Sanger sequencing. We performed MethylCap-Seq/qPCR and ChIP to determine RANKL gene's methylation status and the recruitment of PR and MED12 to the promoter and upstream enhancer regions of RANKL in LM and MM. qPCR was used to examine RANKL mRNA level in the same tissues to determine if epigenetic changes or MED12 mutation status affected transcription factor binding as well as RANKL's transcription activity.

RESULTS: MethylCap-Seq/qPCR demonstrated that the DNA methylation level of the enhancer region located 75kb upstream of RANKL gene, which was previously reported as a PR regulatory element, was significantly lower in LM vs MM ($P<0.05$). Methylation inhibitor DAC decreased the methylation level of RANKL enhancer region and increased mRNA levels in MM and LM cells. In contrast, PR and MED12 bindings towards the RANKL promoter and enhancer regions were significantly higher in LM compared to MM ($N=10$, $P<0.01$). Regression analysis indicated that recruitment of PR and MED12 to the enhancer region of RANKL gene was significant and positively correlated with its mRNA level. RANKL mRNA level and MED12 binding in the RANKL promoter region were higher in LM with the MED12 G44D mutation than those with G44R mutation, suggesting that MED12 mutation influences RANKL's transcription activity.

CONCLUSIONS: Our data suggest that the methylation status of RANKL's enhancer region plays a vital role in controlling differential transcription factor binding as well as RANKL expression in LM vs MM. We also find that distinct point mutations in MED12 may influence its DNA binding and transcriptional regulatory activity. Our studies represent a key step towards the better understanding of mechanisms underlying the pathogenesis of specific LM subtypes and indicate the necessity for personalized disease therapeutics.

O-066

Ulipristal Treatment Highlights the Link of MED12 and Fibrosis Regulation in Leiomyomas. Minnie Malik,[1] Joy Britten,[1] Lynnette Nieman,[2,3] Matthew Wilkerson,[4] Xijun Zhang,[4] Jeris Cox,[1,2,5] William Catherino.[1,2] *[1]Uniformed Services University of the Health Sciences, Bethesda, MD, USA; [2]NIH, Bethesda, MD, USA; [3]NIH, Bethesda, MD, USA; [4]USUHS, Bethesda, MD, USA; [5]Army Medical Center, Fort Belvoir, VA, USA.*

INTRODUCTION: Ulipristal Acetate (UA) decreased leiomyoma size in randomized, placebo-controlled double blind clinical trials. At the completion of one study, patients underwent hysterectomy. Notably the majority of uterine leiomyomas harbor mutations in MED12 gene that encodes a subunit of the mediator complex implicated in transcriptional regulation. We hypothesized that the changes in expression of genes that are characteristic to the MED12 leiomyoma subtype may elucidate the mode of UA action on leiomyoma fibrosis.

METHODS: To examine the impact of UA on the genomics of treated and placebo leiomyomas, we used RNASeq analysis. Three comparisons were performed: treated leiomyoma compared to patient-matched myometrium (paired analysis-T); placebo leiomyoma compared to matched myometrium (paired analysis-P); treated compared to placebo leiomyomas (unpaired analysis). Genes with an adjusted two-sided P-value of less than 0.05 and greater than 2-fold change in expression were considered differentially expressed.

RESULTS: The leiomyoma tissue samples used in this study were positive for MED12 mutation as well as the uniquely expressed genes that are characteristic to this subtype of leiomyomas. In UA treated leiomyomas, paired analysis comparison demonstrated changes in expression of KIAA1199 (+3.0-fold; Hyaluronan depolymerization pathway), Metalloproteinase-16 (+2.1-fold; Collagen breakdown pathway) and THSD4 (-1.74-fold; Fibrillin matrix assembly). Unpaired analysis demonstrated a 2.89-fold increased expression of UNC5D gene in treated leiomyomas, indicating an increased regulation of p53 dependent apoptosis.

CONCLUSIONS: UA-mediated MED12 regulation may decrease leiomyoma size by four different pathways. Increased breakdown of hyaluronan, known to be involved in tissue hydrodynamics, in combination with decreased chondroitin sulfate proteoglycans, may contribute to loss of water resulting in shrinkage of tumor size. MMP16 activates collagenase MMP2 by cleavage leading to breakdown of extracellular collagen. Regulation of expression and assembly of fibrillin (fibrosis indicator) leading to attenuation of the TGFβ pathway. Finally, increase in un-5 netrin receptor D may indicate an increased apoptosis in UA treated leiomyomas.

O-067

Feedback Regulation Between TGF-β3 and miR-29c in Leiomyoma. Tsai-Der Chuang, Omid Khorram. *Harbor-UCLA Medical Center, Torrance, CA, USA.*

INTRODUCTION: Our group previously reported that the expression of miR-29c which targets many extracellular matrix (ECM) genes is downregulated in leiomyomas. Based on this finding we proposed that aberrant expression of miR-29c plays a critical role in accumulation of ECM in leiomyoma. The expression of TGF-β3 which stimulates the expression of ECM components is upregulated in leiomyoma. The objective of this study was to assess the relationship between miR-29c and TGF-β3 in leiomyoma pathogenesis. We hypothesized that TGF-β3 suppresses the transcription of miR-29c, and TGF-β3 might in turn be a target of miR-29c.

METHODS: Myometrium and leiomyoma tissue samples (N=21) from patients without any treatments for at least 3 months prior to surgery were collected for isolation of leiomyoma smooth muscle cells (LSMC) and gene analysis. miR-29c and TGF-β3 mRNA were assessed by QRT-PCR, andTGF-β3 protein abundance was analyzed by Western blot.The direct interaction of miR-29c and 3' UTR of TGF-β3 was determined by the luciferase activity assay.Methylation specific PCR assay was used to determine the methylation levels in miR-29c promoter. Results were analyzed by Student's t-tests and one-way ANOVA with Tukey's HSD for post hoc analysis.

RESULTS: Our results indicated that the expression of TGF-β3 mRNA and protein was elevated, while miR-29c expression was repressed (100%, 21/21 pairs of tissues) in leiomyoma as compared to matched myometrium, and this was independent of race or ethnicity. Using 3'UTR luciferase reporter assay we demonstrated that overexpression of miR-29c in LSMC decreased TGF-β3 translational activity (19%). Gain-of function of miR-29c in LSMC down-regulated TGF-β3 mRNA (28%) and protein expression, while knockdown of miR-29c up-regulated TGF-β3mRNA (137%) and protein expression, thus confirming that TGF-β3 is a direct target of miR-29c. In addition, treatment of LSMC with TGF-β3 (5 ng/ml) decreased miR-29c levels (22%). Furthermore, using methylation specific PCR we demonstrated that treatment of LSMC with TGF-β3 increased the methylation levels in miR-29c promoter (128%), indicating that TGF-β3 regulated miR-29c transcription through an epigenetic mechanism involving DNA methylation.

CONCLUSIONS: Our results indicate that suppression of miR-29c in leiomyoma leads to overexpression of TGF-β3 which in turn could suppress miR-29c expression through methylation of miR-29c promoter. Targeting the expression of miR-29c or TGF-β3may have a potential therapeutic value for leiomyoma treatment.

O-068

Inflammatory and Immunological Processes Are Strongly Dysregulated in Uterine Fibroids Compared to Normal Myometrium and Are Shown to Offer Novel as well as Effective Treatment Options for Uterine Fibroids. Jörg Müller, Anette Sommer, Andrea Wagenfeld, Markus Koch, Thomas M Zollner. *Bayer Pharma AG, Berlin, Germany.*

INTRODUCTION: Uterine fibroids (UFs) are benign tumors and 30-70% of women at reproductive age are affected by symptomatic UFs. Typical symptoms are abnormal uterine bleeding, pelvic pain and reproductive dysfunction. Current treatment options include surgery (hysterectomy, myomectomy, uterine artery embolization) and drug treatments (GnRH agonists, progesterone receptor modulators). UFs are characterized altered extracellular matrix (ECM) deposition and tissue fibrosis as well as impaired inflammatory response. Current anti-hormonal therapies do not address this aspect directly and novel therapies targeting immune response in UFs may provide alternative and effective approaches for treatment. The objective of the study was to uncover pathways and biological processes with a role in inflammation which are dysregulated in UFs and therapeutically accessible.

METHODS: Whole genome gene expression profiling of 92 fibroid and 54 myometrial samples from 71 patients was performed. Significantly regulated genes (FC>1.5, $p<0.01$) were analyzed with regard to their enrichment in biological pathways focusing on inflammation, immune response and chemotaxis. Selected hypothesis were validated in a therapeutic fibroid xenograft mouse model. All UF and myometrial tissue samples were obtained under IRB approval and informed consent.

RESULTS: Genes involved in inflammation-related processes are strongly dysregulated in UFs versus normal myometrium. Significantly dysregulated processes include chemotaxis (recruitment of immune cells), ECM turnover (tissue fibrosis), NK cell activation (better survival of dedifferentiated cells) and interferon alpha (IFNA) signaling. Roferon (IFNA2) treatment in a UF mouse model showed significant xenograft shrinkage.

CONCLUSIONS: The current study underlies the important role of impaired inflammatory response as well as recruitment and activation of immune cells in the development and progression of UFs. Further supporting biological and clinical data are needed to strengthen these hypotheses on the way to novel immune modulatory therapies.

O-069

Rank-Fc Inhibits Growth of Leiomyoma Cells and Decreases Tumor Growth In Vivo. Deborah E Ikhena†, Shimeng Liu, Stacy Kujawa, Serdar E Bulun, Ping Yin*. *Northwestern University, Feinberg School of Medicine, Chicago, IL, USA*.

INTRODUCTION: Rank-Fc is a recombinant protein containing the murine extracellular domain of receptor activator of nuclear factor kappa-B (RANK) fused to the Fc portion of murine immunoglobulin G1. It acts by binding to RANK ligand (RANKL), thus inhibiting RANK/RANKL downstream effects. We previously demonstrated that RANKL acts as a paracrine signal from estrogen/progesterone receptor-rich mature cells to activate the RANKL/RANK pathway in leiomyoma stem cells. Here we aim to determine whether blocking RANK/RANK signaling pathway with RANK-Fc can prevent estrogen and progesterone induced leiomyoma growth.

METHODS: Fibroid tissues were obtained from pre-menopausal women aged 18-45 who did not report a history of menstrual irregularities. We isolated leiomyoma smooth muscle cells from fresh fibroid tissues and maintained them in primary culture (n=3). The cells were treated with vehicle, RANKL (30ng/ml), RANK-Fc (50ng/ml) or both for 48 hours. Protein was extracted and Cyclin D1 (a cell cycle protein required for cell proliferation) protein expression levels were measured.

For in vivo tumor xenograft experiments, freshly isolated smooth muscle cells were suspended in rat-tail collagen (type 1) at 10^6cells/10µl and cultured for 48 hours in floating cultures. Cell pellets were then grafted underneath kidney capsules of NOD scid gamma (NSG) ovariectomized (OVX) mouse hosts supplemented with subcutaneous (s.c.) implantation of estradiol and progesterone releasing pellets (n=20 mice). The mice were treated with or without RANK-Fc (s.c, 10mg/kg, twice a week) for 4 weeks. Then the mice were sacrificed and the tumors were harvested for the measurement of tumor volumes as well as immunohistochemistry (IHC) staining for Ki67 (a marker of cell proliferation).

RESULTS: In primary cultured cells, RANK-Fc treatment reduced Cyclin D1 protein expression in the presence of RANKL. IHC of regenerated fibroid tumors showed significantly lower expression of Ki67 in mice treated with RANK-Fc compared to vehicle-treated ones ($p<0.05$). Importantly, the tumors derived from RANK-Fc treated mice were significantly smaller than those from control mice ($p<0.05$).

CONCLUSIONS: RANK-Fc is an effective inhibitor of leiomyoma cell proliferation and growth, both in the in vitro cell culture and in the in vivo tumor implantation settings. These findings implicate RANKL blockade as a potential strategy in the treatment of uterine leiomyoma.

O-070

Expression of Tumor Suppressor PCDH10 in Uterine Leiomyomas and Leiomyosarcomas. Joie Z Guner†, Gyoung E Kim, Meaghan A Delaney, Triparna Ghosh-Choudhury1, Cecilia Valdes, William Gibbons, Matthew L Anderson*. *Baylor College of Medicine, Houston, TX, USA.*

INTRODUCTION: Despite progesterone's key role in uterine smooth muscle tumorigenesis, the mechanisms by which activation of its receptor promotes growth and metastasis remains unclear. We recently identified the tumor suppressor PCDH10 as a key centralizing feature of progesterone-dependent patterns of gene expression in uterine leiomyomas. However, a role for PCDH10 in uterine smooth muscle tumorigenesis has not been previously described.

METHODS: After obtaining IRB approval, total RNA and protein were prepared from flash frozen specimens of myometrium, leiomyoma and leiomyosarcoma (uLMS), primary cultures, and established uLMS cell lines (sk-LMS, Leio-505, Leio-285). Real time quantitative PCR and Western blot were used to evaluate gene expression. Genomic binding sites for the progesterone receptor (PR) were interrogated by ChIP-PCR. A lentiviral vector was used to drive expression of a full length PCDH10 clone. Proliferation and apoptosis were measured using MTS and Caspase 3/7 assays (Promega).

RESULTS: Our results demonstrate that over-expression of PCDH10 is a robust feature of uterine leiomyomas that varies with menstrual phase. On average, levels of PCDH10 transcript were 2.7-fold lower in leiomyomas collected during the luteal phase (n=8) than proliferative phase specimens (n=8; $p<0.05$). High levels of PCDH10 were also observed in 2/4 uLMS specimens. However, no evidence of PDCH10 overexpression was observed in postmenopausal leiomyomas. Furthermore, only minimal PCDH10 expression was observed in matched, primary cultures of myometrium and leiomyoma (0/12) or established uLMS cell lines (0/4). Use of ChIP-PCR demonstrated that PR binds directly to its sole consensus binding site in the upstream PCDH10 promoter in both leiomyomas and myometrium. *In vitro,* enforced expression of PCDH10 dramatically reduced the number of adherent uLMS cells, decreased rates of proliferation and enhanced apoptosis when compared to control-transfected cultures.

CONCLUSIONS: Overexpression of tumor suppressor PCDH10 is a robust feature of uterine leiomyomas that regulates smooth muscle adhesion, survival and proliferation. Further research is needed to determine how overexpression of PCDH10 and its potential regulation by progesterone contributes to smooth muscle tumorigenesis.

O-071

Human Labour: A Joint Venture of PRA and ERα. Lubna Nadeem,[1] Hedy Romero†,[1] Oksana Shynlova,[1,3] Sam Mesiano,[4] Stephen Lye*.[1,2,3] *[1]Sinai Health System, Toronto, ON, Canada; [2]U of T, Toronto, ON, Canada; [3]U of T, Toronto, ON, Canada; [4]CWRU, Cleveland, OH, USA.*

INTRODUCTION: Myometrial cell connectivity through gap junction (GJ) formation is critical for labour contractions; it is promoted by estrogen (E2), inhibited by progesterone (P4) and regulated by AP-1 transcription factors. We have recently provided evidence of nuclear P4 withdrawal in human myometrium during labour when unliganded nuclear progesterone receptor (PR)A activates the transcription of GJ protein connexin (Cx)43. We have also shown that P4-liganded cytoplasmic PRA promotes Cx43

trafficking and GJ formation while P4/PRB inhibits these processes. Current study investigates the interaction between E2 receptor ERα and PRA/B. We hypothesized that PRA and ERα work synergistically to upregulate Cx43 expression, GJ formation and cell connectivity.
METHODS: Cx43 trafficking was analyzed in human myometrial cells (hTERT-HM$^{A/B}$) engineered to express PRA or PRB. Intercellular connectivity was examined by dye-loading assay. Endogenous ERα and PRA/B protein interactions (cytoplasmic and nuclear) were assessed by immunoprecipitation, Proximity Ligation Assay (PLA) and by flag-pull down assay. Co-localization of ERα and PRs was examined by immunofluorescence. Luciferase assay was performed to examine the ERα/PRs' regulation of Cx43 transcription by using transient transfection of Cx43 promoter, PRA/PRB, ERα and AP-1 factors. In all experiments cells were stimulated with P4, E2, P4+E2 or Vehicle.
RESULTS: hTERT-HM$^{A/B}$ cells transfected with GFP-tagged Cx43 were used to examine Cx43 intracellular trafficking/localization. In PRA cells either P4 or E2 promote forward trafficking of Cx43/cell connectivity which was remarkably enhanced by P4+E2. In PRB cells E2 promotes Cx43 trafficking/cell connectivity but P4 or P4+E2 blocks them. Immunoprecipitation, Flag pull down, immunofluorescence and PLA showed that both PRA/B interact with ERα; nuclear interaction is enhanced when PRA is unliganded and PRB is P4-liganded. Furthermore maximal activity of Cx43 promoter was observed in the presence of unliganded PRA and E2-liganded ERα.
CONCLUSIONS: We concluded that during pregnancy nuclear P4/PRB binds to and inhibits the action of E2/ERα, whereas during labour unliganded nuclear PRA binds to E2/ERα and activates Cx43 transcription, while cytoplasmic P4/PRA- E2/ERα promotes Cx43 forward trafficking, GJ formation and cell-cell connectivity.
FUNDING: CIHR, FDN-143262.

O-072

Thrombin-Induced Decidual CSF2 Induces Abruption-Related Preterm Birth by Weakening Fetal Membranes. Rachel Sinkey,[1] Sefa Arlier,[1] Robert Moore,[2] Frederick Schatz,[1] Nihan Semerci,[1] Chinedu Nwabuobi,[1] Kellie Larsen,[1] Ozlem Guzeloglu-Kayisli,[1] Deepak Kumar,[2] John Moore,[2] Umit Kayisli,[1] Charles Lockwood.[1] *[1]Univ. of South Florida, Morsani College of Medicine, Tampa, FL, USA; [2]Case Western Reserve Univ., School of Medicine, Cleveland, OH, USA.*
INTRODUCTION: Abruption, a leading cause of preterm birth (PTB), is accompanied by excess thrombin (THR) generated by decidual cell (DC)-expressed tissue factor. Although thrombin is a primary coagulation mediator, we showed that THR acts DCs to inhibit progesterone (P_4) receptor (PR) expression, triggering functional P_4 withdrawal leading to PTB. Abruptions are often accompanied by preterm premature rupture of membranes (pPROMs) with THR enhancing DC matrix metalloproteinase (MMP), the neutrophil-activating chemokine, interleukin (IL)-8 and granulocyte-monocyte colony stimulating factor (CSF2) to weaken full thickness fetal membrane (FM). This study investigates regulation and cellular targets of CSF2 in term and abruption-related decidua basalis specimens and CSF2 mediation of THR-induced FM weakening.
METHODS: Decidual basalis sections from normal term (n=10), idiopathic PTB (n=8) and abruption-complicated pregnancies (n=8) were immunostained for CSF2. Microarray and qRT-PCR compared levels of CSF2 and its receptor CSF2R mRNA in cultured term DCs and cytotrophoblasts (CYTs). Term DCs were treated with 10^{-8} M estradiol (E_2) or E_2+ medroxyprogesterone (MPA, 10^{-7} M) ± 1 IU/ml THR for 4 h, washed times x3 to remove THR and incubated for 24 h with control media. The effect of conditioned media supernatant (CMS) on FM weakening were analyzed. Statistical analysis used One-way ANOVA.
RESULTS: CSF2 immunostaining localized primarily in DC cytoplasm and CTB membranes. CSF2 immunoreactivity was higher in DCs and CTBs in decidua basalis of idiopathic PTB or abruption-complicated *vs.* normal term specimens ($p<0.05$). Microarray confirmed by qRT-PCR detected 2-fold higher CSF2 expression in DCs *vs.* CTBs and 25-fold higher CSF2R expression in CTBs *vs.* DCs ($p<1.06E-11$). THR induced CSF2 secretion in DC cultures ($p<0.05$) and MPA reduced this effect by %70. THR-treated DC derived CMS significantly weakened FMs strength ($p = 0.007$), which was inhibited by MPA co-treatment.
CONCLUSIONS: Decidual CSF2 acting via CSFR2 in CTBs mediates thrombin-induced FM weakening that contributes to abruption-related pPROM and PTB, which is counteracted by MPA.
Supported by the MOD Prematurity Research Center Ohio Collaborative grant.

O-073

Uterine Preconditioning Regulates Gestational Length. Judith Ingles,[1] Jennifer Condon,[2] Pancharatnam Jeyasuria.[2] *[1]Wayne State University, Detroit, MI, USA; [2]Wayne State University, Detroit, MI, USA.*
INTRODUCTION: Activation of the uterine unfolded protein response (UPR) has been identified by our laboratory as critical for the regulation of an appropriate gestational length[1]. Stimulation of the uterine UPR acts in a tocolytic fashion by targeting the contractile architecture in a non-apoptotic caspase 3 (CASP3) dependent manner. Growing evidence demonstrates that non-apoptotic CASP3 action can be maintained through the process of preconditioning. In this study we examine if preconditioning events allow myometrial activation of CASP3, which is normally associated with apoptosis and cell death, to be rendered non-apoptotic across gestation.
METHODS: Preconditioning is the application of minor protective insults, prior to a damaging stressor. Human myometrial (hTERT^{HM}) cells were preconditioned with a chemical inducer of the UPR, tunicamycin (TM, 0.1μg/ml, 24hr) prior to exposure of a major stress (TM, 5.0μg/ml, 1hr). Cytoplasmic and nuclear proteins were extracted and analyzed for markers of the UPR and inflammation at via immunoblotting. TNFα release was quantified using an enzyme linked immunosorbent assay. Using a timed pregnant CD-1 mouse model of stress induced preterm birth, mice were given 0.1mg/kg TM (i.p, E13) prior to the delivery of 1.0mg/kg TM (i.p, E15) and gestational length was monitored.
RESULTS: In hTERT^{HM} cells, preconditioning the UPR facilitated the maintenance of CASP3 in a non-apoptotic state. Specifically, significant CASP3 activity ($p<0.02$) was observed in the absence of apoptosis, confirmed by minimal cleavage of poly ADP ribose polymerase. Observed preconditioning-dependent increases in cell viability are likely due to decreased levels of the apoptotic initiators ATF4 and CHOP ($p<0.02$ and $p<0.02$), the preservation of anti-apoptotic markers Mcl-1 and XIAP ($p<0.05$ and $p<0.01$), and reduced inflammation, as seen by diminished NFκB activation and TNFα secretion ($p<0.01$ and $p<0.01$). Preliminary analysis has demonstrated *in vivo* preconditioning of pregnant mice maintains the tocolytic activity of non-apoptotic CASP3 in the presence of exaggerated stress, extending the length of gestation.
CONCLUSIONS: We propose pregnancy related preconditioning like events allow for non-apoptotic tocolytic CASP3 action. We speculate that inappropriate preconditioning may predispose women to an increased risk of preterm labor and delivery.
1) Kyathanahalli, C., et al. (2015). Proc Natl Acad Sci USA 112(45): 14090-14095.

O-074

IL-1 Signaling Is Critical for Neutrophil Recruitment and Activation in a Rhesus Macaque Model of Intrauterine Inflammation. Pietro Presicce,[1] Paranthaman Senthamaraikannan,[1] Courtney Jackson,[2] Cesar M Rueda,[2] Lisa A Miller,[3] Claire A Chougnet,[2] Alan H Jobe,[1] Suhas G Kallapur*.[1] *[1]Cincinnati Children's Hospital Medical Center (CCHMC), Cincinnati, OH, USA; [2]CCHMC, Cincinnati, OH, USA; [3]UC Davis - California National Primate Center, Davis, CA, USA.*
INTRODUCTION: Intrauterine infection/inflammation (IUI) is characterized histologically by neutrophilic infiltration of the placenta and fetal membranes and is frequently associated with preterm labor. Mechanisms of inflammation in IUI are poorly understood.
METHODS: We modeled IUI in the Rhesus macaque with an intra-amniotic (IA) injection of *E. coli* lipopolisaccharyde (LPS) (O55:B5, 1mg) (n=11) or saline (controls, n=13) at ~80% gestation. IL-1 signaling was blocked by recombinant human IL-1 receptor antagonist (rhIL-1ra) (Anakinra) given by maternal subcutaneous (100mg 3h prior to IA LPS) and IA (50mg 1h prior to IA LPS) routes. Fetuses were delivered surgically 16h after IA injections. At delivery, amnion was dissected free of chorion

and decidua parietalis. Chorio-decidua cell suspensions were used for multi-parameter flow cytometry. Detailed inflammation assessments were performed.

RESULTS: IA LPS increased expression of phospho-IRAK1 (p-IRAK1), a critical mediator of TLR signal transduction, and IL-8 and G-CSF mRNAs (neutrophil chemoattractants) in the dissected amnion. LPS caused a massive neutrophil recruitment (mean x 10^6/g±SE: Controls 0.3±0.1 vs. LPS 9.7±2.2, p<.001) in the chorio-decidua. The recruited neutrophils expressed high levels of Neutrophil elastase and IL-8 (by IHC) and a high spontaneous production of TNFa (by intracellular flow cytometry analysis). In the amniotic fluid (AF), LPS increased prostaglandin levels (PGE2: Controls 0.8±0.1 vs. LPS 2.4±0.3 ng/ml, p<.001). rh-IL1ra significantly decreased LPS-induced expression of p-IRAK1 in the disseted amnion by 6-fold (p=.003), and IL-8 and G-CSF mRNAs by 4-fold and 18-fold respectively (p=.01). In the chorio-decidua, rhIL-1ra decreased neutrophil numbers by 14-fold (p=.004) and neutrophil TNFa expression by 17-fold (p=.02). In the AF, PGE2 levels decreased non-significanlty by 1.6-fold upon rhIL-1ra injection.

CONCLUSIONS: Our data emphasize a key role for the amnion in mediating IUI, through an IL-1-dependent neutrophil recruitment and activation in the chorio-decidua. Anti-IL-1 therapy may thus be beneficial in reducing placenta inflammation during IUI.

O-075

Platelet Activating Factor (PAF) Induces Preterm Birth in Mice Through TLR4-Dependant Induction of Pro-Inflammatory Cytokines. Hanan H Wahid,[1] Lachlan M Moldenhauer,[1] Kenner C Rice,[2] Mark R Hutchison,[3] Sarah A Robertson.[1] [1]*University of Adelaide, Adelaide, SA, Australia;* [2]*NIDA & NIAAA, Washington, DC, USA;* [3]*University of Adelaide, Adelaide, SA, Australia.*

INTRODUCTION: Endogenous DAMPs can induce sterile inflammation and initiate the parturition cascade by activating TLRs to drive pro-inflammatory cytokine synthesis. PAF is a potent phospholipid inflammatory mediator that is elevated in amniotic fluid in spontaneous preterm delivery in women, In mice, PAF accumulation in amniotic fluid and fetal lung at term is required for on-time birth and exogenous PAF causes preterm birth (PTB). In vitro experiments suggest pro-inflammatory effects of PAF are dependent on TLR4 (Agrawal et al, Biol Reprod, 2014; Gao et al, J Clin Invest, 2015). We tested the hypothesis that in vivo, cPAF-induced PTB requires TLR4 and can be abrogated by either genetic TLR4 deficiency or the novel small molecule TLR4 antagonist (+)-naltrexone.

METHODS: *Tlr4-/-* and WT Balb/c female mice mated to males of the same genotype were given non-hydrolysable carbamyl PAF (cPAF, 2 ug ip), or vehicle alone on gd 16.5, with or without (+)-naltrexone (60 mg/kg ip) on gd 16.5, 17.0, 17.5 and 18.0 (n=12-14/group). Preterm birth (PTB, delivery within 36 h) was monitored and mice undelivered at gd 18.5 were autopsied to measure fetal survival. Additionally, gestational tissues were recovered from WT females (n=8/group) 4 h after treatment with cPAF and/or (+)-naloxone for qPCR of inflammatory cytokine genes.

RESULTS: cPAF elicited PTB in 64% (9/14) of WT mice but only 17% (2/12) Tlr4-/- mice (p<0.05, Chi2 test). Fetal survival after cPAF exposure was reduced in undelivered WT and in *Tlr4-/-* mice. (+)-naltrexone rescued WT mice from PAF-induced preterm delivery with 0/14 exhibiting PTB (p<0.05), and fetal survival comparable to vehicle control group. cPAF induced *Il1B*, *Il6* and *Il10* expression in the myometrium, decidua and placenta of WT mice, and (+)-naltrexone suppressed cytokine induction (p<0.05, ANOVA).

CONCLUSIONS: In mice, cPAF induction of inflammatory cytokines and preterm delivery is facilitated by TLR4, consistent with a role for TLR4 in regulating PAF signalling. The TLR4 antagonist (+)-naltrexone is a potent inhibitor of cPAF-induced preterm birth and fetal death in utero. Further studies will determine whether (+)-naltrexone protection from aberrant cPAF effects in utero is consistent with normal development of offspring after birth.

O-076

Oxidative Stress Induced p38MAPK Activation in Human Amnion Epithelial Cells Are Independent of ASK1-Signalosome. L Richardson, CL Dixon, R Menon*. *UTMB, Galveston, TX, USA.*

INTRODUCTION: Human parturition at term is associated with oxidative stress (OS) induced fetal cell senescence activated by p38 mitogen activated protein kinase (MAPK).Two independent pathways of p38MAPK activation were investigated: 1) OS induced dissociation of thioredoxin-apoptosis signaling kinase (ASK)-1 complex resulting in ASK1 release and phosphorylation of p38MAPK and 2) TGFb mediated activation of TAK1 (TGFb activated kinase) and TAB 1 (TGFb activated kinase 1 binding protein) leading to phosphorylated p38MAPK. Existence of these two pathways were tested in human amnion epithelial cells (AECs) exposed to cigarette smoke extract (CSE), an OS inducer.

METHODS: AECs were isolated from normal term, not-in-labor human fetal membranes and stimulated with OS inducer CSE for 1 hour. Nuclear and cytoplasmic fractions and total cell lysates were collected from both treated and untreated cells. ASK1-Trx complex and their detachment in response to OS were determined using pull down assays. Western blots determined ASK1, Trx, P-TAB1, and P-p38MAPK and immunocytochemistry (ICC) followed by confocal microscopy localized them in AECs. Statistical analyses were performed using Mann Whitney U Test and Independent Samples T-test $p < 0.05$ was considered significant.

RESULTS: CSE caused OS induced P-p38MAPK in AECs that was reversed by antioxidant N-acetyl cysteine. Pull down assay did not show existence of ASK1-Trx complex in AECs regardless of treatment. Localization of ASK1 (nuclear and cytoplasmic) and Trx (cytoplasmic) were consistent regardless of treatment; however, P-p38MAPK was higher in treated cells. Western blot and ICC co-localization showed that control and treated cells contained low amount of ASK1-Trx complex (Persons R Coefficient 0.57and 0.41) and treated cells were significantly less co-localized then controls (p=0.017). Activation of the TGFb pathway in treated cells was identified by increased intensity of TGFb/TAK1 and TAB1/P-p38MAPK relocation to the nucleus. Western blot analysis confirmed increased expression of P-TAB1 after treatment (p<0.05), an effect that was reversed by NAC (p<0.05).

CONCLUSIONS: CSE mediated OS induced p38MAPK activation in human AECs is independent of ASK1-Trx signalosome dissociation and likely mediated by activation of TGFb mediated pathway. A better knowledge of this pathway and associated mediators will improve our understanding of parturition mechanisms due to fetal tissue senescence prompted by p38MAPK at term (physiologic) and at preterm (pathologic).

O-077

The Detection of Placental Oxygenation by Photoacoustic Imaging and Ultrasound. Liliya M Yamaleyeva*,[1] Yao Sun,[2] Tiffaney Bledsoe,[1] K Bridget Brosnihan.[1] [1]*Wake Forest SC of Medicine, Winston-Salem, NC, USA;* [2]*Wake Forest SC of Medicine, Winston-Salem, NC, USA.*

INTRODUCTION: Placental hypoxia is a major underlying cause of pregnancies at risk for intrauterine growth restriction (IUGR) or preeclampsia. Photoacoustic imaging (PAI) is a novel imaging modality that combines optical contrast of photoacoustic laser technology with the high spatial resolution of ultrasound in real-time. PAI measures tissue oxygen saturation (sO2) due to the differences in absorption spectra for oxygenated and deoxygenated hemoglobin. We tested the sensitivity and accuracy of PAI for the assessments of placental sO2 in normal and pathological pregnancy.

METHODS: Placental sO2 levels were determined in normal C57Bl/6 mice at GD10, 12, 14, and 18 by using PAI features of VEVO LAZR in a 3D mode (VisualSonics). Placental sO2 levels were also determined in a model of hypertensive pregnancy associated with upregulation of circulatory markers of hypoxia (C57Bl/6 mice treated with L-NAME at 50 mg/kg/day; GD 11 to 18) and in IUGR model associated with placental hypoxia (ACE2KO mice). Sensitivity of PA imaging was assessed by measuring sO2 in the blood exposed to various levels of O2 in a tissue-like (phantom) environment.

RESULTS: Longitudinal analysis of placental sO2 in C57Bl/6 mice revealed no differences. Changing the fraction of inhaled O2 from 100 to

20% reduced total placental sO2 by 12.5%. Systolic blood pressures were higher in L-NAME-treated vs. sham C57Bl/6 (215.8±0.8 vs. 99.3±4.4 mmHg; p<0.05). L-NAME infusion decreased sO2 in placental labyrinth (L) (58.6±3.4 vs. untreated 73.6±0.97%, p<0.05) and in the combined decidua (D), junctional zone (JZ) and maternal triangle (MT) region (48.9±1.0 vs. 63.0±2.0%, p<0.05). Similarly, sO2 levels were lower in the placenta of IUGR ACE2KO vs. C57Bl/6 (ACE2 KO L: 58.6±2.0% and D, JZ, MT: 52.4±2.7%; p<0.05). L area had a higher sO2 than D, JZ, MT in sham (73.6±0.97 vs. 63.0±2.0%, p<0.05) and L-NAME infused C57Bl/6 (58.6±3.4 vs. 48.9±1.0%, p<0.05); however no regional differences were detected in the IUGR placenta. Phantom studies revealed that patterns of sO2 obtained by the direct measurement strongly correlate with those measured by the PA imaging (r=0.82, *p<0.01).

CONCLUSIONS: Our data demonstrate that PAI detects differences in sO_2 between fetal and maternal regions of the placenta and between various physiological states such as normal pregnancy, hypertensive or IUGR pregnancy.

O-078

The Human Placental Proteome Secreted into the Maternal and Fetal Circulations. Trond M Michelsen†,[1,2] Tore Henriksen,[2] Theresa L Powell,[1] Thomas Jansson*.[1] [1]*University of Colorado, Aurora, CO, USA;* [2]*Oslo University Hospital, Oslo, Norway.*

INTRODUCTION: Placental dysfunction is implicated in major pregnancy complications. Attempts to establish placental biomarkers in maternal blood are hampered by the inability to distinguish placentally and maternally derived proteins. To increase the specificity of proteomics as a read-out of placental function, we determined human placental proteins secreted into the maternal and fetal circulations by combining our unique placental 4-vessel samples and a novel aptamer-based proteomic methodology.

METHODS: Blood samples were collected from the maternal radial artery and uterine vein and the umbilical artery and vein (4-vessel sampling) at cesarean section in 10 healthy women with normal pregnancies. 1300 proteins were measured by Slow Off-rate Modified Aptamer (SOMA) protein-binding technology. Differences between the radial artery and the uterine vein and the umbilical artery and vein were determined by paired t-test using p<0.005 as significance level to account for multiple testing. We subsequently examined changes across gestation in the proteins significantly secreted from the placenta into the maternal circulation using 1st, 2nd and 3rd trimester maternal blood samples from 3 women. Linear regression testing was used to demonstrate significant changes over gestation.

RESULTS: At term the placenta secreted 24 proteins into the maternal circulation, including Placental Growth Factor, Tissue Factor Pathway Inhibitor, Dickkopf-related Protein 1 and 4, and Noggin, and secreted five proteins into the fetal circulation, including Angiogenin and Cathepsin D. Among the proteins secreted to the maternal circulation, four proteins changed significantly across gestation: Metalloproteinase Inhibitor 3 (p=0.02) and Midkine (p=0.03) decreased while Placental Growth Factor (p=0.02) and Legumain (p=0.04) increased.

CONCLUSIONS: No proteins were secreted into both the fetal and maternal circulations, suggesting a clearly defined directionality in placental protein release. The placenta-specific proteomic profiles across gestation determined by 4-vessel sampling will allow us to identify novel factors that are secreted by the placenta into the maternal circulation. We propose that these proteins represent promising new minimally invasive biomarkers for human placental function across gestation. In addition, these novel proteins may provide new insight into mechanisms by which the placenta regulates maternal and fetal physiology.

O-079

Use of Circulating MicroRNAS to Predict Placental Dysfunction in Women at Risk of Stillbirth. Bernadette C Baker,[1] Sylvia Lui,[1] Alexander EP Heazell,[1] Karen Forbes,[2] Rebecca L Jones*.[1] [1]*University of Manchester, Manchester, United Kingdom;* [2]*University of Leeds, Leeds, United Kingdom.*

INTRODUCTION: Current clinical methods fail to accurately predict women at greatest risk of stillbirth or related adverse outcomes, including fetal growth restriction (FGR). Circulating maternal serum microRNAs offer potential as biomarkers for high risk pregnancies and may also be informative of underlying placental pathology. We hypothesised that a specific maternal serum miRNA signature is associated with placental dysfunction and high risk of FGR and stillbirth.

METHODS: miRNA expression profiles were assessed using miRCURY LNA™ Universal RT microRNA PCR Human panel I+II (Exiqon) on serum miRNAs extracted from maternal serum (36 weeks gestation, n=4) from women who had an FGR fetus (birthweight centile <3rd) matched to healthy controls (20th-80th centile). Significantly altered miRNAs were confirmed by PCR in maternal serum (n=18/group) and placenta (n=22/group). *In silico* analysis was performed to predict downstream targets. Maternal serum human placental lactogen (hPL) was measured by ELISA (n=18).

RESULTS: 11 miRNAs were altered in maternal serum from FGR pregnancies (p<0.05); most significant being miR-28-5p, miR-409-3p, and miR-378a-3p. Several altered miRNAs were placenta specific, e.g. miR-526b-5p and miR-409-3p. Potential targets for these miRNAs included genes involved in placental function and altered in FGR (IGF1, SLC7A5, VEGFA). Circulating miRNAs positively correlated with maternal serum hPL, a biomarker of placental dysfunction, including placental specific miR526b-5p (p<0.01, r=0.447) and miR-454-3p (p<0.01, r=0.477). Decreased placental expression of miR-28-5p and 301a-3p was detected in FGR pregnancies (p<0.05); stratification by infant sex revealed decreased expression in placentas from male (n=10) but not female (n=12) FGR pregnancies.

CONCLUSIONS: These studies identified a 'miRNA signature' in serum of women with FGR which correlate with other biomarkers of placental dysfunction, such as hPL and may indicate a failing placenta. Significantly decreased placental miR-28-5p and 301a-3p expression suggests these miRNAs may have a role in the underlying placental pathology. Sexual dimorphism in placental miRNA expression may be important for future screening strategies and enhance understanding of increased male susceptibility to adverse perinatal outcomes.

This study was funded by Tommy's.

O-080

Insertion of Human Corticotropin-Releasing Hormone and Retroviral Regulatory Element THE1B into the Mouse Genome Delays Birth Timing. Caitlin E Dunn-Fletcher†, Lisa M Muglia, Elizabeth L Huffman, Louis J Muglia*. *Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA.*

INTRODUCTION: In humans, placental corticotropin-releasing hormone (CRH) is detectable in maternal serum and increases exponentially with gestational age, predicting the onset of parturition. CRH production by the placenta may represent one possible mechanism controlling birth timing that is unique to higher primates. Using comparative genomic analysis, we discovered retroviral element THE1B located 3 kb upstream of CRH in perfect correlation with placental expression of CRH in the primate lineage. We hypothesized that introduction of the human THE1B/CRH locus in mice would initiate placental CRH expression under the control of regulatory element THE1B and this production of placental CRH would alter the timing of birth.

METHODS: Zygote microinjection of human BAC RP11-366K18 (CHORI) was used to produce transgenic mice containing the human CRH locus and approximately 180 kb of flanking sequence including retroviral element THE1B. The CRISPR/Cas9 system was used to delete the THE1B element in BAC-containing mice. Placental CRH production was quantitated by qPCR at 18.5 days of gestation. Birth timing data was obtained by allowing males access to females for three hours at weekly intervals and monitoring gravid females for delivery.

RESULTS: Human CRH is expressed in the placentas of BAC-containing transgenic mice in a tissue-specific manner. Female mice crossed to males homozygous for the BAC delivered approximately 10 hours later than females crossed to wild type males. The delay in birth timing was observed for both wild type females (n=15 Tg/+, n=20 +/+, p=0.0028) and BAC-homozygous females (n=5 Tg/Tg, n=20 +/+, p=0.0077) and is thus dependent on placental genotype rather than maternal genotype. In addition, successful genomic deletion of retroviral element THE1B abolished placental expression of human CRH without abolishing expression in other sites (n=3 Tg/+, n=5 KO1/+, n=6 KO2/+, p=0.0199).
CONCLUSIONS: These findings suggest that the retroviral element THE1B is required for placental expression of CRH and that placental expression of human CRH, a known biomarker of preterm birth in humans, is competent to alter birth timing in mice.

O-081

Oxygen-Dependent JMJD6 Regulation of Fibronectin Synthesis and Assembly in the Human Placenta. Sruthi Alahari†,[1,2] Isabella Caniggia*.[1,2,3] *[1]MSH, Toronto, ON, Canada; [2]University of Toronto, Toronto, ON, Canada; [3]University of Toronto, Toronto, ON, Canada.*
INTRODUCTION: Extracellular matrix (ECM) assembly during human placentation is a multi-step process involving the coordinated actions of factors that guide cytotrophoblast differentiation towards a migratory/invasive phenotype typical of extravillous trophoblasts. These events are compromised in preeclampsia (PE), a pathology typified by shallow trophoblast invasion into the maternal spiral arteries. Emerging evidence highlights the Jumonji C family of oxygen-dependent histone demethylases as regulators of the epigenetic code, including several genes mediating epithelial to mesenchymal transitions (EMTs). Hence, we sought to investigate the importance of JMJD6 enzyme in mediating ECM, in particular fibronectin (FN) assembly in the human placenta.
METHODS: Placentae were obtained from first trimester and preeclamptic (n=17), pre-term (n=14) and term (n=15) control pregnancies. Placental mesenchymal cells (pMSCs) and primary trophoblasts were isolated and characterized. qPCR was used to quantify fibronectin (*FN1*) gene expression, while western blotting (WB), immunohistochemistry (IHC) and immunofluorescence (IF) assayed for FN protein expression and spatial distribution.
RESULTS: Overexpression (OE) of JMJD6 in pMSCs in normoxia led to a reduction in FN levels. IF analysis revealed that besides the typical extracellular FN distribution, JMJD6 OE also downregulated intracellular FN, indicating its impact on FN synthesis. *FN1* mRNA was significantly upregulated in primary trophoblasts and pMSCs exposed to low oxygen (i.e. 3% O_2), when JMJD6 is functionally inactive. OE of the inactive JmjC mutant (ΔJMJD6) in pMSCs abolished the negative regulatory effect of JMJD6 on FN expression and prevented its dimerization, required for FN deposition. Consistent with our observation of impaired JMJD6 histone demethylase activity in PE, WB and IHC revealed increased FN expression in PE tissue. Examination of the signalling pathway involved in FN matrix formation, revealed down-regulation of activated β1 integrin and phosphorylated focal adhesion kinase ($pFAK^{Y397}$), upon JMJD6 OE at 8% O_2 but not at 3% O_2.
CONCLUSIONS: The present study demonstrates that JMJD6 controls the synthesis, expression and deposition of FN in the human placenta. We propose that the shallow trophoblast invasion in PE is in part due to altered JMJD6 activity, resulting in aberrant FN deposition.
Supported by CIHR.

O-082

A Distinct Signature of ATP-Binding Cassete Transporter Expression in the Preterm Human Placenta with Chorioamnionitis. Guinever E Imperio†,[1,2] Enrrico Bloise,[2,3] Mohsen Javan,[1] Phetcharawan Lye,[1] Andrea Constantinof,[1] Caroline Dunk,[5] Fernando M Reis,[4] Stephen J Lye,[1,5] William Gibb,[6] Tania M Ortiga-Carvalho,[2] Stephen G Matthews.[1,5] *[1]University of Toronto, Toronto, ON, Canada; [2]Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil; [3]Universidade Federal de Minas Gerais, Belo Horizonte, MG, Brazil; [4]Universidade Federal de Minas Gerais, Belo Horizonte, MG, Brazil; [5]Mount Sinai Hospital, Toronto, ON, Canada; [6]University of Ottawa, Ottawa, OT, Canada.*
INTRODUCTION: The ATP-binding cassette (ABC) transporters actively efflux substrates involved in immunological responses and drug biodisposition in the placenta. Intrauterine infection contributes to neonatal morbidity, thus understanding the expression profile of ABC transporters in the presence of chorioaminionitis is vital to improving fetal health and survival. We hypothesized that chorioamnionitis modifies the expression of ABC transporters in the preterm human placenta (PTDC).
METHODS: Placentas were obtained from PTDC (n=8) and from preterm without chorioaminionitis (PTD; n=7). Gene expression of 47 ABC transporters was assessed using the TaqMan® Human ABC Transporter Array. Expression of selected genes was validated using qPCR and immunohistochemistry. Expression of microRNAs known to regulate P-glycoprotein (P-gp) and breast cancer resistance protein (BCRP) were also examined.
RESULTS: The expression of five ABC transporters *ABCB1, ABCB9, ABCC2, ABCF2* and *ABCG2* was modified in chorioamnionitis, and in all cases the magnitude of the effect correlated to the severity of inflammation. Increased *ABCB1* ($p<0.05$) and *ABCG2* ($p<0.05$) mRNA was validated using qPCR. Immunohistochemistry demonstrated increased BCRP (*ABCG2*, $p<0.05$) but decreased P-gp staining intensity (*ABCB1*, $p<0.05$) in cases of chorioamnionitis. The expression of selected microRNAs involved in P-gp (miR-331-5p, $p<0.01$) and BCRP (miR-328 and miR-519c, $p<0.05$) regulation was increased in chorioamnionitis.
CONCLUSIONS: Given that ABC transporters extrude a range of specific substrates, alterations in their expression associated with inflammation will likely lead to modified fetal transfer of clinically relevant compounds as well as important physiological factors.**Funding:** The Bill and Melinda Gates Foundation, CNPq and Capes.

O-083

Cross-Sex Testosterone Therapy Is Not Sufficient for Bone Development in Female Mice: Implications for Treating Transgender Youth. Laura G Goetz†,[1] Ramanaiah Mamillapalli,[1] Maureen J Devlin,[2] Masoumeh Majidi-Zolbin,[1] Hugh S Taylor*.[1] *[1]Yale University, New Haven, CT, USA; [2]University of Michigan, Ann Arbor, MI, USA.*
INTRODUCTION: Cross-sex hormone therapy (HT) is widely used by transgender people to alter secondary sex characteristics. Very little research has been done on the physiological impact of prolonged HT, though limited-scope observational studies suggest adverse health effects. Here we investigate the long-term effects of HT on bone health and body composition, in a murine model, and compare whether beginning HT during adolescence versus after reaching adulthood affects those outcomes.
METHODS: Female mice underwent ovariectomy (OVX) at 6 weeks (early, E) or 10 weeks (late, L), and with surgery began weekly subcutaneous injections of testosterone (T), estradiol benzoate (E2B), or vehicle (n = 5 per group, with 7 groups, including a no OVX/vehicle group). Dual-energy X-ray Absorptiometry (DXA) and microCT scans were performed at 20 weeks of age to investigate differences in body composition.
RESULTS: E2B treatment at both ages increased spinal bone mineral density by 20% (p=0.01) and content by 20% (p=0.01) compared to controls, but T did not. In the late T group, spine area was 5% greater (p=0.01) and bone mineral content trended 5% greater (p=0.10) than in the early T group, suggesting that early life estrogen exposure is important for adolescent bone development and cannot be sufficiently replaced by T alone. In the femur, hormone treatment, but not age at OVX,

affected trabecular bone density (10-fold higher in E2B mice; p<0.0001) and cortical bone area (higher in E2B mice; p= 0.009). Total body fat percentage decreased in both E2B groups by 20% (E: p=0.01, L: p=0.01) and in vehicle controls by 10% for early (E: p=0.05) and 20% for late (L: p=0.01) compared to the no OVX group. Visceral fat percentage decreased by a third in both E2B (E: p=0.03, L: p=0.03) and vehicle (E: p=0.03, L: p=0.01) groups. In contrast, neither body fat percentage nor total body fat decreased in either T group, implying that T therapy promotes adipose deposition while estrogen does not.
CONCLUSIONS: This suggests that using T alone results in inability to reach peak bone mass, while increasing adiposity. These findings suggest potentially adverse health outcomes related T therapy and offer critical information regarding the effects of sex steroids on bone and body composition, with clinical implications for treating transgender youth.

O-084

Elevated Androgen Levels Impair Connexin43 Function Leading to Decreased EDHF-Mediated Relaxation and Hypertension in Adult Female Rats. Amar More†, Jay Mishra†, Sathish Kumar. *University of Texas Medical Branch, Galveston, TX, USA.*
INTRODUCTION: Women with PCOS are often presented with endothelial dysfunction and elevated blood pressure. PCOS women have hyperandrogenemia, and in rat model of PCOS, anti-androgen treatment decreases blood pressure indicating a key role for androgens in the development of hypertension. However, the underlying mechanism that contributes for androgen-mediated increase in blood pressure is not known. This study determined whether elevated androgens affect endothelium-derived hyperpolarizing factor (EDHF) mediated vascular relaxation responses through alteration in function of gap junction proteins, connexins.
METHODS: Female Sprague Dawley rats were implanted with placebo pellets or dihydrotestosterone pellets (DHT; 7.5-mg, 90-d release) to induce a 2-fold increase in plasma DHT levels similar to that in PCOS women. After 10 weeks of DHT exposure, blood pressure through CODA system and vascular function using wire myography were assessed. Acetylcholine induced EDHF-mediated relaxation was determined in presence of inhibitors of nitric oxide and prostacyclin synthesis. Contribution of connexins (Cx37, 40 and 43) in the EDHF-mediated relaxation was assessed with peptides targeted against connexins. Direct effects of androgens on connexins expression were determined using an *in vitro* cell culture model.
RESULTS: Elevated androgens in females significantly increased mean arterial pressure and decreased endothelium-dependent EDHF-mediated acetylcholine relaxation in mesenteric arteries compared to controls. Inhibition of Cx40 did not affect EDHF relaxation in both control and DHT groups. Inhibition Cx37 decreased EDHF relaxation to a similar magnitude in both controls and DHT females. However, inhibition of Cx43 significantly attenuated EDHF relaxation in mesenteric arteries of controls but not in DHT females. Cx37 and 43 but not 40 were expressed in mesenteric arteries, and elevated androgens did not alter Cx37 but decreased Cx43 expression compared to vehicle controls. In vitro exposure of testosterone to cultured mesenteric artery smooth muscle cells dose dependently downregulated Cx43 expression.
CONCLUSIONS: Increased blood pressure in hyperandrogenic females is due, at least in part, to decreased EDHF-mediated vascular relaxation responses. Cx43 appears to play a predominant role in contributing to androgen-induced decrease in EDHF function in the rat mesenteric arteries.

O-085

Steroidogenic Factor 1 (*Nr5a1*) Is Necessary for Sertoli Cell Differentiation Post Sex Determination. Chandra S Miryala†,[1] Prashanth Anamthathmakula†,[1] Jennifer Ondon,[1] Rebecca Moreci,[1] Jeyasuria Pancharatnam.[1] *[1]C.S. Mott Center for Human Growth and Development, Wayne State University, Detroit, MI, USA; [2]Duke University, Durham, NC, USA.*
INTRODUCTION: Our lab has demonstrated the importance of Steroidogenic Factor 1 (*Sf-1, Nr5a1*) in fetal Leydig cell development and function prior to male gonadal sex differentiation. The function of SF-1 in the developing and differentiating Sertoli cell however is unknown. The high levels of SF-1 in the developing Sertoli cell post sex determination at the peak of SRY (sex determining region of the Y chromosome) expression implies a vital role for this nuclear receptor in the differentiation and/or function of the Sertoli cell.
METHODS: *Sf-1* knockout (KO) mice were generated crossing male *Sf-1*$^{lox/lox}$ mice with Amh-Cre *Sf-1*$^{lox/lox}$ females. Testes were collected from E15.5, 16.5, 17.5 and 18.5 embryos from timed pregnant mice treated with BRDU 4 hours prior to dissection. Sertoli cells were detected using the SOX9 marker by IHC. Proliferating Sertoli cells were determined by merging SOX9 and BRDU IHC. Due to a loss in the Sertoli cell population at E15.5 we used TUNEL assay to determine if apoptosis contributed to this loss.
RESULTS: The E15.5 Sertoli cell population declines following *Sf-1* knockout and SOX9 positive Sertoli cells do not proliferate compared to the wild type (WT). The KO testis was highly apoptotic at E15.5, not seen in the WT or in the KO testes post E15.5. AMH protein levels decline at E15.5 and E16.5 in testes of KO mice when compared to WT. Immunohistochemical analysis using the germ cell specific marker, VASA, points to a reduction in the germ cell population in the KO. Seminiferous cords are well developed in the WT testes at E15.5, E16.5, E17.5 and E18.5 but are disrupted in the KO testes with limited number remaining at E18.5. Some KO 6-week-old adult testes consist of Sertoli cell only seminiferous tubules while very few had some spermatogenesis. This phenotype is consistent with a hypomorph where a few Sertoli cells escaped *SF-1* ablation. Testis weights of 6-week-old adult KO mice was drastically lower than WT ($p \leq 0.05$), however, KO seminal vesicles weights were similar to WT (p>0.05).
CONCLUSIONS: The Sertoli cell specific KO of *Sf-1* at E14.5 recapitulates dysgenesis of the *Sf-1* null mouse as seen in the apoptotic phenotype of the Sertoli cells. This implies that some of the developmental program that leads to cell death is still functioning at this stage.

O-086

Effects of Oxytocin on Atrophic Rat Vagina. Bernhard Lindenthal, Peter Muhn, Ulrike Fuhrmann, Ildiko Terebesi, Ralf Lesche, Qiong Lin, Reinhard Nubbemeyer, Thomas M Zollner, Christina Bartnitzek. *Bayer Pharma AG, Berlin, Germany.*
INTRODUCTION: Low estrogen synthesis during menopause leads to vaginal atrophy, which causes severe symptoms in about 45% of postmenopausal women. Therapy with estradiol restores vaginal physiology comparable to pre-menopausal conditions. However, use of estradiol to treat women with vaginal atrophy is limited due to side effects and possible risks. The nonapeptide oxytocin has been shown in clinical studies to reduce symptoms of vaginal atrophy and may be an alternative treatment option. However, the mechanisms of oxytocin effects on vaginal tissue and a direct comparison to estrogen have not been investigated so far.
METHODS: Ovarectomized rats were treated with oxytocin, estradiol, atosiban or vasopressin, either intravaginally (gel) or systemically (s.c.). Histology, gene expression analysis, organ weights and oxytocin measurements were performed in long term (4-6 days) and short term (0.5-24 h) studies.
RESULTS: Treatment of ovarectomized rats with either oxytocin 4 mg/kg intravaginal or estradiol 1.5 µg/kg s.c. for 6 days showed strong thickening of vaginal epithelium and keratinization. The effect of oxytocin could be antagonized with atosiban, an oxytocin receptor antagonist, whereas vasopressin had no effect. Gene array analysis showed similarities of

gene regulation by oxytocin and estradiol in vaginal tissue. KRT1, SPRR3, DSC1 were identified to be regulated 0.5-24 h after oxytocin or estradiol application and might be therefore useful marker genes for further studies. No effects of oxytocin on the uterus were observed after intravaginal administration.
CONCLUSIONS: Oxytocin and estradiol exerts similar effects on vaginal histology in atrophic vaginal epithelium of ovarectomized rats. The effect of oxytocin is oxytocin receptor dependent. Similarities in gene expression after short and long-term treatments suggest the involvement of similar pathways induced by oxytocin and estradiol. Therefore local oxytocin might be an option for estrogen-free treatment for symptoms of vaginal atrophy in postmenopausal women.

O-087

Obesity Prevents Protective Down-Regulation of Mitogenic Insulin Receptor A in Uteri of Diet-Induced Obese Mice. Clare Flannery, Caitlin Radford, Farrah Saleh, Gina Choe, Jung Dae Kim, Sabrina Diano, Hugh Taylor*. *Yale School of Medicine, New Haven, CT, USA.*
INTRODUCTION: Obesity is a risk factor for endometrial hyperplasia. We hypothesized that high levels of insulin associated with obesity promote endometrial proliferation. We previously found the mitogenic insulin receptor isoform, IR-A, increases dramatically in normal, early proliferative endometrium, and is also raised in hyperplasia. Endometrial expression of IR-A was unaffected by body mass index. However, high levels of insulin reduced IR-A by 60% *in vitro* and in a lean, hyperinsulinemic mouse model. We sought to investigate the effect of excess adiposity on IR-A expression *in vivo*.
METHODS: Female C57Bl6 mice were fed either normal chow (NC; 18% calories from fat; n=7) or high fat chow (HF; 45% fat; n=18) for 12 weeks. After a 16-hour fast, mice underwent a glucose tolerance test and MRI for body composition. Obesity was defined as percent fat 2 standard deviations higher than mean percent fat in NC mice. On HF chow, 10 mice became obese, and 8 mice did not become obese. Uteri were extracted, and IR-A and IR-B were quantified by qRT-PCR. Each group was analyzed by 2-tailed t-test.
RESULTS: HF obese mice had 28±2% body fat versus 15±1% in NC mice ($p<0.0001$). HF obese mice had 60% higher insulin levels than NC (0.90±0.04 vs. 0.55±0.03 ng/mL; $p<0.0001$). Despite similar percent body fat, insulin levels were also 30% higher in HF non-obese (0.71±0.08 ng/mL) than in NC mice ($p=0.02$). The uteri of HF obese mice had similar IR-A and IR-B expression to NC mice (p=NS, respectively). In contrast, the uteri of HF non-obese mice showed a 40% reduction in mitogenic insulin receptor IR-A, relative to NC ($p<0.01$). IR-B was unchanged in HF non-obese mice relative to NC mice (p=NS).
CONCLUSIONS: In summary, we found that obesity prevents down-regulation of mitogenic IR-A in the setting of hyperinsulinemia. This study suggests that the endometrium of obese women remains sensitive to insulin action, and is vulnerable to insulin-driven proliferation.

O-088

Altered Early Luteal Phase miRNA 483-3p Expression in Women with PCOS. Iris Eisenberg-Loebl, Debra Goldman-Wohl, Caryn Greenfield, Ronit Haimov-Kochman, Simcha Yagel, Tal Imbar*. *Hadassah-Hebrew University Medical Center, Jerusalem, Israel.*
INTRODUCTION: Previously we have demonstrated an altered expression pattern of miRNA molecules in granulosa-lutein cells (GLC) from women with Polycystic ovary syndrome (PCOS). Among this panel of dysregulated miRNAs, there was a prominent lower expression of miRNA 483-3p in PCOS patients. This is a conserved sequence encoded in the second intron of the *IGF2* gene. In this study we aimed to examine the role of miRNA 483-3p in the GLC of women with PCOS and its influence on steroidogenesis.
METHODS: Women with PCOS (n=8) and normally ovulating (n=8) women undergoing IVF treatment were enrolled. Serum samples were collected at early follicular phase and at the ovum pick up day along with GLC. Primary GLC cultures were established and the steroidogenic role of miRNA 483-3p was analyzed. Primary human GLC were transfected with miRNA 483 mimics and inhibitor. Culture media was analyzed for estradiol and progesterone expression.
RESULTS: Lower levels of miRNA 483-3p and 483-5p were detected in GLC and in the serum of PCOS patients at the early luteal phase. Early follicular phase serum levels were similar. *IGF2* mRNA levels were significantly decreased in GLC from PCOS patients ($p= 0.03$). Furthermore, direct inhibition of miRNA 483-3p expression in GLC culture, resulted in significantly lower levels of progesterone synthesis as detected by ELISA assay. Bioinformatic analysis, identified that miRNA 483-3p is involved in regulation of TGFβ signaling pathway by targeting SMAD3 and SMAD4.
CONCLUSIONS: There is a different expression pattern of miRNA 483 (GLC and serum) during early luteal phase in PCOS. GLC from PCOS women showed lower expression levels of the miRNA. This was accompanied by a reduction in the cells steroidogenic activity, mainly, progesterone secretion. Our results implicate an aberrant post transcriptional regulation of the steroidogenic pathway in GLC of women with PCOS involving reduced expression of miRNA 483.

O-089

Differential Increases in First Trimester Maternal Weight (MW) by Maternal Age Over the Past Decade in 2.6 Million Pregnancies: Opportunity to Target Teenagers for Obesity Prevention. Shara M Evans†,[1] David A Krantz,[2] Terrence W Hallahan,[2] Mark I Evans*.[1,3] *[1]Fetal Medicine Foundation of America, New York, NY, USA; [2]NTD Eurofins Laboratory, Melville, NY, USA; [3]Mt. Sinai School of Medicine, New York, NY, USA.*
INTRODUCTION: To investigate first trimester MW changes in teenagers over past decade to identify opportunities for pregnancy obesity complication prevention.
METHODS: 1st trimester MW was collected as part of a nation-wide combined screening program for aneuploidy in 2,608,669 pregnancies from 2003-2015 and categorized by MA at del (<20,20-29,30-39, and 40+). Whole age cohort MW and top 10% MW were collected by year for each age group. Our population was 63% Caucasian, 13% Hispanic, 11% African American, 7% Asian, 3% Asian Indian and 3% others. Geometric mean MW values were adjusted for age, gestational age at time of test and ethnicity by determining the least-squares means based on ANOVA using log-transformed weight values. The adjusted geometric mean MW values were then regressed against time (with standard error of the coefficients adjusted for autocorrelation and number of patients during each time period).
RESULTS: Over the study period, MW increased by 5.3% for both entire cohort and for the top 10%. For teenagers, however, there was no overall MW increase, except for the top 10%.

N/Age	<20	20-29	30-39	40+
2,608,669	68,833	867,907	1,521,201	150,728
Total Pop	0.1% (143.0-143.7)	4.4% (148.1-154.2)	5.6% (146.4-153.8	5.3% (149.9-158.1)
Top 10%	4.6% (216.5-226.7)	4.7% (236.5-247.7)	6.3% (228.4-243.0)	4.7% (234.0-245.0)

CONCLUSIONS: The >5% increase in MW is alarming. For both total and top 10%, older patients increased more than younger ones. That the absolute weight gain is nearly double in the heaviest 10% is a public health crisis. We can expect continued increases in diabetes and obesity related complications of pregnancy. Women <20 were the only cohort without an overall increase in MW over the past decade. However, in the top 10% population, even women < 20 had a significant increase. Continued MW increases are concerning and were similar for all women >20 and for the top 10% of women <20. The increase for teenagers in the top 10% identifies a group at high risk for a lifetime of increased pregnancy and other obesity complications that may benefit by targeted public health interventions.

O-090

Adiponectin Prevents Obesity and Hepatic Steatosis in Mouse Offspring Born to Obese Dams. Megan Gossling,[1] Fredrick Rosario,[2] Stephanie Wesolowski,[1] Thomas Jansson,[2] Theresa Powell*.[1,2] *[1]University of Colorado, Aurora, CO, USA; [2]University of Colorado, Aurora, CO, USA.*

INTRODUCTION: Childhood obesity may have its origin in fetal life. Offspring born to obese mothers have an increased lifetime risk of obesity, insulin resistance, and non-alcoholic fatty liver disease. Using a novel mouse model of maternal obesity with similarities to the human condition, including low circulating adiponectin (ADN), we have demonstrated that ADN supplementation in obese pregnant dams prevents fetal overgrowth. We hypothesized that ADN supplementation during pregnancy attenuates the adverse metabolic outcomes in adult offspring of obese dams.

METHODS: Female C57BL/6J mice were fed control or high-fat/high-sugar diets. Pregnant obese (OB) and control (C) mice were given PBS or ADN (0.62 mg/g/d) infusion at E14.5-E18.5. Fasted male offspring were studied at 3 months (N=36). A glucose tolerance test (GTT) was performed. Serum insulin was measured using ELISA and serum triglycerides, hepatic triglyceride and glycogen deposition were measured by colorimetric assays. Hepatic neutral lipid deposition was determined by Oil Red O. Hepatic perilipin-2 and insulin signaling pathway activity were measured by western blot. Hepatic gene expression of the insulin targets G6Pase, PEPCK, PGC-1α, SREBP-1, ACC, FAS, and glycogen phosphorylase was determined using RT-qPCR. Results were analyzed by one-way ANOVA, $p<0.05$ considered significant.

RESULTS: Male offspring of obese pregnant dams (OB/PBS) were 20% heavier than offspring born to both control pregnant dams (C/PBS) and ADN supplemented obese dams (OB/ADN). The GTT area under the curve (+25%), serum insulin (+2.4-fold), and serum triglyceride (+46%) levels were significantly elevated in offspring of OB/PBS dams. Hepatic triglyceride content (+1.6-fold), neutral lipid staining (+5.5-fold), perilipin-2 expression (+1.7-fold), and glycogen deposition (+2-fold) were significantly increased in OB/PBS offspring compared to C/PBS offspring. All metabolic aberrations at 3 months of age were prevented in OB/ADN offspring. Hepatic insulin signaling and gene expression of insulin targets did not differ between groups.

CONCLUSIONS: Adiponectin supplementation in pregnant obese dams prevented obesity, glucose intolerance, hypertriglyceridemia, and hepatic steatosis in adult male offspring born to obese dams. ADN may be a potential therapeutic agent for preventing the long-term metabolic consequences in offspring born to obese mothers.

O-091

A Randomized Controlled Trial of an M-Health Behavioural Lifestyle Intervention to Prevent Gestational Diabetes in Overweight and Obese Pregnancy: PEARS. Maria A Kennelly, Kate M Ainscough, Elizabeth J O'Sullivan, Karen L Lindsay, Fionnuala M McAuliffe*. *School of Medicine and Medical Science, University College Dublin, Dublin, Leinster, Ireland.*

INTRODUCTION: Maternal adiposity confers an increased risk of Gestational Diabetes Mellitus (GDM). Interventions focusing on changing lifestyle behaviours may improve maternal obesity outcomes. Mobile Health (mHealth) technologies hold potential to support such interventions through remote delivery of content. The aim of this study is to assess the impact of an antenatal behavior-change intervention supported by mHealth smartphone app technology compared with usual care on the incidence of GDM in an overweight and obese pregnant population.

METHODS: This is a RCT of 565 women with a BMI ≥ 25 kg/m^2. Women were randomized to standard care, or a 'healthy lifestyle package.' The healthy lifestyle package grounded in behavior change theory consisted of one education session on low glycemic index diet and physical activity in pregnancy, a smartphone app reinforcing this information and fortnightly motivational emails from the research team. The primary outcome was the incidence of GDM at 29 weeks' gestation. Other outcomes included gestational weight gain (GWG), birth weight, and large for gestational age (LGA)(≥90th centile) infants.

RESULTS: There was no difference in the incidence of GDM between the two groups; 37/241 (15.4%) *vs*. 36/255 (14.1%) *P*=0.69 respectively. The intervention group had significantly less GWG compared to controls (11.3 ± 5.6kg *vs.* 12.6 ± 5.6kg; *P*=0.027). At a metabolic level, the intervention resulted in improvement in late pregnancy glucose homeostasis with attenuation of late pregnancy insulin resistance - table 1. Although there was no difference in birth weight between the two groups (3590.0 ± 561.5g *vs.* 3679.6 ± 543.6g; *P*=0.06), fewer infants were born LGA in the intervention group compared to control 12/264 (4.5%) *vs.* 28/274 (10.2%) *P* =0.01).

CONCLUSIONS: An m-health-supported behavioral intervention had no impact on the incidence of GDM in an overweight and obese population. It did, however, have a positive impact on GWG, maternal glucose homeostasis and significantly reduced the number of infants born LGA.

Mean change in metabolic parameters from baseline to 28 weeks	Intervention	Control	P
Fasting glucose mmol/L	-1.15 (0.33)	-0.05 (0.3)	0.02*
Insulin mU/L	3.5 (4.42)	4.56 (5.5)	0.03*
C-Peptide ng/ml	0.43 (0.73)	0.6 (0.9)	0.04*
HOMA2-IR	0.41 (0.58)	0.54 (0.73)	0.04*

O-092

Mild Intraventricular Hemorrhage Is Not Associated with Low Bayley Scores at Age 2. Emilie Vander Haar†, Adina Goldberger†, Cynthia Gyamfi-Bannerman*. *Columbia University Medical Center, New York, NY, USA.*

INTRODUCTION: Severe intraventricular hemorrhage (IVH) has been associated with poor neurodevelopmental outcomes. However, it is unclear whether mild IVH is associated with long-term developmental delay. We aim to determine whether mild IVH is associated with poor neurodevelopmental outcomes.

METHODS: This is a secondary analysis of a multicenter, randomized controlled trial of magnesium for cerebral palsy prevention in pregnancies at risk for preterm delivery. We included singleton pregnancies, and excluded multiples, malformations, and stillbirths. All infants in the study received at least one head ultrasound performed by a trained research sonographer. Our three exposure groups were no IVH, mild IVH (grades I/II), and severe IVH (grade III/IV). Our primary outcome, Bayley II scores at age 2 less than two standard deviations below the mean, was defined by a mental developmental index (MDI) or psychomotor developmental index (PDI) <70. Our secondary outcome was MDI or PDI one SD below the mean. We conducted bivariate analyses, and fit a logistic regression model, adjusting for possible confounders to assess factors related to abnormal MDI or PDI.

RESULTS: Of 1,528 patients, 1,226 (80%) had no IVH, 278 (18%) mild IVH, and 24 (2%) severe IVH. Mean gestational age at delivery was 28 4/7 weeks. Groups differed by race, delivery route, neonatal sepsis, meconium, periventricular leukomalacia (PVL) and gestational age at delivery. There was no difference in antibiotic exposure, magnesium exposure, or number of betamethasone courses. Infants with severe IVH were more likely to have PDI<70, while MDI<70 was more common in both mild and severe IVH. There was no difference between IVH groups for PDI or MDI one SD below the mean. After adjusting for confounders, PDI<70 was associated with severe but not mild IVH (Table 1). PVL was the strongest independent risk factor for abnormal MDI or PDI. PVL remained significantly associated with PDI<70 after removing cases where PVL co-existed with IVH (OR 6.27, CI 1.5-24.9; p=0.01).

CONCLUSIONS: Mild IVH is not associated with abnormal Bayley scores at age 2. PVL appears to be a strong predictor of poor neurodevelopmental outcomes.

**Figure(s) will be available online.*

O-093

Adrenomedullin Is a New Modulator of Lipolysis in Human Adipocytes. Yuanlin Dong, Chandra Yallampalli. *Baylor College of Medicine/Texas Childrens Hospital, Houston, TX, USA.*

INTRODUCTION: Pregnancy complicated with GDM displayed increased adrenomedullin (ADM) and its receptors in adipose tissues as compared with uncomplicated pregnant women, and this is associated with insulin resistance and dyslipidemia, but the molecular effects of ADM on lipid metabolism are unknown. In the present study, we determine the effect of ADM on lipolysis and examine the major signaling of lipolytic cascade in human adipocytes.

METHODS: Human pre-adipocytes were fully differentiated into mature adipocytes and used to measure the release of glycerol as an index of lipolysis. The signaling molecules involved in ADM actions were investigated by using Q- PCR and Western blotting and data analyzed using ANOVA.

RESULTS: ADM stimulates adipocyte glycerol release in a dose- and time-dependent manner ($p<0.01$). These ADM-induced increases in glycerol release were reduced by pre-incubation with ADM receptor components CRLR/RAMP2 blocker, ADM 22-52, and CRLR/RAMP3 blocker, CGRP 8-37 ($p<0.01$). Treatment of cells with ADM (1nM to 100nM for 24 hours) did not significantly affect the gene expressions for insulin receptor substrate-1 (IRS-1), lipolytic enzymes perilipin and hormone-sensitive lipase (HSL) ($p>0.05$), but resulted in a reduction of phosphorylation of IRS-1 at Ser612 ($p<0.01$), implying impaired insulin's anti-lipolytic action by ADM. In parallel with increased release of glycerol, ADM significantly enhanced the phosphorylation of perilipin at Ser522 and HSL at Ser563. In contrast, AM**22-52** (1μM) and CGRP8-37 (1 μl) block ADM actions and inhibit perilipin-Ser522 and HSL-Ser563 phosphorylations in a time-dependent manner, suggesting that the lipolytic action of ADM in adipocytes is mainly mediated by activation of both perilipin and HSL.

CONCLUSIONS: ADM promotes lipolysis in adipocytes, which is triggered by down-regulation of phosphorylation of IRS-1, but up-regulation of phosphorylation of the lipolysis-related proteins perilipin and HSL. Knowledge of the signaling pathways involved in the lipolytic action of ADM is important for our understanding of how metabolic derangements develop in states of GDM, and ADM antagonist may be useful to improve insulin sensitivity and lipid homeostasis in GDM patients.

O-094

The Impact of Altered IL-1 Signaling on Metabolic Dysfunction During Pregnancy. Jasmine Plows†, Thashma Ganapathy, Philip Baker, Mark Vickers, Joanna Stanley, Clare Reynolds*. *University of Auckland, Auckland, New Zealand.*

INTRODUCTION: Adipose inflammation is a hallmark feature of obesity. The release of pro-inflammatory cytokines from adipose tissue can contribute to maternal insulin resistance and may be one mechanism by which obesity predisposes women to gestational diabetes. There is ample evidence that reduced function of the interleukin-1-receptor-1 (IL1R1), which propagates signaling of pro-inflammatory cytokines IL-1α and β, protects against obesity-mediated metabolic dysfunction in male mice. We aimed to investigate the role this receptor plays in metabolism during pregnancy.

METHODS: C57BL/6J (WT) and IL1R1 knockout female mice ($IL1R1^{-/-}$) were randomized to control (CD) or high fat diet (HFD; 45% kcal from fat) two weeks prior to mating and during pregnancy (n=15 per group). Glucose tolerance was assessed at gestational day (GD)16.5, and tissues were collected at GD18.5. Data are presented as mean ± SEM.

RESULTS: There was a significant effect of genotype on energy intake and weight gain over pregnancy; $IL1R1^{-/-}$ mice consumed fewer calories (255.9±4.3 vs 269.6±4.2kcal, p=0.025) and gained less weight (13.4±0.5 vs 15.4±0.5g, p=0.006) than WT mice. HFD resulted in marked glucose intolerance, regardless of genotype ($p<0.0001$). However, the difference in mean area under the curve between CD and HFD-fed mice was smaller in $IL1R1^{-/-}$ mice than WT mice (158.8±73.3mmol/L.min, p=0.04 vs 305.5±65.3mmol/L.min, $p<0.0001$). There was a significant interaction between genotype and diet on plasma insulin concentration post-glucose administration. $IL1R1^{-/-}$ on CD had increased insulin release compared with WT on CD at 30 mins (1.76±0.19 vs 1.16±0.23ng/mL, p=0.002) and 60 mins (1.47±0.15 vs 1.21±0.14ng/mL, $p<0.0001$). There was also a significant interaction between genotype and diet on fasting plasma leptin. $IL1R1^{-/-}$ on HFD had increased fasting plasma leptin compared to both WT on HFD (174.4±17.8 vs 114.0±14.5, p=0.011) and $IL1R1^{-/-}$ on CD (174.4±17.8 vs 97.7±17.8, p=0.004).

CONCLUSIONS: Pregnant $IL1R1^{-/-}$ mice were not protected against HFD-induced glucose intolerance. This differs from the protective effect seen in male $IL1R1^{-/-}$ mice, although some beneficial effects were observed in $IL1R1^{-/-}$ mice, including reduced weight gain, caloric intake over pregnancy, and increased insulin response. These findings suggest that IL1R1 can affect metabolism during pregnancy, and could be an avenue to explore to improve pregnancy outcomes in obese or insulin resistant women.

O-095

Short Interpregnancy Interval After Pregnancy Loss Is Associated with Decreased Risk of Subsequent Miscarriage in a Prospective Cohort. Alexandra C Sundermann†,[1] Katherine E Hartmann,[1,2] Sarah H Jones,[1] Eric S Torstenson,[1] Digna R Velez Edwards*.[1,2] *[1]Vanderbilt University Medical Center, Nashville, TN, USA; [2]Vanderbilt University Medical Center, Nashville, TN, USA.*

INTRODUCTION: Spontaneous abortion, or miscarriage, impacts up to one in five recognized pregnancies. Evidence is inconsistent for how long to delay conception after a loss with some physicians recommending no delay, others recommending a delay of three months, and the WHO guidelines recommending at least six months. The objective of this report is to determine the association between length of interpregnancy interval (IPI) after a loss with risk of subsequent miscarriage.

METHODS: We identified women enrolled in the *Right from the Start* (2000-2012) prospective pregnancy cohort who reported miscarriage as their immediately prior pregnancy outcome. IPI was defined as the number of days between pregnancy loss and self-reported last menstrual period of subsequent pregnancy. Miscarriage was defined as loss of pregnancy prior to 20 weeks of gestation. Cox proportional hazard models were used to estimate crude and adjusted hazard ratios (HR) and 95% confidence intervals (CI). Adjusted models included maternal age, ethnicity, body mass index (BMI), parity, and education selected a priori.

RESULTS: Among the 511 study participants who reported miscarriage as their prior pregnancy outcome, 15.7% had a repeat miscarriage in the study pregnancy. When compared to IPIs of 6-17.99 months, IPIs of less than three months had the lowest risk of subsequent miscarriage (Table, adjusted-HR 0.33, 95% CI: 0.16, 0.71). Neither maternal race or parity acted as effect measure modifiers.

Table. Association between interpregnancy interval length and risk of miscarriage in subsequent pregnancy (n=511)

Interpregnancy interval length, months	N	Crude HR	95% CI	Adjusted HR[1]	95% CI
<3	124	0.31	0.15, 0.65	0.33	0.16, 0.71
3-5.99	177	0.79	0.48, 1.30	0.77	0.46, 1.29
6-17.99	136	1.00	referent	1.00	referent
18	74	0.59	0.29, 1.20	0.53	0.25, 1.12

[1]Adjusted for maternal age, BMI, education, parity and ethnicity

CONCLUSIONS: Contrary to guideline recommendations, we found that IPIs after pregnancy loss of less than three months are associated with the lowest risk of subsequent miscarriage for the first time in a prospective pregnancy cohort. This implies that counseling women to delay conception in the clinic may not be warranted.

O-096

Evaluating the Clinical Burden of Preeclampsia (PEC) on a Tertiary Care Hospital in Harare, Zimbabwe. Lydia L Shook†,[1] Muchabayiwa F Gidiri,[2] Kara M Rood,[3] Irina A Buhimschi*.[4] [1]*Yale School of Medicine, New Haven, CT, USA;* [2]*University of Zimbabwe College of Health Sciences, Harare, Zimbabwe;* [3]*The Ohio State University, Columbus, OH, USA;* [4]*Nationwide Children's Hospital, Columbus, OH, USA.*

INTRODUCTION: PEC is a major cause of maternal morbidity and mortality worldwide, with a disproportionate burden on resource-limited systems. The objectives of this study were to explore the frequency of referrals for PEC evaluation to a major tertiary hospital in Harare; to assess the efficacy of the PEC triage system; and to investigate the outcomes of PEC pregnancies.

METHODS: We performed a retrospective cohort study of pregnant women presenting for evaluation to Mbuya Nehanda Maternity Hospital from Jun-Aug 2015 (N=1259 visits). Indication for evaluation, demographics, referring site and disposition were recorded. Visits were grouped by indication for evaluation (PEC vs Other). Obstetric and perinatal outcome measures for women who were admitted and subsequently delivered (n=820 deliveries) included mode of delivery, NICU admission, and length of hospital stay. Data were analyzed by Wilcoxon rank-sum or Chi-square as appropriate and logistic regression used to control for confounding effects.

RESULTS: Of 1259 triage visits, 245 (19.5%) were for PEC evaluation. Transfers accounted for 89% of PEC visits vs 76% for other obstetric indications (P<.001). Overall, 33% of patients referred for PEC evaluation were discharged from the hospital undelivered. Patients admitted for PEC evaluation were more likely than those admitted for other obstetric indications to be discharged undelivered (PEC: 28.3% vs Other: 12.8%, P<.001). Patients admitted for PEC who then delivered were more likely to have a longer hospital stay (P<0.01), Cesarean delivery (49.3% vs 37.3%, P=0.01) and NICU admission (P<0.01) than those admitted for other obstetric indications. Results maintained following correction for gestational age.

CONCLUSIONS: Concern for PEC accounts for a significant number of referrals with up to one-third of these resulting in "over-triage." Deliveries complicated by PEC, however, were more likely to require resource-intensive care. These findings underscore the importance of correctly identifying true PEC in the community. Optimization of the referral and triage process has the potential to reduce the burden of this disease on constrained health care systems.

O-097

Zika Virus Infects Human Endometrial Stromal Cells. Paola Panina-Bordignon*,[1] Isabel Pagani,[2] Silvia Ghezzi,[2] Adele Ulisse,[1] Alicia Rubio,[2] Elisabetta Garavaglia,[1] Giuseppe Ippolito,[4] Guido Poli,[2] Elisa Vicenzi.[2] [1]*San Raffaele, Milan, Italy;* [2]*San Raffaele, Milan, Italy;* [3]*Spallanzani, Rome, Italy.*

INTRODUCTION: Zika virus (ZIKV) is a re-emerged flavivirus transmitted to humans by mosquito bites but also vertically from mother to fetus and by sexual route. Thus, the female reproductive tract may represent as a potential site of virus infection and propagation to the fetus during pregnancy.

METHODS: Endometrial stromal cells isolated from endometrial biopsies (HESC) and the human endometrial cell line T-HESC were infected *in vitro* with the reference African MR766 or the contemporary INMI-1 strains (moi: 1). *In vitro* decidualization was induced 0.5 mM cAMP and 1 μM MPA for 7 d. Viral growth and localization were analysed by immunofluorescence (IF) with anti-dsRNA or anti-panflavi envelope and anti-vimentin and anti-calreticulin mAbs. Virion production was measured in supernatants by a plaque-forming assay (PFA); absolute quantification of viral NS5 RNA was determined by droplet digital (dd) PCR. Expression of IFN-beta and ISGs (MXA and OAS-2) was detected by RT-qPCR. Surface expression of entry receptors, AXL and MER, was evaluated by FACS.

RESULTS: Primary HESC and the T-HESC line were productively infected with MR766 or INMI-1. The percentage of cells infected with MR766, measured by IF, was ca. 80%, while with INMI-1 was 10-fold lower. Both strains replicated efficiently (PFA and ddPCR) although INMI-1 was 1 $\log_{10}$ less efficient than MR766. In infected cells, ZIKV E-protein co-localized with calreticulin in the ER lumen, while viral dsRNA co-localized with vimentin. Interestingly, a 2-fold increase of the percentage of infected cells was observed in decidualized (d) T-HESC vs. controls. The efficiency of virus replication in dT-HESC cells increased up to 100-fold at 144 h post-infection. Expression of AXL, not MER, increased in dT-HESC. IFN-β transcripts increased 300-fold 6 d after MR766 infection, whereas lower levels were induced with INMI-1. MXA and OAS-2 mRNAs were upregulated in infected vs. uninfected cells. Of note, a more rapid insurgence of IFN-β was observed in T-HESC vs. dT-HESC.

CONCLUSIONS: Primary and immortalized HESC are highly permissive to ZIKV infection and replication, particularly after *in vitro* decidualization, suggesting that these cells likely represent a crucial target of sexual virus transmission and a relevant source of ZIKV spreading to placental trophoblasts.

O-098

Zika Virus Infection Damages the Testes in Mice. Jacques Halabi†,[1] Prabagaran Esakky,[1] Suzanne Scheaffer,[1] Andrea Drury,[1] Michael S Diamond,[2] Kelle H Moley*.[1] [1]*Washington University School of Medicine, St. Louis, MO, USA;* [2]*Washington University School of Medicine, St. Louis, MO, USA.*

INTRODUCTION: Zika virus (ZIKV) infection of pregnant women can cause congenital malformations including microcephaly, which has focused global attention on this emerging pathogen. In addition to transmission by mosquitoes, ZIKV can be detected in the seminal fluid of affected males for extended periods of time and transmitted sexually. In this work, we evaluated the consequences of ZIKV infection in the male reproductive tract of mice.

METHODS: We performed a longitudinal study in wild-type (WT) C57BL/6 mice infected with ZIKV (strains H/PF/2013 French Polynesia 2013 or Dakar 41519) or Dengue virus (DENV, serotype 2, strain D2S20). Testis, Epididymus, and sera were removed from virus exposed or uninfected WT mice (six mice in each group at each timepoint) at 7, 14 or 21 days post infection.

RESULTS: Seven days following infection, we detected high levels of viral RNA and infectious virus in the testis and epididymis with either ZIKV but not the closely related Dengue virus (DENV). By in situ hybridization (ISH) ZIKV was present in spermatogonia, primary spermatocytes, and Sertoli cells. No signs of tissue damage were seen, however CD45 positive cells were present, indicating an inflammatory response. By day 14, the mice infected with ZIKV experienced significant reduction in testes size with loss of normal architecture, absence of the blood-testis-barrier, decrease numbers of TRA98 positive germ cells, lin28a positive spermatogonia, and detachment of Sertoli cells from the basement membrane of the seminiferous tubules. By day 21, the testes were 10% of their original weight and this was associated with extensive tissue injury resulting in testicular involution, diminished testosterone and inhibin B levels, and oligospermia.

CONCLUSIONS: In conclusion, ZIKV preferentially infected spermatogonia, primary spermatocytes, and Sertoli cells in the testes, resulting in cell death and destruction of the seminiferous tubules. Thus, ZIKV infection of males has implications beyond sexual transmission including deleterious effects on testes function, sperm production and viability, and fertility.

O-099

Hyperemesis Gravidarum: Risk of Recurrence in Subsequent Pregnancies. Michael J Fassett,[1] Morgan R Peltier,[2] Darios Getahun*.[3] [1]*Kaiser Permanente West Los Angeles Medical Center, Los Angeles, CA, USA;* [2]*Winthrop University Hospital, Mineola, NY, USA;* [3]*Kaiser Permanente Southern California, Pasadena, CA, USA.*

INTRODUCTION: The purpose of this study was to examine whether the recurrence risk of hyperemesis gravidarum (HG) is modified by the timing of diagnosis, severity of illness and prepregnancy BMI categories.

METHODS: We used the KPSC 2007-2014 longitudinally-linked medical records to examine the recurrence risk of HG in women with first two (n=22,120) successive pregnancies. Timing of diagnosis- and severity of illness-specific recurrence risks were examined. Adjusted odds ratios (ORs) were used to estimate risks.
RESULTS: Risks of HG in the second pregnancy among women with and without previous HG were 24.8% and 4%, respectively (OR, 7.02; 95% confidence interval [CI], 5.99-8.21), especially when the condition occurred during the first (OR, 7.76; 95% CI, 6.54-9.22) and second (OR, 4.74; 95% CI, 3.38-6.64) trimesters, but not during the third trimester of the first pregnancy. The increased risk of HG recurrence was found for women with a history of first and second trimester diagnosis of HG resulting in preterm and term gestation. Women requiring in-hospital treatment were at significantly increased risk of recurrence compared with those managed on an outpatient basis. Risk of recurrence remained significant regardless of maternal prepregnancy BMI categories.
CONCLUSIONS: We demonstrated that a history of HG in the first pregnancy was associated with increased risk of recurrence regardless of maternal prepregnancy BMI, especially when the condition occurred during the first and second trimesters of pregnancy.

O-100

Zika Infection in Pregnant Rhesus Macaques Results in Placental Injury and Altered Brain Development Independent of Microcephaly. Peta L Grigsby,[1] Victoria H Roberts,[1] Alec J Hirsch,[2] Matthias C Schabel,[3] Chris D Kroenke,[3] Jamie O Lo,[4] Xiaojie Wang,[3] Zheng Liu,[3] Jessica Smith,[2] Nicole Haese,[2] Meredith Kelleher,[1] Rebecca Broeckel,[2] Craig N Kreklywich,[2] Christopher J Parkins,[2] Patricia Smith,[2] Victor DeFillppis,[2] William Messer,[5] Jay A Nelson,[2] Jon D Hennebold,[1] Marjorie Grafe,[6] Lois Colgin,[7] Anne Lewis,[7] Rhonda MacAllister,[7] Terry K Morgan,[8] Antonio E Frias,[4] Daniel N Streblow*.[2] *[1]Oregon National Primate Research Center, Portland, OR, USA; [2]Oregon National Primate Research Center, Portland, OR, USA; [3]Oregon Health & Science University, Portland, OR, USA; [4]Oregon Health & Science University, Portland, OR, USA; [5]Oregon Health & Science University, Portland, OR, USA; [6]Oregon Health & Science University, Portland, OR, USA; [7]Oregon National Primate Research Center, Portland, OR, USA; [8]Oregon Health & Science University, Portland, OR, USA.*
INTRODUCTION: As global reports of Zika virus (ZIKV) affected pregnancies continue to rise, so does the pressing need to understand the detrimental consequences of this virus on fetal development. Here, we describe a novel and highly translational non-human primate pregnancy model of ZIKV infection.
METHODS: At 50 days of gestation (term=168 days) pregnant animals were infected with ZIKV (strain PRVABC59; 1x105 ffu SQ). The pregnancy was monitored for 85 days by serial physical exams, blood counts, total chemistry panel and ultrasound/MRI. C-section delivery was performed at 135dGA at which time maternal and fetal tissues were collected.
RESULTS: A transient fever as well as axillary lymphadenopathy and a rash that was present on the upper torso and arms in all animals. Persistence of maternal infection was observed up to 12 weeks. ZIKV initiated a robust feto-placental inflammatory response characterized by elevated cytokines, chemokines and reduced placental perfusion.
CONCLUSIONS: ZIKV infection during the 2nd trimester results in persistence of maternal/fetal infection and viral transfer. Importantly, despite seemingly normal fetal growth, we provide compelling evidence of placental injury and alterations in fetal brain development independent of microcephaly.

O-101

The Impact of the Cholesterol Metabolite 27-Hydroxycholesterol on Endometrial Proliferation. Douglas A Gibson†,[1] Frances Collins,[1] Arantza Esnal,[1] Alistair RW Williams,[2] Philippa TK Saunders.[1] *[1]University of Edinburgh, Edinburgh, United Kingdom; [2]University of Edinburgh, Edinburgh, United Kingdom.*
INTRODUCTION: Endometrial cancer (EC) is the most common gynaecological malignancy and 4th most common cancer in women. Obesity is a major modifiable risk factor in EC and is thought to contribute to risk by increasing estrogen exposure and inflammation. Obesity is also associated with hypercholesterolaemia resulting in increased exposure to cholesterol metabolites such as 27-Hydroxycholesterol (27HC). 27-HC can act as an estrogen receptor (ER) agonist and is also the endogenous agonist for the 'adopted' orphan nuclear receptor LXR (Liver X Receptor). Recent studies demonstrate a role for 27HC in promoting ER-dependent growth and LXR-dependent metastasis in mouse models of breast cancer however the impact of 27HC on EC risk/progression is unknown.
METHODS: A patient sample cohort of 270 graded endometrial cancers was collected from post-menopausal women undergoing total abdominal hysterectomy using a method approved by the local institutional ethics committee. The expression of LXR receptors (LXRα and LXRβ) as well as enzymes required for the synthesis (CYP27A1) and breakdown (CYP7B1) of 27HC was assessed by qPCR and Western blot. The activity of LXR- and ER-dependent transcription was by assessed reporter assay in epithelial cell lines representative of well-, moderate- and poorly-differentiated endometrial cancers.
RESULTS: LXRα and LXRβ expression was detected in EC but did not change with grade. Expression of CYP7B1 decreased with disease severity ($p<0.05$) consistent with an association between increased bioavailability of 27HC and progression of EC. Profiling of endometrial cancer cell lines demonstrated that 27HC ($p<0.001$, n=6) or the synthetic ligand GW-3965 (LXR agonist; $p<0.001$, n=6) could promote transcription via LXR. Importantly, we found that 27HC could also activate ER-dependent transcription ($p<0.001$; n=6) and promoted proliferation of endometrial epithelial cancer cells ($p<0.001$; n=6).
CONCLUSIONS: These results provide novel insight into the impact of 27HC on endometrial proliferation and suggest that altered cholesterol metabolism may contribute to development or progression of endometrial cancer.

O-102

SYD985 Shows Antitumor Activity in Uterine and Ovarian Carcinosarcoma with HER2/Neu Expression. Gulden Menderes†,[1] Elena Bonazzoli,[1] Jonathan D Black,[1] Stefania Bellone,[1] Francesca Pattinelli,[1] Alice Masserdetti,[1] Luca Zammataro,[1] Gary Altwerger,[1] Natalia Buza,[2] Pei Hui,[2] Serena Wong,[2] Elena Ratner,[1] Babak Litkouhi,[1] Dan-Arin Silasi,[1] Masoud Azodi,[1] Peter E Schwartz,[1] Peter Goedings,[3] Patrick Beusker,[3] Miranda van der Lee,[3] Marco Timmers,[3] Wim Dokter,[3] Alessandro D Santin*.[1] *[1]Yale University School of Medicine, New Haven, CT, USA; [2]Yale University School of Medicine, New Haven, CT, USA; [3]Synthon Biopharmaceuticals BV, Nijmegen, Netherlands.*
INTRODUCTION: The objective of this study was to compare the anti-tumor activity of SYD985 to T-DM1 in carcinosarcoma (CS) which has significant heterogeneity of HER2/neu expression.
**Figure(s) will be available online.*
METHODS: The cytotoxicity of SYD985 and T-DM1 was evaluated using eight CS primary cell lines with differential HER2/neu expression. Antibody-dependent cellular cytotoxicity (ADCC), proliferation, viability and bystander killing experiments were performed using Cr^{51}-release assays, propidium iodide-based and flow cytometry assays, respectively. SYD985 and T-DM1 *in vivo* activity was also studied in mouse xenograft models.
RESULTS: Similar ADCC were induced by SYD985 and T-DM1. In contrast, SYD985 was significantly more cytotoxic compared to T-DM1. Specifically, in HER2/neu 0/1+ cell lines the mean IC_{50}'s were 0.060 μg/mL and 3.221 μg/mL for SYD985 vs T-DM1 ($p<0.0001$) and in HER2/neu 3+ cell lines 0.013 μg/mL and 0.096 μg/mL, ($p<0.0001$), respectively. Unlike T-DM1, SYD985 induced efficient bystander killing of HER2/neu

0/1+ CS cells admixed with HER2/neu 3+ cells. *In vivo* studies confirmed that SYD985 is more active than T-DM1 in CS and effective against HER2/neu 3+ xenografts

**Figure(s) will be available online.*

CONCLUSIONS: We demonstrate for the first time that SYD985 is a novel ADC with remarkable activity against CS not only with strong (3+) but also with low (0/1+) HER2/neu expression .

O-103

Serum MicroRNA Sequencing for Early Diagnosis of Invasive Ovarian Cancer. Kevin M Elias†,[1,3,5] Wojciech F Fendler,[4] Konrad Stawiski†,[4] Allison Vitonis,[5] Ross S Berkowitz,[1] Daniel W Cramer,[5] Dipanjan Chowdhury*.[2] *[1]Brigham and Women's Hospital, Boston, MA, USA; [2]Dana-Farber Cancer Institute, Boston, MA, USA; [3]Brigham and Women's Hospital, Boston, MA, USA; [4]Medical University of Lodz, Lodz, Poland; [5]Brigham and Women's Hospital, Boston, MA, USA.*

INTRODUCTION: Effective screening for ovarian cancer has proven elusive. Ovarian cancers have abnormal microRNA (miRNA) processing. We hypothesized that a distinct circulating miRNA signature might identify early stage ovarian cancers.

METHODS: We constructed a heterogeneous patient cohort of pre-treatment blood samples from 179 women and divided samples 3:1 into a 135 patient training set and 44 patient validation set. Total serum RNA was extracted, converted into miRNA next generation sequencing libraries, and sequenced. Eleven machine learning algorithms were used to separate the cases of invasive cancer from the healthy controls or benign/borderline masses. Models were graded in terms of receiver operating characteristic area under the curve (ROC AUC) and validated both by qPCR on the study samples as well as by external validation on an independent publicly available dataset of 454 patients.

RESULTS: After qPCR validation, we produced a neural network model comprised of 7 miRNAs and 2 normalizers. The neural network (AUC 0.93; 95%CI 0.88-0.97) outperformed CA-125 (AUC 0.74; 95%CI 0.65-0.83) in terms of overall operating characteristics (p=0.001). In the independent dataset, the neural network perfectly classified patients in the training set (AUC 1.00, 95%CI 1.00-1.00) and provided very good discriminatory power on the testing set (AUC 0.93, 95%CI 0.81-1.00), with an overall sensitivity of 75% and specificity of 100%. The miRNA signature was unique to ovarian cancer compared to 12 other diagnoses.

CONCLUSIONS: A properly trained neural network derived from miRNA sequencing can reproducibly discriminate both early and late stage invasive ovarian cancer cases. This offers the potential for a novel screening strategy.

**Figure(s) will be available online.*

O-104

Exosomal Content in the Plasma of Patients with Ovarian Cancer Reflect Tumor State and Induce the Epithelial to Mesenchymal Transition in Target Cells. Shayna Sharma,[1] Katherin Scholz-Romero,[1] Richard Kline,[2] Katrina Wade,[2] Jacob Estes,[2] Carlos Palma,[1] Dominic Guanzon,[1] Andrew Lai,[1] John Hooper,[3] Gregory E Rice,[1,2] Carlos Salomon.[1,2] *[1]The University of Queensland, Brisbane, QLD, Australia; [2]Ochsner Baptist Hospital, New Orleans, LA, USA; [3]Mater Research Institute, University of Queensland, Brisbane, QLD, Australia.*

INTRODUCTION: Recently, the role of extracellular vesicles in cancer progression, specifically, in metastasis and in the capacity of several tumours to invade and colonize specific organs has been established. The aim of this project was to characterize the exosomal and tumor protein profile from patients at different stages of ovarian cancer (OvCa).

METHODS: Plasma samples and biopsies from patients with ovarian cancer were obtained from Ochsner Medical Center (New Orleans, USA). Exosomes were characterized by the presence of enriched TSG101 using Western Blot, size distribution (Nanosight™), and morphology by electron microscopy. The exosomal protein profile and protein tumor profile was determined using a Liquid Chromatography (LC)/ Mass Spectrometry (MS) LC-MS/MS on a 5600 Triple TOF mass spectrometer (AB Sciex, Framingham, U.S.A.). The effects of exosomes on Epithelial to Mesenchymal Transition (EMT) were validated by the ratio of E-cadherin (epithelial marker) to N-cadherin (mesenchymal marker) by Western Blot and the expression of 84 key genes involved in the EMT (RT² Profiler™ PCR Array, QIAGEN).

RESULTS: Exosomes were identified as spherical vesicles with a typical cup-shape, diameters ranging from 50 to 100 nm, with the expression of TSG101. We identified stage disease specific proteins in exosomes. Exosomes isolated from stage III OvCA induce EMT (increased N-cadherin/E-cadherin ratio) compared to the control. Exosomes regulated the expression of a set of transcription factors associated with EMT such as SNAIL1/SNAIL2, bHLH (E47, E2-2, and TWIST1/TWIST2), and ZEB1/ZEB2 on target cells.

CONCLUSIONS: Exosomes derived from patients with disease are able to communicate messages to induce EMT in target cells.

O-105

Targeting Integrin αV/β1 Receptor Manifests Intriguing Anti-Tumor Effects in Sensitive and Chemoresistant Ovarian Cancer Cells: Potential Therapeutic Target. Ghassan M Saed*,[1] Nicole M Fletcher,[1] Ira Memaj,[1] Mohammed G Saed,[1] Michael P Diamond,[2] Robert T Morris.[1] *[1]Wayne State University, Detroit, MI, USA; [2]Augusta University, Augusta, GA, USA.*

INTRODUCTION: The lack of early warning symptoms, ineffective diagnostic tests, and the development of chemoresistance are major causes of the high death rate from ovarian cancer. It has been recently reported that integrins play an important role in proliferation and survival of ovarian cancer cells. The objective of this study was to determine the efficacy of killing sensitive and chemoresistant ovarian cancer cells utilizing αV and β1 integrin monoclonal antibodies.

METHODS: A2780 and SKOV-3 human epithelial ovarian cancer (EOC) cells and cisplatin resistant counterparts were utilized. Integrin αV and β1 expression were determined by ELISA. Cytotoxicity of integrin αV and β1 antibodies alone (15 or 40 μg/ml) and in combination were assessed by MTT Cell Proliferation Assay (24 hrs). Two-tailed *t*-tests were used to compare groups for ELISA data.One-way ANOVA followed by Tukey's post hoc tests was performed for cytotoxicity comparisons, $p<0.05$. Significant synergistic effects were determined by CompuSyn Software.

RESULTS: A2780 Cisplatin resistant EOC cells manifested higher integrin αV protein levels than their sensitive counterpart (173.2 ± 46.6 vs 56.3 ± 12.3 pg/ml) while no difference was observed in integrin β1 protein levels. There was a decrease in cell viability, in a dose-dependent manner, in both sensitive and resistant EOC cells in response to treatment with antibody against integrin αV or β1 alone or in combination. More importantly, there was a synergistic effect in decreasing viability when combining the antibodies with cisplatin in the cisplatin resistant A2780 EOC cells.

		% Viable Cells	
Integrin antibody	**Dose (μg/ml)**	**Sensitive**	**Cisplatin Resistant**
Untreated	0	100±0.0	100±0.0
αV	15	69.5±15.6*	72.3±7.0**
αV	40	50.6±11.2*	50.2±7.4**
β1	15	70.2±13.4*	68.5±3.8**
β1	40	53.6±10.2*	56.7±10.0**
αV +β1	15	58.8±14.0*	53.1±3.9**
αV + β1	40	36.0±9.9*#	33.7±2.2**##
p<0.05 as compared to *untreated sensitive, **untreated resistant, #all sensitive cell treatments, ##all resistant cell treatments			

CONCLUSIONS: Here we identify novel targets that may serve as a treatment not only for killing tumor cells but also for sensitization of patients to chemotherapy.

O-106

FDG-PET/CT Kinetic Modeling Provides Detailed Information of Glucose Metabolism in Ovarian Cancer. Xiaohua Yang,[1] Kuan-Hao Su,[1] Jung-Wen Kuo,[1] Mustafa Tunc,[2] Stefanie Avril,[2] Analisa DiFeo,[3] Raymond F Muzic Jr,[1] Norbert Avril*.[1] *[1]CWRU, Cleveland, OH, USA; [2]CWRU, Cleveland, OH, USA; [3]CWRU, Cleveland, OH, USA.*

INTRODUCTION: Platinum-based chemotherapy is the most important treatment for ovarian cancer; however drug resistance poses a major challenge, which could potentially be overcome by inhibiting metabolic pathways. Positron Emission Tomography (PET) using radiolabeled Fluorodeoxyglucose (^{18}FDG) allows a detailed analysis of tumor glucose metabolism by kinetic modeling approaches including three-compartment and Michaelis-Menten models.

METHODS: Patient-derived cell lines of high-grade ovarian cancer (platinum-sensitive OV81 and paired platinum-resistant CP10 and CP40) were subcutaneously injected into nude rats (RNU316). Arterial and venous catheters were inserted to obtain an accurate tracer input function. Dynamic ^{18}FDG-PET imaging was performed in rats before and after treatment using cisplatin (5mg/Kg) alone or in combination with an inhibitor (WZB117 10mg/Kg) of the glucose transport protein (GLUT1). Standard and detailed ^{18}FDG kinetic models using rate constants, maximum velocity, and other parameters were implemented using COMKAT.

To validate the parameter estimates, tumor tissue samples from 6 rats before treatment and 3 rats after each treatment were collected to evaluate GLUT1, hexokinase II (HK-II) and lactate dehydrogenase A (LDHA) expressions by qPCR and WB.

RESULTS: Before treatment, CP10 and CP40 tumors showed 30-40% higher glucose metabolism than OV81 measured as SUVmax, k_3 rate constant, ^{18}FDG metabolic rate, V_{max} of glucose transport and phosphorylation, and phosphorylation rate of glucose. This was confirmed by higher GLUT1, HK-II and LDHA gene expression ($p<0.05$). Cisplatin reduced values of the kinetic model parameters as well as the level of gene expression by 30-40% in OV81 tumors. WZB117 plus cisplatin treatment resulted in a further 30-60% reduction in CP40 tumors.

CONCLUSIONS: Kinetic analysis of ^{18}FDG-PET provided a detailed insight regarding intracellular changes of glucose metabolism before and after treatment in platinum sensitive and resistant ovarian cancer. Using an inhibitor of GLUT1 together with platinum resulted in a more significant reduction of glucose metabolism in platinum resistant than in platinum-sensitive tumors. PET kinetic modeling is helpful for evaluating metabolic changes in patients during their course of disease to monitor and target metabolic pathways in cancer.

O-107

ATG4D Silencing Abrogates Autophagy and Induces a Fibroid-Like Transformation in Normal Human Myometrium Cells. Abdeljabar El Andaloussi,[1] Nahed Ismail,[2] Ayman Al-Hendy.[1] *[1]MCG, Augusta University, Augusta, GA, USA; [2]University of Pittsburgh, Pittsburgh, PA, USA; [3]MCG, Augusta University, Augusta, GA, USA.*

INTRODUCTION: Autophagy is a very important physiological process to keep the cell homeostasis. Defect in autophagy lead to sever disorders: neoplasia, neurodegeneration or aging. ATG4D is required for autolysosome formation from autophagosome/ lysosome fusion to complete degradation. The functional relevance of ATG4D in uterine fibroid (UF) biology is unknown. We showed recently, a defect in ATG4D in 90% of UF tested.

Hypothesis: Lack of ATG4D expression in human normal myometrium cells block autophagy and mimic fibroid phenotype.

METHODS: We knocked-down ATG4D expression by specific shRNA in human normal myometrium UTSM cell line vs. scramble appropriate control. The proliferation and production of inflammatory cytokines by ATG4D-deficient UTSM was evaluated by Ki67, MTT assay and cytokines, respectively, and analysis of the mean fluorescence intensity (MFI) using flow cytometry. Real time PCR was used to test the expression of ATG4D knock-down in the treated UTSM cells and expression of extracellular matrix genes was analyzed by western blot.

RESULTS: ATG4D silencing in UTSM-shATG4D show 206 folds decreases of RNA expression vs. scramble control ($P<0.008$). Compared to control cells, UTSM-shATG4D exhibited significant increase in proliferation (Ki67 MFI of 1860 ± 281.42 in control cells vs. 10346 ± 258.8 in UTSM-shATG4D) ($p<0.001$) and confirmed by MTT assay. Furthermore, ATG4D loss of function promote proinflammatory profile vs. to scramble RNA control.

MFI ± SD	TNFα	IL-1β	IL-6	IL-9	TGF-β1	IL-10	IL-17A
UTSM SC	347.5 ±40.3	677 ±0.7	4869 ±48	3358.5 ±242.5	3958 ±53.74	4742.5 ±167.6	5222 ±229.1
UTSM KD	3519.5 ±106.8	906.5 ±41.7	4042 ±377.6	5119 ±63.6	4813 ±32.52	2808 ±80.6	4318 ±156
p value	0.0006	0.016	0.09	0.0099	0.002	0.004	0.035

Finally, UTSM-shATG4D exhibited a defective autophagy marked by increased LC3-I (LC3-I MFI: 41264.5 ± 3008.7) compared to the scramble control (LC3-I MFI: 22682 ± 1258.6) ($P=0.015$). The extracellular matrix markers Collagen, Fibronectin and PAI-1 are induced in the absence of ATG4D.

CONCLUSIONS: We conclude that autophagy plays a central role in the transformation of normal myometrium into fibroid tumor status. Thus, enhancing autophagy in uterine fibroid would provide a novel medical therapeutic approach for treatment of non-invasive UF.

O-108

Can Preimplantation Genetic Screening (PGS) Be Applied to Previously Untested Cryopreserved Blastocysts? Jessica Rubin†*,[1] Alfred Wun,[2] Cecilia Valdes,[1] Randall Dunn.[2] *[1]Baylor College of Medicine, Houston, TX, USA; [2]Houston Fertility Specialists, Houston, TX, USA.*

INTRODUCTION: Limited data is known on the thaw survival rate & clinical pregnancy rate (CPR) from embryos previously cyropreserved without PGS then thawed for PGS. Retrospective compilation of patients undergoing autologous IVF cycles with cryopreservation prior to PGS was compiled. Patients who elected to thaw embryos & biopsy for PGS between December 2013 and May 2015 were included. Patients were subdivided by age <35 & ≥ 35.

METHODS: All IVF candidates electing for PGS after embryo cryopreservation on day 5 or 6 were included. After thaw #1, trophectoderm cells were biopsied using laser on day 5 or 6, based on blast development. Blastocysts were cryopreserved using vitrification. Biopsy samples were sent for Next Generation Sequencing. Further analysis was done with the embryos that have undergone thaw #2 for embryo transfer.

RESULTS: Among all ages, 120 embryos were thawed following initial cryopreservation & 100 survived. There was no difference in the survival rate for thaw #1 between age groups. Comparing age groups, there was no difference in the incidence of euploid, aneuploid, or "no result," likely due to small sample size. Of the 100 embryos that survived thaw #1 for PGS, 58 were euploid. 23 euploid embryos were subsequently thawed for embryo transfer & 19 survived thaw #2. The CPR for all ages was 57.9% & there was no significant difference between groups.

Table 1:PGS & CPR following embryo vitrification, PGS biopsy, & revitrification.

	<35 years old	>35 years old	All ages
Euploid	38/59 (64.4%)	20/41 (48.8%)	58/100 (58.0%)
Aneuploid	18/59 (30.5%)	17/41 (41.5%)	35/100 (35.0%)
No result	3/59 (5.1%)	4/41 (9.8%)	7/100 (7.0%)
# of embryos that did not survive thaw to perform PGS	13/72 (18.0%)	7/48 (14.6%)	20/120 (16.7%)
# of embryos thawed for ET	13	10	23
# embryos transferred	11	8	9
Clinical pregnancy rate	6/11 (54.5%)	7/8 (87.5%)	11/19 (57.9%)

CONCLUSIONS: There was no significant difference in embryo thaw survival rate for PGS biopsy between age groups. Surprisingly there was no difference in euploid rates between age groups. The option to thaw cryopreserved embryos for PGS should be considered for women with cryopreserved embryos and a new diagnosis of a genetically inherited condition in a parent or child, recurrent pregnancy loss, or cryopreservation of embryos prior to PGS.

O-109

The Impact of Excisional Treatment for Cervical Intraepithelial Neoplasia on the Vaginal Microbiota. Anita Mitra†,[1] David MacIntyre,[1] Jonathan Lai,[1] Yun Lee,[1] Ann Smith,[2] Julian Marchesi,[2] Deirdre Lyons,[3] Phillip Bennett,[1] Maria Kyrgiou.[1] *[1]Imperial College London, London, United Kingdom; [2]Cardiff University, Cardiff, United Kingdom; [3]Imperial College London, London, United Kingdom.*

INTRODUCTION: The vaginal microbiota (VMB) is usually *Lactobacillus spp.* dominant appears to protect the female reproductive tract against infections including HPV. CST (community state type) III and the high-diversity *Lactobacillus spp.* deplete CST IV have both been associated with HPV acquisition, persistence and increased severity of cervical intraepithelial neoplasia (CIN). These CST's have also been associated with pre-term birth (PTB) which is a known complication of excisional treatment. We aimed to investigate the impact of excisional treatment for CIN on VMB composition.

METHODS: Population: Non-pregnant, premenopausal women attending the colposcopy clinic for excisional treatment of histologically-proven CIN.

Setting: Imperial College NHS Trust, London, UK

Interventions: Vaginal swabs were collected from the posterior vaginal fornix immediately prior to treatment, and at 6 month follow-up. Bacterial DNA was extracted and Illumina MiSeq platform was used to sequence 16S rRNA gene amplicons.

Analysis: Heirarchical clustering of sequence data was used to examine bacterial species classification data.

RESULTS: One hundred and three women provided both pre- and post-treatment samples. Excisional treatment did not significantly alter the distribution of CSTs within the cohort (Table 1). There was no association with post-treatment HPV status.

TABLE 1.	Pre-treatment	Post-treatment
CST I (*L. crispatus*)	44/103 (43%)	40/103 (39%)
CST II (*L. gasseri*)	4/103 (4%)	4/103 (4%)
CST III (*L. iners*)	32/103 (31%)	39/103 (38%)
CST IV (*High diversity*)	21/103 (20%)	20/103 (19%)
CST V (*L. jensenii)*	2/103 (2%)	0/103 (0%)

CONCLUSIONS: Excisional treatment does not appear to have a significant impact on VMB composition. CST III and IV remained more prevelant than in a previously described normal population. These results suggest that the increased prevalence CST III and IV in women with CIN may be due to intrinsic host factors rather than as a result of disease, which supports a hypothesis that there are genetic factors influencing an individuals VMB composition, which may also predispose this specific group of women to PTB.

O-110

Progestin-Only Contraceptives Induce Decidualization by Enhancing ZBTB16 Expression: Implications for Abnormal Uterine Bleeding. Sefa Arlier, Ozlem Guzeloglu-Kayisli, Nihan Semerci, Kellie Larsen, Umit Kayisli, Frederick Schatz, Charles Lockwood. *Univ. of South Florida, Morsani College of Medicine, Tampa, FL, USA.*

INTRODUCTION: Medroxyprogesterone acetate (MPA, a mixed progestin-glucocorticoid) etonogestrel (ETO), and levonorgestrel (LNG) are used in progestin-only long-acting reversible contraceptives (pLARCs), whose adherence is reduced by abnormal uterine bleeding (AUB). Previously, we showed that pLARCs induce human endometrial stromal cell (HESC) decidualization-dependent tissue factor (TF) overexpression, which generates excess thrombin to enhance VEGF, IL–8 and MMP–1 expression, causing aberrant angiogenesis, inflammation and excessive proteolysis. Our prior microarray analysis showed that MPA and ETO induce Zinc finger and BTB domain containing 16 (ZBTB16), a transcription factor regulating progesterone/glucocorticoid receptor (PR/GR) function. Thus, we posit that pLARCs induce HESC decidualization by increasing ZBTB16 expression and/or transcriptional activity.

METHODS: HSCORE analysis of ZBTB16 immunostained paired endometria from pre- and 3 months post-Depoprovera (Depo) treated women (n=7) and ovariectomized guinea pigs (GPs; n=20) treated 21 d with placebo (Pla) or estradiol (E_2) or E_2+MPA. Immunoblotting and qRT-PCR evaluated ZBTB16 levels in primary HESC cultures treated 7 d with E_2 or E_2+dexamethasone (Dex), E_2+MPA, E_2+ETO, E_2+LNG or E_2+Org2058 (a pure progestin). qRT-PCR assessed ZBTB16 levels in pLARC-induced HESCs treated with control *vs.* GR siRNA for 48h (n=3).

RESULTS: Compared to pre-Depo treatment, post-Depo treated specimens displayed significantly increased ZBTB16 immunostaining HSCOREs in endometrial stromal cells (Mean±SEM 90.4±14.1 *vs.* 184.9±10.8; $p<0.001$) and glandular cells (57.5±19.1 *vs.* 181.0±20.4; $p<0.001$). In GP endometrial stromal cells, E_2+MPA significantly increased ZBTB16 immunoreactivity *vs.* Pla or E_2 (147.7±15.3 *vs.* 62.0±13.2 or 43.7±7.1, respectively, $p<0.001$). In cultured HESCs, significantly enhanced ZBTB16 mRNA and protein levels were found in response to E_2+MPA or E_2+ETO or E_2+LNG or E_2+DEX, but not by E_2+Org2058 *vs.* E_2 ($p<0.01$), indicating glucocorticoid regulation of ZBTB16 by pLARCs. Inhibition of LAPC-induced ZBTB16 expression by GR siRNA *vs.* control siRNA treated HESCs ($p<0.01$) further confirmed this premise.

CONCLUSIONS: pLARCs decidualize HESCs by GR-dependent enhanced ZBTB16 expression. Such ZBTB16 may indirectly promote AUB by inducing excess thrombin generation via decidualized HESC expressed TF.

O-111

A Calcium Channel Blocker Used to Treat Hypertension Alters Contractility of the Uterosacral Ligament: Implications for Pelvic Organ Prolapse. Marsha K Guess, Joshua Johnson, Ritsuko Iwanaga, Kathleen A Connell*. *University of Colorado School of Medicine, Aurora, CO, USA.*

INTRODUCTION: Hypertension (HTN) has been shown to be associated with a pelvic organ prolapse (POP), although the link between HTN and POP has not been studied. Uterosacral ligaments (USLs) are composed of connective tissue, abundant smooth muscle (SM) fascicles, adipose, neural bundles and a rich vascular network. POP is believed to originate due to aberrant homeostasis of the USL resulting in altered contractility. We previously showed that oxytocin (OXT) induces contractions in USLs in vitro. We hypothesized that the calcium channel blocker nifedipine, used to treat patients with HTN, would inhibit OXT-induced USL contractility in vitro.

METHODS: USLs were harvested from nulliparous Sprague Dawley rats. We performed organ bath studies and stimulated smooth muscle contractions with OXT at a concentrations of 50nM and 100nM. Following stimulation, we then added nifedipine ($1x10^{-7}$) and measured contractions per minute, area under the curve and peak hight of contractions. Data were analyzed using labchart.

RESULTS: Administration of nifedipine to actively contracting USLs resulted in significant reduction of contractions per minute, reduction in area under of the curve of contractions and calcium and reduced height of contractions (all $p<0.05$). Using calcium free medium, contractions were significantly reduced but not completely abrogated.

CONCLUSIONS: We have demonstrated that smooth muscle in rat USLs are functional and have contractile properties. We have demonstrated that OXT action can be abrogated by blocking calcium channels. Increased risk of POP exhibited by women with HTN may in turn be abrogated by calcium channel blockers.

O-112

LGR5 Is Expressed by Human Endometrial Epithelial Cells and Regulated by Progesterone. Nicola Tempest†, Dharani Hapangama*. *University of Liverpool, Liverpool, Merseyside, United Kingdom.*

INTRODUCTION: Monthly regeneration of the human endometrium is thought to have a stem cell basis; but definitive epithelial stem cell markers are yet to be confirmed. Leucine-rich repeat-containing G-protein coupled receptor 5 (LGR5) is an established epithelial stem cell marker of tissues including hair, skin and intestine, thus LGRS has been proposed as a universal epithelial stem cell marker. Endometrial expression of LGR5 is not fully described.

Aim-Examine the cellular localisation and hormone regulation of LGR5 in human endometrium.

METHODS: LGR5 expression was analysed using qPCR, Insitu hybridisation (ISH) and Immunohistochemistry (IHC) in healthy full thickness human endometriam (EN) and fallopian tube (FT) mucosa from the same women in proliferative and secretory phases (n=5/group). The effect of exogenous progestagen treatment on LGR5 expression was examined in vitro (endometrial explant cultures n=5) and in vivo, women on oral/intrauterine Levenorgestrel (n=10), using qPCR and ISH. In silico meta-analysis included 6 published microarray datasets containing 85 endometrial samples.

RESULTS: LGR5 mRNA expression was limited to epithelial cells. Luminal epithelium showed the highest expression compared to all other EN epithelial locations. FT expressed significantly higher LGR5 mRNA ($p=<0.01$) than matched EN; with the levels higher in proliferative vs secretory phase in both EN and FT.

Antibodies available for LgR5 (N and C terminal) were not reliable or specific.

Progesterone treatment significantly down regulated LGR5 in vivo (EN) and in vitro (explants) vs controls.

In silico analysis demonstrated differential expression in 39/50 LGR5 regulated genes in the secretory vs proliferative phase EN; only 5/50 LGR5 regulated genes were differentially regulated in microarray data of sorted epithelial side population cells vs unsorted epithelial cells.

CONCLUSIONS: This is the first comprehensive study examining LGR5 expression in full thickness EN employing the gold standard method, ISH. LGR5 shows a dynamic spatial and temporal expression pattern, suggesting hormonal regulation. Progestagens appear to inhibit expression in EN and FT. The interrogation of microarray data shows a differential expression of LGR5 regulated genes in the secretory phase suggesting functional relevance. Further studies are needed to distinguish the role of LGR5 in the endometrial epithelium and its role as a universal epithelial stem cell marker.

O-113

VEGF Stimulates Macrophage Recruitment and M2-Polarization in the Decidua: Potential Relevance to the Pathogenesis of Preeclampsia. Karen C Wheeler†, Manoj Jena, Bhola S Pradhan, Bo Pei, Neha Nayak, Subhendu Das, Sabita Dhal, Kang Chen, Nihar R Nayak*. *Wayne State University, Detroit, MI, USA.*

INTRODUCTION: Decidua- and trophoblast-derived cytokines and growth factors play pivotal roles in immune tolerance of the allogeneic fetus and the establishment of pregnancy. Vascular endothelial growth factor (VEGF) was initially considered to have endothelial cell-specific functions. However, it is now clear that VEGF interacts with a number of other cell types, including macrophages. Both VEGF levels and macrophage numbers concomitantly increase at the implantation sites during early pregnancy and are believed to be critical to establishment of pregnancy. In this study we examined the roles of decidual VEGF in macrophage recruitment and polarization toward the immunosuppressive M2 phenotype.

METHODS: We used a human monocyte cell line, THP1 cells, and decidualized endometrial stromal cells as an in vitro model to examine the effect of decidual VEGF on macrophages. Macrophage recruitment was assessed using a transwell migration assay, and the various M1/M2 phenotype markers were assessed using real-time PCR (qPCR) and flow cytometry. Human endometrial and decidual tissue samples were analyzed for the presence of M1/M2 macrophages using immunohistochemistry and qPCR.

RESULTS: We show that VEGF treatment significantly enhanced macrophage recruitment and polarized M1 macrophages to an M2 phenotype. Moreover, treatment with conditioned media from decidualized endometrial stromal cells induced changes in macrophage recruitment and polarization similar to VEGF treatment, an effect that was abrogated using a potent VEGF inhibitor, the recombinant soluble VEGF receptor 1 (sFlt1). In addition, qPCR and immunohistochemical analyses revealed that M2 macrophages predominate in human decidual tissue during the first trimester of pregnancy.

CONCLUSIONS: These results suggest that VEGF has a significant role in macrophage recruitment and M2-polarization, and that inhibition of VEGF function may trigger the shift in macrophage polarity from the M2 to M1 phenotype observed in several pregnancy disorders, such as in preeclampsia, that are associated with increased production of the VEGF inhibitor sFlt1.

O-114

Syncytiotrophoblast Extracellular Vesicles Alter Angiotensin-II Induced Vasoconstriction in Mouse Uterine Arteries. Floor Spaans†,[1,2] Jude S Morton,[1,2] Dionne S Tannetta,[3] Ian L Sargent,[3] Sandra T Davidge*.[1,2] *[1]University of Alberta, Edmonton, AB, Canada; [2]University of Alberta, Edmonton, AB, Canada; [3]University of Oxford, Oxford, United Kingdom.*

INTRODUCTION: The development of hypertension and proteinuria in preeclampsia (PE) is thought to be due to the release of placental factors, including syncytiotrophoblast extracellular vesicles (STBEVs), leading to maternal endothelial dysfunction. The lectin-like oxidized LDL receptor-1 (LOX-1) is a multi-ligand scavenger receptor; both STBEVs and LOX-1 expression are increased in women with PE. To further investigate a role for LOX-1 in pathological pregnancies, we propose to use genetically modified mice. Our aim was to investigate the role of STBEVs and the LOX-1 receptor in vascular dysfunction using LOX-1 deficient (knock-out; KO) mice. We hypothesized that STBEVs activate LOX-1 and contribute to vascular dysfunction in mouse uterine arteries, and that this effect will not be evident in LOX-1 KO mice.

METHODS: Uterine arteries were obtained from late pregnant (gestational day 18; term = day 19) C57BL/6 (WT) and LOX-1-KO mice. Isolated vessels were incubated for 24hrs in the absence (n=4) or presence of STBEVs (200 μg/ml, n=4). A recent report showed that LOX-1 activation is associated with AT-1 receptor activation, and vice versa. We therefore used angiotensin II (Ang II) mediated vasoconstriction using wire myography to assess vascular (dys)function.

RESULTS: Our results showed that responsiveness to Ang II was increased after incubation with STBEVs as compared with controls, i.e. a prolonged response to Ang II was observed (AUC: 3.3±0.9 controls vs. 4.9±0.9 STBEVs; $p<0.03$) in uterine arteries from WT mice. In uterine arteries from LOX-1 KO mice this response to STBEV incubation was not observed (AUC: 4.1±2.3 controls vs. 3.5±2.0 STBEVs).

CONCLUSIONS: STBEVs induced hyper-responsiveness to Ang II which was LOX-1 dependent. Further studies are required to determine the mechanisms: i.e. whether this effect is AT-1 receptor mediated and whether AT-1 receptor expression is altered by STBEV activation of LOX-1. In addition, the possible activation of LOX-1 by STBEVs in the WT mice will be further investigated using LOX-1 blocking antibodies. These data indicate that elevated levels of circulating STBEVs in pregnancy could contribute to the development of vascular dysfunction via the LOX-1 receptor.

O-115

Severe Preeclampsia Is Associated with Resistance to Decidualization. Tamara Garrido-Gomez†,[1,2] Francisco Dominguez,[1,3] Alicia Quiñonero,[3] Patricia Diaz-Gimeno,[3] Mirhan Kapidzic,[2] Matthew Gormley,[2] Katherine Ona,[2] Pablo Padilla,[4] Olga Genbacev,[2] Alfredo Perales,[4] Susan J Fisher,[2,5,6] Carlos Simon.[1,7,8,9] *[1]INCLIVA, IUIVI, Valencia University, Valencia, Spain; [2]Center Reprod Sciences, San Francisco, CA, USA; [3]Fundación IVI, Valencia, Spain; [4]Hospital La Fe, Valencia, Spain; [5]Eli&Edythe Broad Center, San Francisco, CA, USA; [6]UCSF, San Francisco, CA, USA; [7]Valencia University, Valencia, Spain; [8]Stanford University, Stanford, CA, USA; [9]Igenomix, Valencia, Spain.*

INTRODUCTION: Preeclampsia (PE) is a third trimester pregnancy complication that affects ~8% of first pregnancies. Deficient cytotrophoblast (CTB) invasion of the decidua and uterine vasculature is thought to play a causal role. However, little is known about a possible decidual contribution to this phenomenon. We hypothesized that aberrant decidualization of human endometrial stromal cells (hESCs) might be involved.

METHODS: hESCs were established from women who developed severe PE (sPE) and decidualized in vitro. In parallel, we used a laser capture microarray approach to isolate gestational age-matched samples of the decidua parietalis in pregnancies complicated by sPE (cases) or non-infected preterm birth (nPTB; controls). Both sample sets were subjected to global transcriptional profiling. We also asked whether decidual cells from sPE pregnancies could decidualize immediately after they were isolated or redecidualize once they de-differentiated in culture. Finally, we cultured CTBs in conditioned medium from sPE vs. control decidua cells and assayed the effects on CTB invasion.

RESULTS: Marker expression suggested that hESCs from women with a previous sPE pregnancy failed to decidualize *in vitro*. Global transcriptional profiling revealed the modulation of 129 genes in controls whose expression did not change in the sPE cultures. Microarray analyses of decidua parietalis samples from control vs. sPE pregnancies revealed numerous molecular defects *in situ*. Immunolocalization confirmed the near absence of decidualization markers in sPE pregnancies. Stromal cells established from decidual samples obtained at the time of sPE deliveries failed to decidualize in culture. Conditioned medium from these cells reduced CTB invasion.

CONCLUSIONS: sPE was associated with decidualization resistance, which could contribute to restricted CTB invasion. These findings suggested novel strategies for developing predictive biomarkers and prophylactic measures.

O-116

Placental Extracellular Vesicles Can Sequester VEGF to Induce Endothelial Cell Activation: Relevance for Preeclampsia. Mancy Tong†, Qi Chen, Jo L James, Peter R Stone, Larry W Chamley*. *The University of Auckland, Grafton, Auckland, New Zealand.*

INTRODUCTION: Preeclampsia is a life-threatening hypertensive disease that affects 3-5% of pregnant women. While the pathogenesis of preeclampsia remains unclear, endothelial cell activation is a central hallmark, and toxin(s) released by the placenta are responsible for endothelial activation. Potential toxins include the soluble VEGF receptor (sFlt-1) and placental extracellular vesicles (EVs). This study aims to investigate whether preeclamptic EVs carry Flt-1 and whether EV-associated Flt-1 can activate endothelial cells.

METHODS: Micro- and nano-vesicles were collected from preeclamptic (PE-EVs) and control placentae by sequential ultracentrifugation. Flt-1 was detected by western blot. HMEC-1 endothelial cells were cultured with PE-EVs or control-EVs, with/without a Flt-1 antagonist (10µg/mL), or PE-EVs that had been exposed to exogenous VEGF to quench free Flt-1 (100ng/mL). HMEC-1 activation was quantified by ELISA of ICAM-1 expression and monocyte adhesion. Flt-1 in conditioned media (CM) from preeclamptic or control placentae was quantified by ELISA. Statistical significance was assessed by t-tests.

RESULTS: PE-EVs carried significantly more Flt-1 than control-EVs ($p=0.0184$ for micro-; $p=0.0415$ for nano-vesicles, n=9). PE-EVs significantly increased endothelial cell activation as measured by ICAM-1 expression ($p<0.0001$, n=6) and monocyte adhesion ($p<0.002$, n=7), which was reduced by antagonizing Flt-1 ($p<0.0005$, n=7). Pre-treatment of PE-EVs with VEGF also significantly reduced their ability to activate endothelial cells compared to untreated PE-EVs ($p<0.03$, n=3). The level of sFlt-1 in PE-CM was significantly higher than that in control-CM (12.5±0.3ng/mL vs 10.2±0.4ng/mL, $p=0.0013$, n=6). Ultracentrifugation had no effect on the level of Flt-1 in control-CM but reduced Flt-1 by 7% in PE-CM, demonstrating that this portion of Flt-1 is EV-associated.

CONCLUSIONS: PE-EVs can activate endothelial cells by expressing Flt-1, which sequesters free/circulating VEGF. While EV-associated Flt-1 did not constitute a major portion of the total sFlt-1 secreted by preeclamptic placentae, EV-associated Flt-1 may be targeted to specific organs, potentially leading to the organ-specific symptoms observed in preeclampsia. Therefore, EVs may be one key placental toxin that mediates the endothelial activation that occurs prior to the onset of preeclampsia and may be a potential biomarker or treatment target in the future.

O-117

Evidence for Partial Overlap of Molecular Etiology Between Preeclampsia and Decidualization Disorders. Maria B Rabaglino†,[1] Emiel D Post Uiterweer,[2] Kirk P Conrad.[3] *[1]CONICET, Córdoba, Argentina; [2]University Medical Center Utrecht, Utrecht, Netherlands; [3]University of Florida, Gainesville, FL, USA.*

INTRODUCTION: Although the transcriptomics of delivered preeclamptic (PE) placentas are well documented, the molecular etiology of PE is likely to be found only in placental tissues of an earlier origin. In previous work (Hypertension 65:421-9, 2015), we reanalyzed our own microarray dataset in the GEO database (GSE12767) of chorionic villous samples (CVS) from women at ~11.5 gestational weeks who developed severe PE 6 months later (PE-CVS) matched to CVS from women with normal pregnancies. We found a significant association ($p<0.05$) between the up or down-regulated differentially expressed genes (DEG) identified in PE-CVS (396 in total) with DEG expressed in the opposite direction during normal endometrial maturation, suggesting PE etiology involves compromised (pre)decidualization. Thus, we hypothesize that other disorders associated with impaired endometrial maturation may overlap with PE. The objective was to compare DEG in PE-CVS with those in decidualization disorders, as well as delivered PE placenta.

METHODS: Publically available microarray datasets downloaded from the gene expression omnibus database (GEO) were re-analyzed with the Bioconductor software. DEG were determined by modified t-test for implantation failure (IF; GSE26787 and GSE16532), miscarriage (MC; GSE26787) and basal plate from delivered placentas in preterm PE (BP; GSE14722). Up or down-regulated DEG between PE-CVS and each disorder were compared by Pearson's chi-square test to determine relatedness.

RESULTS: There was significant overlap ($p<0.05$) between up-regulated DEG in PE-CVS and up-regulated DEG in IF for both datasets and MC. Likewise, the overlap between down-regulated DEG in PE-CVS and down-regulated DEG in IF (for both datasets) or MC was also significant. There was no association for DEG in opposite directions between PE-CVS and IF or MC. Also, there was no significant overlap between DEG in PE-CVS and DEG in BP, neither in the same nor opposite directions.

CONCLUSIONS: These results support the concept that PE shares at least partial molecular etiology with other endometrial diseases that disrupt endometrial maturation, and that the molecular pathology of the delivered placenta in PE is probably different from that of first trimester, possibly reflecting consequence rather than cause of the disease.

O-118

High Resolution Flow Cytometry Reveals Abnormal Distribution of Placental Extracellular Vesicles in Murine Placental Insufficiency Model. Nicole Marek, Mayu Morita, Pam Canaday, Terry K Morgan. *OHSU, Portland, OR, USA.*

INTRODUCTION: Our group has developed a new multiparametric high-resolution flow cytometry (HRFC) method that can reliably identify, quantitate, and purify cell- and size-specific extracellular vesicles (EVs) from any cell of interest. We hypothesized that we could use this novel approach to identify differences in placental EV numbers and sizes

comparing maternal blood from wild-type (WT) controls (C57B6) to maternal blood from our transgenic (TG) (AGTdupC57BL6) mouse model of placental insufficiency (pregnancy-induced hypertension, placental damage, fetal growth restriction).

METHODS: Prospective HRFC study of maternal blood (100ul) was collected from WT and TG dams near term (day 17.5). To highlight placental-specific EVs we had two approaches: First, we crossed dams with ubiquitous GFP males, which generates a placental trophoblastic cytosol-rich green fluorescent signal. Second, we employed fluorescently labeled antibodies targeted against placental alkaline phosphatase (PLAP) and a less specific EV marker (Annexin). Male plasma served as negative control for PLAP and positive control for GFP positive EVs. Submicron-sized polystyrene beads (100, 160, 200, 240, 300, 500, 900nm) were used as sizing controls.

RESULTS: Cell and size-specific EVs from pregnant mouse blood could be resolved at 50nm resolution. Using male blood to accurately set gates for HRFC positive EV signals, we determined that WT dams near term have a predominantly exosome-sized EVs (< 150nm); whereas TG dams matched for gestational age showed predominantly larger microparticles (250-500nm range). This difference in placental EV size distribution between WT and TG dams was reproducible and consistent using either GFP or PLAP as the placental-specific marker.

CONCLUSIONS: Although more work is needed, such as characterizing patterns throughout gestation and sorting these EVs to confirm expected placental specific signals, our preliminary data suggest differences in placental EV profiles may be related to differences previously observed in placental damage by maternal genotype.

O-119

Granulocyte-Colony Stimulating Factor Reverses Detrimental Effects of High-Fat Diet on Ovarian Reserve. Delaney C Swindle, Alex J Polotsky, Malgorzata E Skaznik-Wikiel*. *University of Colorado School of Medicine, Aurora, CO, USA.*

INTRODUCTION: We previously reported that high-fat diet (HFD) is associated with decreased ovarian reserve and subfertility, independent of obesity. The effects are most likely mediated by increased inflammation in the ovary *(Skaznik-Wikiel, et al. Biol Reprod 2016)*. It is unclear if treatment with anti-inflammatory compounds can alleviate the deleterious effects of HFD on primordial follicle pool. Granulocyte-colony stimulating factor (G-CSF) is commonly used in clinical practice to treat neutropenia due to its anti-inflammatory and anti-apoptotic properties. The goal of this study was to assess if G-CSF administration reverses HFD-induced diminished ovarian reserve.

METHODS: In this prospective laboratory study, 5 wk old C57BL/6 mice were assigned to receive different dietary interventions for 10 weeks: HFD (60% fat calories) or low-fat diet (LFD, 10% fat calories). HFD mice received daily intra-peritoneal injections for five consecutive days during last week of feeding of either G-CSF (n=4) or normal saline (n=4). LFD mice received no other intervention. Ovaries were collected after 10 weeks of dietary exposure for assessment of resting (primordial) and growing (primary, secondary, antral) follicles. Animal weight and percentage of body fat were measured by quantitative MRI at the time of ovary collection. One-way ANOVA with Bonferroni correction was used for statistical analysis.

RESULTS: The average weight and percentage of body fat are presented in Table 1. The mean body weight and fat mass were not different between HFD G-CSF and saline group (p=0.83; p=0.91; respectively). There were significant differences between groups in the number of primordial follicles, as described in Table 1.

	LFD	HFD+ G-CSF	HFD+saline	p-value
Weight (g ± SEM)	21.3 ± 0.3	24.6 ± 1.5	25.0 ± 1.4	0.09
Fat mass (% ± SEM)	7.1 ± 1.4	16.2 ± 4.3	17.1 ± 4.7	0.14
Primordial follicle number (± SEM)	1105 ± 26	935 ± 187	390 ± 82	**0.01**

There were no differences in the number of primary, secondary, and antral follicles between the groups.

CONCLUSIONS: As expected, HFD alone resulted in significant decrease of resting ovarian follicles. Notably, G-CSF reversed this detrimental impact of HFD exposure on primordial follicle pool. The findings are novel and can have significant clinical applications in the future. Further studies are needed to elucidate the exact mechanism behind these findings.

O-120

High-Fat Diet and Aging Affect Ovarian RAGE Gene Expression. Erkan Buyuk,[1] Maureen Charron,[1,2] Kimberley Thornton,[1] Obehi Asemota,[1] Zaher Merhi.[3] *[1]AECOM/Montefiore Medical Center, Bronx, NY, USA; [2]AECOM, Bronx, NY, USA; [3]NYU, New York, NY, USA.*

INTRODUCTION: Advanced glycation end products (AGEs) are inflammatory molecules that form after glycation of lipids and proteins. Serum AGEs and their receptor RAGE are elevated with aging and obesity. AGE-RAGE interaction induces inflammation potentially altering ovarian function. High-fat diet (HF) increases inflammation and weight gain in a RAGE-dependent manner. Effect of HF diet on ovarian RAGE expression has not been studied. We thus hypothesize that HF diet and aging increase ovarian RAGE expression.

METHODS: 6-week old C57BL/6J mice were fed normal chow (NC) for 12 weeks and then had oophorectomy at either "young" age (20 week-old) before (n=4) or after (n=6) superovulation (SO); or at "old" age (32 week-old) before (n=5) or after (n=5) SO. Another group of mice were given HF and then had oophorectomy at either young age before (n=4) or after (n=6) SO; they were then switched to NC (for weight loss) and sacrificed at 32 weeks of age before (n=6) or after (n=5) SO. Oocytes were collected from each mouse following SO. RNA extraction and RT-PCR for RAGE expression was performed on the ovaries. Data were expressed as mean±SEM.

RESULTS: *Before SO:* All old mice (2.7±0.1) had higher RAGE mRNA levels compared to all young mice (1.9±0.4, p=0.004). Old mice on HF (2.7±0.2), but not on NC, had higher RAGE mRNA levels compared to young mice on HF (2.0±0.3, p=0.03). *After SO*: SO increased RAGE mRNA levels in both young and old mice on HF only. Despite being reverted to NC and subsequent weight loss, old mice exposed to HF had higher RAGE mRNA levels compared to old mice on NC throughout the study. Young mice on HF (1.8±0.9) had lower number of oocytes compared to young mice on NC (6.7±1.8, p=0.03). Mice on HF that were reverted to NC (7.2±1.8) had similar number of oocytes compared to mice that were on only NC throughout the study (6.7±1.8, p>0.05).

Mice	Before SO	Weight (g)	RAGE mRNA	After SO	Weight (g)	RAGE mRNA
Young	NC	18.4±0.6[a]	1.9±0.2	NC	18.5±0.4[e]	2.0±0.3
	HF	29.7±1.8[b]	2.0±0.3[c]	HF	28.7±1.8[f]	4.4±1.3
Old	NC	21.0±0.2	2.6±0.3	NC	22.9±1.1	2.6±0.3[g]
	HF	21.6±0.4	2.7±0.2[d]	HF	21.6±0.6	3.8±0.4[h]

p<0.05 for a *vs* b; c *vs* d; e *vs* f; g *vs* h.

CONCLUSIONS: Aging and HF may adversely impact ovarian function in a RAGE-dependent manner. RAGE blockers could represent a potential ovary-protective agent for older women consuming unhealthy diet rich in fat.

O-121

AKAP13-Deficient Oocytes Show Signs of Precocious Exit from Prophase I Arrest. Carter M Owen†,[1,2] Ophelia Yin†,[2] Sinnie Ng,[2] Pola Olczak†,[3] Janice P Evans,[3] James H Segars*.[2] *[1]NICHD/NIH, Bethesda, MD, USA; [2]Johns Hopkins SOM, Baltimore, MD, USA; [3]Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA.*

INTRODUCTION: The localization of cAMP-dependent protein kinase A (PKA) plays a critical role in maintenance of prophase I arrest in mammalian oocytes. AKAP13 is a multifunctional regulator of cell signaling that nucleates actin and binds the regulatory (RII) subunit of PKA determining its subcellular localization and specificity of substrate

phosphorylation. Given PKA's central role in oocyte meiotic arrest, we sought to characterize localization of AKAP13 and the consequences of AKAP13 knockdown in murine oocytes arrested at prophase of meiosis I.
METHODS: Prophase I, germinal vesicle (GV)-intact, oocytes were isolated from ovarian tissue of CF-1 mice (6-8 wks old). For localization experiments, oocytes were fixed and stained with or without affinity-purified rabbit polyclonal antisera directed against AKAP13. Control staining included Phalloidin (actin) and DAPI (DNA). Oocytes were imaged with a Zeiss fluorescent microscope. For knockdown experiments, 50 uM *Akap13* siRNA or non-targeting (NT) siRNA were microinjected into GV-intact oocytes. Following injection, oocytes were cultured for 48 hrs in dibutryl-cAMP containing medium to maintain oocytes in prophase I arrest. Observations of oocyte morphology were undertaken at 44-48 hours post-injection. At 48 hrs post-injection, RNA was isolated from oocytes and relative expression of *Akap13* mRNA was determined by quantitative real-time polymerase chain reaction (qPCR).
RESULTS: Immunofluorescence demonstrated that AKAP13 appeared as a punctate pattern throughout the cytoplasm of GV-intact oocytes compared to no primary antibody controls. In RNAi-mediated knockdown experiments, 22.4% of oocytes (17/76) injected with *Akap13* siRNA were not GV-intact by 48 hrs after injection and had phenotypes including GV-loss and cleavage. This was in contrast to 1/53 oocytes injected with NT siRNA exhibiting GV-loss (P=0.0009). qPCR demonstrated a ~72% knockdown of *Akap13* expression of oocytes injected with *Akap13* siRNA compared to NT siRNA injected oocytes.
CONCLUSIONS: These data demonstrate the presence of diffuse cytoplasmic AKAP13 in oocytes arrested at prophase I of meiosis. GV-loss after *Akap13* siRNA microinjection with confirmed knockdown of *Akap13* expression by qPCR suggests that AKAP13, possibly through affecting PKA localization, plays a role in prophase I arrest.

O-122

Maternally Expressed NLRP2 Links the Subcortical Maternal Complex (SCMC) to Fertility, Embryogenesis and Epigenetic Reprogramming. Sangeetha Mahadevan†,[1,2,6] Varsha Sathappan,[3] Budi Utama,[4] Isabel Lorenzo,[5] Khalied Kaskar,[1] Ignatia Van den Veyver*.[1,2,5] *[1]Baylor College of Medicine, Houston, TX, USA; [2]Texas Children's Hospital, Houston, TX, USA; [3]Rice University, Houston, TX, USA; [4]Rice University, Houston, TX, USA; [5]Baylor College of Medicine, Houston, TX, USA; [6]Baylor College of Medicine, Houston, TX, USA.*
INTRODUCTION: Mammalian parental genomes contribute differently to early embryonic development. Before activation of the zygotic genome, the maternal genome provides all transcripts and proteins required for the transition from a highly specialized oocyte to a pluripotent embryo. Depletion of these maternally-encoded transcripts frequently results in failure of preimplantation embryonic development, but their functions in this process are incompletely understood.
METHODS: We generated global *Nlrp2* knockout mice to study the effect of maternal loss of NLRP2 on fertility and embryogenesis.
RESULTS: We found that female mice lacking NLRP2 are subfertile because of early embryonic loss and the production of fewer offspring that have a wide array of developmental phenotypes and abnormal DNA methylation at imprinted loci. *In vitro* culture of embryos from *Nlrp2*-null females exhibit a striking inability to undergo normal embryonic cleavage. We demonstrate that NLRP2 is a member of the subcortical maternal complex (SCMC), an essential cytoplasmic complex in oocytes and preimplantation embryos with poorly understood functions. We identified imprinted DNA methylation maintenance as a new role of the SCMC, likely by directing subcellular localization of proteins involved in this process, such as DNA methyltransferases 1 (DNMT1).
CONCLUSIONS: This work highlights an understudied group of maternally provided cytoplasmic proteins which cause complex epigenetic disturbances, subsequently compromising reproductive fitness and early development.

O-123

DMPS (Dimercapto-1-Propanesulfonic Acid), a Heavy Metal Chelator, Induces Oocyte Deterioration. Sarah R Aldhaheri, Roohi Jeelani†, Mili Thakur†, Marisa Hildebrandt†, Farnoosh Qadri†, Husam M Abu-Soud*. *Wayne State University, Detroit, MI, USA.*
INTRODUCTION: Given the recent lead poisoning crisis in Flint, MI, investigational research and media attention has turned towards the safety profile of many commonly used chelators. Dimercapto-1-propanesulfonic acid (DMPS) is commonly used in the treatment of arsenic, copper, and mercury poisoning. Given as series of high doses (0.2-0.4 g/day) over a period of up to 15 days, its long half-life, and ability to enter into the cell, although to a limited extent, we sought to investigate the impacts of DMPS on: 1) reproductive function as judged by changes in microtubule morphology (MT) and chromosomal alignment (CH) of metaphase II mice oocyte; and 2) the ability of DMPS to reduce hemoprotein model compounds and subsequent formation of ferrous-deoxy complexes and the generation of superoxide.
METHODS: Metaphase II mouse oocytes (n=180) were exposed to increasing concentrations of DMPS (10- 200 μM), for 2h after which all oocytes were fixed, stained and scored based on the MT and CH as an indicator of the oocyte's capacity to sustain exposure and then compared to untreated controls.Oocyte were scored based on a 1-4 scoring system in which oocytes with good quality were scored 1 and 2 and oocyte with poor quality were scored 3 and 4. Variety of spectroscopic techniques were utilized to investigate the mechanism through which DMPS impacts oocyte quality.
RESULTS: A statistically significant difference in poor scores for MT was found between groups treated with 0-25 μM versus 100 - 200 μM (66-75 %, respectively) (p=0.04). For CH alignment a statistically significant difference in poor scores was noted between groups treated with 0-10 μM versus 100-200 μM (p=0.05). Furthermore, our results indicated that DMPS was capable of mediating the reduction of a series of hemoprotein model compounds and thus subsequent formation of their corresponding deoxy-complexes. Heme reduction not only inhibits the catalytic activity of hemeproteins but also allows these enzymes to potentially serve as a source of superoxide generating system (reactive oxygen species) which further adds to the deterioration of oocyte quality.
CONCLUSIONS: Our current work showed for the first time the link between oocyte quality deterioration and DMPS exposure, highlighting the possibility of these agents to negatively affect fertility through a mechanism that involves enzyme inhibition and reactive oxygen species generation.

O-124

***Med12* Is Critical in Reproductive Tract Development.** Xinye Wang,[1,4] Priya Mittal,[2,5] Aleksandar Rajkovic.[1,2,3] *[1]Magee-Womens Research Institute, Pittsburgh, PA, USA; [2]Graduate School of Public Health, Pittsburgh, PA, USA; [3]University of Pittsburgh, Pittsburgh, PA, USA; [4]Tsinghua University, Beijing, China; [5]St. Jude Children's Research Hospital, Memphis, TN, USA.*
INTRODUCTION: *Med12*, the mammalian Mediator Complex Subunit 12, is a transcriptional factor that is highly conserved among eukaryotes. The global deficiency of *Med12* is lethal in mouse embryos while somatic gain of function *Med12* mutations in the human uterus cause uterine leiomyomas. The role of *Med12* in reproductive tract development is not well understood.
METHODS: We used *Amhr2-Cre, Gdf9-Cre and Zp3-Cre* to deplete *Med12* (*Med12$^{fl/fl}$ Amhr2-cre* mouse model) in granulosa cells, uterine mesenchyme, oviduct and oocytes. We performed detailed histomorphologic, biochemical and molecular analyses to determine effects of *Med12* deficiency on various components of the reproductive tract.
RESULTS: We discovered that the conditional knockout of *Med12* caused infertility in *Med12$^{fl/fl}$ Amhr2-cre* mice, without causing reproductive tract tumors. The histomorphologic analyses showed abnormal development in the *Med12$^{fl/fl}$ Amhr2-cre* uteri and ovaries. The *Med12$^{fl/fl}$ Amhr2-cre* uteri were hypo-plastic while ovaries showed abnormal granulosa cell morphology. Mating studies showed absent vaginal plugs from *Med12$^{fl/}$*

^{fl} *Amhr2-cre* females. *Med12$^{fl/fl}$ Amhr2-cre* female estrous cycles are disrupted contributing to the infertility. The serum analyses showed low level of estrogen in *Med12$^{fl/fl}$ Amhr2-cre* mice, which is likely due to the impaired granulosa cell functions. Molecular studies on *Med12$^{fl/fl}$ Amhr2-cre* granulosa cells discovered down-regulation of *Nr5a2*, *Fshr* and *Cyp19a1*. We also examined the effects of *Med12* deficiency in primordial and primary oocytes. *Gdf9-cre* or *Zp3-Cre* mediated inactivation of Med12 in primordial and primary oocytes, respectively, led to infertility without affecting overall ovarian development and histomorphology. These results are consistent with the critical role of maternal *Med12* in early embryo development, but not in postnatal oocyte differentiation. *Med12* is therefore also a maternal effect gene.

CONCLUSIONS: *Med12* plays multiple critical roles in the development of female reproductive system that include regulation of granulosa cell function, uterine development, and maternal gene effects in the embryo.

O-125

Predictive Modelling of Stress-Related Behavior Through Gene Expression Following Prenatal Glucocorticoid Exposure. Andrea Constantinof†,[1] Vasilis Moisiadis†,[1] Stephen Matthews*.[1,2,3] *[1]University of Toronto, Toronto, ON, Canada; [2]University of Toronto, Toronto, ON, Canada; [3]University of Toronto, Toronto, ON, Canada.*

INTRODUCTION: Prenatal exposure to excess glucocorticoids increases risk for psychiatric disease. We have demonstrated that antenatal synthetic glucocorticoids (sGC) program gene transcription in the hypothalamic paraventricular nucleus (PVN), with strongest effects in females. Understanding the relationship between gene expression and phenotype allows for predictive modelling, which has broad implications for the use of gene profiles in disease detection. Here, we hypothesized that transcriptional programming of the PVN is correlated to behavioral outcomes and can be used in predictive modelling.

METHODS: Pregnant guinea pigs received 3 courses of betamethasone (Beta;1mg/kg) or saline (C) in late gestation. Total locomotor activity in open-field (OFA) was measured in female offspring on postnatal day 24 and brains collected at day 40. PVN was micro-punched (C;n=5, Beta;n=5);RNA extracted for RNA-seq; data analyzed using standard bioinformatics. Principal component analysis (PCA), which uses the underlying variance of a dataset to show how factors are related, was carried out on normalized expression profiles of significantly up-regulated genes, and OFA scores. Relationships were analyzed by linear regression. Multiple regression combined gene profiles to predict OFA, linear regression determined the correlation of predicted and observed OFA.

RESULTS: PCA showed OFA is associated with expression of *Greb1l* (estrogen receptor signaling), *Prlr* (prolactin receptor),& *Trim66* (transcriptional regulator). Linear regression revealed the correlation to be significant (*Greb1l*: R^2=0.71, p=0.002, *Prlr*: R^2=0.51, p=0.019, *Trim66:* R^2=0.58, p=0.01), and significant correlation between predicted and observed OFA (R^2=0.80, p=0.015).

CONCLUSIONS: This is the first evidence of a correlation between stress-activated locomotor behavior and gene expression in the PVN following prenatal sGC. Interestingly, this association focused on a subset of genes involved in regulation of sex-hormone signaling. These findings provide insight into the potential mechanisms of antenatal sGC and how these molecular events relate to behavior. Furthermore, we demonstrated that predictive modelling using gene expression accurately predicts stress-activated locomotor behavior, providing proof of principal for the use of gene expression modelling in disease prediction, detection, and prevention.

O-126

Treatment with Prenatal Glucocorticoids in Baboons Predisposes Male Offspring (F1) to Obesity in Adulthood. Hillary F Huber†,[1] Anderson H Kuo†,[2] Cun Li,[1] Susan L Jenkins,[1] Peter W Nathanielsz*.[1] *[1]University of Wyoming, Laramie, WY, USA; [2]University of Texas Health Science Center, San Antonio, TX, USA.*

INTRODUCTION: During pregnancy, the threat of premature delivery is frequently treated with glucocorticoids (GC) to accelerate fetal lung development. This approach improves neonatal morbidity and mortality. However, there are few investigations of long-term effects in nonhuman primates. We developed a baboon model of prenatal GC administration and have been studying the effects on offspring for nearly 13 years. The animals have reached adulthood and full body size. We previously reported in the GC male baboons greatly increased pericardial fat and liver lipids. Therefore, we hypothesized that GC offspring would be predisposed to obesity compared to controls (CTR).

METHODS: Maternal GC treatment was 3 courses of 2-day IM injection of betamethasone (175 μg/kg day) at 0.6, 0.64, and 0.68 gestation. We measured morphometrics in 5 GC males for comparison with age-matched controls (ages 10-12.5 yrs, 10 males). Regional fat depots were measured by MRI. We measured HbA1c in a subset of 5 GC and 5 CTR males. One-tailed *t*-tests were performed in SPSS 23 to compare each measurement in CTR vs GC. Pearson's correlation was used to determine if morphometric parameters can help predict the amount of pericardial fat we previously examined, a known marker of metabolic cardiac health.

RESULTS: GC males had larger sizes compared to CTR in BMI (p=0.07), weight (p=0.03), waist circumference, (p=0.02) hip circumference (p=0.04), neck skinfold (p<0.01), and triceps skinfold (p=0.05). HbA1c was higher in GC (p=0.1). Triceps skinfold correlates to both apical (p=0.002) and midventricular (p=0.03) pericardial fat thickness on MRI. Hip circumference correlates with amount of apical fat (p=0.02) and amount of midventricular fat (p=0.07) on MRI. Neck skinfold correlates better with midventricular pericardial fat thickness (p=0.05) than apical fat (p=0.14) on MRI.

CONCLUSIONS: Prenatal GC treatment affects offspring morphometry into adulthood, resulting in fatter males, suggesting male GC offspring may be predisposed to obesity related complications. This is further supported by the slightly higher HbA1c levels as well as the previously reported increased pericardial and hepatic fat. Triceps skinfold, neck skinfold, and hip circumference correlate to amount of pericardial adiposity and may be useful markers for assessing metabolic cardiac health. (NIH-OD011183).

O-127

Maternal Obesity Is Associated with Decreased Dopamine Signaling in Juvenile Offspring: A Transgenerational Obesity Cycle. Larissa H Mattei†,[1] Chang Xue,[2] Rachel Zeuner,[3] Emmanuel N Pothos,[2] Andrea G Edlow†*.[1] *[1]Tufts Medical Center/Tufts SOM, Boston, MA, USA; [2]Tufts Univ School of Graduate Biomedical Sciences, Boston, MA, USA; [3]Tufts Univ SOM, Boston, MA, USA.*

INTRODUCTION: Maternal obesity (MATOB) is associated with increased risk of obesity in offspring, but causative mechanisms are not known. Aberrant dopamine (DA) signaling has been implicated in reward-based eating. Using a mouse model of maternal diet-induced obesity, we evaluated offspring mesolimbic DA signaling, weight trajectory, and adult body composition.

METHODS: Female (F) C57BL/6 mice were fed a 60% high-fat diet (HFD) or 10% fat control diet (CD) for 12 wks prior to mating. Obese dams continued on HFD in pregnancy/lactation (HFD/HFD), lean dams remained on CD (CD/CD). Male (M) and F offspring were weaned to CD at 3 wks. Offspring were weighed at 4 and 11 wks (juvenile and adult). Adult body composition was determined using EchoMRI. Electrically evoked DA release was quantified in the nucleus accumbens (NAcc), prefrontal cortex (PFC) and dorsal striatum (Str) of juveniles.

RESULTS: M and F HFD/HFD juvenile offspring had significantly decreased DA signaling in the NAcc, PFC and Str compared to controls. The effect was more pronounced in Fs (Fig 1).

**Figure(s) will be available online.*

Offspring weight differences were significant in Fs only (Fig 2), with HFD/HFD Fs lighter at 4 wks (p<0.001) and heavier by 11 wks (p=0.01).

**Figure(s) will be available online.*

CONCLUSIONS: MATOB is associated with significantly reduced DA signaling in juveniles (F>M). Significant weight differences in offspring were observed in Fs only. Differences in DA signaling and weight despite offspring consumption of CD suggest a profound impact of the *in utero* environment. These findings may contribute to a mechanistic link between maternal and offspring obesity, with Fs more vulnerable to malprogramming of reward-based eating.

O-128

Accelerated Ovarian Ageing Induced by Chronic Fetal Hypoxia. CE Aiken†,[1] JL Tarry-Adkins,[1] AM Spiroski,[2] AM Nuzzo,[2] SE Ozanne,[1] DA Giussani*.[2] *[1]Institute of Metabolic Science, Cambridge, Cambridgeshire, United Kingdom; [2]University of Cambridge, Cambridge, Cambridgeshire, United Kingdom.*

INTRODUCTION: Exposure to chronic hypoxia *in utero* programmes dysfunction in various organ systems of the developing fetus. However, it is unknown whether the female reproductive system may be similarly susceptible. Ovarian development is highly sensitive to developmental programming via maternal diet (Aiken et al. *FASEB J*. **30(4)**:1548, 2016). Therefore, we hypothesise that chronic fetal hypoxia may also result in accelerated ovarian ageing.

METHODS: Wistar rat dams were subjected to normoxia (N, 21%) or hypoxia (H, 13%) from gestational days 6-21. Offspring were raised in normoxia. Ovaries were collected from 1 female per litter at 4 months of age. Ovarian gene and protein expression (q-rtPCR and western blotting), and telomere length (Southern blotting) were determined.

RESULTS: Chronic fetal hypoxia did not affect ovarian weight (N:0.08g±0.01 *vs.* H:0.07g±0.01, p=0.17). Ovaries from offspring exposed to gestational hypoxia had reduced telomere length ($p<0.01$; Figure 1A) and increased markers of cellular senescence (p53 $p<0.001$, p16Ink $p<0.05$; Figure 1 C & D) compared to controls. Hypoxia-exposed offspring had increased expression of DNA-damage sensing genes compared to controls (Ogg1 $p<0.05$ and Neil1 $p<0.05$), but reduced expression of Ku70 ($p<0.001$; Figure 1B), a key component of the main DNA repair complex. Furthermore hypoxia-exposed offspring had up-regulation of NOX2-mediated oxidative stress (Gp91phox and P22phox, $p<0.05$) and compensatory increase in anti-oxidant defence enzymes (CuZnSOD, $p<0.05$).

CONCLUSIONS: Chronic fetal hypoxia results in accelerated ageing of the somatic ovary, with evidence of shortened telomere length, impaired DNA repair, and increased oxidative stress. These novel findings suggest that female reproductive physiology is exquisitely sensitive to gestational hypoxia, which may impair female fertility and health in the next generation.

Supported by *The British Heart Foundation, Academy of Medical Sciences, and Newton Trust/Wellcome Trust ISSF/University of Cambridge*

**Figure(s) will be available online.*

O-129

***In Utero* Bisphenol-A Exposure Leads to Altered Uterine Stromal Cell Migration and Adenomyosis.** Myles H Alderman III†, Demetra Hufnagel†, Hugh S Taylor*. *Yale School of Medicine, New Haven, CT, USA.*

INTRODUCTION: Bisphenol-A (BPA) is a commonly used precursor in polycarbonate plastic production that is nearly ubiquitous in modern society. Previous research has indicated that *in utero* exposure to toxicologically relevant doses of BPA leads to aberrant developmental programming and estrogen response in the adult murine uterus through alterations of the epigenome. Here we identify increased migratory ability of uterine stromal cells leading to adenomyosis as a result of this altered developmental programming.

METHODS: Pregnant CD-1 Dams were treated with BPA by intraperitoneal osmotic minipump from day 9-21 of gestation resulting in mean maternal and fetal blood serum levels of BPA commensurate to that of exposed humans (8.2ng/ml and 7.52ng/ml). Isolated endometrial stromal cells from the offspring's uteri were analyzed at 10 weeks of age by trans-well migration assay (N=6). The uteri were also assessed by immunohistochemistry for smooth muscle actin (N=14).

RESULTS: Uterine stromal cells from animals treated in utero with BPA demonstrated an increased migratory rate compared to controls (23%, P=0.0002). In utero BPA exposure also led to an increased migratory rate towards both serum and CXCL12 containing media compared to controls (22% and 32%, $P<0.0001$ and P=0.002, respectively). None of the control animals displayed any uterine histological disorganization or abnormal glandular development. 100% of animals exposed to BPA *in utero* displayed glandular invasion of the myometrium and general myometrial disorganization, the hallmark characteristics of adenomyosis.

CONCLUSIONS: We demonstrate that in utero exposure to BPA can lead to altered endometrial stromal cell migration leading to adenomyosis. Prenatal BPA exposure epigenetically programs endometrial stromal cells leading to significant and potentially clinically relevant pathology.

O-130

Nutrient Sensor-Epigenome Regulation of Adipogenesis Programs Obesity in Offspring of Obese Mothers. Mina Desai,[1] Guang Han,[1] Kavita Narwani,[1] Elaheh Mossayebi,[1] Marie H Beall,[2] Michael G Ross.[1] *[1]LABioMed at Harbor-UCLA, Torrance, CA, USA; [2]LA Perinatal Assoc, Los Angeles, CA, USA.*

INTRODUCTION: Our mouse model of maternal obesity and a high fat diet (HF) mimics the human scenario wherein the newborn pups are heavier at birth and develop obesity. Enhanced adipogenesis results, in part, from early induction of PPARγ which facilitates preadipocyte differentiation to mature adipocytes which store fat. However, the mechanism for increased fetal adipose PPARγ in unknown. SIRT1, a nutrient sensor and a histone deacetylase, may be suppressed in response to increased nutrient energy. SIRT1 interacts with developmental histone methyltransferase (EZH2; regulates cell differentiation) which modulates Wnt10b, a known inhibitor of PPARγ. We hypothesized that in HF newborns, SIRT1-EZH2 mediated effects suppress Wnt10b promoting increased PPARγ and preadipocyte differentiation.

METHODS: Female mice were fed either a control (10% k/cal) or high fat (HF; 45% k/cal) diet to create maternal obesity prior to mating, and diets continued throughout pregnancy and lactation. Inguinal adipose tissue was collected from one day old males. Isolated preadipocytes were cultured for 48h (time 0) and subsequently induced to differentiate. Protein was extracted at day 0, 2, 4 and 6 of induction for expression of SIRT1, EZH2, Wnt10b and PPARγ. Values are shown as fold change (mean±SE).

RESULTS: In HF preadipocytes, prior to differentiation at day 0, SIRT1 and Wnt10b expression was downregulated whereas that of EZH2 and PPARγ was upregulated as compared to Control. With differentiation, both HF and Control cells showed progressively decreased expression of SIRT1 and Wnt10b with increased expression of EZH2 and PPARγ, though HF cells maintained decreased SIRT1 and Wnt10b and increased EZH2 and PPARγ as compared to Controls.

**Figure(s) will be available online.*

CONCLUSIONS: In HF newborns, the decreased SIRT1 with increased EZH2 suppresses Wnt10b and likely promotes adipogenesis, contributing to obesity. Ex vivo culture results indicate an intrinsic programming of WAT adipogenesis in HF offspring, independent of the body hormonal milieu.

O-131

Cardiac Assessment by 4D Echocardiography of Fetal Guinea Pigs. Shifa Turan, Graham W Aberdeen, Loren P Thompson*. *Univ. of Maryland, Baltimore, MD, USA.*

INTRODUCTION: We have previously reported that chronic hypoxia (HPX) increases oxidative/nitrosative stress in the fetal guinea pig (GP) heart at term. We sought to assess heart structure and function *in utero* using 4D echocardiography with spatio-temporal image correlation and tomographic ultrasound (US)(STIC-TUI) along with color and pulse Doppler US in the fetal GP. We hypothesized that chronic HPX reduces fetal heart function as a contributing factor to fetal complications.

METHODS: Pregnant GPs were exposed to normoxia (NMX; N=6) or hypoxia (HPX, 10.5%O_2; N=8) at 25d gestation. At term (65d), Doppler US was performed on lightly anesthetized fetal GPs (NMX; N=17, HPX; N=18). Myocardial performance [or Tie Index = (IVT+IRT)/ET)] was calculated from isovolumic contraction (IVT), relaxation (IRT), and ejection (ET) time intervals of left ventricles (LV) obtained from spectral Doppler images at the mitral/aortic valves. E/A ratio (early passive/active atrial diastolic filling) was obtained from LV/RV of NMX/HPX fetuses as an index of diastolic function. After the exam, fetal GPs were excised, and body and organ wts obtained. Statistical increases/decreases were identified ($P<0.02$) and comparisons were NMX vs HPX.

RESULTS: HPX had no effect on the Tie index in either male (M) (0.60±0.04 vs 0.62±0.03) or female (F)(0.58±0.02 vs 0.62±0.04) fetal

GPs or on individual time intervals (IVT, IRT, ET). HPX increased E/A ratios in LV of hearts of M (0.54±0.03vs0.70±0.05) and F GPs (0.62±0.02vs0.73±0.04) but had no effect on E/A ratios of the RV of either sex. Chronic HPX reduced FBW (M: by 16.7%; F: by 28.2%) and fetal heart wt (M: by 21.5% and F: by 27.5%), but had no effect on heart wt/FBW ratios. Placental weight was similar between treatments (M: 5.0±0.4 vs 5.2±0.1g; F: 5.1±0.3 vs 5.2±0.3) although placental wt/FBW ratios of both M (0.052±0.002 vs 0.067±0.003) and F GPs (0.047±0.001 vs 0.071±0.005) were increased with HPX.

CONCLUSIONS: 4D STIC-TUI fetal echocardiography is a novel application for imaging the fetal GP heart. We identified that chronic HPX increased diastolic filling with less reliance on atrial contraction and had no effect on LV systolic function. This suggests a greater preload in HPX fetuses due to a greater placental size relative to FBW and no change in UmbA indices. Further, the HPX fetal heart undergoes an adaptive response in the presence of fetal growth restriction and placental compensation. Further study is needed to examine the permanence of these changes postnatally. (NIH-HL126859-LPT).

O-132

Neuronal Exosome Synaptopodin: An Early Predictor of Therapeutic Response to Controlled Hypothermia. Laura Goetzl*,[1] Diana Martirosyan,[1] Nune Darbinian,[1] Nana Merabova,[1] Keri Fugarolas,[2] Ogechukwu Menkiti.[2] *[1]Temple University, Philadelphia, PA, USA; [2]St. Christopher's Hospital, Philadelphia, PA, USA.*

INTRODUCTION: Neonatal controlled hypothermia for hypoxic ischemic encephalopathy (HIE) is current standard of care and is associated with some improvement in neurologic outcome. However reliable biomarkers for estimating therapeutic response are lacking. Accurate biomarkers would be invaluable in classifying neonates into prognostic subsets to guide further therapy and aid in counseling.

METHODS: A secondary analysis was performed on neonatal samples collected at 8, 10 and 14 hours after the initiation of therapeutic controlled hypothermia for HIE. Neonatal neuronal exosomes were purified from serum as previously described. Synaptopodin (SYNPO), Neuron Specific Enolase (NSE), and Mitochondrial Cytochrome C Oxidase (COX4I1) protein levels were quantified using standard ELISA methods. The primary study outcomes were length of stay (LOS) and discharge on seizure medication (DCMED).

RESULTS: 13 subjects were included. The slope of change for biomarker levels was calculated between 8 and 14 hours. Among short term clinical markers (5 minute APGAR, cord pH or Base Excess (BE)), only pH was weakly correlated with LOS ($r= -0.54$, $p=0.05$) and none correlated with DCMED. In contrast, neural exosome SYNPO slope was highly correlated with LOS (-0.91, $p<0.001$) and SYNPO slope predicted DCMED (Figure 1, $p=0.02$). SYNPO improved in 6/8 without DCMED and 1/5 with DCMED. Neuronal exosome NSE and COX4I1 were not useful biomarkers of outcome in this cohort.

CONCLUSIONS: Improving levels of the neuronal survival protein SYNPO in neural exosomes released into the neonatal circulation between 8 and 14h of controlled hypothermia are a powerful indicator of favorable short term clinical outcomes and are superior to predictions based on cord blood pH or BE. Our results indicate that neuronal exosomes provide a plastic and non-invasive window into neuronal membrane status. Further research is needed to identify the optimal sampling strategy and to refine the negative and positive predictive value with regards to long term outcomes.

**Figure(s) will be available online.*

O-133

Volumetric and Vascular MRI Placental Changes with Exposure to Intrauterine Inflammation: Biomarker of Fetal Brain Injury. Jun Lei†,[1] Dan Wu,[2] Solange Eloundou†,[1] Wael Alshehri†,[1] Jiangyang Zhang,[2] Irina Burd*.[1] *[1]Johns Hopkins University School of Medicine, Baltimore, MD, USA; [2]Johns Hopkins University School of Medicine, Baltimore, MD, USA.*

INTRODUCTION: To determine whether *in vivo* MRI techniques could detect acute volumetric and vascular changes in placentas exposed to intrauterine inflammation.

METHODS: Mouse model of intrauterine inflammation was utilized. Lipopolysaccharide (LPS; 25 µg per dam, n=5) or PBS (n=4) were injected intrauterine at E17. *In vivo* MRI studies were performed utilizing 11.7T Bruker scanner, with a 72mm quadrature transmitter. Placental volume, blood volume and velocity were measured. Fetal brains and placentas were collected at 6 h. Histochemical analysis was performed to confirm results.

RESULTS: MRI analyses indicated that the mean volume for LPS placentas was decreased to 135 mm3 as compared to 155 mm3 in the controls. Furthermore,blood volume within placenta (0.22±0.01 vs 0.18±0.01) and velocity (5.8±0.2 x10-4 mm2/s vs 4.5±0.4 x10-4 mm2/s) demonstrated significant decreases ($p<0.05$) in LPS compared to PBS

**Figure(s) will be available online.*

H&E staining of placenta indicated thinning on maternal side (MS) following LPS exposure. MS was significantly decreased with LPS exposure ($P<0.05$) when compared to the fetal surface (FS). The LPS-exposed fetal brains also demonstrated reduced fetal brain cortical thickness. The changes in placenta correlated with changes in cortical thickness in the fetal brain.

CONCLUSIONS: Exposure to intrauterine inflammation caused changes in MRI placental volume and vascular system. These changes correlated with fetal cortical brain injury. Our study demonstrated that *in vivo* MRI is a possible translational tool to predict fetal brain injury exposed to intrauterine inflammation.

O-134

Chronic Hypoxia Alters Fetal Cerebrovascular Responses to Endothelin-1. Jinjutha Silpanisong†, Dahlim Kim†, James M Williams, Olayemi O Adeoye, William J Pearce. *Loma Linda University School of Medicine, Loma Linda, CA, USA.*

INTRODUCTION: In utero hypoxia influences the structure and function of most fetal arteries, including those of the developing cerebral circulation. Whereas the signals that initiate this hypoxic remodeling remain uncertain, these appear to be distinct from the mechanisms that maintain the remodeled vascular state. The present study explores the hypothesis that chronic hypoxia elicits sustained changes in fetal cerebrovascular reactivity to endothelin-1 (ET-1), a potent vascular contractant and mitogen.

METHODS: All tissues used in these experiments were obtained from normoxic and chronically hypoxic term fetal (139–142 days gestation) and young (18–24 month-old) nulliparous adult sheep. Normoxic animals were maintained at the LLU animal care facility (353 m altitude), where arterial oxygen tensions (PaO_2) averaged 23 ± 1 Torr and 102 ± 2 Torr in fetal and adult sheep respectively. Chronically hypoxic sheep were maintained for the final 110 days of gestation at the Barcroft Laboratory, White Mountain Research Station, Bishop, CA (altitude 3,820 m). At high altitude, PaO_2 values averaged 19 ± 1 and 64 ± 2 Torr for fetal and adult sheep respectively.

RESULTS: In fetal lambs, chronic hypoxia had no significant effect on plasma ET-1 levels or ETA receptor density in cerebral arteries but enhanced contractile responses to ET-1 in an ETA-dependent manner. In organ culture (24h), 10 nM ET-1 increased medial thicknesses less in hypoxic than in normoxic arteries, and these increases were ablated by inhibition of PKC (chelerythrine) in both normoxic and hypoxic arteries, but were attenuated by inhibition of CaMKII (KN93) and p38 (SB203580) in normoxic but not hypoxic arteries. As indicated by Ki-67 immunostaining, ET-1 increased medial thicknesses via hypertrophy. Measurements of colocalization between MLCK and SMaA revealed

that organ culture with ET-1 also promoted contractile dedifferentiation in normoxic, but not hypoxic, arteries through mechanisms attenuated by inhibitors of PKC, CaMKII, and p38.
CONCLUSIONS: These results support the hypothesis that chronic hypoxia elicits sustained changes in fetal cerebrovascular reactivity to endothelin-1 (ET-1) through pathways dependent upon PKC, CaMKII, and p38 that cause increased ET-1-mediated contractility, decreased ET-1-mediated smooth muscle hypertrophy, and a depressed ability of ET-1 to promote contractile dedifferentiation.

O-135

Role of Uric Acid and GLUT9 in Pregnancy on Neonatal Development. Benjamin P Lüscher, Daniel V Surbek, Camilla Marini, Marc U Baumann. *University Hospital of Bern, Bern, Switzerland.*
INTRODUCTION: High maternal uric acid serum levels are often associated with preeclampsia. The regulation of the placental uric acid transport system and its major uric acid transporter glucose transporter 9 (GLUT9) are not fully understood yet. We hypothesized that the lack of GLUT9 in the placenta leads to exposure of high uric acid levels in the fetus. Using a systemic GLUT9 knockout mice model we aim to understand the effect of fetal hyperuricemia on the growth of the pups and the development of their internal organs.
METHODS: Six-week-old female GLUT9$^{(+/-)}$ mice, maintained on regular chow diet, are mated with GLUT9$^{(+/-)}$ male mice. After the mating the diet is changed to regular chow diet plus inosine for the entire pregnancy period (21 days), which will lead to hyperuricemia in GLUT9$^{(-/-)}$ fetal mice, but not in the maternal mice. Starting from day 7 after birth the pups are daily weighted until day 70 after birth. At day 70 the pups are sacrificed and after perfusion organs (pancreas, liver and kidney) are weighted and used for tissue analysis to identify possible abnormal organ development.
RESULTS: First of all we saw a significant difference in body weight between neonatal GLUT9$^{(+/+)}$ and GLUT9$^{(-/-)}$ female mice from day 12 till day 35. Neonatal GLUT9$^{(-/-)}$ female mice were smaller than GLUT9$^{(+/+)}$ female mice . When kidneys from neonatal GLUT9$^{(+/+)}$ were compared with GLUT9$^{(-/-)}$ female mice, we observed a decreased in size of 25±0.15% (n=7; p=0.007, Student's T-test) in the left kidney and of 35±0.21% (n=7; p=0.011) in the right one. Hematoxylin & eosin staining of kidney paraffin sections revealed normal kidney tissue in GLUT9$^{(+/+)}$ and GLUT9$^{(+/-)}$ mice, whereas the morphology of the kidney in GLUT9$^{(-/-)}$ mice was altered and showed multiple areas with necrotic tissue.
CONCLUSIONS: The impaired growth pattern of neonatal GLUT9$^{(-/-)}$ mice may be due to hyperuricemia in pregnancy. Further characterization of this systemic GLUT9 knockout mice model may elucidate the underlying pathomechanism between hyperuricemia and altered neonatal development.

O-136

Cardiac miRNA Expression in the Fetus and Six Month Old Sheep in Response to Myocardial Infarction. Mitchell Lock†,[1] Jia Yin Soo†,[1] Jack Darby†,[1] Doug Brooks,[1] Enzo Porrello,[2] Ross Tellam,[3] Janna Morrison*.[1] *[1]University of South Australia, Adelaide, Australia; [2]University of Queensland, Brisbane, Australia; [3]Queensland Biosciences Precinct, Brisbane, Australia.*
INTRODUCTION: The adult heart has very little capacity to repair after damage because adult cardiomyocytes lack the ability to proliferate. Some miRNAs that have roles in cell cycle and regeneration change expression at the time when proliferation ceases in both rodents and sheep. We investigated the expression of miRNAs and their predicated target genes after myocardial infarction in sheep hearts before and after birth when the response to injury is different.
METHODS: To investigate the effect of age on response to cardiac damage, we ligated the second diagonal of the left anterior descending (LAD) coronary artery in 102 day gestation sheep fetuses (MI, n=5; Sham, n=5) and six month old sheep (MI, n=4; Sham, n=4). Heart tissue from the infarct, border and remote zone of the left ventricle was dissected and frozen in liquid nitrogen or fixed in paraformaldehyde three days after surgery. Total RNA was extracted and analysed using a custom designed miRNA microarray and validated with qRT-PCR and histology.
RESULTS: The differentially expressed probes from the microarray (Fig 1A) were subjected to k-means clustering in CLCBIO (k=10 revealed profile stability). The miRNA in each cluster were used as input into MiRWalk for mRNA target prediction. Predicted targets were assessed for Gene Ontology (GO) term enrichments using DAVID. Target genes of fetal miRNAs showed enrichment for *apoptosis* and *regulation of development*. In contrast, target genes in the six month old sheep showed enrichment for *negative regulation of apoptosis* and *cell migration*. Supporting this finding, qRT-PCR showed the fetus and six month old sheep had opposite expression profiles (Fig 1B).
CONCLUSIONS: miRNAs that are downregulated in the fetus following injury may have significant roles in regulating cardiomyocyte proliferation in sheep. Low expression of these miRNAs in the fetus allows repair after damage with high expression after birth resulting in limited capacity for repair.
**Figure(s) will be available online.*

O-137

Effect of Amnion Derived Exosomes on Feto-Maternal Gestational Cells: Novel Signalers in the Labor Cascade? Emily E Hadley†,[1] Samantha Sheller†,[1] Rheanna Urrabaz-Garza,[1] Talar Kechichian,[1] George Saade,[1] Sam Mesiano,[2] Robert Taylor,[3] Ramkumar Menon*.[1] *[1]UTMB, Galveston, TX, USA; [2]Case Western Reserve University, Cleveland, OH, USA; [3]Wake Forest School of Medicine, Winston-Salem, NC, USA.*
INTRODUCTION: Labor is associated with inflammatory overload in uterine tissues. Term amnion epithelial cells (AEC) are senescent and release exosomes that carry inflammatory signals. We hypothesize AEC derived exosomes promote labor by increasing inflammatory load in feto-maternal compartments. We determined the functional role of AEC derived exosomes in promoting inflammation in placental syncytiotrophoblast, decidua and myometrium.
METHODS: Exosomes were isolated from media of AECs from term non labor placental membranes grown in normal (control) and oxidative stress (OS) conditions. OS was induced by cigarette smoke extract (CSE) mimicking term labor. Exosomes were characterized and quantified using nanoparticle tracking analyzer. Placental (BeWo), myometrial and decidual cells were treated with three doses of control or OS exosomes ($2e^5$, $2e^7$, $2e^9$/well) for 24 hours (n=7). Confocal microscopy of fluorescent labelled exosomes showed their entry into each cell type. Exosome effect was confirmed by exposing cells to incubation at 4°C to block endocytosis or by heating or sonicating exosomes prior to treatment. IL-6 and PGE_2 levels in media were quantitated by ELISA. Statistical analysis performed with ANOVA.
RESULTS: AECs produce ~50 nm, cup shape exosomes with 923 and 1273 exosomes/cell in control and OS cells respectively. After treatment, exosomes were localized inside all cell types. Treatment had no effect on IL-6/PGE_2 production in BeWo cells compared to untreated cells. A significant ($p<0.05$) dose dependent increase in IL-6 was seen in decidua and myometrial cells treated with control and OS exosomes compared to untreated cells. PGE_2 was significantly higher ($p<0.05$) in decidual and myometrial cells treated with OS exosomes, but not with control exosomes. Exposure to cold, or treatment with sonicated or heated exosomes produced IL-6 and PGE2 similar to that of untreated cells.
CONCLUSIONS: Term AEC derived exosomes increased IL-6 in decidua and myometrium suggesting an inflammatory load increase. OS induced exosomes induced PGE_2 production suggesting a uterotonic response specifically in maternal compartments. Fetal tissues can increase inflammation and signal initiation of parturition via exosomes.

O-138

Collagen Type 1 Gels Augment Healing of Ruptured Amnion in Mouse PROM. Haruta Mogami, Annvarapu H Kishore, R Ann Word*. *University of TX Southwestern Med Ctr, Dallas, TX, USA.*
INTRODUCTION: Clinically, there is no effective treatment for preterm rupture of membrane (PROM), a major cause of preterm birth. Here, we tested the hypothesis that collagen type 1 gels would alter healing of the amnion in a mouse model of non-infectious sterile PROM. Mechanisms were investigated using primary human epithelial and mesenchymal amnion cells in culture.

METHODS: sUterus and fetal membrane of pregnant mice were punctured with a sterile 20G needle at 15 dpc. After puncture, rat type 1 collagen (2 mg/ml, 20 µl/fetus) or PBS was injected between membrane and myometrium. In vitro, primary human amnion cells were used for wound scratch assay and immunoblots.
RESULTS: In this model of 20 G (0.91 mm) sterile ruptured membranes, expression of proinflammatory cytokines and COX-2 increased 2 h after rupture [*IL1β* (5-fold), *IL6* (9-fold), *TNF* (3-fold), and COX-2 (4-fold), all $p < 0.01$]. Despite these significant increases in proflammatory cytokines, 40% of PBS-injected membranes healed spontaneously after 72 h. Injection of collagen gels, however, improved healing to 90% (n=25-28, $P<0.01$ χ^2) (0.2 ± 0.1 vs 1.2 ± 0.3 mm, $P<0.01$) with no effect on proinflammatory cytokines. Collagen gels also stimulated healing of choriodecidua to 42% compared with 6% for PBS (n=17-19, $P=0.05$). Histologically, collagen accelerated migration and proliferation of amnion mesenchymal cells in vivo. In vitro, collagen gels increased migration of amnion mesenchymal, but not epithelial, cells compared with medium alone (90 vs 51% closure at 72 h, $P<0.01$). Neutralizing antibodies of α1β1, α2β1 integrins or discoid receptor 1 (DDR1) did not block collagen-induced migration of mesenchymal cells. Inhibition of the collagen receptor, DDR2, however, blocked collagen-induced cell migration compared with vehicle (46 vs 90% closure at 48 h, $P<0.01$). Myosin regulatory light chain (RLC) is a key molecule in the contraction of actin-myosin fiber and subsequent cell migration. Collagen gels induced dramatic, but transient, phosphorylation of myosin RLC at 1 h and this effect was mitigated by DDR2 inhibitor.
CONCLUSIONS: Collagen gels induce proliferation and migration of amnion mesenchymal cells through activation of DDR2 signaling. Further, collagen gels significantly improved healing of ruptured fetal membranes in a mouse model of sterile inflammation. Collectively, these results suggest that collagen gels may promote healing of non-infectious PPROM.

O-139

Mechanisms Underlying the Effects of Retosiban/GSK221149A on the Response to Mechanical Stretch in Human Myometrial Explants. Irving LMH Aye†, Alex Moraitis, D Stephen Charnock-Jones, Gordon CS Smith*. *University of Cambridge, Cambridge, Cambridgeshire, United Kingdom.*
INTRODUCTION: Prolonged stretch of myometrium stimulates its contractility, and this may explain higher rates of spontaneous preterm birth in multiple pregnancy. We have previously shown that retosiban, an orally active, non-peptide oxytocin receptor (OTR) antagonist, prevents this effect of high stretch in human myometrial explants. We hypothesized that stretch activates signaling events downstream of the OTR and that this is inhibited by retosiban.
METHODS: Myometrial biopsies (n=75) obtained at term from non-laboring women were dissected into strips and cultured for 20h under low (0.6g) or high (2.4g) tension with or without one or more of the following: retosiban, atosiban (peptide OTR antagonist), two ERK inhibitors (U0126 & SCH772984) or vehicle (DMSO). Explants were flash frozen, or transferred to an organ bath for isometric tension studies. Downstream signaling events were studied using phospho-kinase arrays or ELISA (both R&D).
RESULTS: In strips maintained at high stretch, retosiban (1µM) attenuated the contractile responses to KCl (P=0.005) and oxytocin (P=0.004) by 40%. Phospho-kinase arrays demonstrated that high stretch increased ERK phosphorylation (P=0.003) and decreased β-catenin expression (P=0.04). Technical (n=6) and biological (n=10) replicates using ELISAs confirmed both findings (P<0.01). High stretch increased phosphorylation of ERK by 2 fold, and this was prevented by retosiban (10nM & 1µM; P<0.001) but not atosiban (concentrations up to 1µM). However, the inhibitory effect of 10nM retosiban on stretch-induced ERK phosphorylation was prevented by 1µM atosiban (P=0.01). Finally, inhibition of ERK activity using U0126 (10µM) or SCH772984 (10µM) attenuated the contractile responses to KCl and oxytocin (40% and 80% reductions respectively) of strips incubated in high stretch (P<0.05).
CONCLUSIONS: Prolonged stretch of human myometrium activates signaling events downstream of the OTR. The effect of stretch can be inhibited by therapeutically relevant concentrations of retosiban, but not atosiban. This effect of retosiban can itself be blocked by 100-fold molar excess of atosiban. We interpret these data as follows: (1) myometrial stretch induces activation of the OTR, (2) retosiban reverses this effect through inverse agonism of the OTR. Collectively, our findings indicate that retosiban is a potential therapeutic approach to preventing spontaneous preterm birth in multiple pregnancy.

O-140

Characterization of Peptides Against Neuromedin U Receptor 2 in Preterm Labor. Amarilys Boudreault†,[1,2] Christiane Quiniou,[1] Xin Hou,[1] Mathieu Nadeau-Vallée,[2] Sylvain Chemtob*.[1,2] *[1]CHU Ste-Justine, Montreal, QC, Canada; [2]Université de Montréal, Montreal, QC, Canada.*
INTRODUCTION: Preterm birth (delivery before 37 weeks of gestation) is the leading cause of neonatal mortality and morbidity worldwide and induce long-term disabilities. To date, no pharmacological agent (tocolytic) is efficient to prolong gestation for more than 48h and all of the agents used in clinic have maternal and/or fetal side effects. Recently, a pro-contractile system involving the neuropeptide neuromedin U and its receptor neuromedin U receptor 2 (NmU-R2) was discovered in our laboratory. Our group has developed five different small peptide-antagonists of NmU-R2. The objective of this project is to characterize these NmU-R2-antagonists and to choose a potential lead compound for the development of a new tocolytic agent.
METHODS: To know which peptide is the best to inhibit uterine contraction, we performed *ex vivo* contraction assays of uterine segments in organ tissue baths with or without the different peptides and murine NmU (10^{-7} or 10^{-8}M). We assessed the inhibition of intracellular release of calcium *in vitro* using isolated murine primary myometrial cells to perform calcium assays with the five NmU-R2-antagonists. Also, cells were pre-incubated with several doses of best performed peptides (chosen from the *ex vivo* assay) or vehicle for 30 minutes followed by a stimulation with 10^{-7}M of NmU and incubation of 10 minutes at 37°C. Afterward, we analyzed by Western Blot the phosphorylation of kinases (Erk and Akt).
RESULTS: Peptides 3 and 5 were the best to inhibit *ex vivo* uterine contraction (respectively about 40 and 50% inhibition) and inhibited the release of calcium *in vitro* (about 50-60% inhibition). Then, dose-response curves were performed with these peptides using calcium assays and they showed a dose-response inhibition of calcium release (IC_{50}: 0.63nM for peptide 3 and 23nM for peptide 5). The immunoblots of Erk and Akt showed an inhibition of the phosphorylation in a dose-dependant manner with these peptides.
CONCLUSIONS: Results indicated that two out of the five peptides have better antagonist capacities against NmU-R2. Peptide 5 has more consistent results than peptide 3 *in vitro* and *ex vivo*. Hence, we have a potential lead antagonist peptide to serve as a potential tocolytic agent against NmU-R2. Further studies will be conducted for binding and *in vivo* in a mouse model of preterm birth.

O-141

Adiponectin Receptor Activation Mediates Myometrial Tocolysis: A Mechanism for Obesity Related Preterm Birth. Vibhuti Vyas,[1] Nathan Anderson,[1] Rachael Bok,[1] Theresa Powell,[2] Thomas Jansson,[1] Kenneth J Hurt.[1] *[1]University of Colorado, Aurora, CO, USA; [2]University of Colorado, Aurora, CO, USA.*
INTRODUCTION: Obese women have increased risk for preterm delivery, however the underlying mechanisms are poorly understood. The circulating levels of adiponectin are reduced in obese pregnant women. We hypothesized that adiponectin inhibits myometrial contractility.
METHODS: The adiponectin receptor (AdipoR) agonist, AdipoRon was used to activate adiponectin receptors in pregnant and non-pregnant (NP) mouse myometrial strips in a physiologic organ bath. The effect of AdipoRon on spontaneous and oxytocin-induced contractions was studied. We determined AdipoRon concentration-response curves (0.1 – 45µM) for mouse myometrial strips from estrogen-primed NP and pregnant mouse uterus (gestational day [GD] 15 and 18). Signaling pathways were investigated using the AMP Kinase (AMPK) inhibitor Dorsomorphin (50µM). Myometrial strips were flash frozen, homogenized, and

prepared for western blot (WB) analysis of AMPK activation monitored by phosphorylation of AMPK (Thr172). Statistical significance was established using two-way ANOVA followed by Bonferroni's multiple comparisons test.

RESULTS: In NP myometrium, AdipoRon inhibited contractions measured as the area under the curve (AUC), peak height (PH) and cyclic frequency (CF; all $p<0.05$) of both spontaneous (n=12) and 4nM oxytocin-stimulated contractions (AUC $p<0.05$, n=12). AdipoRon also inhibited AUC, PH and CF ($p<0.05$) of 2nM oxytocin-induced contractions in GD15 and GD18 myometrium (n=12 strips). In GD15 and 18 uterine strips, AdipoRon increased AMPK phosphorylation 2-fold ($p<0.001$). Dorsomorphin caused a 2-fold inhibition of AMPK in GD15 tissues (n=4-8 strips) and pretreatment with dorsomorphin did not prevent the inhibitory effect of AdipoRon on myometrial contractility.

CONCLUSIONS: Activation of myometrial adiponectin receptors inhibits both spontaneous and oxytocin induced contractions in NP and pregnant myometrium, by a mechanism that does not involve AMPK. We propose that adiponectin functions as a quiescence factor prolonging pregnancy. In maternal obesity, low adiponectin levels may contribute to the increased risk of preterm birth in these women. We speculate that these findings identify novel therapeutic targets to prevent preterm parturition and improve pregnancy outcomes in obese women.

O-142

Functional Pharmacology Coupled with Metabolomics Reveals Novel Pathways of Chlorophyll Compounds on Myometrial Activity.

Enitome E Bafor†,[1,2] Edward G Rowan,[2] RuAngelie Edrada-Ebel*.[2] *[1]University of Benin, Benin, Edo State, Nigeria; [2]Strathclyde Institute of Pharmacy and Biomedical Sciences, Glasgow, North Lanarkshire, United Kingdom.*

INTRODUCTION: Chlorophyll compounds are now considered as potential novel sources of drugs for pre-term labour. We therefore hypothesized that unique signaling interplay are involved in the myometrial activity of chlorophyll-derived compounds.

METHODS: Uteri from female virgin C57BL/6 mice were excised, mounted in Krebs-Henseleit buffer-filled organ baths. Single concentrations (200 µg/ml) of the chlorophyll compounds were added for 10 min to the isolated tissues and without washing, the tissues and buffers were collected and flash-frozen in liquid nitrogen. In the presence of dry ice, each flash-frozen tissue was homogenized and extracted first with methanol and then dichloromethane solvents. The buffer was freeze-dried and similarly extracted. High resolution mass spectrometry (HRMS) and proton nuclear magnetic resonance spectroscopy (1H-NMR) were performed on the extracts. The resulting HRMS data were pre-processed, analyzed and identified with the online metabolomic data analysis program, XCMS. The XCMS output were further analyzed using the Ingenuity Pathway Analysis tool. All NMR datasets were pre-processed using Mnova v. 8.1 and analyzed using SIMCA-P software package.

RESULTS: Significant pathways for the chlorophyll compounds ($p < 0.05$) were extracted via HRMS. For chlorophyll compounds with inhibitory effects, detected pathways included upregulation of cAMP, endocannabinoid, ceramide and catecholamine signaling with accompanying downregulation of myoinositol (MI), gamma aminobutyric acid (GABA), sphingosine and phosphatidylinositol signaling. Bioinformatics showed strong correlations of the compounds' action with MI signalling, cytidine diphosphate diacylglycerol, serotonin, nicotinic acid, eicosanoid and GABA pathways

**Figure(s) will be available online.*

CONCLUSIONS: This study has enabled the innovative detection of a unique interplay of signaling pathways involved in the myometrial activity of chlorophyll-derived compounds which makes them potential agents for combating pre-term labour.

O-143

Inhibition of the Auto-Inflammation Suppressor Protein ISG15 Triggers Preeclampsia by Blocking Trophoblast Migration and Invasion.

Nihan Semerci, Ozlem Guzeloglu-Kayisli, Sefa Arlier, Kellie Larsen, Chinedu Nwabuobi, Frederick Schatz, Antony Odibo, Charles Lockwood, Umit Kayisli. *Univ. of South Florida, Morsani College of Medicine, Tampa, FL, USA.*

INTRODUCTION: Covalent binding of proteins (aka ISGylation) by interferon-induced ubiquitin-like modifier 15 protein (ISG15) negatively regulates IFN-α/β responses. In humans, homozygous loss-of-function mutations in the ISG15 gene suppresses interferon (IFN)-γ production in lymphocytes and induces an abnormally hyper-IFN-α/β mediated immune response causing severe auto-inflammation. Elevated plasma and decidual interleukin (IL)-6 expression and impaired decidual IFN signaling are associated with preeclampsia (PE). Using microarray analysis, we found that IL-6 inhibits ISG15 expression in primary cytotrophoblast (CTB) cultures. Our *in situ* analysis showed that interstitial CTBs in PE *vs.* control placentas exhibit significantly lower ISG15 immunoreactivity. This study investigated the role of ISG15 on CTB migration and invasion.

METHODS: Immunohistochemistry was performed on term decidua basalis specimens to determine cell specific ISG15 expression (n=4). Migration and invasion assays were performed on normal and ISG15-siRNA silenced HTR8/SVneo cells (human first-trimester chorionic villi explant-derived immortalized cytotrophoblasts) using non-coated and matrigel coated trans-wells and 24-h wound healing assays in 12-well culture plates. Statistical analysis used student's t-test.

RESULTS: Among decidua basalis cells, immunostaining revealed the highest *in situ* ISG15 expression in interstitial CTBs. Immunoblotting and qRT-PCR of HTR8 cultures confirmed significantly reduced ISG15 protein and mRNA levels following ISG15 siRNA *vs.* control siRNA treatment. Phase-contrast microscopy observed flattened and larger cells in HTR8 cultures following ISG15 siRNA *vs.* control siRNA treatment. Moreover, ISG15 siRNA silencing reduced HRT8 migration (Mean ± SEM 0.410±0.05 *vs.* 0.679± 0.080; p = 0.026; n=6), invasion (0.373±0.02 *vs.* 0.573±0.06; p= 0.024; n=5) and delayed *in vitro* wound healing compared to control siRNA treatment at 4 to12 h.

CONCLUSIONS: These results indicate that ISG15 expression levels are crucial for trophoblast morphology and function (migration/invasion). By blocking trophoblast invasion, reduced ISG15 levels could contribute to impaired spiral artery transformation that reduces utero-placental blood flow in PE. Thus, induction of ISG15 expression is likely to be therapeutic in PE.

Supported by U01HD087213 by NICHD.

O-144

Rosiglitazone Reduces Endotoxin Mediated Effects on Inflammation and Trophoblast Differentiation in First Trimester Human Placenta.

Leena T Kadam†,[1,2] Brian Kilburn,[2] Aalem Singh,[2] Hamid Reza Kohan-Ghadr,[2] Sascha T Drewlo.[2] *[1]Wayne State University, School of Medicine, Detroit, MI, USA; [2]Wayne State University, School of Medicine, MI, USA.*

INTRODUCTION: Abnormal placental function and inflammation are common features in the wide spectrum of pregnancy-related disorders. In the current study we aimed to evaluate the relationship between inflammation and trophoblast cell physiology. PPAR-γ is known to regulate gene expression in inflammation, cell differentiation and oxidative stress and can be specifically induced by the drug Rosiglitazone. We hypothesized that endotoxin exposure induces an inflammatory response in the placenta and impairs trophoblast differentiation and induction of PPAR-γ activity will reverse these effects.

METHODS: First trimester placental villous explants exposed to 1µg/ml of bacterial endotoxin Lipopolysaccharide (LPS) +/- 10µM Rosiglitazone for 24hrs. The effects of LPS treatment on expression of genes involved in inflammatory signaling and trophoblast differentiation was assessed by qPCR, immunoblotting & ELISA. Trophoblast cell apoptosis & proliferation was assessed by TUNEL assay and IHC.

RESULTS: Exposure to LPS significantly upregulated the expression of inflammatory cytokines (n=12,≥1.7 fold) CCL5 (p=0.03),IL-1β (p=0.01) and IL-10(p=0.03). LPS exposure also induced apoptosis (≥1.5

fold,p=0.02) and decreased proliferation in treated explants (by ≥40%, p=0.03).The expression of the LPS receptor TLR4 measured by semi-quantitative IHC was significantly upregulated by LPS in the placental villi. The expression of genes involved in trophoblast differentiation was also significantly downregulated (~40%)-β-hCG (p=0.009) and Gcm1(p=0.03). Rosiglitazone treatment significantly downregulated the levels of inflammatory proteins, TLR4 and also reduced apoptosis. It rescued the expression of β-hCG and GCM1 and restored the proliferation rate.

CONCLUSIONS: We report for the 1st time that exposure of first trimester human placenta to endotoxins,in addition to inducing an inflammatory response also regulates receptor expression & factors involved in trophoblast differentiation suggesting a link between inflammation & altered placental function. Further, these effects were rescued by Rosiglitazone treatment. The current study indicates the crucial role of PPAR-γ in regulating trophoblast differentiation and placental inflammatory response providing a potential target for future treatments.

O-145

SDF2 Is a Novel Component of ER Stress-Induced Apoptosis Pathway in Trophoblast Cells via PERK-eIF2 Alpha-ATF4 Branch. Aline R Lorenzon-Ojea†,[1] Clarissa R Rocha,[2] Estela Bevilacqua*.[1] *[1]Institute of Biomedical Sciences - University of Sao Paulo, Sao Paulo, SP, Brazil; [2]Institute of Biomedical Sciences - University of Sao Paulo, Sao Paulo, SP, Brazil.*

INTRODUCTION: Our previous studies showed stromal cell-derived factor 2 (SDF2) as a novel factor in endoplasmic reticulum stress pathway, involved in apoptosis/ survival cell fate. CHOP is the primary factor involved in apoptosis in ER stress, mainly produced by the PERK branch of the Unfolded Protein Response. Herein, we investigated a possible role of SDF2 in PERK branch of UPR in ER-stress stimulated trophoblast cells: the choriocarcinoma cell lineage BeWo and HTR8-SVneo – an immortalized first-trimester cell lineage.

METHODS: BeWo and HTR8-SVneo were induced to ER stress with tunicamycin in the presence or not of PERK inhibitor, GSK2606414. ER stress markers were evaluated by qRT-PCR (sXBP1, CHOP, GADDA34, and SDF2) and Western Blot (p-eIF2alpha, total eIF2-alpha, GRP78/BiP, and SDF2). Cells were also silenced for SDF2 with siRNA and superexpressed with plasmid, induced to ER stress and evaluated for apoptosis (caspase-3) and cell survival (ATP production) by luminescence assays.

RESULTS: Cells treated with tunicamycin and PERK-inhibited showed upregulation of SDF2 gene expression (5-fold) in both cell lineages. CHOP expression pattern did not change in BeWo, but it was downregulated (20-fold) in HTR8/SVneo. GADD34 expression was upregulated in BeWo and downregulated in HTR8-SVneo (12-fold). SDF2 and GRP78/BiP protein expression were downregulated in this condition for both cell lineages. p-eIF2alpha/total eIF2alpha ratio was lower in the presence of PERK inhibitor, regardless tunicamycin treatment. Apoptosis was induced when SDF2 was superexpressed in tunicamycin-treated cells and decrease in silenced cells for both cell lineages.

CONCLUSIONS: Changes in SDF2 expression during PERK inhibition in stressed-trophoblast cells suggest a role played by this factor in this UPR branch. Moreover, SDF2 superexpression was able to induce apoptosis in ER-stressed cells. Differences in ER stress markers in these lineages – mainly in GADD34 – reinforce the characteristics of tumoral cells (BeWo) in escaping apoptosis control during ER stress. As SDF2 is strategically positioned in this pathway for regulation of cellular fates, potentially driving the cells to the apoptosis, it becomes a paramount importance target to the understanding of gestational diseases, as preeclampsia, and tumoral cells.

O-146

Human Placental Endothelial Cells Are Capable of Recovering from Failed Angiogenesis Secondary to Impaired Wnt Signaling. Toluwalope O Junaid†, Paul Brownbill, Edward D Johnstone, John D Aplin*. *University of Manchester, Manchester, United Kingdom.*

INTRODUCTION: Impaired wingless protein [Wnt] signalling alters endothelial cell [EC] behaviour and disrupts angiogenesis, leading to detrimental effects on placental vascularisation and fetal growth [Monkley et al. Dev 122(11):3343, 1996]. We hypothesised that augmenting Wnt signalling may improve placental angiogenesis.

Objective: To determine whether the angiogenic potential of placental ECs can be restored following failed angiogenesis secondary to impaired Wnt signalling.

METHODS: Tube-like structure [TLS] formation assays were performed using human placental arterial endothelial cells [HPAECs] isolated from placentas from normal and fetal growth restriction [FGR] complicated pregnancies [n=5/group]. HPAECs, seeded on matrix-coated coverslips, were incubated in endothelial growth medium [EGM] under normoxic conditions for 6 hours [h], and then in EGM containing 1uM of niclosamide [NIC], a broad spectrum Wnt inhibitor, for 24h. Subsequently, NIC's effect was withdrawn by culturing the cells in fresh EGM for further 24h. The TLS covered area on the coverslips, quantity and length of TLS formed pre- and post-withdrawal of NIC were quantified on Wimtube TLS analysis software. EC viability was assessed by immunofluorescence staining for expression of known markers of proliferation [Ki67] and apoptosis [cleaved caspase 3].

RESULTS: Compared to vehicle control, NIC significantly impaired TLS formation by both normal and FGR HPAECs *in vitro*, evidenced by reduced TLS covered area [$p<0.05$] with fewer [$p<0.01$] and shorter [$p<0.05$] TLS formed. EC viability was maintained; cells could proliferate and there was no difference in incidence of apoptotic cells. 24h after withdrawal of Wnt inhibition, in normal and FGR HPAECs respectively, median TLS covered area increased by 4% and 45% [$p<0.05$], median quantity of TLS increased by 24% and 56% [$p<0.01$] and median length of TLS increased by 26% and 51% [$p<0.05$]. Thus TLS formation by both HPAEC groups recovered, but this occurred significantly more rapidly in FGR cells.

CONCLUSIONS: Our findings signify that the detrimental effects of impaired Wnt signalling on EC behaviour are reversible. This discovery may represent a novel lead in therapeutic angiogenesis, suggesting the need to investigate Wnt agonists as potential agents for improving placental angiogenesis in pregnancy diseases characterised by impoverished placental vascularity.

O-147

mTOR Inhibition Down-Regulates Mitochondrial Function in Primary Human Trophoblast Cells and Is Associated with Decreased Expression of Electron Transport Chain Complexes in IUGR Placentas. FJ Rosario†,[1] MB Gupta,[2] L Cox,[3] TL Powell,[1,4] T Jansson*.[1] *[1]University of Colorado Anschutz Medical Campus, Aurora, CO, USA; [2]University of Western Ontario, London, ON, Canada; [3]TFBRI, San Antonio, TX, USA; [4]University of Colorado Anschutz Medical Campus, Aurora, CO, USA.*

INTRODUCTION: Placental protein synthesis and active transport are dependent on energy generated by mitochondria and decreased number and/or impaired function of placental mitochondria may contribute to restricted fetal growth. Reports on placental mitochondrial number and function in human IUGR are inconsistent. We have previously shown that placental mechanistic Target of Rapamycin (mTOR) signaling is inhibited in human IUGR. mTOR Complex 1 (mTORC1) regulates mitochondrial function in cell lines. We tested the hypothesis that mTORC1 is a positive regulator of mitochondrial respiration in cultured primary human trophoblast (PHT) by modulating mitochondrial biogenesis and that human IUGR is associated with decreased placental expression of electron transport chain complexes (ETCC).

METHODS: We silenced raptor (mTORC1 inhibition), rictor (mTORC2 inhibition) or DEPTOR (mTORC1/2 activation) in cultured PHT cells. We performed transcriptome profiling and measured mitochondrial

respiration (Seahorse Bioscience XF24), mtDNA copy number (RT-PCR), citrate synthase activity and cellular ATP levels in PHT cells. Placental tissue from pregnancies complicated by IUGR (n=25) and gestational age-matched appropriately grown pregnancies (n=19) were collected, mTORC1 signaling activity and mitochondrial ETCC expression were determined using Western blot.
RESULTS: Inhibition of mTORC1, but not mTORC2, resulted in down-regulation of genes in networks related to oxidative phosphorylation, decreased mitochondrial respiration ($P<0.01$) and cellular ATP levels ($P<0.001$). Furthermore, mTORC1 inhibition decreased the abundance of mtDNA ($P<0.002$) and citrate synthase activity ($P<0.001$), markers of mitochondrial biogenesis. In contrast, activation of mTORC1/2 had opposing effects. Placental mitochondrial ETCC expression was downregulated in IUGR ($P<0.02$) and was positively correlated with placental mTORC1 signaling ($P<0.001$).
CONCLUSIONS: Based on evidence from both cultured PHT cells and placentas of IUGR pregnancies, we propose that reduced placental mTOR activity inhibits mitochondrial respiration mediated by decreased mitochondrial biogenesis and contributes to placental insufficiency in IUGR.

O-148

Sexual Dimorphism in the Regulation of Placental Metabolism and Fetal Growth by miR-210. Yu Wang†,[1] Matthew S Bucher,[1] Bailey L Simon,[2] Alina Maloyan,[2] Leslie Myatt*.[1] *[1]Oregon Health & Science University, Portland, OR, USA; [2]Oregon Health & Science University, Portland, OR, USA.*
INTRODUCTION: microRNA-210 is a hypoxamir that significantly alters metabolism in hypoxic and inflammatory states e.g. obesity. We showed that overweight and obese (BMI>30) compared to lean (BMI 18-25) women have significantly higher placental miR-210 with appropriately grown female fetuses, but not males. Moreover, miR-210 overexpression lowered mitochondrial respiration in primary human trophoblasts. We hypothesized that placental miR-210 expression would relate to fetal size but in a sexual dimorphic manner.
METHODS: Placental villous tissue was collected from uncomplicated singleton pregnancies at term c. sections in the absence of labor (M=17, F=20). Pre-pregnancy BMI and birth weight were recorded. mRNA expression of villous tissue miR-210, protein levels of mitochondrial complexes I-V and succinate dehydrogenase complex subunit b (SDHB), a target for miR-210, were assessed. Data were analyzed by nonparametric spearman correlations.
RESULTS: Placental miR-210 expression positively correlates with birth weight centiles where fetuses are female ($p<0.01$, $r=0.6497$, $n=20$), whilst miR-210 levels did not differ in placentas from male fetuses irrespective of birth weight. We confirmed that placental miR-210 levels were higher in overweight and obese women compared to lean in appropriately grown female fetuses. However, miR-210 correlates with BMI in only lean and overweight women ($p<0.05$, $r= 0.5495$, $n=13$). No correlations were found between miR-210 and mitochondrial complexes, however miR-210 does negatively correlate with its target SDHB ($p<0.05$, $r=-0.3256$, $n= 37$).
CONCLUSIONS: The association between placental miR-210 and birth weight centiles in female fetuses, suggests this increase in miR-210 with fetal size may be an adaptive mechanism regulating fetal growth via glucose availability in the female. In larger fetuses, high miR-210 may suppress mitochondrial respiration, whilst increasing the less energetically efficient glycolysis, thus higher placental glucose usage; conversely, lower miR-210 levels seen in low birth weight fetuses may result in a more metabolic efficient placenta, by increasing mitochondrial respiration and reducing glycolysis, thus conserving glucose for fetal metabolism. Hence female fetuses may have an adaptive placental mechanism via miR-210 to regulate metabolism and growth that is not operative in the male fetus.

O-149

Disruption of Mitochondrial Proteostasis Results in Impaired Mitochondrial Dynamics and Female Infertility. Tianren Wang†,[1] Tim Sanchez,[2] Daniel Neddleman,[2] Denny Sakkas,[2] Tamas Horvath,[1] Emre Seli*.[1] *[1]Yale School of Medicine, New Haven, CT, USA; [2]Harvard School of Engineering and Applied Sciences, Cambridge, MA, USA.*
INTRODUCTION: CLPP (caseinolytic peptidase P) maintains mitochondrial protein hemostasis (proteostasis) by degrading misfolded mitochondrial proteins and activating mitochondrial unfolded protein response (mtUPR). We hypothesized that mitochondrial proteostasis is required for oocyte mitochondrial function, and assessed fertility parameters and mitochondrial dynamics (fusion and fission) in mice lacking CLPP.
METHODS: *ClpP* knockout ($ClpP^{-/-}$) female mice were compared to wild type (WT). Serial ovarian sections were stained with hematoxylin and eosin to assess follicle development. PMSG and hCG (5IU) injection +/- mating with WT males was performed to assess oocyte and embryo development. Oocyte mitochondrial redox activity (NADH and FAD generation) was determined non-invasively using fluorescence lifetime imaging microscopy (FLIM). Mitochondrial dynamics (fusion and fission) were evaluated using electron microscopy and expression of genes that regulate mitochondrial dynamics (mitofusin 1 [*Mfn1*]; mitofusin 2 [*Mfn*]; mitochondrial dynamin like GTPase [*Opa1*]) were assessed using quantitative RT-PCR.
RESULTS: $ClpP^{-/-}$ and WT mice ovaries had similar number of primordial, primary, secondary and antral follicles. However, $ClpP^{-/-}$ mice generated a significantly lower number of MII oocytes (7.8 vs 25, $p<0.05$) and 2-cell embryos (3 vs 24.4, $p<0.01$), and no blastocysts (0 vs 12.75, $p<0.05$). FLIM measurements showed altered redox activity ($p<0.01$) in $ClpP^{-/-}$ oocytes, which also had and increased amount of reactive oxygen species (ROS) ($p<0.01$). Electron microscopy revealed $ClpP^{-/-}$ oocyte mitochondria to be smaller (0.127 vs. 0.142 um2; $p<0.01$), with lower aspect ratio (length/width; 1.32 vs. 1.38; $p<0.05$), suggesting impaired fusion. This finding was associated with significantly decreased expression of *Mfn1*, *Mfn2*, and *Opa1* in $ClpP^{-/-}$ oocytes ($p<0.05$ for each).
CONCLUSIONS: Loss of mitochondrial proteostasis by homozygous deletion of *ClpP* results in female infertility and abnormal oocyte and embryo development, associated with impaired mitochondrial dynamics and energy metabolism. Future studies are required to determine whether this pathway is involved in infertility and/or age-related decline in reproductive potential.

O-150

Independent Serum Markers of Corpora Lutea Function After GnRH Agonist Trigger and Low Dose hCG in IVF. Leah A Kaye†, Erica Anspach Will†, Evelyn I Neuber, John C Nulsen, Claudio A Benadiva, Lawrence Engmann*. *University of Connecticut, Farmington, CT, USA.*
INTRODUCTION: Two strategies using low dose hCG have developed after GnRH agonist (GnRHa) trigger to rescue corpora lutea (CL) from early luteolysis and facilitate pregnancy without greatly increasing OHSS risk. However, CL function has not been evaluated after the use of such protocols. Our objective was to compare independent markers of CL function – serum 17α-hydroxyprogesterone (17OHP) and prorenin – in the luteal phase and early pregnancy after GnRHa trigger with adjuvant hCG at trigger (1000 IU) or 35 hours later (1500 IU) at vaginal oocyte retrieval (VOR).
METHODS: This is a secondary analysis of a prospective double-blind randomized trial. We enrolled 65 high responders, 30 of whom provided blood for this study. After a GnRH antagonist cycle, 10 women received hCG with their GnRHa trigger (dual trigger) and 20 received hCG at VOR. Serum levels of 17OHP and prorenin were collected after trigger, the day of VOR, and 5 (early luteal), 9 (mid-luteal), and 16 days (pregnancy test) after trigger, continuing weekly in pregnancy. $P<.05$ was significant using Mann-Whitney U and independent t-tests.
RESULTS: The groups had equivalent peak estradiol (2377±1066 pg/mL vs 2258±1027 pg/mL) and oocytes retrieved (18.0±6.8 vs 20.4±6.8). Three women had moderate OHSS, all after hCG at VOR.

In both groups, mean 17OHP peaked in the early luteal phase (18.98 ng/mL) with a decrease by mid-luteal phase (3.37 ng/mL) and subsequent increase only with pregnancy. Early luteal levels were higher after hCG at VOR compared with dual trigger (21.77±8.5 vs 13.68±11.0 ng/mL, p=0.04). All 17OHP levels in pregnancy were higher after hCG at VOR. In both groups, mean prorenin peaked the day of VOR (3.00 ng/mL), followed by a nadir at the mid-luteal phase (0.70 ng/mL). By day 16, patients with pregnancies had an increased prorenin, higher in those receiving hCG at VOR than at trigger (mean 2.22±1.6 vs 1.13±0.8, p=0.04).

**Figure(s) will be available online.*

CONCLUSIONS: The higher 17OHP and prorenin levels after adjuvant hCG at VOR suggests rescue of more CL, but may not be worth an increased risk for early or late-onset OHSS.

O-151

Creating a Hormonally Active 3-Dimensional Ovarian Follicle via a Microfluidic System. Mae W Healy†,[1] Shelley N Dolitsky,[1] Meera Raghavan†,[2] Alex Tillman,[2] Maria Villancio-Wolter,[2] Nicole Y Morgan,[2] Alan H DeCherney,[1] Erin F Wolff,[3] Solji Park*.[1] *[1]NIH, Bethesda, MD, USA; [2]NIH, Bethesda, MD, USA; [3]Celmatix, New York, NY, USA.*

INTRODUCTION: Roughly half of female pediatric cancer patients receive gonadotoxic therapy, resulting in diminished ovarian reserve and a shortened reproductive window. Prior studies show that 3-dimensional capsules simulating an ovarian environment are capable of in vitro maturation of early secondary oocytes, which can be cryopreserved for future use with ART . However, prior techniques have relied on low throughput methods that are not amenable to scaling for clinical purposes. We have created an artificial ovarian follicle with a microfluidic system to mimic a more supportive environment necessary for the maturation of murine primary oocytes.

METHODS: Using a microfluidic system with controlled syringe pump rates, 3-D capsules were created. Murine granulosa cells suspended in 0.8 mg/ml collagen + 0.05% alginate created the core of the capsule. Murine theca cells suspended in 2% alginate created the shell of the capsule. Capsules were placed in culture media, which was changed every 2-3 days. Viability testing, performed in triplicates, was performed on days 1, 8, 13, 21, and 26. Hormonal ELISA assays were performed on culture media collected on those same days and levels of estradiol, progesterone, and androstenedione were analyzed.

RESULTS: Confocal microscopy confirmed appropriate compartmentalization of fluorescent-labeled murine granulosa and theca cells to the inner capsule and outer shell, respectively. Viability testing showed that <15% cells present in capsules were dead up to 26 days after collection. Hormonal assays of culture media revealed preserved endocrine function, where estradiol levels ranged from 0.3 pg/ml to 17.3 pg/ml, progesterone levels ranged from 37.3 pg/ml to 1,257.8 pg/ml, and androstenedione levels ranged from 4.15 pg/ml to 12.49 pg/ml.

CONCLUSIONS: Using a microfluidic device amenable for adaptation for high throughput clinical grade uses, a 3-dimensional capsule with alginate and collagen was created to simulate an ovarian follicle. Within each capsule, murine granulosa and theca cells were spatially distributed, demonstrated long term viability, and were hormonally active. Further research is needed to evaluate if this environment can support the maturation of a primary oocyte, which has the potential for substantial clinical impact to the field of in vitro maturation for prepubescent patients.

O-152

Discovery-Based Proteomic Profiling of Tubal Fluid in Hydrosalpinx Reveals Candidate Biomarkers. Morgan E Lindsay†,[1] Elizabeth H Yohannes,[2] Avedis A Kazanjian,[2] Ryan J Heitmann,[1] Richard O Burney*.[1,2] *[1]Madigan Army Medical Center, Tacoma, WA, USA; [2]Madigan Army Medical Center, Tacoma, WA, USA.*

INTRODUCTION: Hydrosalpinx describes the intratubal acculumulation of fluid due to distal obstruction, and is associated with chronic pelvic pain, infertility, and early pregnancy loss. Current approaches to the detection of hydrosalpinx include dynamic studies that are expensive and associated with infectious morbidity and post procedural pain. A comparison of the proteome in healthy and hydrosalpinx affected Fallopian tubes is an important step toward identifying biologically plausible candidate markers.

METHODS: Tubal fluid was collected from women with surgically confirmed hydrosalpinx (n=5) and compared with cycle-phase matched tubal lavages from fertile women undergoing tubal reversal (n=7). Aliquots were normalized and processed for LC/MS. Automated protein identification and differential quantification in the comparison of samples was conducted using Proteome Discoverer, with proteins evidencing fold change greater than 1.5 and P-value adjusted for multiple comparison less than 0.05 considered signficant. Immunoblot of select differentially expressed proteins was performed.

RESULTS: Comparative proteomic analysis of hydrosalpinx fluid and lavage samples from fertile controls revealed 61 differentially expressed proteins. Proteins involved in the regulation of ROS were down-regulated in hydrosalpinx fluid, while proteins involved in inflammation were upregulated. Among the most upregulated proteins in hydrosalpinx was mesothelin, a secreted glycoprotein also increased in epithelial ovarian cancer. The upregulation of mesothelin in hydrosalpinx fluid was confirmed by immunoblot.

**Figure(s) will be available online.*

CONCLUSIONS: We observed striking differences in the proteomic composition of hydrosalpinx fluid compared to the secretome of healthy fallopian tubes. The increase in inflammation-associated proteins and other analytes such as mesothelin defines an array of potential candidates for serologic biomarker discovery. Further analysis is necessary to elicit the potential role for mesothelin in the pathophysiology of hydrosalpinx.

O-153

Oocyte/Embryo Utilization Rates and Disposition Decisions in Fertility Preservation Patients. Molly B Moravek,[1] Rafael Confino,[2] Angela K Lawson,[2] Kristin N Smith,[2] Susan C Klock,[2] Mary Ellen Pavone*.[2] *[1]University of Michigan, Ann Arbor, MI, USA; [2]Northwestern University, Chicago, IL, USA.*

INTRODUCTION: Cancer patients presenting for fertility preservation (FP) often question the likelihood of using frozen gametes and embryos in the future, and struggle with oocyte/embryo disposition choices at the time of cryopreservation, but there is little data to guide physician counseling. The objective of this study was to assess utilization of cryopreserved specimens and describe disposition decisions in an FP patient population.

METHODS: A retrospective chart review was performed on all female cancer patients who pursued FP at an urban medical center from 2006 to 2015. Chi-squared analysis was used to compare characteristics of patients who returned to use oocytes/embryos with those who did not.

RESULTS: Of 214 FP patients, 19 (8.9%) returned to use cryopreserved specimens, and 9/19 (47%) had live births, including 2 sets of twins. 8/19 patients (42%) elected to use a gestational carrier (GC). 15 patients (7%) experienced a spontaneous pregnancy, resulting in 13 live births. Average time from FP to return to use cryopreserved specimens was 1069 days (range 201-2274). Patients who returned to use oocytes/embryos were more likely to be married at the time of cryopreservation (84.2% vs 46.2%, p=0.002). There was no difference in age, AMH, or cancer type between patients who returned and those who did not. For oocyte/embryo disposition elected at the time of cryopreservation, 27.2% of patients chose to donate to research, 26.8% to continue cryopreservation, 9.9% to donate to another couple or family member, 4.3% to discard, and elections were unknown or undocumented in 32% of patients.

CONCLUSIONS: Few FP patients returned to use cryopreserved oocytes or embryos, but live birth rate was reasonable in those who did. Given the resource-intense nature of cryopreservation for FP, more research is needed to understand why the utilization rate is so low, and better predict which patients will return for cryopreserved specimens. Additionally, a large proportion of FP patients needed a GC, suggesting that providers should counsel women about this possibility at the time of cryopreservation, and ensure appropriate infectious disease testing is performed. Finally, oocyte and embryo disposition decisions among this population are particularly important given the low specimen utilization rate.

O-154

Utility of PGS to Determine the Need for Repeat Embryo Cryopreservation Cycles and Improve Fertility Preservation Success in Cancer Patients. Ozgur Kan†, Kutluk Oktay. *New York Medical College, Valhalla, NY, USA.*

INTRODUCTION: It is often assumed that the embryos cryopreserved from cancer patients would ensure fertility preservation. However, without the knowledge of embryo normalcy and with the significant threat of losing ovarian function after chemotherapy, this is a risky assumption. If the aneuploidy status is known among the embryos cryopreserved, patients will have the option to repeat the cycle or resort to alternative FP technologies. Here we hypothesized that the utility of PGS will ensure FP to cryopreserve euploid embryos in cohort of women with breast cancer.

METHODS: Twenty fertility preservation cycles from 11 women with stage I-II breast cancer were included. Ovarian stimulation was performed with an antagonist protocol utilizing aromatase inhibitors plus rFSH. All biopsies were performed at blastocyst stage and subjected to aCGH for PGS. The main outcome measures were the number euploid embryos and the percentage of cycles that were repeated for all-aneuploidy and resulted in the recovery of at least one euploid embryo.

RESULTS: Mean age at cryopreservation was 40.1±2.73 years. Average AMH level was 1.32 ng/mL, AFC 7.81±5.21 and mean total FSH dose per cycle was 2423.5±1027.39 IU. In 20 FP cycles, a total of 274 oocytes were retrieved (13.7±8.42 per cycle) and 75 resultant blastocysts were biopsied (3.75±2.21/cycle). Of the biopsied blastocysts, 9 were found to be euploid (12%), 59 had abnormal chromosomal status (78.6%) and 7 (9.3%) were inconclusive-3 were rebiopsied. Of the 3 rebiopsied embryos, 2 were found to be euploid, bringing the total euploid yield to 14.6%. Of the 20 cycles, 12 (60% of cycles in 72.7% of all patients) resulted in all-aneuploid embryos. Based on the findings of all-aneuploidy, we performed 6 repeat cycles in 5 women. This resulted in at least one euploid embryo (range 1-2) in 4/6 cycles. Overall, the probability of obtaining a euploid embryo increased from 27.2% to 41.1% on second FP cycle, but plateaued on the third (40%).

CONCLUSIONS: Routine PGS may improve fertility preservation success and aid in the decision making for repeat embryo cryopreservation cycles. If first cycle does not result in a euploid embryo, the cycle should at least be repeated once to increase the likelihood of cryopreserving a chromosomally normal embryo.

O-155

Cytoskeletal Tension and YAP Regulation Modulate Mechanosensation in Oogonial Stem Cells. Julie A MacDonald†, Dori C Woods, Jonathan L Tilly. *Northeastern Univeristy, Boston, MA, USA.*

INTRODUCTION: Recent work has shown the sensitivity of oogonial stem cells (OSCs) to the composition of the extracellular environment as well as applied mechanical force. We propose a mechanism of action to modulate this mechanosensation, from receiving the extracellular stimuli at the cell surface via integrin receptors, propagating the signal through the cytoskeleton, and resulting in transcriptional activity mediated by Yes-associated protein (YAP), all of which enhance *in vitro* oogenesis.

METHODS: Feeder cell-free cultures of OSCs (passage 30-35) were propagated with small-molecule RGD peptides to antagonize integrin receptor binding with the tissue culture substratum coated in 10 μg/cm^2 of an equal mixture of collagen type I and IV, and assayed for the formation of *in vitro* derived (IVD) oocytes. To evaluate cytoskeletal tension in response to mechanical strain, OSC cultures were subjected to uniaxial cyclic strain (10% elongation, 0.1 Hz, 24 hours) using a Flexcell FX-5000T in the presence of ROCK-inhibitor Y-27632 (10 μM) and analyzed by confocal microscopy for the formation of actin stress fibers. RNA was isolated to evaluate expression levels of *Stimulated by retinoic gene 8 (Stra8)* by quantitative PCR. Western blots were used to quantitatively evaluate expression levels of YAP, as well as levels of YAP phosphorylation. All experiments were replicated 3 times, and statistical significance was determined by ANOVA and Student's *t*-test.

RESULTS: Integrin receptor antagonism by RGD-peptides, compared to control OSC cultures, reduced expression levels of *Stra8,* and ameliorated matrix-mediated increases in IVD oocyte formation (-30%, n=3, P<0.05). Treatment with Y-27632 prevented the formation of F-actin stress fibers. OSCs cultured on collagen matrices for 48 hours show decreased levels of YAP phosphorylation (-45.7%) when compared to control cultures, as well as decreased levels of YAP phosphorylation following mechanical stimulation (-40.8±0.05% at 12 hours post-stretch, n=3).

CONCLUSIONS: In summary this work details the ability of mechanical stimuli to impact OSC differentiation. The capacity of OSCs to sense and respond to the microenvironment *in vivo* has broad implications for the impact of age-related changes of ovarian tissue. Targeting this mechanism provides opportunities to potentially overcome environment-dictated quiescence of OSCs and restore oogenesis in the aging ovary. Supported by NIH R37-AG012279.

O-156

Identification of Novel Epigenetic Reprogrammed Genes in Myometrial Stem Cells Developmentally Exposed to Endocrine Disrupting Chemicals. Qiwei Yang,[1] Lindsey S Treviño,[2] Aymara Mas,[1] Michael P Diamond,[1] Cheryl Lyn Walker,[2] Ayman Al-Hendy.[1] [1]*Augusta University, Augusta, GA, USA;* [2]*Baylor College of Medicine, Houston, TX, USA.*

INTRODUCTION: Uterine fibroids (UF) are monoclonal tumors arising from aberrant stem cells in the myometrium. We have identified Stro-1$^+$/CD44$^+$ myometrial stem cells (MSCs) capable of self-renewal and regeneration of myometrium tissues upon xenotransplantation, and demonstrated that early life exposures to endocrine disrupting chemicals (EDCs) reprogrammed estrogen responsive genes (ERGs) in MSCs. However, little is known about the reprogramming of non-ERGs in response to developmental exposure to EDCs which may contribute to UF development.

METHODS: Female newborn Eker rats were treated subcutaneously with vehicle (VEH) or 10 μg of diethylstilbestrol (DES) on postnatal days 10-12, a critical period of uterine development. MSCs were isolated from 5 month-old myometrium tissues (N=5 for each group). RNA-seq, ChIP-seq (anti-H3K4me3 antibody) and bisulfite next generation sequencing (NGS) were performed. ChIP- and q-PCR were used to validate ChIP- and RNA-seq data respectively. Fisher's exact, Student T and Wilcoxon test were used for statistical analysis.

RESULTS: RNA-seq showed that 9.52% of genes were upregulated in DES-MSCs compared to VEH-MSCs. Eight of non-ERGs (*Grem2, Ptgis, Slit3, Cpne8, Grb14, Synm, Ptprk and Fam111A)* are involved in important pathways (e.g. synthesis of steroids, cell growth, and cell cycle) and were significantly upregulated in DES-MSCs ($p<0.05$). Bisulfite NGS demonstrated that 7/8 genes showed hypomethylation within their CpG islands in DES-MSCs. Wilcoxon test analysis showed significantly different DNA methylation levels of 126 CpG sites for 8 genes between DES- and VEH-MSCs ($p<0.05$). Notably, all of the 71 CpG sites for 5 genes (*Grem2, Ptgis, Slit3, Grb14, Ptprk),* 24/25 and 10/11 CpG sites for *Synm and Cpne8*,respectively,showed decreased methylation levels in DES-MSCs. The methylation status of these 7 non-ERGs were inversely correlated with gene expression and H3K4me3 enrichment ($p<0.05$). Moreover, ChIP-seq exhibited increased H3K4me3 enrichment at the promoter regions of all 8 non-ERGs in DES-MSCs, and a significant correlation with their RNA expression ($p<0.05$).

CONCLUSIONS: These data suggest a novel paradigm whereby developmental EDC exposure increases the risk of UF by reprograming the epigenome of MSCs towards a pro-fibroid epigenomic landscape in non-ERGs genes.

O-157

Maternal Mesenchymal Stem Cell Administration Alleviates Intrauterine Inflammation-Induced Perinatal Brain Injury Through CD8$^+$ T Cell Suppression in Placenta. Li Xie†,[1,3] Hongxi Zhao,[1,4] Jun Lei,[1] Lu Zong,[1,5] Hattan Arif,[1] Michael McLane,[1] Irina Burd*.[1,2] *[1]Johns Hopkins University School of Medicine, Baltimore, MD, USA; [2]Johns Hopkins University School of Medicine, Baltimore, MD, USA; [3]Northwestern Polytechnical University, Xi'an, Shaanxi, China; [4]Tangdu Hospital, Xi'an, Shaanxi, China; [5]Xi'an Jiaotong University, Xi'an, Shaanxi, China.*

INTRODUCTION: Using a model of intrauterine (IU) inflammation, we have previously shown that maternal administration of mesenchymal stem cells (MSCs) decreases perinatal brain injury and improves behavioral outcomes. The aim of this study was to determine immune mechanisms by which bone marrow derived-MSCs ameliorate perinatal brain injury, induced by lipopolysaccharide (LPS) IU injection.

METHODS: A mouse model of inflammation-induced perinatal brain injury at embryonic (E) day 17 was utilized (n = 119). Bone-marrow MSCs were isolated from green fluorescent protein (GFP) transgenic mice and administered IP. To deplete CD8$^+$ T cells, 200 mg anti-CD8 antibody was administered IP at E14 and E16. Flow cytometry of mesenchymal stem cell and CD8$^+$ markers was used for confirmation. CD-1 dams were assigned to 6 groups: PBS+PBS, PBS+MSCs, LPS+PBS and LPS+MSCs, LPS+CD8 depletion (LPS+DEP), PBS+DEP. Fetal brain and placentas were collected at 6h after LPS administration. Cell trafficking *in vivo* was examined by Bruker Imager. Immunecards (qPCR) were utilized to evaluate inflammatory marker expression in placenta. Cliff aversion behavioral test was performed at PND5.

RESULTS: GFP-MSCs were confirmed to be CD44$^+$, Sca-1$^+$ and CD45$^-$,CD34$^-$, CD11b$^-$ and CD11c$^-$. LPS+PBS placentas were found to have a higher fraction of CD8$^+$ T cells ($P < 0.05$). Maternally administered-MSC were found to home to placenta, following LPS exposure, with a decreased fraction of CD8$^+$ T cells (similar to LPS+DEP), and in contrast to LPS+PBS ($P < 0.05$). These data were confirmed with qPCR analysis. Furthermore, LPS+DEP and LPS+MSC demonstrated improved performance on neurobehavioral testing as compared to LPS+PBS ($P < 0.05$).

CONCLUSIONS: Maternal MSC treatment alleviated adverse neurological outcomes of pups exposed to IU inflammation through immunomodulation at maternal-fetal interface. Our data support CD8$^+$ T cells' role in mediating perinatal brain injury and a mechanisms for MSC brain injury rescue.

O-158

Trophoblast Spheroid Model Derived from hiPSCs to Study Trophoblast Functions Under Pathological-Like Conditions. Mehboob Ali,[1] Mark Hester,[1] Lisa Zhao,[1] Irina A Buhimschi.[1,2] *[1]Nationwide Children's Hospital, Columbus, OH, USA; [2]The Ohio State University College of Medicine, Columbus, OH, USA.*

INTRODUCTION: Dysregulated trophoblast invasion and abnormal secretory function are known to associate with pregnancy complications such as preterm birth, preeclampsia and IUGR. Studies on 2nd and 3rd trimester human placenta with pathologic affections, placentas at term and animal models are incapable in deciphering molecular events deregulated early in placental development or in response to fluctuating environmental stressors. We aimed to fill this gap by developing a human trophoblast spheroid (TS) model derived from induced pluripotent stem cells (hiPSC).

METHODS: Human episomal-derived iPSCs were maintained under feeder-free and defined, serum free medium at 37°C and 5% CO_2 for 10 days to generate embryoid bodies (EBs). EBs were then grown into TS as adherent culture (2D differentiation) or encapsulated into matrigel droplets (3D differentiation) using BMP4 and inhibitors of TGFβ & FGF2 signaling for 11 days and were challenged with endotoxin (LPS, 50-100 ng/ml for 24 h on day 6 of culture) to mimic an inflammatory condition. Morphology, surface marker expression, release of prototype placental hormones, and invasive phenotypes were assessed using phase contrast microscopy, western blot, ELISA and confocal microscopy in media supernatants, cell lysate and TS bodies at different days.

RESULTS: TS develop three distinct cellular zones which displayed hallmarks of 1) the core zone, representative of cytotrophoblast 2) the confluent zone, representative of villous trophoblast (cyto- and syncytiotrophoblast;); and lastly 3) the migratory zone, (large cells with prominent nucleus and invasive structures characteristic of EVT). Trophoblast-specific transcription factor, CDX2, invasive trophoblast phenotypes surface markers, placenta growth hormones, human corticotrophin hormone (CRH) and human chorionic gonadotropin (hCG) were observed to change over the time of growth in sequential manner recapitulating 1st trimester human placental development. LPS challenge increased both CRH and HCG in culture medium.

CONCLUSIONS: Our data demonstrated that hiPSC-derived TS 2D and 3D cultures exhibit temporal and spatial trophoblast diversity associated with expression of surface and functional markers and growth hormones. Further studies will validate the model as a mimic for first term placenta trophoblast diversity and function.

O-159

High Throughput Screen (HTS) Using Viable Fluorescent ESC Reporters of Stressed-Forced Differentiation of the First Lineage. Erica D Louden, Elizabeth E Puscheck, Quanwen Li, Kang Chen, Daniel A Rappolee*. *Wayne State University, Detroit, MI, USA.*

INTRODUCTION: To validate stress-forced potency decrease and differentiation increase in fluorescent reporter mouse Embryonic Stem Cells (ESCs; Rex1-RFP/**r**ed **f**luorescent **p**rotein reports potency status, PDGFRa-GFP/**g**reen **f**luorescent **p**rotein reports first lineage differentiation status) despite potency-maintaining culture conditions. We test ESCs for first lineage differentiation using our High Throughput Screen (HTS) for toxicology stress for pharma and IVF and validate the PDGFRa-GFP ESCs using co-markers of first lineage differentiation (Dab2), laminin and direct GFP tests in dose- and time-dependent responses.

METHODS: ESC transgenic GFP knocked into a PDGFRa are regulated by the PDGFRa promoters: PDGFRa-GFP ESCs were tested for stress-forced differentiation. A key test was stress-forced differentiation in the presence of LIF, which maintains proliferation and potency. Microplate, Immunofluorescence and Immunoblot assays tested PDGFRa-GFP ESC responses and quantified with Simple PCI. Dose and kinetic responses were tested using hyperosmotic sorbitol as a positive stress control. Retinoic acid (RA) is a first lineage inducer used as a positive control.

RESULTS: Hyperosmotic stress +/- LIF initiated decreased ESC and potency and increased differentiation as shown by Hoechst staining and by microplate reader, co-localization of PDGFRa-GFP, Dab2 and laminin co-marker for first differentiated lineage. Microplate reader assays for stress-induced PDGFRa-GFP differentiation were corroborated by Immunoblot for Dab2 and GFP and showed similar dose responses. Preliminary flow cytometric results suggest that 1-5% of Pdgfra-GFP cells are bright after 3day induction with retinoic acid, LIF- or sorbitol despite LIF and that another 10-15% of intermediate bright GFP cells are induced.

CONCLUSIONS: Stress decreases stem cell growth and the response to this "runting" is forcing differentiation of remaining ESCs hypothetically to provide sufficient nutrient-acquiring function from fewer cells. Rex1-RFP potency reporter decrease and PDGFRa-GFP differentiation reporters increase with strong stress exposures. These two assays should thus provide complementary HTS for measuring pharma and IVF-ART stress.

O-160

Endothelial Progenitor Cells Contribute to Vasculogenesis of the Pregnant Mouse Uterus. Reshef Tal†, Dong Dirong, Shafiq Shaikh, Ramanaiah Maimillapalli, Hugh S Taylor*. *Yale School of Medicine, New Haven, CT, USA.*

INTRODUCTION: Angiogenesis plays an important role in cyclic endometrial growth, implantation and maintenance of pregnancy. Previously, bone marrow (BM)-derived endothelial progenitor cells (EPCs) have been shown to contribute to endometrial vasculature in a process termed vasculogenesis, but their role in pregnancy is unknown.

METHODS: To investigate the contribution of BM-derived EPCs to the vascularization of the pregnant uterus, we utilized transgenic

mice expressing GFP (green fluorescent protein) reporter gene under regulation of the Tie2 endothelial-specific promoter as BM donors in a non-gonadotoxic bone marrow transplantation (BMT) model. Submyeloablation was induced by 5-fluorouracil (5-FU) administration to wild-type FVB/N female mice (125 mg/kg), followed by reconstitution with BM from FVB/N-Tie2/GFP donors. Following 1-month recovery, Tie2-GFP BM–transplanted mice were bred with proven fertility male mice and sacrificed on various days of gestation (ED6.5, ED10.5, ED13.5, ED18.5 and postpartum). Bone marrow-transplanted non-pregnant mice and saline-injected pregnant mice served as controls (n= 5-6/group). Implantation sites of uteri were collected and analyzed by flow cytometry, immunohistochemistry and immunofluorescence.

RESULTS: While no GFP-positive cells were found in non-pregnant or early pregnant uteri of BM-transplanted mice, GFP-positive EPCs were first detected in the pregnant uterus on ED13.5 (1.14% of total uterine cells) and increased as pregnancy progressed, peaking on ED18.5 (1.42%) followed by decrease in the postpartum period (0.91%) ($p<0.001$ for ED13.5, ED18.5 and postpartum vs. other groups). The percentage of endothelial cells that were BM-derived out of the total endothelial cell population of the implantation site (GFP+CD31+/CD31+) was 9.3%, 15.8% and 6.1% on ED13.5, ED18.5 and postpartum, respectively. Immunohistochemical staining with GFP antibody demonstrated that EPCs incorporated into decidual vasculature, and immunofluorescence showed that GFP-positive EPCs colocalized with CD31 in blood vessels endothelium of uterine implantation sites, confirming their endothelial differentiation.

CONCLUSIONS: Our findings indicate that BM-derived EPCs contribute to the vascularization of the pregnant uterus and that this contribution increases as pregnancy progresses.

T-001

Uterine Contraction Parameters Before and After Epidural Analgesia. Rebecca Benfield,[1] Du Feng,[1] Jan Salstrom,[2] Melydia Edge,[3] Denise Brigham,[3] Edward Newton*.[3] *[1]University of Nevada, Las Vegas, NV, USA; [2]Dartmouth-Hitchcock Medical Center, Lebanon, NH, USA; [3]East Carolina University, Greenville, NC, USA.*

INTRODUCTION: In 2011-2012, epidural or spinal analgesia was used for pain by 67% of the women who gave birth in the US. Risks associated with epidural analgesia, include trends toward prolonged first stage labor, disturbances in labor progress, and increased incidences of oxytocin augmentation up to two fold.

We measured change in uterine contraction peak amplitude intensity at baseline and 30 and 60 min post epidural test dose.

METHODS: Retrospective review of 3025 charts, identified 24 healthy women (17 nullipara, 7 multipara, age range =18 ~ 28 yrs) at term with Intrauterine Pressure Catheters (IUPCs) who received epidural only (n=15) or combined epidural/intrathecal (n=9) labor analgesia. Exclusion criteria included magnesium sulfate therapy or chorioamnionitis. Twenty women received pitocin and four did not. The baseline (BL) epoch began up to 60 min prior to the IV bolus initiation: Epoch length varied (all had at least 4 contractions). Amplitude (mmHg), i.e. intensity, was extracted from the monitor strip grid. Measurements were cross-checked by an independent observer. Data were analyzed using hierarchical linear modeling.

RESULTS: Women who received epidural only analgesia had an average BL contraction intensity of 59 (SD = 18), which dropped to the lowest level at 30 min (M=57, SD=19), and remained low at 60 min (M=57, SD=19). Women who received combined epidural labor analgesia show a similar but slightly different pattern of change in contraction intensity, having an average BL contraction intensity of 57 (SD = 15), which dropped to the lowest level at 30 min (M=55, SD=15), but increased at 60 min (M=57, SD=15). The overall effect is significant for women who received epidural only labor analgesia (b= -5.438, $\chi^2(1)=5.90$, $p = .015$), but not significant for women who received combined epidural/intrathecal labor analgesia (b=-3.255, $\chi^2(1)=2.58$, $p = .108$).

CONCLUSIONS: Despite the small sample size, both types of epidural analgesia decreased uterine contraction intensity. Contraction intensity returned to baseline at 60 min with combined epidural/intrathecal analgesia but remained decreased with epidural only analgesia. The addition of intrathecal narcotic modified the negative effects of local anesthetic.

T-002

Histologic Chorioamnionitis Induces Higher Lipid Oxidative Damage in Amniochorion Membranes from Pregnancies Complicated by Spontaneous Prematurity. Laura F Martin†,[1] Natália P Moço,[1] Jossimara Polettini,[2] Moisés D de Lima†,[1] Hélio A Miot,[1] Márcia G da Silva*.[1] *[1]Botucatu Medical School, São Paulo State University, Botucatu, São Paulo, Brazil; [2]The University of Western São Paulo , UNOESTE, Presidente Prudente, São Paulo, Brazil.*

INTRODUCTION: Despite of multifactorial etiology of spontaneous preterm birth, the exacerbation of maternal inflammatory response resulting from intra-amniotic infection (IAI) is present in 25-40% of preterm pregnancies. Histologic chorioamnionitis (HC) is defined by the presence of polymorphonuclear cells (PMNs) infiltrate in the amniochorion membranes in response to bacterial IAI. PMNs activation trigger an antimicrobial mechanism with generation and release of reactive oxygen species (ROS), leading to exacerbation of oxidative stress (OS). Additionally, the OS can initiate intracellular signaling cascade that increase proinflammatory mediators production. Thus, we aimed to evaluate oxidative damage and antioxidant capacity in amniochorion membranes from preterm pregnancies in the presence of HC.

METHODS: Preterm group was composed of 27 pregnant women who presented preterm labor with intact membranes (PTL) and 27 pregnant women who presented preterm premature rupture of membranes (pPROM). Term group was composed of 30 normal pregnant women in labor. Groups were subdivided according to infiltrate inflammatory status. Protein oxidative damage (3-NT production) was assayed by ELISA, lipid oxidative damage (MDA production) was analyzed using TBARS Assay Kit, and total antioxidant capacity (TAC) was assessed using Antioxidant Assay Kit. Generalized Linear Models were employed to compare 3-NT, MDA and TAC among the groups.

RESULTS: There was no statistically significant difference in 3-NT levels among the groups regardless of the HC status. MDA levels were statistically higher in PTL group [0.32 (0.15-0.58)] than pPROM [0.12 (0.09-0.27), p=0.00] and term [0.13 (0.06-0.38), p=0.007] groups. In addition, the TAC were higher in PTL [0.16 (0.09-0.24)] when compared to pPROM [0.01 (0.00-0.13), p=0.05] and term [0.05 (0.00-0.14), p=0.05] groups regardless HC status. In the presence of HC PTL group [0.36(0.31-0.41] showed significantly higher MDA concentration than pPROM [0.12 (0.08-0.22), p=0.02] and term [0.08 (0.04-0.24), p=00.5] groups. MDA levels did not differ among the groups in the absence of HC.

CONCLUSIONS: Lipid oxidative damage exacerbation is associated with HC in amniochorion membranes in preterm labor.

Support CNPq 142419/2013-3.

T-003

Use of Mass Spectrometric Measurements to Determine Differential Expression of Prostaglandins and Prostamides in Amniotic Fluid of Women with Preterm Labor Delivering at Term and Women at Term in Labor. Hassendrini N Peiris†,[1] Robert J Romero,[2,3] Kanchan Vaswani,[1] Sarah Reed,[1] Piya Chaemsaithong,[2] Sonia Hassan,[2] Eli Maymon,[2] Murray D Mitchell.[1] *[1]University of Queensland, Herston, QLD, Australia; [2]Wayne State University, Detroit, MI, USA; [3]National Institutes of Health, Detroit, MI, USA.*

INTRODUCTION: An increase in intrauterine prostaglandin production from arachidonic acid is critical for the onset and progression of labour in women. Endocannabinoids can act as substrates for enzymes of the prostaglandin biosynthetic pathways to generate other related compounds such as prostamides. The related end products are indistinguishable by radioimmunoassay due cross-reactivity's of the antisera. However, mass spectrometry is able to separate these compounds and allows the accurate and relative expressions of prostaglandins to be made in a single sample. **Aim:** To explore the use of mass spectrometric measurements in

identifying the relative expressions of prostaglandins in amniotic fluid of women with preterm labor delivering at term (PTL-TD; n=20) and women at term in labor (TDL; n=28).

METHODS: Standards and samples were subjected to an extraction in methanol/formic acid containing internal standards (PGE_2-d4, $PGF_{2\alpha}$-d4, PGFM-d4). Standards and samples were measured by LC-MS/MS. Following normality testing data were log transformed (Mean±SD)and Mann Whitney U test was used for analysis.

RESULTS: The mean gestational age at delivery was similar in PTL-TD (38.79±1.3 weeks) and TDL (39.25±1.26 weeks). Amniotic fluid concentrations (Mean±SD)of PGE_2 (12.38±1.32), $PGF_{2\alpha}$ (11.47±1.66), PGFM (11.87±1.32) in the TDL group were significantly higher than in the PTL-TD group: PGE_2; (5.9±1.12), $PGF_{2\alpha}$; (7.5±0.63), PGFM; (7.13±0.55). ($p<0.05$).

CONCLUSIONS: Using mass spectrometric measurements we describe the differential expression of prostaglandins in the amniotic fluid of women with preterm labor delivering term and women at term in labor. We propose that separation of these products using mass spectrometry might reduce variability in current results and lead to potential utilisation for their measurement in the diagnosis of preterm labor.

T-004

Fetal Sex Differences in Prediction of Spontaneous Preterm Birth. Leonardo M Pereira,[1] Kim A Boggess,[2] George R Saade,[3] Terry K Morgan,[1] Ashoka D Polpitiya,[4] ChienTing Hsu,[4] Amir J Lueth,[4] Angela C Fox,[4] Tracey C Fleischer,[4] J Jay Boniface,[4] Durlin E Hickok,[4] Todd L Randolph.[4] *[1]Oregon Health & Science University, Portland, OR, USA; [2]University of North Carolina, Chapel Hill, NC, USA; [3]University of Texas Medical Branch, Galveston, TX, USA; [4]Sera Prognostics, Salt Lake City, UT, USA.*

INTRODUCTION: Prior studies show that spontaneous preterm birth (sPTB, <37 weeks) is more common in women carrying male compared to female fetuses. One cause for the higher rate of sPTB in males may include fetal sex differences in placental gene expression. Insulin-like growth factor binding protein 4 (IBP4) and sex hormone binding globulin (SHBG) are expressed early in pregnancy and may reflect placental development. We hypothesized that the outcome of the sPTB predictor (log of the ratio of levels of IBP4 to SHBG) would be influenced by fetal sex.

METHODS: This is a secondary analysis of the PAPR trial that enrolled 5501 women with singleton pregnancies from eleven U.S. centers. We analyzed blood samples by the sPTB predictor assay from 411 asymptomatic subjects (82 sPTB cases, 329 term controls; 1 to 4 cases to controls) from the gestational age of 17 0/7-21 6/7 weeks. High predictor score was defined as greater than -1.42. Differences in fetal sex proportions by predictor score among sPTB subjects were tested using a Fisher's Exact Test. Pregnancy duration by fetal sex was evaluated by a Log-rank test, censoring at 37 weeks.

RESULTS: Among sPTB subjects, a higher proportion of males than females have a high predictor score (79% vs. 51%, p = .02). Among subjects with a high score, Log-rank test showed that males delivered earlier than females (p = .04).

CONCLUSIONS: The analysis demonstrates that male sPTB cases are more likely to have a high preterm predictor score than are females. Also, among those with high score, gestational age at birth for males was less than for females. Since the proteins in the classifier reflect placental development, higher predictor scores may reflect a greater degree of placental insufficiency, lending support to the theory that sPTB in male fetuses is more frequently associated with compromised placentation.

T-005

Biaxial Mechanical Properties of the Murine Uterus and Cervix. Cassandra Conway,[1] Laurephile Desrosiers,[2] Leise Knoepp,[2] Kristin Miller*.[1] *[1]Tulane University, New Orleans, LA, USA; [2]Ochsner Clinical School, New Orleans, LA, USA.*

INTRODUCTION: Preterm birth is the leading cause of infant morbidity and mortality. Two potential causes of preterm birth, uterine overstretch and cervical insufficiency, are hypothesized to arise, in part, from altered tissue mechanical properties. The evolving tension on the uterus and cervix from the growing fetus is determined by the extracellular matrix proteins (ECM) which dictate the mechanical properties of a tissue. For example, the ECM constituent elastin provides resilience and recoil to tissues. Relationships between ECM proteins and mechanical function, however, are not well established in the uterus and cervix. Hence, elucidating these relationships may aid in the formation of predictive models of preterm birth with mechanical etiology in order to design effective intervention strategies. Therefore, the objective of the study is to measure the regional biaxial mechanical properties of the murine uterus and cervix pre- and post-elastase digestion. We hypothesize that the vaginal cervix will demonstrate decreased compliance and the greatest change in behavior post-elastase treatment compared to the uterus and uterine cervix.

METHODS: Uteri and cervices from female C57/BL/6 mice at 4-6 months of age (IACUC approved, n=5 at estrus) were subjected to pressure-diameter tests at three different axial extensions and to axial force-length tests at four different pressures. Specimens were then intraluminally exposed to 1mL of pancreatic elastase and the tests were repeated. A bilinear curve fit was applied to the local stress-strain data to quantify the moduli in the toe- and linear-regions for each test. Two-way ANOVAs (location, treatment) were used to identify difference in geometry and mechanical properties.

RESULTS: Mechanical properties of elastase treated samples for the internal and external os were found to be significantly different than the properties of the treated uterus. Stress differed significantly for the treated vaginal cervix against the treated uterus.

CONCLUSIONS: Significant differences between location and treatment suggest that there are regional variations for the role of elastin. Our methods demonstrated a way to biomechanically phenotype the murine uterus and cervix, as well as the role of each ECM protein. We submit that the data from this study can be leveraged to develop predictive models of preterm birth in order to improve clinical strategies.

T-006

Exosomal Profile in Amniotic Fluid Is Associated with Parturition Signal. Christopher L Dixon,[1] Vyjayanthi Kinhal,[2] Carlos Palma,[2] Kechichian Talar,[1] Rheanna Urrabaz-Garza,[1] Poorna R Menon,[1] Carlos Salomon,[2] Ramkumar Menon.[1] *[1]The University of Texas Medical Branch, Galveston, TX, USA; [2]The University of Queensland, Brisbane, Australia.*

INTRODUCTION: While there is considerable contemporary interest in elucidating the role of exosomes in normal and adverse pregnancies and their utility as biomarkers and therapeutic interventions, the characterisation of exosomes in amniotic fluid (AF) has never been done. The aim of this study was to determine the concentration of exosomes present in AF in women with different signal of parturition.

METHODS: Amniotic fluid samples were collected by transvaginal amniocentesis from group 1: term not-in labor (TNIL); group 2: term in labor (TL), group 3: Preterm premature rupture of membranes (pPROM); and group 4: preterm birth (PTB). Exosome were isolated by differential buoyant density centrifugation and characterised by morphology, enrich of exosomal proteins and size distribution by electron microscopy, western blot and nanoparticle tracking analysis, respectively. The exosomal protein profile was analysed by Liquid Chromatography (LC)/ Mass Spectrometry (MS) LC-MS/MS on a 5600 Triple TOF mass spectrometer (AB Sciex, Framingham, U.S.A.).

RESULTS: Exosomes were identified as spherical vesicles, with a typical cup-shape and diameters around of 100 nm and positive for enrich exosomal proteins CD63 and TSG101. We did not find different in the physical properties of isolated exosomes between the groups. The total number of exosomes (exosomes/ ml fluid) present in AF was significantly lower in PTB (2.4×10^{10}) compared to TNIL (4.2×10^{10}), TL (5.8×10^{10}) and PROM (4.7×10^{10}). Interestingly, the number of total exosomes was significantly higher ~1.4-fold in TL compared to TNIL. Exosomes positive for PLAP (placental and amnion specific marker) was present in exosomes isolated from AF. The ratio PLAP/total exosomes was significantly higher ~7.2-fold and ~45-fold in PTB compared to TL or pPROM, and TNIL, respectively. MS/MS analysis identified over 100 different exosomal proteins associated with signals of parturition.

CONCLUSIONS: To the best of our knowledge, this study is the first to report exosomes characteristics in AF. Exosomes specific changes in AF might be used to understand the mechanism responsible for human parturition.

T-007

Tumor Necrosis Factor-α and Interferon-γ Promote Preeclampsia-Related Decidual Inflammation by Synergistically Inducing Decidual Cell Expressed Inflammatory Cytokines via STAT5 Signaling. Ozlem Guzeloglu-Kayisli, Nicole Teal, Nihan Semerci, Kellie Larsen, Rachel Sinkey, Sefa Arlier, Frederick Schatz, Umit Kayisli, Charles Lockwood. *Univ. of South Florida, Morsani College of Medicine, Tampa, FL, USA.*

INTRODUCTION: Preeclamptic decidua displays excess macrophages/dendritic cells and impaired natural killer (NK) cell numbers/functions. We found synergistic induction of the NK cell–recruiting chemokine CXCL10 (aka IP-10) in decidual cell (DC) cultures by tumor necrosis factor (TNF)-α and interferon (IFN)-γ co-treatment. Markedly higher CXCL10 levels in 1st trimester sera of women who later develop preeclampsia and in 3rd trimester preeclamptic decidua suggest that this synergistic impact on decidual inflammation occurs during very early pregnancy and persists. We posit that TNF-α+IFN-γ synergistically induce a broad range of inflammatory genes mediated by specific signaling pathway(s) whose identification will provide novel therapeutics to block preeclamptic decidual inflammation.

METHODS: First-trimester DC cultures (n=3) treated 6 h with estradiol (E_2) or E_2+medoxyprogesterone acetate (MPA)±TNF-α or IFN-γ alone or together were evaluated by Microarray followed by GeneSpring and Ingenuity Pathway Analyses (IPA). Immunoblotting assessed JAK2, STAT5 and NFκB activation (phosphorylation) levels. qRT-PCR and ELISA measured the impact of STAT5 and JAK2 inhibitors on synergistically induced cytokine levels. Statistical analysis used One-way ANOVA/post hoc Tukey test.

RESULTS: Microarray identified 22 genes synergistically increased up to 150-fold by TNF-α+IFN-γ *vs.* TNF-α or IFN-γ alone ($p<0.0005$). 8 of these genes encode pro-inflammatory/leukocyte recruiting cytokines, with 5 genes confirmed by qRT-PCR. Microarray also determined that TNF-α+IFN-γ co-treatment specifically increased total JAK2, STAT5 and p65 signaling proteins. IPA predicted JAK2, STAT5A and NFκB over-activation by TNF-α+IFN-γ treatment ($p<0.01$). Immunoblotting detected increased phospo-JAK2 and STAT5a levels and prolonged NFκB activation by TNF-α+IFN-γ *vs.* control or TNF-α and IFN-γ alone. A specific STAT5, but not JAK2 inhibitor, completely blocked TNF-α+IFN-γ induced synergistic impact on cytokine production ($p<0.02$).

CONCLUSIONS: These results suggest: 1) TNF-α+IFN-γ mediated synergistic increase in inflammatory cytokine expression amplifies decidual inflammation and impairs decidual leukocyte recruitment; 2) the potential therapeutic benefit of STAT5 inhibitors in preventing preeclampsia-related inflammation.

T-008

Development of a Novel Co-Culture Model Studying Maternal/Fetal Interactions Driving Uterine Transformation for Labour. Kelycia B Leimert†,[1] Angela Messer†,[2] Theora Gray†,[2] Megan Malach†,[2] Xin Fang,[2] David M Olson*.[1,2] *[1]U Alberta, Edmonton, AB, Canada; [2]U Alberta, Edmonton, AB, Canada.*

INTRODUCTION: Transformation of the pregnant uterus into the active, contractile uterus of delivery is essential for parturition. IL-1β and PGF2a are key mediators in this process, inducing pro-inflammatory and pro-labour genes through positive feedback. Interactions of the myometrium and fetal gestational tissues in regulating uterine transformation are largely unknown. We developed a human fetal membrane explant (FME) and primary myocyte co-culture model to characterize these interactions. We hypothesize that communication between maternal and fetal tissues promotes transformation, enhancing IL-6 and COX-2 responses to PGF2a and IL-1β compared to each individual tissue.

METHODS: 6mm FME were excised from term non-labouring (TNL) placentas and acclimatized for 48h in transwells with 15% FBS. Primary TNL human myometrium smooth muscle cells (HMSMC) were plated in 12-well plates. After 48h, FME transwells were added to each well in indirect contact with HMSMC via shared culture medium. FME/HMSMC were then stimulated with 5ng/mL IL-1β or 10μM PGF2a, followed by collection of shared supernatant and extraction of RNA/protein from each tissue. *IL-6* and *COX-2* mRNA abundance was measured by qPCR in response to both monoculture/co-culture conditions. N=4, two-way ANOVA, $p<0.05$.

RESULTS: HMSMC co-cultured for 6h shows 14x increased *IL-6* mRNA and 3.5x increased *COX-2* mRNA compared to HMSMC alone. 24h co-culture increase *IL-6* and *COX-2* levels 17 and 49x from 24h monocultures, respectively ($p<0.01$). 6h co-incubated FME has 31x higher levels of *IL-6* and 7x higher *COX-2* than FME alone; after 24h co-culture *COX-2* increases 6x from FME alone but *IL-6* does not change ($p<0.01$). After 6h PGF or IL-1 stimulation, co-incubated HMSMC expresses 7 and 5x higher *IL-6* and 3 and 2x higher *COX-2* than treated HMSMC monocultures. Co-cultured FME treated with either agonist increases *IL-6* levels 13-16x from FME controls ($p<0.001$), and *COX-2* increases 14x after PGF but 1.5x after IL-1 ($p<0.05$).

CONCLUSIONS: A better understanding of the role of inflammatory mechanisms in labour physiology is crucial. Our novel model uses primary term tissues to study *in vitro* interaction between gestational layers. HMSMC/FME co-culture results in amplified expression of *IL-6* and *COX-2* and increases the responsiveness of both tissues to PGF2a and IL-1β, suggesting that crosstalk between maternal and fetal tissue drives transformation. Funded by WCHRI,CIHR.

T-009

Progesterone and the Repression of Myometrial Inflammation: The Roles of MKP-1 and the AP-1 System. Kaiyu Lei†,[1] Ektoras X Georgiou†,[1] Angela Yulia†,[1] Suren R Sooranna,[1] Jan J Brosens,[2] Phillip R Bennett,[1] Mark R Johnson*.[1] *[1]Imperial College London, London, United Kingdom; [2]University of Warwick, Coventry, United Kingdom.*

INTRODUCTION: Progesterone (P4) plays an important role in normal human physiology, primarily in the uterus, where it is essential for the initiation and maintenance of pregnancy. During pregnancy, P4 represses *COX-2* expression in the myometrium and amnion. The underlying mechanism has been studied in breast cancer cell line, in which P4 was shown to act via its receptor (PR) to inhibit NF-κB. However, previous studies suggested that GR is also involved in regulating labour-associated gene expression. Further, we recently reported that in human myometrial cells, PR knockdown almost had no effect (only 0.025% genes) on MPA's anti-inflammatory effect and P4 actually acted via GR to modulate the expression of P4-responsive genes, such as *FKBP5* and *HSD11B1*, and to repress IL-1β-induced *COX-2* expression. However, the mechanism is still unclear.

METHODS: Primary cultures of human myometrial cells were grown from myometrial biopsies obtained at the time of elective LSCS. A several molecular biology techniques were employed in this study including gene silencing, gene overexpression, qPCR, nuclear/cytosolic protein assay, western blotting, co-IP and an Affymetrix Human Genome U133 plus 2.0 Array analysis.

RESULTS: We now report that P4 also acts via GR to induce mitogen-activated protein (MAP) kinase phosphatase-1 (MKP-1) and knockdown of MKP-1 impairs the ability of P4 to repress IL-1β-dependent *COX-2* induction. Microarray analysis revealed that P4 repressed preferentially AP-1 responsive genes in response to IL-1β. Consistent with these observations, we found that the ability of P4 to reduce c-Jun activation was lost upon GR as well as MKP-1 knockdown. Interestingly, c-Jun levels in human myometrial cells declined upon GR and MKP-1 knockdown, which suggests the presence of an AP-1 feedback loop. This is supported by our observation that c-Jun levels declined following an initial rise in primary myometrial cells treated with PMA, a potent activator of c-Jun N-terminal kinase. Finally, we show that MKP-1 is an intermediate in P4-mediated repression of some but not all IL-1β responsive genes. For example, P4 repression of *IL11* and *IRAK3* was maintained upon MKP-1 knockdown.

CONCLUSIONS: Taken together, the data show that P4 acts via GR to drive MKP-1 expression, which in turn inhibits IL-1β-dependent c-Jun activation and *COX-2* expression.

T-010

Pre-Maternal High-Fat Diet Consumption Initiates Preterm Birth by Potentiating the Actions of Lipopolysaccharide at Toll-Like Receptor 4 and Decreasing Utero-Placental Antioxidant Capacity. Clarence Manuel,[1] Sandra E Reznik*.[1,2] [1]*St. John's University, Queens, NY, USA;* [2]*Montefiore Medical Center/Albert Einstein College of Medicine, Bronx, NY, USA.*

INTRODUCTION: Previous studies reveal that pre-maternal high-fat diet (HFD) consumption increases the risk of adverse pregnancy outcomes by creating a lipotoxic utero-placental environment consisting of robust inflammation and oxidative stress. Despite such findings, the mechanism of HFD induced preterm birth (PTB) remains unresolved. We hypothesize that pre-maternal HFD consumption increases the incidence of PTB by potentiating the inflammatory actions of LPS at toll-like receptor 4 (TLR-4), and by decreasing the antioxidant capacity of the utero-placental milieu.

METHODS: C57BL6/J timed pregnant mice were continually maintained on either a HFD (60 % fat), or normal chow diet (NCD, 13.4 % fat), beginning eight weeks before pregnancy. A weekly subclinical dose (0.2mg/kg) of LPS (*E.coli,* O111:B4) was administered intraperintoneally (ip) throughout the regimen. Mice were then administered 0.3 mg/kg of LPS ip on E15.5 and the time of onset of delivery and number of pups delivered were recorded. Differences in expression of inflammatory proteins (TLR-4, NF-κB, IL-6, IL-8, and MCP-1) and oxidative stress markers (Nrf-2, HMGB-1, lipid peroxidation, protein carbonylation and total antioxidant capacity) between the two groups were evaluated, using immunohistochemistry, enzyme-linked immunosorbent assay (ELISA) and colorimetric assays. In addition, human primary placental HTR-8/SVneo (HTR-8) trophoblasts cells grown in media containing either saturated fats (palmitic acid) or unsaturated fats (linoleic acid) in the absence or presence of LPS were tested for markers of oxidative stress.

RESULTS: Preliminary results reveal pre-maternal HFD increases the onset of premature delivery compared to NCD, and HTR-8 cells treated with 0.2 mM palmitic acid for 72 hr decreases antioxidant capacity compared to cells treated with linoleic acid. Studies are currently ongoing.

CONCLUSIONS: These studies shed light on the contributions of maternal HFD on the incidence of PTB, and explore how pre-existing metabolic disease and metabolic status may increase a mother's risk of delivering prematurely.

T-011

Progesterone Receptor B Blocks Inflammation by Increasing Expression of IL-1β Inhibitory Receptors, IL-1R2 and IL-1RN in Human Term Decidual Cells. Nihan Semerci†, Vidya Krishan, Ozlem Guzeloglu-Kayisli, Kellie Larsen, Sefa Arlier, Frederick Schatz, Umit Kayisli, Charles Lockwood. *Univ. of South Florida, Morsani College of Medicine, Tampa, FL, USA.*

INTRODUCTION: Progesterone (P_4) maintains uterine relaxation during pregnancy and P_4 withdrawal induces labor in most mammals. In human labor, reduced P_4 receptor (PR) expression and/or activity may mediate functional P4 withdrawal. Previously, we found significantly decreased decidual cell (DC) PR levels in human term labor *vs.* non-labor and in chorioamnionitis vs. control decidua and that interleukin (IL)-1β inhibits PR levels and increases IL-6, IL-8, cyclooxygenase-2, and matrix metalloproteinase-1 and 3 levels in term DC cultures. IL-1 receptor (IL1R)1 and IL1RAcP activate, whereas IL1R2 and IL1RN inhibit IL-1β mediated signaling. Thus, we hypothesize that changes in IL1R activator/inhibitor ratios is associated with labor and that PR-B protects against pro-inflammatory gene expression by regulating levels of IL-1Rs in DCs.

METHODS: Serial decidua basalis sections from gestational-age matched term pre-labor (n=5) *vs.* in-labor (n=5) placentas were immunostained for IL1R1, IL1R2, IL1RN or the DC marker vimentin and analyzed by HSCORE. Term DC cultures (n= 4) primed for 7 days with 10^{-8} M estradiol (E_2) + 10^{-7} M medroxyprogesterone acetate (MPA) were transfected with control or PR-B expression vectors for 48 h to assess IL1Rs and IL-1β mRNA levels by qRT-PCR.

RESULTS: HSCORE analysis revealed that compared to pre-labor specimens, in-labor decidua basalis sections showed: 1) increased IL1R1 immunoreactivity (Mean±SEM 55.2±20.5 *vs.*190±17.5, p=0.001); 2) decreased IL1RN immunoreactivity (160.7±36.0 *vs.* 40.9±14.0; p<0.02); and 3) unchanged IL1R2 immunoreactivity. Compared to control vector transfections, PR-B overexpression in term DCs did not affect IL1R1 and IL1RAcP, but significantly enhanced IL1R2 (1±0.01 *vs.* 1.82± 0.26, p<0.03) and IL1RN (1± 0.01 *vs.* 3.73± 2.19; p<0.03) mRNA levels and repressed IL-1β mRNA levels (1±0.01 *vs.* 0.78±0.003, p<0.01).

CONCLUSIONS: Our results reveal IL1R switching (increase in IL1R1/IL1RN) between pre-labor and in-labor decidua basalis that may cause hyper-activation of IL1β signaling during labor. Moreover, PR-B induced IL1R2 and IL1RN levels in DCs may prolong gestation by promoting an anti-inflammatory milieu in the decidua suggesting a crucial role for PR-B in preventing inflammation-induced pre-term birth.

Supported by the MOD Prematurity Research Center Ohio Collaborative grant.

T-012

Dysbiosis Leads to Cervical Remodeling *In Vivo*. Luz-Jeannette Sierra†,[1] Gillermo O Barila,[1] Amy G Brown,[1] Michael Humphrys,[2] Jacques Ravel,[2] Michal A Elovitz*.[1] [1]*Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA;* [2]*University of Maryland School of Medicine, Baltimore, MD, USA.*

INTRODUCTION: Microbial communities are important to health and disease. Emerging data in diverse biological systems has demonstrated that disruption of these normal microbial communities or a dysbiotic state may be important, if not critical, in the pathogenesis of disease states. We hypothesize that dysbiotic states in the cervicovaginal space and/or gut may be involved in the pathogenesis of spontaneous preterm birth (PTB). The objective of this study was to determine if disrupting normal microbial communities during pregnancy will result in a dysbiotic state and initiate premature cervical remodeling.

METHODS: Time-pregnant CD-1 mice were gavaged with 50 mg/g body weight azithromycin (AZT) or water on embryonic day 12 (E12). Stool and cervicovaginal fluid (CVF) were collected before antibiotic treatment and every 24 hours post-drug administration until E17. Genomic DNA was extracted from stool, amplicon sequencing libraries were prepared targeting the V4 region of the 16S gene, and normalized libraries were sequenced using the Illumina Hiseq 2500. Jensen-Shannon distances in the treatment and control groups were computed to assess the achievement of a dysbiotic state within the mouse. Rate of PTB, pup number and pup weight were recorded. Cervical changes were assessed in the cervical vaginal fluid (CVF) by measuring soluble E-cadherin (se-cad) and hyaluronan (HA) via ELISA of E17 mice.

RESULTS: No difference in PTB rate, pup weight and count was observed between the groups. AZT treated dams showed decrease bacterial counts in the gut as assessed via the Jensen-Shannon Index (p=8.698e-05). SE-cad and HA levels were increased in the CVF of animals exposed to AZT (p=0.0041, p=0.0039 respectively) at E17.

CONCLUSIONS: As would be expected from both human and mouse studies, a single dose of antibiotic can create a dysbiotic state. We have now demonstrated that a commonly used drug during human pregnancy significantly alters the gut microbiota. Importantly, the presence of a dysbiotic state was also associated with molecular changes in the cervix that are markers of premature cervical remodeling. These data suggest that a dysbiotic state might be a significant risk factor for spontaneous preterm birth by inducing changes in cervical function. (MOD Prematurity Research Center at PENN).

T-013

The Mid-Gestational Changes in Cervicovaginal RANTES and IL-1β Correlate with Fetal Fibronectin in Asymptomatic Pregnant Women and Are Predictive Markers of Inflammation-Associated Preterm Birth. Emmanuel Amabebe†, Victoria Stern†, David Chapman, Dilly Anumba*. *University of Sheffield, Sheffield, United Kingdom.*

INTRODUCTION: Intrauterine infection and the subsequent inflammatory processes that ensue can disrupt the maternal choriodecidual tissue with concomitant leakage of fetal fibronectin (FFN) into the cervicovaginal space. We hypothesized that changes in cervicovaginal

inflammatory cytokines in mid-gestation would correlate with FFN expression levels and may improve its predictive capacity for preterm birth (PTB). We therefore examined the relationship between mid-trimester changes in cervicovaginal fluid (CVF) FFN, IL-1β and RANTES and determined their combined predictive capacity for PTB in asymptomatic pregnant women.

METHODS: CVF collected serially at 20-22 wks (n=70: Preterm=35, Term=35) and 26-28 wks (n=70: Preterm=26, Term=44) from 93 asymptomatic high-risk pregnant women, part of a prospectively obtained biorepository of specimens (ECCLIPPx™ studies), were examined. Quantitative FFN level and vaginal pH were measured using the 10Q Rapid FFN analyser (Hologic, MA), and a narrow range pH paper (Macherey-Nagel, DE) respectively. Levels of IL-1β and RANTES were analyzed by BD™ Cytometric Bead Array. The 20-22/26-28 wks ratios of FFN, pH and cytokines were compared between preterm and term women using Receiver Operating Characteristics curves and binary logit models, to determine their predictive capacity for PTB. Associations between these markers were determined by Pearson's correlation coefficients.

RESULTS: Compared to 20-22 wks, FFN at 26-28 wks increased and correlated with IL-1β (r=0.3, P=0.006) and RANTES (r=0.4, P=0.0002) for term- and preterm-delivered cohorts. The increase in pH at the later gestation only correlated with IL-1β (r=0.4, P<0.0001). The change in RANTES levels between 20-22 and 26-28 wks expressed as a ratio indicated the highest predictive capacity for PTB (AUC=0.87, CI=0.73-1.0) compared with FFN (AUC=0.76, CI=0.57-0.94), IL-1β (AUC=0.75, CI=0.58-0.93) and pH (AUC=0.65, CI=0.46-0.85). Combination of RANTES with FFN ratios showed similar predictive capacity as the ratio of RANTES alone (AUC=0.87, CI=0.70-0.96).

CONCLUSIONS: CVF expression levels of RANTES and IL-1β in mid trimester of pregnancy correlate with FFN levels. The rate of change of CVF RANTES across these gestations shows good predictive potential for PTB. However, larger studies are required to confirm these observations and determine any potential clinical utility.

T-014

Cervicovaginal Levels of Human Beta-Defensin 1, 2, 3 and 4 of Reproductive-Aged Women with *Chlamydia trachomatis* Infection. Larissa B Bastos†, Nathália M Noda-Nicolau†, Márcia G Silva*. *São Paulo State University, Botucatu, SP, Brazil.*

INTRODUCTION: Elimination of *Chlamydia trachomatis* infection by the host requires activation of innate and adaptive immune responses. Human beta-defensins (hBD)-1, -2, -3 and -4 represent the main group of human natural antimicrobials and are produced by epithelial and immune cells in response to infection.

The goal of this study was to assess the cervicovaginal levels of hBD-1, 2, 3 and 4 during *Chlamydia trachomatis* infection.

METHODS: A total of 74 cervicovaginal samples were collected for Pap-testing and assessing the presence of infection by *C. trachomatis,* human papillomavirus (HPV), *Neisseria gonorrhoeae* and *Trichomonas vaginalis.* Vaginal smears were taken to evaluate local microbiota. HBD levels were determined using ELISA assay in cervicovaginal fluid samples.

RESULTS: Seventy-four women with normal vaginal microbiota and no evidence of *N. gonorrhoeae*, HPV and *T. vaginalis* infection were included in hBD quantification assays; 37 tested positive for *C. trachomatis* and 37 were negative. Women positive for *C. trachomatis* had significantly lower cervicovaginal hBD-1, hBD-2 and hBD-3 compared with those who tested negative [hBD-1 [0 pg/mL (0-2.1) vs 1.6 pg/mL (0-2.4); p<0.0001], hBD-2 [(0 pg/mL (0-3.9) vs 0.61 pg/mL (0-8.9); p=0.0097] and hBD-3 [0 pg/mL (0-4.3) vs 0.28 pg/mL (0-8.4); p=0.0076]. HBD-4 was not detected.

CONCLUSIONS: The association of *C. trachomatis* infection with lower levels of hBD-1, -2 and -3 in cervicovaginal fluid suggests either the proteolytic action of *C. trachomatis* on hBDs or the downregulation of production of these natural antimicrobials.

T-015

The Effect of TLR3 Receptor Priming on TLR 2,4 and 6 Agonist-Induced Inflammation in Placental Explants. Eberechi Anucha†, Zahirrah Begam Mohamed Rasheed†, Lee S Yun, David A MacIntyre, Phillip R Bennett, Lynne Sykes†*. *Imperial College London, London, United Kingdom.*

INTRODUCTION: The causes of spontaneous preterm labour are multifactorial. Most research has focused on the role of bacterial infection. Emerging evidence indicates a potential role for viruses in increasing susceptibility to bacterial-induced preterm labour. This study investigates the effect of priming the TLR3 receptor with the agonist poly I:C and its impact upon TLR2, 4 and 6 agonist-induction of inflammation in human placental explants.

METHODS: Placenta was collected from women undergoing pre-labour elective caesarean at term or following labour. A comparison between pre and post labour TLR2, 3 and 4 mRNA expression was determined by qRT-PCR. To investigate the effect of viral priming, explants were stimulated with the TLR3 agonist Poly I:C (100μg) on day 5 of culture followed by either TLR2, TLR4 or TLR6 agonists on day 6. Western immunoblotting was used to examine activation of transcription factors NF-κB and AP-1 and expression of COX-2. Tissue culture cytokine concentration was determined by multiplex- ELISA.

RESULTS: An increase in mRNA expression of TLR2 and 3 was seen in post-labour placentas (p< 0.01 and 0.05 respectively). Priming of explants with the TLR3 agonist led to augmented NF-κB activation following TLR2 stimulation compared with no prior priming (p <0.05). Although an augmented response was also seen in the primed explants for TLR4 and TLR6 agonists, this was not statistically significant. No effect was seen on AP-1 with any treatment condition. COX-2 was not significantly increased with TLR 2,3,4 or 6 agonists in primed explants compared with non-primed explants. Production of the pro-inflammatory cytokines IL-1β (p<0.01), TNF-α (p<0.05), and IL-6 (p<0.05) was significantly increased upon treatment with the TLR3 agonist, however, no further increase was seen with addition of the TLR2, 4 and 6 agonists. (n≥ 4).

CONCLUSIONS: TLR3 stimulation leads to a significant pro-inflammatory effect in placental explants. Although NF-κB activation can be further augmented with subsequent treatment to bacterial TLR receptor agonists, no augmented response in cytokine production was demonstrated. Since NF-κB is a key regulator of *both* labour associated and pro-inflammatory proteins, it is plausible that viral priming may act upon alternative proteins not tested in this study to increase susceptibility to bacterial-induced preterm labour.

T-016

An Anti-IL-6R Peptide as a Potential Therapeutic Agent in Inflammation- and Infection-Induced Preterm Birth. Estefania Marin Sierra†,[1,2] Christiane Quiniou,[1] Mathieu Nadeau-Vallée,[1,3] Xin Hou,[1] Barbara Hales,[2] Sylvain Chemtob*.[1,2,3] *[1]CHU Sainte-Justine Research Center, Montreal, QC, Canada; [2]McGill University, Montreal, QC, Canada; [3]Université de Montréal, Montreal, QC, Canada.*

INTRODUCTION: Preterm birth (PTB, delivery before 37 weeks of gestation) is ranked as the leading cause of mortality under 5 years old. PTB has a multifactorial aetiology where just infection is confirmed as a causal link. Current studies showed the importance of inflammation in PTB, marked as an increase of IL-6 levels before the onset of PTB. Neonate morbidity is shown to be linked to increased levels of IL-6 in amniotic fluid (AF), fetal blood and gestational tissues (GT). Here we present a small peptide IL-6R antagonist, named 633, as a potential therapy in a mouse model of LPS- or IL-6-induced PTB.

METHODS: We studied 633 effect in IL-6 signalling in HEK-IL6R cells by immunoblotting. We analyzed the effect of IL-6 and 633 in mice GT *ex vivo* and performed dose-response curves of proinflammatory cytokines in HEK-IL6R and mice uteri. We performed IL-6- and LPS-induced PTB mice models to test 633 efficacy and collected tissues (fetal membranes (FM), uterus, placenta, leukocytes, plasma and AF) respectively 24 or 12 hours after induction to analyze gene expression by quantitative RT-PCR or protein expression by ELISA. We determined the effect of 633 on neonatal survival and weight.

RESULTS: 633 can modulate IL-6 signalling by blocking STAT3 ($p<0.001$) without affecting the Akt and Erk1/2 pathway. 633 decreased IL-6-induced IL-1β gene expression in FM ($p<0.05$); as well as Casp1 ($p<0.05$) and TNFα ($p<0.01$) in uterus. 633 has a dose response inhibitory effect of IL-6-induced IL-1β, IL-6 and TNFα gene expression in HEK-IL6R cells and of TNFα gene expression in uterus (IC_{50} 0.76, 2.07, 0.26 and 1.05nM, respectively). 633 was able to prevent IL-6- and LPS-induced PTB ($p<0.001$ and $p<0.01$, respectively) in mice by selectively blocking proinflammatory gene expression in leukocytes, uterus and FM; and downregulating the levels of CRP in maternal blood ($p<0.05$) and IL-1β in AF ($p<0.001$). 633 is able to increase neonatal survival ($p<0.05$) and rescued neonatal weight ($p<0.001$).
CONCLUSIONS: 633 is a potential prophylactic treatment for PTB by reducing the inflammatory outcome. The characterization of 633 will encourage further tests on its potential to reduce neonatal morbidity.

T-017

Activation of the TLR3 Receptor: A Possible Mechanism for Virally Induced Preterm Labour. Zahirrah Begam Mohamed Rasheed†, Yun S Lee, David A MacIntyre, Phillip R Bennett, Sykes Lynne†*. *Imperial College London, London, United Kingdom.*
INTRODUCTION: Ascending infection is a common cause of preterm birth, often attributed to bacterial pathogens. However, epidemiological studies show that certain viruses can also increase the risk of preterm labour. A 'double-hit' hypothesis exists whereby a viral infection leads to increased susceptibility to bacterial infection and increased risk of preterm delivery. When treated with the TLR3 agonist Poly(I:C) 14% of mice deliver preterm compared with 22% if treated with the TLR2 agonist PGN. This increases to 100% if treated with both agonists (Ilievski, 2010). We sought to determine the responsiveness of human amnion and myometrium to the TLR3 agonist Poly(I:C).
METHODS: Amnion and myometrium were collected from women undergoing a pre-labour caesarean section at term. Amniocytes and myocytes were cultured and stimulated with Poly(I:C) at varying doses and timepoints. Protein expression of TLR3, the inflammatory transcription factors NF-κB and AP-1, and COX-2 was determined using western blotting. Experiments were performed with ≥ three biological replicates, and statistical analysis was performed with GraphPad Prism.
RESULTS: In amniocytes a dose-dependent increase in TLR3 expression was seen with Poly(I:C) treatment at 5, 10 ($p<0.05$), and 25ug/ml ($p<0.01$) and in myocytes at 5 ($P<0.01$), 10 ($P<0.001$) and 25ug/ml ($P<0.001$) at 12hrs. Activation of both NF-κB ($p<0.01$) and AP-1 ($p<0.05$) was seen with 5ug/ml of Poly(I:C) in amniocytes at 12hrs. However, in myocytes, 25ug/ml was required to see a consistent increase in NF-κB activation. At 25ug/ml a 9-fold increase was seen in NF-κB activation in amniocytes ($P<0.05$), compared with a 3.6 fold increase in myocytes ($p<0.05$). A 6-fold increase was seen in AP-1 activation in amniocytes ($p<0.05$) whereas no consistent effect was seen in myocytes. Although COX-2 expression was seen with Poly(I:C) treatment in amniocytes, this increase is seen at 4hrs, which precedes significant activation of NF-κB and AP-1. In contrast, COX-2 activation is seen much later at 12hrs in myocytes with concentrations as low as 5ug/ml of Poly(I:C); a concentration that does not significantly activate NF-κB or AP-1 in myocytes.
CONCLUSIONS: Amniocytes are more responsive than myocytes to the TLR3 agonist Poly(I:C). Although COX-2 expression is induced by TLR3 stimulation, this may be via an alternative transcription factor than NF-κB and AP-1. These data support the role of TLR3 in a polymicrobial aetiology of preterm labour.

T-018

Simvastatin Treatment Reduces the Incidence of Preterm Birth in an Infection-Induced Mouse Model. Ashley K Boyle†,[1] Sara F Rinaldi,[1] Adrian J Thomson,[2] Adriano G Rossi,[3] Philippa T Saunders,[3] Jane E Norman.[1] *[1]University of Edinburgh, Edinburgh, International, United Kingdom; [2]University of Edinburgh, Edinburgh, International, United Kingdom; [3]University of Edinburgh, Edinburgh, International, United Kingdom.*
INTRODUCTION: Around 11% of global births are preterm (PTB). Current tocolytic therapies are largely ineffective. Intrauterine infection/inflammation is the most common cause of PTB. Statins lower cholesterol but also have pleiotropic effects, including immunomodulation and anti-inflammatory properties. We hypothesised that treatment with the statin simvastatin would reduce inflammation and delay PTB in a mouse model of LPS-induced PTB.
METHODS: On gestational day (D)16, C57Bl/6 mice received an intraperitoneal (IP) injection of simvastatin (20μg or 40μg) or PBS (200μl). On D17, LPS (1μg; *E.Coli* 0111:B4) or PBS was injected into the uterus (IU) between two amniotic sacs using ultrasound guidance, followed by a further IP PBS or simvastatin injection 2h later (n=5-16/group). Time from IU injection to first pup delivery was recorded (PTB defined as delivery <30h post-IU injection). Experiments were repeated in a second cohort, with mice sacrificed 6h post-IU injection. Serum and tissues were collected for qPCR and ELISA (n=6/group).
RESULTS:
**Figure(s) will be available online.*
Mice receiving intrauterine LPS delivered significantly earlier than PBS treated mice (31±18h (76.5% PTB) vs 61.8±1h (0% PTB); $p=0.0034$). Simvastatin reduced the rate of LPS-induced PTB (20μg simvastatin: 46.8±6h (43.8% PTB); 40μg simvastatin: 48.7±7h (28.6% PTB), $p>0.05$ vs PBS (0% PTB)). Uterine inflammatory gene expression of *Il-6*, *Cxcl1*, *Ccl2* and serum IL-6 were all significantly greater in LPS-treated mice ($p<0.001$ vs PBS). Treatment with 40μg simvastatin significantly reduced levels of these cytokines and contraction-associated gene *Cx43* ($p<0.05$ and $p<0.014$ vs LPS).
CONCLUSIONS: Simvastatin treatment reduced rates of PTB, uterine inflammatory gene expression and circulating IL-6 in an LPS-induced mouse model. Simvastatin warrants further investigation for the treatment of preterm labour.

T-019

Involvement of the Nicotinic Acetylcholine Receptor (nACHR) Pathway in RU486-Induced Preterm Delivery in Rats. Aihua Ye, Junjie Bao, Min Zhang, Yuanyuan Liu, Shao-Qing Shi, Robert E Garfield, Huishu Liu*. *Guangzhou Women & Children's Medical Center, Guangzhou Medical University, Guangzhou, China.*
INTRODUCTION: Nicotine is known to delay delivery in pregnant rats through an action on the inflammatory pathways. **OBJECTIVES**: The aims of this study were to examine the effects of nicotine (nicotinic acetylcholine receptor (nAChR) agonist) and alpha-bungarotoxin (α-BGT, a nicotine receptor antagonist) on RU486-induced preterm delivery.
METHODS: Timed pregnant Sprague Dawley rats were treated with RU486 (1mg in sesame oil/rat s.c. on day 18 of gestation,GD), RU486 + nicotine (1 mg in saline/kg s.c.bid, GD 16-18), α-BGT (1ug in saline/kg, bid), RU486 + α-BGT, RU486 + nicotine + α-BGT or vehicles (control groups). All groups (n=6 rats/group) were sacrificed at 6 and 12 hours after treatments or during delivery at term (control group without treatments) and the number of preterm births, fetal and placental weights determined and myometrium and serum collected for inflammatory cytokine assays by Luminex.
RESULTS: RU486 resulted in 100% preterm delivery (GD 19) compared ($P<0.001$) to delivery of controls (GD 22). Gestation is significantly prolonged after nicotine treatment (26.40±0.71h) compared to RU486 alone (24.44±0.48h)($P<0.05$) and RU486+nicotine+α-BGT group (23.46±0.61h). In addition, fetal weights were significantly higher in nicotine group (8.16±0.14g, $P<0.05$) than in other groups, but there is no significant differences ($P>0.05$) among RU486 (2.67±0.03g) , RU486 +nicotine (2.76±0.03g) and RU486+Nic+α-BGT (2.64±0.35g) groups.

RU486 increased (P<0.05) the levels of IL-1β and TNF-α in serum and IL-1β, IL-6 and TNF-α (P<0.05) in myometrium both at 6 hours and 12 hours. Cytokines , were decreased (P<0.05) by nicotine treatment. All effects of nicotine on RU486-induced preterm birth were inhibited (P<0.05, delivery time, fetal weights and cytokines) by α-BGT.

CONCLUSIONS: 1) RU486 induces preterm birth that is suppressed by nicotine and this effect is reversed by α-BGT through action on cytokine synthesis or release. 2) The effects of RU486 are in part mediated through the nAChR pathway. 3) Nicotine and nicotine receptor antagonists may respectively be used to inhibit or improve the effects of RU486. 4) Nicotine and other agonists might be used to treat preterm birth.

T-020

The *Escherichia coli* Nissle 1917-Based Probiotic (EcN) Promotes Anti-Inflammation by Inhibiting Decidual Cell Expressed Pro-Inflammatory Cytokines. Kellie Larsen,[1] Rachel L Hardison,[2] Sheryl S Justice,[2] Fred Schatz,[1] Sefa Arlier,[1] Nihan Semerci,[1] Ozlem Guzeloglu-Kayisli,[1] Charles J Lockwood,[1] Umit A Kayisli*.[1] [1]*University of South Florida, Tampa, FL, USA;* [2]*The Ohio State University School of Medicine, Columbus, OH, USA.*

INTRODUCTION: EcN is a gram-negative enterobacterium exhibiting potent immuno-regulatory properties and protection against infections as well as a specific pattern of fitness factors unaccompanied by virulence effectors. Uropathogenic *E. coli* (UPEC) account for 90% of urinary tract infections. Bacteriuria is an independent risk factor for low birth weight and preterm birth (PTB). We previously showed that EcN induces decidual cell (DC) survival by preventing UPEC-induced DC death. This study investigated the impact of EcN on pro- and anti-inflammatory gene expression in DCs in the presence of either infection or inflammation.

METHODS: Cultured term DCs were primed with 10^{-8} M estradiol (E2) and 10^{-7} M medroxyprogesterone acetate (MPA) for 7 days. In the first set of experiments, DC cultures were incubated with vehicle control or EcN (10^7 CFU) ± UPEC (10^7 CFU) for 4 h followed by whole genome microarray evaluation using GeneSpring and Ingenuity Pathway Analyses (IPA). In the second set of experiments, DC cultures were incubated with vehicle or EcN ($5x10^6$ CFU) ± 10ng/ml interleukin (IL)-1β or ± 5 μg/ml lipopolysaccharide (LPS) for 4h for RT-PCR analysis. Statistical analysis was performed using SigmaStat software.

RESULTS: Microarray analysis and IPA evaluation revealed that EcN inhibits UPEC-induced expression of several pro-inflammatory cytokines including tumor necrosis factor (TNF)-α, IL-1β, C-C motif chemokine ligand 2 (CCL2), CCL20 and C-X-C motif chemokine 10 (CXCL10) in DC cultures (p<0.03) associated with several inflammatory signaling pathways dominated by IL-1β/IL1 receptor and LPS/TLR4 signaling (p<3.46E-45). Moreover, qRT-PCR analysis of DC cultures determined that EcN significantly blocks IL-1β and LPS-stimulated CCL2, IL-1β, CXCL10 levels and induces expression of the anti-inflammatory gene TNFAIP3 (p<0.05).

CONCLUSIONS: These findings provide evidence that by increasing TNFAIP3 and suppressing several pro-inflammatory cytokine levels such as CCL2, IL-1β and TNF, EcN acts as an anti-inflammatory factor in the presence of infection and/or inflammation. Therefore, therapeutic use of EcN may prevent infection and/or inflammation associated pregnancy complications leading to PTB.

T-021

Pharmacological Inhibition of the Dimethylarginine-Dimethylaminohydrolase 1 (DDAH1) Enzyme Improves Survival and Haemodynamic Function in a Rodent Model of Severe Sepsis in Pregnancy. Julia Zöllner†,[1] Simon Lambden,[2] Noor Mohd Nasri,[1] Mark Johnson*,[2] James Leiper.[1] [1]*Imperial College London, London, England, United Kingdom;* [2]*Imperial College London, London, England, United Kingdom.*

INTRODUCTION: Maternal sepsis is a major cause of maternal mortality worldwide. Nitric oxide (NO) release during pregnancy may exacerbate sepsis-induced hypotension. The endogenous inhibitor of nitric oxide synthase, asymmetric dimethylarginine (ADMA), is an important regulator of vascular NO production in sepsis. DDAH1 regulates ADMA concentrations in the vasculature. We investigated the impact of treatment with L-257, a DDAH1-selective inhibitor on maternal outcomes during septic shock in pregnancy.

METHODS: Female CD1 mice had radiotelemetry probes implanted and were time-mated for experiments on day 16 of pregnancy. Mice underwent cecal ligation and puncture (CLP) and were treated six hours following CLP with L-257, imipenem, vehicle, or a combination of imipenem and L-257. Haemodynamic function, bacterial load, arterial blood gas, aortic tissue ADMA and plasma Nitrate+Nitrite (NOx) were measured.

RESULTS: DDAH1 inhibition improved survival to 33% compared to 13% in the control group. L-257 treatment in combination with imipenem led to a further increase in survival to 50% (p<0.045). Median survival in the imipenem+L-257 group was 88 hours compared to 22 hours in the vehicle group. Analysis of haemodynamic function following DDAH1 inhibition demonstrated that mean arterial pressure (MAP) and heart rate (HR) were preserved compared to the control group (p<0.001). Circulating NOx levels were comparable between groups. Aortic cell lysate ADMA concentrations were significantly elevated following DDAH1 inhibition as compared to control, (Control 0.18 ± 0.01 vs L-257 0.24 ± 0.02 pmol/mg, p<0.032). L-257 levels in aorta were detectable. Base excess, haemoglobin and haematocrit were significantly improved in the combination group. Bacterial load was decreased following L-257 and combination treatment (p<0.022).

CONCLUSIONS: These findings indicate that treatment with L-257 improves haemodynamic function and improves survival in experimental sepsis. This approach which provides cardiovascular support without impairing the pathogen-specific immune response may offer a new therapeutic pathway for pregnant women with septic shock.

T-022

A Light-Producing Mouse Model of Ascending Vaginal Infection-Related Preterm Birth. Natalie Suff†,[1] Rajvinder Karda,[1] Suzanne MK Buckley,[1] Mark Tangney,[2] Simon N Waddington,[1] Donald Peebles,[1] Donald Peebles.[1] [1]*UCL, London, United Kingdom;* [2]*UCC, Cork, Ireland.*

INTRODUCTION: Preterm birth (PTB) is the leading cause of neonatal mortality with a high incidence of neurological impairment in survivors. Approximately 40% of PTB cases are preceded by microbial invasion of the uterus, with ascent from the vagina thought to be the most common route. It is thought that the ensuing inflammatory response causes preterm birth and also damages the fetal brain.

In this study, we aim to develop a light-emitting mouse model that mimics the ascending infection seen in spontaneous PTB using bioluminescent *E.coli*. Furthermore, we aimed to assess the relationship between intrauterine infection and neonatal brain inflammation.

METHODS: Pregnant C57BL/$6^{J\text{-}Tyrc\text{-}2J}$ mice received *E.coli* (K12 with luxABCDE operon) intravaginally at E16.5 and bacterial ascent was monitored by daily bioluminescence imaging. *E.coli* localization was determined using immunofluorescence staining. Neonatal brains were harvested on postnatal day 2 for cytokine ELISAs, neuronal dendritic counts and CD68 immunohistochemistry.

RESULTS: Pregnant mice showed evidence of ascending infection within 24 hours of administration.

**Figure(s) will be available online.*

E.coli was localised to both the maternal and fetal sides of the placenta, as well as the fetal membranes. There was no difference in delivery timing or fetal survival compared with non-infected controls.

There was an increase in brain IL1-β levels in neonates from infected dams compared with uninfected controls (*p=0.002*), but there was no difference in other brain cytokine levels. Neuronal dendritic counts were reduced in infected brains compared to uninfected controls (*p=0.0001*). Activated microglia appeared to be upregulated in infected neonatal brains.

CONCLUSIONS: We have demonstrated that *E.coli* can ascend from the vagina of pregnant mice, resulting in colonisation of fetal membranes and placenta and transplacental passage of bacteria. This resulted in evidence of immune activation in the developing brain, without causing fetal demise. We propose to use this model to test novel treatments for the prevention of PTB and the associated neonatal neurological sequelae.

T-023

Membranous Progestogen Receptors May Be Important in Controlling Fetal Membrane Weakening. Robert Moore,[1] Deepak Kumar,[1] Brian Mercer,[2] Sam Mesiano,[2] John J Moore*.[1,2] *[1]CWRU, Cleveland, OH, USA; [2]CWRU, Cleveland, OH, USA.*

INTRODUCTION: Biochemically mediated fetal membrane (FM) weakening is a necessary prerequisite before FM can rupture at term or preterm gestation. Using an in-vitro model system with human FM tissue we previously reported that FM weakening induced by both TNF (modeling inflammation) and thrombin (modeling bleeding) are mediated through the generation of a required intermediate, GM-CSF. The FM weakening pathway can thus be divided into two parts: steps involved in the generation of GM-CSF and others involved in the action of GM-CSF. We have also reported that progestogens (P4, MPA and 17-OH Progesterone) inhibit this FM weakening pathway at multiple points, inhibiting both GM-CSF production and GM-CSF action. Nuclear P4 receptors are reportedly present only in FM decidual epithelial cells; they are not present in amnion cells, trophoblast cells or other decidual cells (T cells, NK cells, Macrophages or dendritic cells). These cells all reportedly contain membranous progesterone receptors of both the mPR and PGRMC families. Others have shown that decidual epithelial cells produce GM-CSF in response to both TNF and thrombin; this GM-CSF production is blocked by MPA. GM-CSF action thus likely occurs in cells with no nuclear progesterone receptor (nPR). These studies were conducted to test the hypothesis that progestogens block the GM-CSF action pathway steps via action on mPRs.

METHODS: RT-PCR and IHC were used to identify mPR and PGRMC family members in isolated amnion and choriodecidua samples from FM of "term in labor" (TIL) and "not in labor" (NIL) patients . Intact FM fragments from uncomplicated term repeat c-sectioned patients were pre-incubated with specific mPR (Org OD 02-0) or nPR (R5020) agonists (10^{-8}M/24h) then treated with GM-CSF(200ng/ml/48h) prior to strength testing.

RESULTS: RT-PCR and IHC data indicated PGRMC1 & 2, and mPRa, in AM and CD of both groups. nPRB and nPRA+B were found only in the CD of both groups. mPRβ and mPRγ were not detected in the AM or CD. GM-CSF treatment weakened FM by 43%. mPR, but not nPR, agonist inhibited GM-CSF induced FM weakening.

CONCLUSIONS: Progestogen inhibition of FM weakening may be mediated by nPRs on decidual cells that produce GM-CSF and by mPRs on other cells in the FM which GM-CSF acts upon to cause FM weakening and rupture. Speculation: Progestogens that significantly engage both nPRs and mPRs may be better therapeutic agents to prevent FM weakening and pPROM.

T-024

Isolated Human Amnion Epithelial Cells Contain Multiple Cell Populations. Brittany L Sato,[1] Anthony D Junker,[1] Eric S Collier,[1] Claire E Kendal-Wright.[1,2] *[1]Chaminade University of Honolulu, Honolulu, HI, USA; [2]JABSOM, University of Hawai'i at Manoa, Honolulu, HI, USA.*

INTRODUCTION: The integrity of the amnion epithelium (AEC) is vital as a barrier against invading pathogens. However, there are contradictory accounts of the nature of AEC as gestation nears term; some studies report on their stem cell-like properties, while others describe that they undergo senescence. AEC have also been reported to contribute to sterile inflammation by production of danger-associated molecular patterns (DAMPs). The objectives of this study were to investigate the characteristics of AEC and determine if the presence of cell sub-populations explain the varying reports on AEC that may contribute to sterile inflammation by DAMP production.

METHODS: AEC were isolated from normal, term, fetal membranes from repeat caesarean section at Kapi'olani Medical Center for Women and Children with IRB approval. The potential of AEC (n=4) to maintain telomerase was investigated with the Qiagen Human Telomeres and Telomerase RT^2 Profiler Assay. Human embryonic kidney (HEK, n=3) and mouse neuroblastoma/rat glioma hybrid (NG108, n=3) cells terminally differentiated with 1mM cAMP were used as comparisons. Sub-populations of AEC were identified by expression of stem cell surface markers, TRA-1-60 and SSEA4, using immunohistochemistry, immunocytochemistry and flow cytometry. BrdU incorporation was used to determine if proliferating cells retain stem cell surface markers *in vitro*.

RESULTS: AEC exhibited similar expression of telomerase and telomere maintenance genes with that of HEK cells (80%). Interestingly, three genes (BLM, PRKCB, and TERT) had higher expression in HEK compared to AEC ($p<0.05$). PAX8 ($p=0.06$) demonstrated higher expression in AEC compared to HEK. The expression of 60% of genes were higher in AEC ($p<0.05$) than the NG108 cells, with the greatest fold increases in SSB, XRCC5, and HNRNPA2B1. Preliminary flow cytometry data demonstrated that 95% of freshly isolated AEC expressed either or both SSEA4 and TRA-1-60. AEC grown in culture expressed these markers at lower levels (84.9% and 18.4%, respectively) and nearly all *in vitro* proliferating AEC expressed at least one of these markers.

CONCLUSIONS: This data highlights the need to characterize amnion cells because they contain different cell sub-populations. In addition, this data suggests that growing these cells *in vitro* may not be truly representative of the *in vivo* sub-populations.

T-025

Relationships of Cervical Collagen Content, as Determined by Light-Induced Fluorescence (LIF), During Normal Pregnancy, Preterm Birth and Association with Cervical Length. Zheng Zheng, Lele Wang†, Weijuan Zhang†, Shao-Qing Shi, Robert E Garfield, Huishu Liu*. *Guangzhou Women and Children's Medical Center, Guangzhou Medical University, Guangzhou, China.*

INTRODUCTION: The aim of this study was to estimate the concentration of cervical collagen by LIF in pregnant women during normal progress of pregnancy and in women with preterm delivery (PTD) and to compare the latter to cervical length.

METHODS: Nonpregnant (n=10) and pregnant women (primigravida, n=155), were analyzed at various times of gestation with a collascope (an instrument specifically designed to measure cervical collagen fluorescence which is proportional to cervical collagen concentration, see: BJOG: 2005;112(1):103-108). Patients (n=38) were also measured at various times prior to preterm delivery (25 to 36 weeks gestation). The relationships between cervical LIF vs. time to delivery in preterm patients, LIF vs. Bishop Scores, LIF vs. duration of 1st and 2nd stages of labor and LIF vs. cervical length were also estimated. Cervical length was measured by transvaginal ultrasound using (Voluson E8, GE, USA set at 7.5 MHz)**.** Calculation of Pearson's correlation coefficient (R) was used to estimate relationships.

RESULTS: LIF values (photons of fluorescent light/unit time) declined progressively from the nonpregnant state to late gestation patients ($R=-0.8390$, $P<0.001$). LIF also decreased ($R=-0.714$, $P<0.001$) in patients that delivered prematurely.The relationship between the 1st stages of labor were positively correlated to LIF ($R=0.526$, $P<0.005$) but not, 2nd stage ($R=0.374$, $P=0.06$). There was a statistical positive correlation between cervical LIF and Bishop Score ($R=0.382$, $P=0.028$). There was also a significant negative correlation of LIF and cervical length in pregnant patients ($R=-0.393$, $P=0.026$) but not in cervical length vs. weeks to delivery in preterm patients ($R=0.191$, $P=0.251$).

CONCLUSIONS: : 1) Cervical LIF gives valuable information about cervical collagen concentration in nonpregnant and pregnant patients (patients that deliver at term and preterm). 2) Higher LIF values are representative of elevated levels of collagen and rigidity of the cervix. 3) Higher cervical collagen concentrations are also associated with longer 1st stage of labor but not 2nd stage and a lower Bishop Score. 4) Cervical length is associated with increased LIF in normal pregnant patients but not in patients that deliver preterm.

T-026

Progestins Inhibit IL1β Induced MMP9 Activity and GM-CSF Production from Primary Chorion Cells. TK Allen,[1] L Feng,[2] W Marinello,[1] IA Buhimischi,[3] AP Murtha.[2] *[1]Duke University Hospital, Durham, NC, USA; [2]Duke University Hospital, Durham, NC, USA; [3]Nationwide Children's Hospital, Columbus, OH, USA.*

INTRODUCTION: Progestins inhibit inflammatory mediators (GM-CSF and MMP9) that weaken fetal membranes (FM) and are released from the choriodecidua of fetal membrane (FM) explants in vitro. The role of the chorion layer in this weakening process and its response to progestins remains unclear. Our objective was to determine whether progestins inhibit IL1β induced MMP9 and GM-CSF production in primary cytotrophoblasts cells.

METHODS: Primary chorion cells were harvested using an enstablished method that selects cytotrophoblast cells from the FM of term non-laboring women (n=11) at cesarean delivery and were grown to confluence. The cultures were treated with vehicle (ethanol) and Progesterone (P4), 17α hydroxyprogesterone caproate (17P) and Medroxyprogesterone (MPA) all at 10^{-6} M for 6h and challenged with or without IL1β 1ng/ml for 18h. Cells were harvested for MMP9 mRNA quantification by RT-qPCR and cell culture media collected for GM-CSF quantification by ELISA and MMP9 activity by zymography. Basal MMP9 activity was normalized to the unstimulated vehicle control and the IL1β-induced MMP9 activity was normalized to the vehicle control stimulated with IL1β. GM-CSF levels were normalized to total RNA levels for each experimental arm. Groups were compared using the Mann Whitney U test or Kruskal-Wallis ANOVA test.

RESULTS: IL-1β significantly induced MMP9 mRNA expression ($p<0.001$) and activity ($p<0.001$) when compared with the unstimulated control. There were no differences in basal MMP9 mRNA or activity between the unstimulated control and progestin only treated groups. There were no differences in IL1β-induced MMP9 mRNA expression between IL1β stimulated control and the progestin pre-treated groups stimulated with IL1β. P4 ($p=0.016$), 17P (0.004) and MPA ($p<0.001$) inhibited IL-1β induced MMP9 activity when compared with IL1β stimulated control. IL1β significantly increased GM-CSF levels in media when compared with the unstimulated control ($P<0.001$). MPA only ($p=0.031$) significantly decreased IL1β induced GM-CSF levels in the cell culture media when compared with the IL1β treated groups.

CONCLUSIONS: Progestins, specifically MPA, inhibit the IL1β-induced inflammatory response from the primary chorion cells, suggesting that the the chorion layer may also be a site of action for progestin therapy in preventing FM weakening.

T-027

Cervical Smooth Muscle Cells from Women with a History of Premature Cervical Remodeling Exhibit Altered Migrational Contractile Behavior. Victoria Yu†,[1] Sudip Dahal,[1] James Lohner†,[2] Conrad SternAscher†,[1] Cande V Ananth,[1] Kristin Myers,[3] Ron Wapner,[1] Jan Kitajewski,[4] George Gallos,[5] Michael Sheetz,[2] Joy Vink*.[1] *[1]Columbia Univ. Medical Center, New York, NY, USA; [2]Columbia Univ., New York, NY, USA; [3]Columbia Univ., New York, NY, USA; [4]Univ. of Illinois, Chicago, IL, USA; [5]Columbia Univ. Medical Center, New York, NY, USA.*

INTRODUCTION: Since premature cervical tissue remodeling (PCR)/ softening precedes preterm birth (PTB), we evaluated if the type and stiffness of the extracellular matrix (ECM) influences migrational contractile behavior of cervical smooth muscle cells (CSMC) from pregnant women with and without a history of PCR.

METHODS: After IRB approval, CSMC were isolated from cervical tissue obtained prior to cerclage from 4 pregnant women (13-16 weeks) with a history of PCR resulting in PTB <30 weeks (study group) and 4 gestational age-matched controls (CTL) undergoing pregnancy termination. CSMC were seeded on ***hard*** (60 nN/μm) or ***soft*** (3 nN/μm) polydimethylsiloxane pillar arrays coated with collagen or fibronectin. Migrating CSMC were imaged by time-lapse microscopy and average max contractile force was calculated from pillar displacements. After logarithmic transformation, groups were compared by linear regression modeling to account for clustered responses.

RESULTS: All CSMC generate weaker migrational contractile force on soft versus hard pillars (Figure 1A). CSMC from the study group produce stronger migrational contractile force on collagen versus fibronectin-coated pillars (hard or soft), whereas CTLs did not show a difference (Figure 1B, C). On *soft* pillars, CSMC from the study group generate stronger migrational contractile force on collagen-coated soft pillars compared to CTL (Figure 1C).

**Figure(s) will be available online.*

CONCLUSIONS: ECM stiffness influences human CSMC behavior. While all CSMC generate weaker migrational contractile forces on softer substrates, CSMC from women with a history of PCR exhibit altered migrational contractile force based on type and rigidity of the ECM compared to controls. This suggests that a tissue's microenvironment may influence CSMC behavior in women with premature cervical remodeling leading to PTB.

T-028

17α-Hydroxyprogesterone Caproate Is Not an Optimal Progestogen for Inhibition of *In-Vitro* Fetal Membrane Weakening. Deepak Kumar,[1] Robert M Moore,[1] Mercer M Brian,[2] Sam Mesiano,[2] John J Moore*.[1,2] *[1]Case Western Reserve Univ., Cleveland, OH, USA; [2]Case Western Reserve Univ., Cleveland, OH, USA.*

INTRODUCTION: Inflammation/infection and abruption are leading causes of preterm premature rupture of the membranes (pPROM). We previously reported that granulocyte macrophage-colony stimulating factor (GM-CSF) is a critical intermediate in both tumor necrosis factor-α (TNF) (modeling inflammation) and thrombin (modeling abruption) induced fetal membrane (FM) weakening. We also reported that pretreatment with progesterone (P4), medroxyprogesterone acetate (MPA) or 17α-hydroxyprogesterone (OHP) inhibits both TNF and thrombin induced FM weakening in conjunction with inhibition of the induced increase in GM-CSF. In addition these progestogens also inhibit the GM-CSF induced FM weakening. They thus inhibit the FM weakening pathway at two distinct points, the production and the action of GM-CSF. In this report, we characterize the inhibitory effects of clinically relevant 17α-hydroxy-progesterone caproate (17-OHPC) on TNF and thrombin induced FM weakening.

METHODS: Full thickness FM fragments from uncomplicated term repeat cesarean section deliveries were mounted in 2.5cm Transwell inserts and cultured with/without 17-OHPC (10^{-9}-10^{-7}M) added to the choriodecidua (CD) side. After 24h, medium was removed/replaced with/without addition of TNF, thrombin or GM-CSF added to the CD side. After 24-48h culture, medium from each side of fragments was clarified by centrifugation and assayed for GM-CSF content by ELISA. Each Transwell mounted FM fragment was ruptured using our strength testing equipment.

RESULTS: TNF(20ng/ml) and thrombin(10U/ml) both weakened FM (by 43% and 62%) after 48h incubation and increased GM-CSF levels (3.7 and 5.9 fold) on the CD side of treated FM after 24h. Pretreatment with 17-OHPC (10^{-9}-10^{-7}M) inhibited both TNF and thrombin induced FM weakening, and inhibited induced increases in GM-CSF, in a dose dependent manner. Unlike other progestogens, however, it did not inhibit GM-CSF induced FM weakening.

CONCLUSIONS: 17α-OHPC blocks TNF and thrombin induced fetal membrane weakening by inhibiting the production of GM-CSF, a mediator of the weakening process; but unlike MPA and progesterone, it does not inhibit the action of GM-CSF. Thus instead of currently clinically used 17-OHPC, MPA and P4 may be more efficacious in preventing pPROM related pre-term birth because they inhibit both GM-CSF production as well as GM-CSF action at the choriodecidua.

T-029

Alternative-Activated Macrophages from Amniotic Fluid Home to the Prematurely Ruptured Amnion. Haruta Mogami, Annavarapu Hari Kishore, Jesus Acevedo, R Ann Word*. *University of TX Southwestern Medical Center, Dallas, TX, USA.*

INTRODUCTION: Preterm rupture of membranes (PROM) is a major cause of preterm birth. Interestingly, a small proportion of women remain undelivered for weeks to months after PROM and spontaneous sealing of the membranes occurs occasionally. During wound healing, alternative-activated macrophages (M2-MΦ) are necessary for phagocytosis of matrix debris and release of cytokines and growth factors. In this study, we investigated mechanisms of healing of PROM in relation to innate immunity.

METHODS: Fetal membranes of pregnant mice were punctured with a sterile 20 G (0.91 mm) needle by laparotomy under general anesthesia on 15 dpc. In each uterus, half were punctured and half were not. Tissues were collected at various time points after rupture. Macrophage phenotype was identified by immunofluorescence staining of CD68 (pan-MΦ marker), NO synthase-2 (NOS2, M1-MΦ marker), and Arginase-1 (Arg1, M-2 MΦ marker).

RESULTS: In this model of non-infectious PROM, 7% healed spontaneously within 24 h and 50% within 72 h (n=41-64). Histologically, proliferation and migration of amnion mesenchymal cells and immune cells were observed in healing amnion throughout the puncture site, but not in intact nor ruptured edge of choriodecidua. CD68 positive macrophages aggregated to the edge of healing of amnion likely to increase expression of VCAM1 (from 1.1 ± 0.2 to 2.2 ±0.4 R.U./*β2m* at 2h; from 1.1 ± 0.1 to 3.0 ± 0.7 at 6 h), E-selectin (from 1.1 ± 0.1 to 2.0 ± 0.3 at 2 h), and long-term upregulation of P-selectin (from 1.2 ± 0.3 to 5.8 ± 2.1 at 2 h to 15.6 ± 4.8 at 72 h). Whereas CD68-positive MΦs were numerous and strongly positive for Arg1, NOS2 immunostaining was rarely present at 24 h. Using qPCR and std curves, Arg1 and NOS2 mRNA was quantified. In intact amnion, baseline levels of Arg1 were increased relative to low levels of NOS2 (0.99 ± 0.14 vs 0.28 ± 0.03/*CPHA*) and increased 8-fold in ruptured membrane ($p < 0.01$ at 24 h). In contrast, NOS2 was increased modestly (2.5-fold). Interestingly, macrophages homed to the edge of the rupture site as early as 2 h and within 24 h invaded the membrane from the fetal side. In amniotic fluid, CD68+ MΦs increased significantly in ruptured sacs compared to intact sacs at 6 h.

CONCLUSIONS: Amniotic fluid-derived fetal macrophages home to the ruptured amnion as alternative-activated M-2 MΦ. We conclude that amniotic fluid behaves as an immune tissue providing innate immunity to healing of the ruptured avascular amnion.

T-030

Evidence That MPRIP Targets Phosphatases and Kinases to Myosin to Regulate Relaxation and Contraction in the Human Myometrium. Trent Butler†,[1,2] Minoo Heidari Kani†,[1,2] Eng-Cheng Chan,[1,2] Roger Smith,[1,2] Jonathan W Paul*.[1,2] *[1]University of Newcastle, Newcastle, NSW, Australia; [2]Hunter Medical Research Institute, Newcastle, NSW, Australia.*

INTRODUCTION: Understanding the biochemistry of human myometrial contractions is central to the development of rational methods to modulate clinical disorders of myometrial function. The expression and regulation of myosin phosphatase holoenzymes containing MYPT1 regulatory and PP1c catalytic subunits are thought to be critical in the control of myosin MLC20 phosphorylation that is essential for myometrial contraction. Inhibitors of ROCK1/2 kinases that lie upstream of both MLC20 and MYPT1 reduce the amplitude of myometrial contractions. MYPT1 can be anchored to myosin by scaffolding proteins, including MPRIP, but this possibility has not been investigated in myometrium. We tested whether MYPT1, ROCK1/2, and the scaffolding protein MPRIP co-localize to the actin-myosin contractile machinery in immortalised pregnant human myometrial cells.

METHODS: Immunofluorescence microscopy was used to localize proteins in hTERT-immortalized human myometrial cells. We demonstrated that these cells are contractile using Ca^{2+} imaging and video microscopy of oxytocin stimulation. Immunofluorescence imaging was performed using a Nikon C2 confocal microscope. Antibody specificity was tested using concentration-matched immunoglobulin isotype controls. The reliability of co-localization was assessed using single-label controls and Tetraspeck beads. Masks were used to confirm protein co-localization.

RESULTS: Filamentous and non-filamentous staining was seen for MYPT1, MPRIP and ROCK2. Only non-filamentous ROCK1 staining was observed. Filamentous MYPT1, MPRIP and ROCK2 staining was observed to co-localize to myosin filaments, suggesting that these proteins were localized to the actin-myosin contraction machinery. MYPT1 staining co-localized with myosin and partially with ROCK2. MPRIP staining was compartmentalized and co-localized with myosin and partially with ROCK2.

CONCLUSIONS: This study supports interactions of MYPT1, MPRIP and ROCK2 with the actin-myosin contractile machinery and further suggests functional interactions between ROCK2 and MYPT1. MPRIP binding to myosin filaments may be critical in localizing MYPT1 and kinases to myosin and allow compartmentalized regulation of myosin phosphatase activity, which promotes relaxation, and pro-contractile kinase activity in human myometrium.

T-031

HoxA Proteins Regulate the Expression of Contraction Associated Genes in Human Uterine Myometrium. Ning Xie,[1] Yinan Li,[1] Donna Slater,[2] Stephen Lye,[3] Xuesen Dong*.[1] *[1]University of British Columbia, Vancouver, BC, Canada; [2]University of Alberta, Calgary, AB, Canada; [3]University of Toronto, Toronto, ON, Canada.*

INTRODUCTION: Human myometrium possesses regionalized myometrium contractility to accommodate fetal growth during pregnancy and fetal delivery at term. A relaxed fundus (FUN) and a contracted lower uterine segment (LUS) are requiredduring pregnancy to prevent fetal pressure on the cervix. With the onset of labor, this regionalization of myometrial function is reversed as the FUN becomes contractile and the LUS is relaxed to allow descent of the fetus and expulsion of the fetus through the birth canal. How this regional myometrium function is regulated is unclear. We have reported that the homeobox protein A13 (HoxA13) is highly expressed in LUS and can enhance myometrial cell contractility. Whether HoxA10 and HoxA11 are also expressed in the myometrium and regulate the expression of contraction associated proteins (CAPs) remain to be determined. Investigation on the expression and functions of HoxA 10 and 11 genes in human myometrium would enhance our understanding of human pregnancy and labour, and may inform development of therapeutic strategies for pre-term labour.

METHODS: Paired myometrium tissues and primary myometrial cells from FUN and LUS were also collected and cultured *in vitro*. Human myometrial cell line (hTERT) was used to overexpress exogenous HoxA10 and 11 by lentivirus. The expression of HoxA10, HoxA11 and CAPs including IL-1b, IL-6, IL-8, Cx43, Cox2 and OTR were determined by real-time PCR and immunoblotting assays.

RESULTS: In contrast to HoxA13 that is highly expressed in LUS, the mRNA levels of HoxA10 and 11 genes in FUN were four-fold higher than that in paired LUS tissue. HoxA10 and 11 mRNA levels in primary FUN myometrial cells were also 2-4 fold higher than that in LUS myocytes. When overexpressed in hTERT cells, HoxA10 and 11 resulted in 90% decrease in IL-1b, 40-50% decrease in IL-6, Cx43 and Cox2 mRNA levels. HoxA10 and 11 also induced a 2-3 fold increase in OTR, but did not alter IL-8 mRNA levels. Consistently, the protein expression of these CAPs was similarly regulated by HoxA10 and 11 in hTERT myometrial cell lines.

CONCLUSIONS: HoxA 10, 11 and 13 genes are differentially expressed between FUN and LUS, creating regionalized myometrium phenotypes in human myometrium. These proteins may regulate regional myometrium contractility during pregnancy and labour.

T-032

Characterizing Preterm Labor Through Muti-Sensor Electrical Activity Propagation. Hari Eswaran*,[1] Diana Escalona-Vargas†,[1] Sarah Theriot†,[1] Eric R Siegel,[2] Curtis L Lowery.[1] *[1]UAMS, Little Rock, AK, USA; [2]UAMS, Little Rock, AK, USA.*

INTRODUCTION: The objective of this study was to track the propagation speed from uterine electrophysiological signals recorded over the abdomen in order to characterize the preparatory phase before reaching active labor in preterm and term women.

METHODS: The uterine magnetomyographic (MMG) signals were recorded with a 151 channel SARA (SQUID Array for Reproductive Assessment) system from 92 pregnant women between 24 and 40 weeks of gestational age. The recordings were performed serially every other day until they reached active labor. The MMG signals were scored and segments were classified based on presence of uterine contractile burst activity. The sensor space was then split into four quadrants and the delay between burst activity was calculated within quadrants. Propagation speeds were calculated from the delays for the six possible pairwise combinations of quadrants. Wilcoxon rank sum test was used to compare the speed characteristics between the groups.

RESULTS: MMG recordings were successfully processed and 66 women who had at least speed values in three pairwise combinations of quadrants were included for further analysis.The average values of propagation speeds ranged from 2-8 cm/s. Overall no significant difference was found ($p=0.82$) between the ones who went in to active labor at preterm versus the ones who did at term. There were 22 and 25 women who went in to active labor more than 24 hours since the last recording in the preterm and term labor group, respectively. Also, no significant difference was observed in both preterm and term women who went in to active labor more than 24 hours later compared to the ones who did before 24 hours. **Figure(s) will be available online.*

CONCLUSIONS: The speed of propagation between the preterm labor and term labor group were within the physiological range. The fact that no difference in propagation speed observed between the women who delivered at term versus preterm before they reached active labor probably points to the fact the preparatory phase is similar in both cases. Further analysis of other parameters such as synchrony of activity needs to be performed to confirm this observation.

T-033

Global Uterine Signaling During Labor Is Not Progressive Propagation. Lauren Miller†,[1] Neil Sligman,[1] Eva Pressman,[1] Roger Young*.[2] *[1]URMC, Rochester, NY, USA; [2]PreTel Health, Memphis, TN, USA.*

INTRODUCTION: It has been hypothesized that a contraction initiates in a single location and propagates in a progressive, wave-like form, to encompass the entire uterus. Neither high, nor low resolution EMG mapping has convincingly confirmed this hypothesis. Correlating high and low resolution results has been limited by difficulty in examining large areas of the uterus. Using a new method of global mapping based on directional EMG sensors, we evaluated for the existence of progressive signal propagation as the basis for synchronized global uterine contractions.

METHODS: Directional EMG sensors were designed with a square shape, with lengths between 6 and 10cm. We've previously shown that area sensors exhibit spatial resolution similar to the sensor size. Up to seven directional EMG sensors were placed on 5 women in spontaneous labor and uterine bioelectrical activities recorded for 30 to 60 minutes. Contractions were identified by traditional tocodynamometry. Contraction coordination by EMG was defined by the presence of bioelectrical activity ($\geq 75\mu V$) in all area sensors. Contractions were assessed for starting location, propagation direction and speed.

RESULTS: Contractions did not originate from a single site in any subject. The timing of activation was variable from sensor to sensor. Bioelectrical signal latency ranged from 0 to 11 seconds (±1). There was no clear pattern of sensor activation between contractions. Propagation speeds were calculated, and showed no clear pattern. Similarly, there was no pattern to propagation direction, with signals changing directions and entirely skipping some areas. No contraction demonstrated progressive linear propagation of contractile activity across the entire anterior wall.

CONCLUSIONS: Data acquired using a new method of global uterine EMG mapping do not support the hypothesis that propagation of a uterine contraction starts at a single location and progressively propagates point-to-point across the uterus. Since surface EMG technique is limited to probing the anterior uterus, there is a possibility that signals from the posterior wall contribute to the enigma of propagation. However, based on our anterior wall data, an elusive wave-like posterior propagation is unlikely. The most parsimonious explanation of this data is that the uterus uses an alternate mechanism of long-distance signaling, such as pressure-tension mechanotransduction.

T-034

The Estrogen Receptor 1 (ESR1) Exon 7 Skip Isoform Functions by Blocking ESR1 Action Prior to Labor. Prashanth Anamthathmakula†,[1] Chandra S Miryala,[1] Jennifer C Condon,[12] Pancharatnam Jeyasuria.[12] *[1]Wayne State University, Detroit, MI, USA; [2]NICHD, Detroit, MI, USA.*

INTRODUCTION: The Central view of ESR1 action during pregnancy is that it upregulates contractile associated proteins (CAPs such as connexin43, oxytocin receptor) at term. A conundrum in this opinion is that estrogen levels are high throughout pregnancy and cannot be the differential signal. We have recently shown that three ESR1 isoforms; ERα66 (full-length), ERα46 (exon 1 skip) and ERΔ7 (exon 7 skip) are found in the pregnant uterus and are regulated gestationally. ERΔ7 has been show to function in a dominant negative fashion against ERα66. Previous work has shown that binding of splice factor hnRNPG to exon 7 of the ESR1 unprocessed RNA transcript causes exon 7 to be excluded in an Endometrial adenocarcinoma cell line.

METHODS: Utilizing non-laboring human myometrial tissue, (32 weeks versus 39 weeks; n=3) we compared the two gestational periods for hnRNPG and ERΔ7 expression. hnRNPG was knocked down using lentiviral shRNA in a human myometrial cell line ($hTERT^{HM}$). We overexpressed the ERΔ7 isoform using a lentiviral Tet-On inducible expression system in $hTERT^{HM}$ cells and assessed connexin43 and oxytocin receptor expression using western blotting. Immunocytochemistry and 3D collagen contraction assays were performed in ERΔ7 overexpressing $hTERT^{HM}$ cells.

RESULTS: There was a significant decrease at term (39 weeks) of ERΔ7 isoform when compared to the preterm (32 weeks) myometrium at the mRNA ($p<0.05$) and protein level. ERΔ7 overexpression in $hTERT^{HM}$ cells led to a significant reduction ($p<0.05$) in CAPs; connexin43 and oxytocin receptor. The ratio of ERΔ7 to hnRNPG protein was significantly higher in preterm compared to term myometrium samples ($p<0.05$). Lentiviral shRNA knockdown of hnRNPG led to a decrease in ERΔ7 levels in $hTERT^{HM}$ cells, implying that hnRNPG binding causes the exon 7 skip. Additionally collagen contraction assays reveal reduced contractile responsiveness in the ERΔ7 overexpressed $hTERT^{HM}$ cells.

CONCLUSIONS: Alternative splicing plays an important role in the control of the contractile status of the myometrium through splice factors like hnRNPG that control the expression of the ERΔ7 isoform. The dominant negative ERΔ7 controls CAP expression by acting antagonistically to ERα66 thus blocking CAP expression. At term ERΔ7 is reduced and ERα66 can again upregulate CAP expression allowing for a contractile myometrium.

T-035

Placentally Derived Serotonin in Highly Seasonal Pregnant Women. Maria H Sqapi†,[1] Stephen G Matthews,[1,2] Robert Levitan*.[1,3,4] *[1]University of Toronto, Toronto, ON, Canada; [2]University of Toronto, Toronto, ON, Canada; [3]University of Toronto, Toronto, ON, Canada; [4]University of Toronto, Toronto, ON, Canada.*

INTRODUCTION: Preclinical studies have demonstrated that serotonin synthesized from maternal tryptophan at the placenta is an important trophic signal for establishing fetal brain circuitry. Furthermore, perturbations to the placental serotonin system have been shown to induce

permanent brain deficits in adult mouse offspring. Serotonin (5-HT), among monoamine neurotransmitters, has a pronounced seasonal pattern in its availability and/or metabolism with decreases during the winter months. Moreover, people who exhibit strong seasonal changes in mental health have greater decreases in brain extracellular 5-HT compared to healthy controls in the fall/winter period. It is possible that this seasonal rhythm of 5-HT parallels the peripheral placental serotonin system important for fetal neurodevelopment during pregnancy in highly seasonal women. Our objective is to study placental 5-HT synthesis/metabolism in highly seasonal and healthy women enrolled in the Ontario Birth Study (located at Mount Sinai Hospital, Toronto) during the fall and winter. We hypothesize that placentas from highly seasonal pregnant women delivering during the fall/winter period will show decreased 5-HT content and this will be associated with reduced expression of 5-HT-synthesizing/metabolizing enzymes.

METHODS: Women with a score >11 on the Seasonal Pattern Assessment Questionnaire, administered at 12-16 weeks gestational age, were categorized as highly seasonal. Frozen placental tissues were collected from highly seasonal women (N=7) and healthy controls (N=15) who delivered between November 2015 and April 2016. The placental mRNA and protein expression of *LAT1, IDO1, TPH1, MAOA* and *SERT* were measured by qPCR and western blotting. Metabolites along this pathway were measured in placenta by mass spectrometry (LC-MS/MS).

RESULTS: qPCR, western blot and mass spectrometry revealed no significant differences ($p>0.05$) in mRNA and protein expression of key rate-limiting enzymes and metabolite in the serotonin synthesis pathway between highly seasonal women and controls.

CONCLUSIONS: Collectively, our pilot data suggest that placental 5-HT does not decrease markedly with the onset and progression of hypo-serotonergic symptoms during the fall and winter period in highly seasonal women, though much larger sample sizes are needed.

T-036

Evaluation of One or Both Umbilical Arteries in Fetal Growth Restriction. Teresa Harper, Mary Pinter, Diane Gumina, Allison Gillan, John Hobbins*. *University of Colorado School of Medicine, Aurora, CO, USA.*

INTRODUCTION: The umbilical artery (UA) wave forms indirectly reflect placental blood flow. As surrogates of placental function they have been used alone or in conjunction with wave forms from the middle cerebral artery (MCA) to assess fetal condition. The ratio of the two values, the cerebral placental ratio (CPR) is currently being employed in decision-making regarding the timing of fetal surveillance or even the need for delivery. Currently, recommendations are to sample only one UA. We hypothesize that the resistance variance between the two umbilical arteries in FGR is significant enough to impact clinical management.

METHODS: Forty-nine patients, who presented between 24 and 38 weeks with estimated fetal weights (EFW) <10th percentile were examined. At each visit waveforms were obtained from both UAs. To assess placental resistance, pulsatility indexes (PIs) from UA waveforms were tabulated and a discordance was defined as one UA above the 95th percentile and the other UA below. The magnitude of the discordance was expressed as a percent difference between the arteries. The CPR was calculated for each of the paired UA pulsatility indices (PIs).

RESULTS: The study involved a total of 235 visits. Umbilical artery Doppler results revealed that 51% (25 patients) had discordant UA PI values during at least one examination over the course of their pregnancy. The average percent difference between the arteries was not significantly different across gestational age. Most differences between UAs at the same visit were within 20% of each other. However, 23 of the paired artery values were between 20-40% discordant. When CPRs were abnormal, 62% were abnormal in both UA. Whereas in the other 38%, only one UA generated an abnormal CPR.

CONCLUSIONS: We have found that 51% of FGR fetuses in our cohort had discordant UA PI values during at least one visit in their pregnancy. Additionally, 38% of abnormal CPR findings were attributed to only one UA. Therefore, we conclude that assessing only one UA waveform, or even averaging two random waveforms (representing a 50% chance of sampling the same vessel) could mislead clinicians who are using these methods to guide timing of further surveillance or delivery decisions.

T-037

Reducing Primary Cesarean Delivery: Adherence to National Guidelines for Management of Labor Arrest in a Single Center. Mesk Alrais, Nana-Ama E Ankumah, Farah H Amro, Rachel Landgren, Baha M Sibai, Sean C Blackwell*. *McGovern Medical School at UTHealth, Houston, TX, USA.*

INTRODUCTION: The Society for Maternal Fetal Medicine (SMFM) and the American Congress of Obstetricians and Gynecologists (ACOG) have published guidelines for the labor arrest (LA) management to decrease primary cesarean delivery (CD). Our objective was to evaluate the degree of adherence to the guidelines and to assess outcomes between deliveries compliant with the guidelines vs those not compliant.

METHODS: This is a retrospective analysis of prospectively collected data from April through July 2016 of total 844 patients. Inclusion criteria were term, singleton gestations admitted for vaginal delivery and undergoing CD for LA. Exclusion criteria were fetal death, major fetal anomaly, and prior CD. Women were categorized based on the last cervical exam prior to decision for CD: <6 cm (latent), 6-9 cm (active), and 10 cm (2nd stage). According to LA definitions, we compared adherence rates, use of intrauterine resuscitation, Apgar scores, cord pH, and NICU admission. Chi-square test and Student's t-test were utilized as appropriate.

RESULTS: 73 deliveries satisfied criteria for LA. Among these, 22 arrested in latent phase, 27 in active phase, and 24 in the 2nd stage. 31 cases were adherent to the guidelines (43%), and 42 cases were non-adherent(57%). The non-compliance rate by phase of arrest was: latent 15(68%); active 13(48%); and second stage 14(58%). There were no differences in demographics, intrauterine resuscitation, or neonatal outcome between groups.

	Adherent N=31(%)	Non-adherent N=42(%)	p-value
‹6 cm 6-9 cm 10 cm	7(23) 14(45) 10(32)	15(36) 13(31) 14(33)	0.37
Age	26±4.9	29±7.1	0.06
BMI	34±6.1	34±7.4	0.71
Nulliparous	24(77)	38(90)	0.19
Labor duration(hr)	21±6	23±13	0.97
Oxytocin Cessation	19(61)	14(33)	0.05
O_2 use	15(48)	23(55)	0.64
Chorioamnionitis	1(3.2)	6(14)	0.23
Birth weight(gm)	3403±427	3521±461	0.27
APGAR<7 at 5mins	0	2(5)	0.5
PH<7.1	0/25	3/26(11)	0.13
NICU admission	4(13)	7(17)	0.75

CONCLUSIONS: Despite guidelines to reduce the primary CD, almost 60% of CD performed for LA were not in compliance. Additional studies are needed to determine whether non-compliance is due to physician behavior, patient factors that would not allow safe prolongation of labor, or unrealistic clinical endpoints in current guidelines.

T-038

Utility of Perinatal Autopsy for Stillbirth ≤ 20 Weeks. Karen J Gibbins,[1] Robert M Siver,[1] Yajing Xiong†,[3] Jessica M Comstock*.[2] *[1]University of Utah Healthcare, Salt Lake City, UT, USA; [2]Intermountain Healthcare, Salt Lake City, UT, USA; [3]University of Utah, Salt Lake City, UT, USA.*

INTRODUCTION: The utility of perinatal autopsy in ascertaining a potential cause of death is well established in evaluation of stillbirth after 20 weeks. However, autopsy is not routinely performed prior to 20 weeks gestation, and these early fetuses may be too immature to glean useful information. Thus, our objective was to describe our experience with perinatal autopsy in fetuses ≤ 20 weeks.

METHODS: Descriptive study of the 211 fetal autopsy reports with gestational age listed as 12-20 6/7 weeks from 2000-2015. Demographics, indication for delivery (antepartum stillbirth (AS), intrapartum stillbirth (IS), or termination for fetal anomalies), mode of delivery, clinical and pathologic gestational age estimates, degree of maceration, and autopsy findings were abstracted. Autopsy findings were categorized by organ system and recorded as normal, abnormal, or indeterminate.
RESULTS: Pathologic mean gestational age was 17.4 weeks (SD 2.2 weeks). 67% were AS, 13% IS, and 20% pregnancy terminations. Delivery was via spontaneous vaginal delivery in 191 (92%), Cesarean delivery in 2 (1%) and dilation & evacuation (D&E) in 13 (6.3%). Maceration ranged from none in 63 (31%) to grade IV in 85 (42%). Anatomic anomalies were detected in 122 (58%), with skeletal anomalies in 30%, head and neck 23%, abdominal 22%, chest 21%, cardiac 21%, genitourinary 13%, and central nervous system (CNS) 8%. Only 10 fetuses (5%) were so macerated or damaged from D&E so as to preclude any evaluation. Detection of anomalies by gestational age is shown in Figure 1. In fetuses with grade IV maceration, 39 (46%) had an anomaly detected. In D&E cases, anomalies were detected in 54%, although 38% of D&Es were indeterminate. CNS anomalies were unable to be evaluated in 110 (55%) due to postmortem liquefaction of the brain.
**Figure(s) will be available online.*
CONCLUSIONS: Fetal autopsy yields useful results in fetuses below 20 weeks gestation. CNS autopsy is limited, but other organ systems permit complete evaluation, even in the presence of significant maceration.

T-039

Maternal Plasma Hyperglycosylated hCG in Abnormally Invasive Placenta (AIP). Maegan Ford†, Stacy Zamudio, Michael Sbarra, Sonia DaSilva-Arnold†, Nicholas P Illsley, Abdulla Al-Khan*. *Hackensack University Medical Center, Hackensack, NJ, USA.*
INTRODUCTION: AIP can be life-threatening if physicians are unaware the condition is present or if delivery occurs emergently. Even with optimal imaging resources, detection early in pregnancy or of milder cases (accreta) is difficult. As the incidence of AIP is increasing rapidly, a circulating biomarker would be useful. Free ß-hCG protein and message (cell free mRNA) levels are higher in the maternal circulation when AIP is present, but they lack sensitivity and specificity. Hyperglycosylated hCG (h-hCG) is produced by human extravillous trophoblast cells (EVT) and released into the maternal circulation. Elevated h-hCG is a biomarker of gestational trophoblastic disease, but has not been examined in AIP. We hypothesized that the over-invasive EVT in AIP would produce more h-hCG, and that such increase would be greater in severe vs. mild disease. Total ß-hCG levels were also measured, and the h-hCG/ ß-hCG ratio calculated to normalize for differences in placental mass.
METHODS: Plasma samples were obtained between 15–35 weeks from normal pregnancies (n=15), placenta previa (n=10), placenta accreta (n=8) and placenta increta/percreta (n=41 percreta, 2 increta) and stored at -80°C. ß-hCG and h-hCG were measured in these samples by ELISA (Genway, MyBiosource). Correlation was used to examine ß-hCG and h-hCG across gestational age. Levels of hCG in the 4 groups were analyzed by Kruskal Wallis with Dunn's multiple comparison test. Mann-Whitney U was used for 2-group comparison.
RESULTS: There was no correlation between gestational age and ß- or h-hCG levels. Women with placenta previa and normal controls had similar levels of circulating ß- and h-hCG. Likewise, women with the mildest AIP (accreta) had ß- and h-hCG levels similar to the increta/ percreta group. In all controls (previa+normal) compared with all AIP (accreta, increta, percreta) h-HCG levels were similar, whilst ß-hCG was lower in AIP. The h-hCG / ß-hCG ratio was elevated in AIP (median 2.87 [1.2, 4.6 IQR] versus control (1.01 [0.60, 2.6], $p < 0.005$.
CONCLUSIONS: Median levels of the h-hCG / ß-hCG ratio were greater in AIP, but there was significant overlap between cases (0.15 - 9.27) and controls (0.24 – 8.79). hCG levels did not differ in mild versus severe disease. We conclude that hCG, whether considered as cell free mRNA, circulating free- or total ß-hCG, or the h-hCG produced by the EVT are not useful in discriminating AIP from normal pregnancies.

T-040

Single Dose Anti-D Prophylaxis in Pregnancy: Is It Time to Change? Craig E Pennell*,[1] Janice C Cheng,[1] Blagica Penova-Veselinovic,[1] Carol A Wang,[1] Bernie Ingleby,[2] Chris C Arnold,[2] Andrew L Barr,[2] Melanie K White,[1] Scott W White.[3] *[1]The University of Western Australia, Perth, Western Australia, Australia; [2]King Edward Memorial Hospital, Perth, Western Australia, Australia; [3]King Edward Memorial Hospital, Perth, Western Australia, Australia.*
INTRODUCTION: Despite a national program of anti-D prophylaxis in Australia, sensitisation still occurs in ~0.33% of pregnancies due to: 1) lack of prophylaxis (43%); 2) non-obstetric sensitisation (25%); and 3) sensitisation despite adequate prophylaxis (32%). At a global level there are two approved regimens for providing antenatal prophylaxis – double-dose of 500IU or more at 28- and 34-weeks' GA; and single-dose of 1500IU at 28-weeks' GA. To date, compliance and maintenance of circulating anti-D levels at delivery between the regimens have not been well studied.
Aim: To assess compliance and maintenance of circulating anti-D levels at delivery comparing single- and double-dose regimens of prophylaxis.
METHODS: A RCT (n=273) was performed comparing a single 1500IU dose of anti-D at 28-week to the current Australian regimen (28- and 34-week 625IU regimen). An antibody screen at delivery assessed the circulating anti-D levels. Analyses were performed based on intention to treat (ITT) and treatment received (TR). Appropriate statistical tests were used to evaluate differences in compliance, detectability of residual circulating anti-D at delivery, and maternal and neonatal outcomes. Multivariate logistic regression assessed factors contributing to undetectable anti-D at delivery.
RESULTS: Demographic, obstetric and neonatal outcomes were similar between groups. No women became sensitised during the study. Based on analyses by ITT and TR, the single-dose group had a higher proportion of undetectable anti-D at delivery (ITT OR 5.0; 45.4% vs. 14.2%, $p<0.001$). Compliance was improved in the single-dose group (81.2% vs. 60.7%, $p<0.001$). Time elapsed since last dose and third trimester weight were significant predictors for undetectable anti-D at delivery. Multivariate regression indicated anti-D regimen group was not a significant predictor for undetectable anti-D at delivery.
CONCLUSIONS: Despite improving compliance, the single-dose regimen resulted in nearly half of the Rh-negative women having no circulating anti-D at delivery. Translating recent WA data to an Australian context, a single dose regimen could result in an additional 580 sensitisations per year.

T-041

A Retrospective Assessment of Periviable Outcomes Involving Vertex Presentations Depending on Delivery Method. Nicole R Albino, Clark T Johnson*. *Johns Hopkins School of Medicine, Baltimore, MD, USA.*
INTRODUCTION: Delivery method of the periviable infant is determined to optimize fetal outcome, balanced against maternal risks. There is some consideration that cesarean delivery may be protective for the periviable infant depending on fetal presentation, with limited evidence basis. Cesarean delivery can have significant maternal risks, and these risks must be weighed against potential benefits when considering delivery method.
METHODS: This is a retrospective cohort study of all singleton births from the vertex presentation between January 1 of 2008 and June 30 of 2016 limited to delivery between 22 weeks and 26 6/7 weeks of gestation. Primary outcome is neonatal death prior to discharge. We further stratified cesearean deliveries based on whether or not the active segment was involved in the hysterotomy. Secondary outcomes include presence of hysterotomy extension into the active segment, maternal blood loss, and 5 minute Apgar score. We reviewed general morbidities from each case. This study was approved by the IRB at Johns Hopkins, #IRB00104294. Statistics including Fisher's Exact test and t-tests were performed using Stata 14.
RESULTS: A total of 107 cases met criteria for inclusion, including 42 cases delivered by cesarean and 65 delivered vaginally. Of the 42 cesarean

deliveries, 25 included extension into the active segment including classical hysterotomies. Neonatal death was not significantly different between the groups even when stratified by gestational age.

Gestational Age in Completed Weeks	Vaginal Delivery			Cesarean Delivery			p-value
	Live at Discharge	Demise	Percentage Survival	Live at Discharge	Demise	Percentage Survival	
22	0	4	0%	0	1	50%	
23	5	7	41.67%	0	1	0%	0.62
24	9	0	100%	10	1	90.9%	0.55
25	19	3	86.36%	111	2	84.96%	0.63
26	17	1	94.44%	15	1	93.75%	0.73

Average estimated blood loss was significantly more for cesarean deliveries (799 cc vs 325 cc, p<0.01). 5 minute APGAR score was not significantly different between the groups.

CONCLUSIONS: In our population, cesarean delivery does not clearly improve rates of neonatal survival at time of discharge across gestational ages. Frequently, the active segment is involved in the cesarean delivery of these premature infants.

T-042

Novel Factors Associated with Spontaneous Onset of Preterm Labor. Elise N Erickson, Leonardo Pereira, Frances M Biel, Jonathan M Snowden*. *OHSU, Portland, OR, USA.*

INTRODUCTION: Many factors, like maternal race/smoking are associated with increased preterm birth (PTB). Often studies reporting outcomes of spontaneous PTB include "external" pathologies such as infection or placental insufficiency. The objective of this study was to examine risk factors for PTB in a large cohort of women with spontaneous labor grouped by different identifiable causes of labor. Using this approach we aim to better understand the contribution of certain modifiable and non-modifiable covariates in timing of labor.

METHODS: We conducted a retrospective cohort study using linked hospital discharge and vital records for all births (23-42 wk gestation) in California between 2007-10 (N=2,094,220). We excluded subjects with cesarean without labor, induction, fetal demise, multiple gestation, noncephalic presentation, placenta previa, prelabor/preterm ruptured membranes and fetal anomalies. The remaining 1,125,951 were divided into 3 groups with spontaneous labor: 1) obstetric infection, 2) conditions associated with placental insufficiency, and 3) labor with no known pathology.

RESULTS: 3.11% (n=31,967/1,030,756) of births in Group 3 were < 37 weeks of gestation, compared to 30.86% (n=22,006/71,784) of births in Group 2 and 4.27% (n=1,066/24,963) of Group 1. Risks of PTB are presented in Table 1. Across all 3 groups, Asian maternal race, younger age, lower education, high and low levels of prenatal care (PNC), tobacco use, nulliparity, prior PTB all predicted **increased** risk of PTB. Black/Hispanic race was only a risk factor for Group 1 and 2. No factors were associated with **decreased** risk of PTB in all 3 groups.

**Figure(s) will be available online.*

CONCLUSIONS: Odds of PTB differed among 3 groups of women; 1) infection, 2) placental insufficiency, 3) those without identified pathology. Surprisingly, Black/Hispanic women in Group 3 were not at higher risk for PTB. Novel findings prompt further investigation into the contributions of Asian race and level of PNC to PTB risk. Given that the majority of spontaneous PTB was not associated with infection or placental pathology, research to reduce risk of PTB may be informed by analyzing the underpinnings of **spontaneous** labor timing in the absence of identified pathology.

T-043

Characteristics of Uterine Inertia in Uterine Electromyography at the Active Phase of Labor. Pin Li†, Lele Wang, Xueya Qian, Abraham Morse, Robert E Garfield, Huishu Liu. *Guangzhou Women and Children's Medical Center, Guangzhou Medical University, Guangzhou, Guangdong, China.*

INTRODUCTION: The purpose of this study was to identify and analyze the uterine electromyography patterns in patients who develop uterine inertia in the active phase of labor. Patients with and without Patient-Controlled Epidural Analgesia and with and without oxytocin augmentation were included in the study.

METHODS: Uterine electromyography was recorded using 4 silver/silver chloride electrodes placed periumbilically. 30 women not requiring augmentation in the spontaneous active phase of labor were enrolled as a comparison group. Uterine electromyography was recorded in 10 patients with uterine inertia who were using patient controlled epidural anesthesia and 10 patients who were not. Electromyography was recorded before and during treatment with oxytocin. Electromyography signals were characterized by analysis of multiple variables including burst duration and amplitude, RMS and power density spectrum peak frequency.

RESULTS: Representative uterine electromyography tracings from women with or without uterine inertia in active phase of labor are shown in (Figures 1).The mean burst amplitude in the uterine inertia patients was significantly lower than in patients without uterine inertia (21.9±10.44μV vs 52.9±12.82μV, p < 0.001).Significant differences were also seen in the RMS(0.04±0.017mV vs 0.081±0.024mV, p<0.001)and duration of electromyographic bursts (25.6±7.25s vs 53.8±12.59s, p<0.001).There was no significant difference in any parameters measured in patients with and without patient controlled epidural anesthesia. Electromyography parameters were significantly increased in the uterine inertia groups after the administration of oxytocin.

CONCLUSIONS: Uterine electromyography in patients with uterine inertia is easily differentiated from patients progressing in spontaneous active labor. Patient controlled epidural anesthesia does not appear to affect the uterine electromyography.Uterine electromyography is a quantitative, non-invasive assessment tool that may contribute to the evaluation and management of patients with uterine inertia.

T-044

Is a History of a Prior Term Birth Associated with a Reduction in the Risk of Recurrent Preterm Birth? Moeun Son†, William A Grobman, Anna Palatnik, Emily S Miller*. *Northwestern University, Feinberg School of Medicine, Chicago, IL, USA.*

INTRODUCTION: It is well established that women with a history of a prior spontaneous preterm birth (sPTB) are at an increased risk for preterm birth (PTB) in a subsequent pregnancy. However, it remains unclear whether and to what degree also having a prior term birth modifies the recurrence risk in these women. We sought to examine whether a prior term birth is associated with a reduction in the frequency of PTB in women with a prior sPTB.

METHODS: A secondary analysis of data from two multicenter randomized clinical trials evaluating the role of 17 alpha-hydroxyprogesterone caproate (17P) and omega-3 fatty acid in women with a history of sPTB. Women with more than one prior sPTB, those with multiple prior term deliveries, and those missing delivery data were excluded. Women with one prior sPTB and a prior term birth were compared to those whose only birth was a sPTB using bivariable and multivariable analyses. The primary outcome was PTB before 37 weeks of gestation. Secondary outcomes were PTB before 35 weeks and 32 weeks, and sPTB before 37 weeks, 35 weeks, and 32 weeks of gestation.

RESULTS: Of the 705 eligible women, 204 (29%) had a prior term birth. Women with a prior term birth were less likely to be black (44.6% vs. 57.3%, p=0.012), married or living with a partner (56.4% vs. 67.7%, p<0.001), and had less years (y) of education (12 (IQR 11-14) vs. 13 (IQR 12-16) y, p<0.001) compared to those without a prior term birth. The frequencies of PTB and sPTB before 37 weeks of gestation were significantly lower in women with a prior term birth compared to women without a prior term birth (Table). These differences persisted after adjusting for potential confounders in multivariable regression (Table).

CONCLUSIONS: A history of a prior term birth is associated with a reduction in the frequency of recurrent PTB and sPTB before 37 weeks in women with a history of a prior sPTB.
**Figure(s) will be available online.*

T-045

15-Hydroxy Prostaglandin Dehydrogenase Is a Target for Induction of Cervical Ripening and Labor. Annavarapu Hari Kishore,[1] Bruce Posner,[2] Joseph Ready,[2] Sanford Markowitz,[3] R Ann Word*.[1] *[1]Univ TX Southwestern Med Ctr, Dallas, TX, USA; [2]Univ of TX Southwestern Med Ctr, Dallas, TX, USA; [3]Case Western Reserve Univ, Cleveland, OH, USA.*
INTRODUCTION: Induction of cervical ripening with prostaglandins (PGs) is common. The rate of PG-induced cervical ripening is highly variable and 10% do not respond. The underlying mechanisms of this non-responsiveness in some women and hyperstimulation in others are not known. The objective of this study was to decipher the mechanism of PGE2 actions on the cervix.
METHODS: To determine if inhibition of 15-PGDH is important in cervical ripening and preterm birth, a 15-PGDH inhibitor was employed.
RESULTS: Treatment with 15-PGDH inhibitor alone did not alter gestational length or fetal outcomes.

Treatment group	Dose (d15-d18)-BID	Delivery time (h from initiation of treatment) (n)	Resting dilation of cervix (mm) Mean±SEM (n)	Maximum Force (N)	Distensibility (mm/N) mean±SEM
Control	None	96 ± 2.5 (6)	2.32 ± 0.55 (4)	0.48 ± 0.03	10.89 ± 0.21
PGE_2	PGE_2 (1.6 mg/kg)	93 ± 1.3 (5)	2.84 ± 0.52 (5)	0.49 ± 0.01	11.46 ± 1.33
15-PG-DHi	(2.5 mg/kg)	99 ± 3.5 (10)	2.38 ± 0.33 (5)	0.43 ± 0.03	11.34 ± 2.23
PGE_2 + 15-PG-DHi	PGE_2 + PGDHi	40 ± 2.5* (10)	4.77 ± 0.37* (5)	0.41 ± 0.05	23.25 ± 4.39*

Interestingly, a combination of PGE_2 and PGDH inhibitor induced preterm labor within 36-48 h. Perhaps, the most interesting aspect of this treatment is that mice delivered only two pups closest to the cervix whereas the remaining pups delivered on d19 alive and healthy. Cervical tissues prior to delivery (d17, n=4-6/group) were comprised of a dense organized collagenous stromal matrix in vehicle, PGE_2 or PGDH inhibitor alone. In contrast, treatment with PGE_2+PGDH inhibitor resulted in increased mucus-laden epithelial cells and dramatic remodeling of the collagenous matrix surrounding stromal fibroblasts and smooth muscle cells. Biomechanical properties confirmed increased baseline dilation and increased distensibility in combination-treated animals.
CONCLUSIONS: 15-PGDH plays a crucial role in maintenance of cervical competency. Downregulation of cervical PGDH is a prerequisite for PGE_2-induced cervical ripening. Treatment with PGDH inhibitors may not only increase success of PG-induced cervical ripening but also facilitate use of lower doses and decrease the induction-to-delivery interval.

T-046

Antenatal Glucocorticoid Therapy Protects the Chronically Hypoxic Fetus from Programmed Endothelial Dysfunction and Hypertension in Adulthood. KJ Botting†, Y Niu, KL Skeffington, BJ Allison, KL Brain, N Itani, C Beck, DA Giussani*. *University of Cambridge, Cambridge, United Kingdom.*
INTRODUCTION: Antenatal glucocorticoid therapy (AGT) in threatened preterm labour is globally implemented as it reduces respiratory distress and death in preterm infants (*Cochrane Dat Syst Rev*. **3**:CD004454, 2003). Despite benefits, AGT may programme adverse cardiovascular function in the offspring (*J Dev Orig Health Dis*. **6(2)**:127, 2015). This knowledge base is mostly derived from AGT studies in healthy animal models. Conversely, the effects of AGT in models of pregnancy complicated by chronic fetal hypoxia and/or IUGR are comparatively unknown. Here, we isolated the long-term effects of AGT on cardiovascular function at adulthood in sheep which were born at term and were either normally grown or IUGR due to chronic fetal hypoxia.
METHODS: From 0.7 of gestation, pregnant ewes were exposed to normoxia (N) or chronic hypoxia (H, 10% maternal inspired air) followed by AGT (0.8 gestation; 2x12mg dexamethasone maternal i.m. 24h apart; ND: n=7, HD:10) or saline vehicle i.m. (N: n=10, H:10). A week before natural delivery, all ewes were returned to normoxia. Offspring were maintained until 9 months, then chronically instrumented under general anaesthesia to determine *in vivo* cardiovascular physiology followed by *ex vivo* femoral vascular function with wire myography. Data were analysed by 2-way ANOVA.
RESULTS: Offspring of hypoxic pregnancy were smaller at birth (A) and showed hypertension (B) with peripheral endothelial dysfunction (C) at adulthood (Fig.1). AGT in hypoxic pregnancy restored the programmed hypertension in adulthood via mechanisms including increased NO bioavailability. Offspring of hypoxic pregnancy with AGT had a greater fall in femoral vascular conductance during *in vivo* NO blockade and protection against the programmed impairment in peripheral endothelial function (C, D).
CONCLUSIONS: Antenatal glucocorticoid therapy in human clinically-relevant doses protects the chronically hypoxic IUGR fetus from programmed hypertension by increasing NO bioavailability and improving peripheral vascular function.
Support: British Heart Foundation
**Figure(s) will be available online.*

T-047

Low Maternal BMI and Associated Pregnancy Outcomes. Kaitlin Hanmer†,[1] Ann Thomas,[2] David Cantonwine,[2] Thomas McElrath*.[2] *[1]Brigham & Women's Hospital, Boston, MA, USA; [2]Brigham & Women's Hospital, Boston, MA, USA.*
INTRODUCTION: To determine how low prepregnancy body mass index (BMI) affects fetal growth, development of pregnancy-related comorbidities, delivery outcomes and neonatal outcomes. We also sought to compare weight gain patterns and attainment of the Institute of Medicine (IOM) standards for pregnancy weight gain between women with low and normal prepregnancy BMI.
METHODS: We included 1823 pregnancies from the POPS and LIFECODES pregnancy cohorts (Boston, MA) in a retrospective study. We compared pregnant women with a prepregnancy BMI <18.5 (underweight) to those with a prepregnancy BMI 18.5-24.9 (normal).
RESULTS: We had 92 women in the low and 1730 in the normal groups. Overall, 5% of pregnancies had a low prepregnancy BMI. Gestational weight gain was equivalent (11.0 vs. 11.3 kg respectively; p= 0.24) in both groups as was the rate of weight gain (0.5 kg per week). Women in the low BMI group were less likely to have gestational hypertension (p = 0.03). The rate of preeclampsia was not significantly lower in the low BMI group (4.3% vs 5.4%, p = 0.67). Other pregnancy comorbidities occurred at equal rates with no tendency for women in the low BMI group to deliver preterm (p=0.28). Prepregnancy BMI did not significantly affect mode of delivery (p = 0.13). However, infants born to mothers with low BMI weighed less at birth (p = 0.03) and trended toward lower Apgar scores at 1 and 5 minutes (p = 0.05 and p = 0.08).
**Figure(s) will be available online.*
CONCLUSIONS: Prepregnancy BMI is associated primarily with infant birth weight, but not obstetric comorbidities or mode of delivery. Women with low and normal prepregnancy BMI tend to gain the same amount of weight and gain at the same rate during pregnancy. Our results suggest that attaining a normal prepregnancy BMI is important for fetal growth and subsequent birth weight.

T-048

Maternal BMI Regulates the Exosomal Bioactivity on Cytokine Release from Endothelial Cells. Omar Elfeky,[1] Sherri Longo,[2] Andrew Lai,[1] Gregory Duncombe,[1] Gregory E Rice,[1,2] Carlos Salomon.[1,2] *[1]The University of Queensland, Brisbane, QLD, Australia; [2]Ochsner Baptist Hospital, New Orleans, LA, USA.*

INTRODUCTION: Obesity is one of the largest and most serious health issues we face today. Recent studies have shown that the placenta releases exosomes into maternal circulation across gestation. There are no studies, however, that have defined the relationship between maternal BMI and exosome concentration and bioactivity during gestation. We hypothesized that maternal BMI regulates the effect of exosomes present in maternal circulation on the release of cytokines from endothelial cells (EC).

METHODS: A time-series study design was used to establish the relationship between maternal BMI and exosome concentration during pregnancy. Blood samples were obtained from pregnant women at Ochsner Baptist Medical Center (New Orleans, USA) at different times of gestation (10-38 weeks), then classified by maternal BMI into lean (n=15, BMI 18.5-24.9 Kg/m2), overweight (OW, n=15, BMI 25-29.9 Kg/m2), and obese (n=15, BMI >30 Kg/m2) at the moment of sample collection. The total number of exosomes and specific placenta-derived exosomes were determined by Nanoparticle Tracking Analysis (NanoSight™) using quantum dots coupled with CD63 or PLAP antibodies. The effect of exosomes on cytokine (IL-6. IL-8, IL-10 and TNF-α) release from EC was established by the protein solution array analysis (Bioplex-200).

RESULTS: The total number of exosomes present in maternal circulation was strongly correlated with maternal BMI. The contribution of placental exosomes to the total exosomal population decreases with higher maternal BMI across gestation. Exosomes present in maternal circulation increase IL-6, IL-8 and TNF-α release from EC, an effect significantly higher when exosomes were isolated from obese women compared to Lean and OW.

CONCLUSIONS: We suggest that exosomes may contribute to the maternal systemic inflammation during pregnancy.

T-049

Gestational Diabetes Prevalence at Moderate & High Altitude. Anna G Euser,[1,2] Andrew Hammes,[3] Jared T Ahrendsen†,[1] Cassie Geremaia†,[1] Barbara Neistadt†,[1] David W Weitzenkamp,[3] Colleen G Julian,[4] Lorna G Moore*.[1] *[1]University of Colorado, Aurora, CO, USA; [2]University of Colorado, Aurora, CO, USA; [3]University of Colorado, Aurora, CO, USA.*

INTRODUCTION: Altitude affects pregnancy physiology. Prior studies showed decreased fasting glucose & increased insulin sensitivity in pregnancy at HA vs. sea level. We sought to determine gestational diabetes (GDM) prevalence at moderate (MA) & high altitude (HA) in Colorado with the hypothesis that there would be less GDM at HA.

METHODS: In a retrospective cohort design, we compared demographic & pregnancy data for women receiving prenatal care at MA (4000-7000ft) & HA (>8000ft). GDM diagnosis was determined using Carpenter-Coustan criteria. Exclusions were: twins, preexisiting diabetes, unavailable GDM results or moving from a different altitude in pregnancy. One pregnancy was included per patient. Demographic & pregnancy data were compared by t-test (continuous variables) & Chi-squared tests (categorical variables). Univariate, multivariate & stepwise models were used to assess the impact of altitude, maternal age, ethnicity, BMI, parity & GA at testing. In all models, unavailable data was treated as missing & an alpha level of 0.05 was used to assess significance.

RESULTS: We analyzed 2925 MA & 552 HA pregnancies. Overall, there was no difference in GDM prevalence. In all pregnancies, maternal age, Hispanic ethnicity, higher BMI category & GA at testing increased the odds of GDM. In MA univariate analysis, maternal age, Hispanic, BMI & GA at testing were significant. In HA univariate analysis, maternal age, Hispanic & higher parity were significant. Altitude of residence was not significant in any analysis.

CONCLUSIONS: GDM prevalence was not difference and adjusting for possible confounders did not change this result. BMI & GA at testing significantly increased the odds of GDM at MA but not at HA.

Characteristic	MA	HA	p value
Maternal age (y), mean (SD)	29.1 (5.2)	29.8 (5.8)	0.015
Maternal BMI (kg/m^2), n (%)			<0.001
BMI <25.0	1672 (57.2%)	379 (68.7%)	
BMI 25.0-29.9	710 (24.3%)	114 (20.7%)	
BMI ≥30.0	543 (18.6%)	59 (10.7%)	
Parity, n (%)			0.114
0	1,260 (43.1%)	258 (46.7%)	
1	959 (32.8%)	181 (32.8%)	
2+	706 (24.1%)	112 (20.3%)	
Hispanic, n (%)	561 (19.2%)	134 (24.3%)	<0.001
GA at GDM testing (days), mean (SD)	194 (29.4)	200 (13.8)	<0.001
GDM, n (%)	118 (4.0%)	22 (4.0%)	1.0

T-050

Pre-Pregnancy Obesity and Metabolomic and Transcriptomic Networks in Early-Mid Pregnancy. Alison G Paquette†,[1] Pandora L Wander,[2] Vineet Sangar,[1] Tanya K Sorensen,[3] Michelle Williams,[4] Nathan Price,[1] Daniel Enquobahrie*.[3,5] *[1]Institute for Systems Biology, Seattle, WA, USA; [2]University of Washington, Seattle, WA, USA; [3]Swedish Medical Center, Seattle, WA, USA; [4]Harvard T.H Chan School of Public Health, Boston, MA, USA; [5]University of Washington, Seattle, WA, USA.*

INTRODUCTION: Pre-pregnancy obesity has been associated with pregnancy complications for both mothers and offspring. Mechanisms mediating these relationships have not been fully described. We investigated effects of pre-pregnancy obesity on early-mid pregnancy transcriptome and metabolome.

METHODS: Maternal plasma was collected at 20 weeks of gestation from 10 women who were obese prior to pregnancy (body mass index, BMI≥30 kg) and 10 women who were lean prior to pregnancy (BMI<20 kg) in the Omega study, a prospective cohort study of pregnancy outcomes in Seattle, WA. Gene expression was profiled using Affymetrix arrays, and metabolites were measured using gas chromatography-mass spectrometry. Perturbations in gene networks were identified using differential rank conservation(DIRAC). Integrated pathway analysis of metabolomic and transcriptomic data was performed using metaboanalyst 3.0.

RESULTS: We identified 239 genes and 8 gene networks differentially expressed in relation to pre-pregnancy obesity. 15 metabolites were significantly different in individuals with pre-pregnancy obesity. Through integrated transcriptomic-metabolomic analysis, we identified 7 significantly perturbed pathways in women with pre-pregnancy obesity, with amino sugar and nucleotide sugar metabolism displaying the most connected pathways with the highest enrichment in perturbed genes and metabolites.

**Figure(s) will be available online.*

CONCLUSIONS: Women with pre-pregnancy obesity exhibited significant differences in circulating levels of gene transcripts and metabolites in pathways involving sugar metabolism, glutathione metabolism, and gluconeogenesis. Similar studies can inform mechanisms linking pre-pregnancy obesity and adverse pregnancy complications and outcomes.

T-051

An Innovative Bioinformatics Approach to Identify New Potential Therapeutic Targets in Gestational Diabetes. Jeffery A Goldstein†,[1] Lisa A Bastarache,[2] Joshua C Denny,[2] David M Aronoff*.[3] *[1]Vanderbilt University Medical Center, Nashville, TN, USA; [2]VUMC, Nashville, TN, USA; [3]VUMC, Nashville, TN, USA.*

INTRODUCTION: Gestational diabetes mellitus (GDM) is associated with short-term and long term complications for both mothers and their children. Normalizing blood sugar prevents some but not all complications of GDM. New therapeutic approaches are needed, but face difficulties in translating research concepts into clinically useful therapies while also ensuring that new medications are safe in pregnancy. We sought to use

electronic health record (EHR)-based genetic associations to investigate whether drugs currently considered safe in pregnancy might be potential candidates to treat, or prevent complications of, GDM.

METHODS: We compiled a list of 139 systematically active drugs considered safe in pregnancy that target the products of 288 genes. Using Vanderbilt University's BioVU DNA biobank associated with EHRs, we identified SNPs in the 288 genes associated with GDM and type 2 diabetes (DM2). Findings were correlated with gene expression in pancreatic beta cells and the placenta in health and diabetes. Using data from the EHR, we examined the association between medication use and markers of glycemic control including the 50 gram glucose tolerance test (GTT) and glycated hemoglobin (A1C). Multivariate analyses controlled for age, BMI, gender, race, and ethnicity.

RESULTS: We identified SNPs in 20 genes associated with GDM and 44 associated with DM2. Variants in the *MTNR1B* were associated with GDM and DM2 and use of the MTNR1B agonist agomelatine is associated with reduced A1C. Variants were identified in *5HTR3D* and the HTR3-antagonist anti-nausea medications (e.g. ondansetron), were associated with a 3.7 mg/dL increase in GTT. Conversely, hyperemesis gravidarum was associated with a 7.2 mg/dL decrease in GTT. Variants in muscarinic and nicotinic acetylcholine receptors, targeted by the Alzheimer medication galantamine were associated with GDM and DM2. Galantamine was associated with a 0.38% increase in A1C.

CONCLUSIONS: This innovative approach identified novel potential therapies aimed at GDM that are known to be safe in pregnancy. Future directions include study of candidate therapies in controlling blood glucose and preventing the negative complications of GDM and extending this method to other diseases of gestation.

T-052

Nonalcoholic Fatty Liver Disease in the First Trimester and Subsequent Development of Gestational Diabetes: A Prospective Cohort Study. SM Lee,[1] JS Park,[1] ER Norwitz,[2] JN Koo,[3] IH Oh,[3] JE Kwon,[3] BJ Kim,[4] SM Kim,[4] SY Kim,[5] GM Kim,[6] W Kim,[7] SK Joo,[7] S Shin,[8] CW Park,[1] JK Jun.[1] *[1]Seoul National University College of Medicine, Seoul, Republic of Korea; [2]Tufts University School of Medicine, Boston, MA, USA; [3]Seoul Women's Hospital, Incheon, Republic of Korea; [4]Seoul Metropolitan Government Seoul National University Boramae Medical Center, Seoul, Republic of Korea; [5]Seoul National University College of Medicine, Seoul, Republic of Korea; [6]Yonsei University College of Medicine, Seoul, Republic of Korea; [7]Seoul Metropolitan Government Seoul National University Boramae Medical Center, Seoul, Republic of Korea; [8]Seoul Metropolitan Government Seoul National University Boramae Medical Center, Seoul, Republic of Korea.*

INTRODUCTION: Recent evidence suggests that nonalcoholic fatty liver disease(NAFLD) is associated with impaired glucose tolerance and may be a manifestation of metabolic syndrome. We examined the association between NAFLD diagnosed in early pregnancy and the subsequent risk of developing gestational diabetes(GDM).

METHODS: This prospective cohort study included singleton pregnant women presenting for prenatal care at 10-14 weeks of gestation between November 2014 and March 2016. NAFLD was assessed by two different approaches:(1)the appearance of the liver on ultrasound;(2)the Fatty Liver-Index (FLI) incorporating BMI, waist circumference, triglycerides and gamma-glutamyl-transferase. All patients were screened for GDM using two-step approach at 24-28 weeks.

RESULTS: A total of 469 women were enrolled. The prevalence of NAFLD was 23% based on liver ultrasound, and 32% based on FLI. The risk of subsequent GDM was significantly increased in cases with NFALD, and appeared to be related to the severity of the disease (Table). This relationship remained significant after adjustment for confounding variables.

**Figure(s) will be available online.*

CONCLUSIONS: The presence of NAFLD in early pregnancy is associated with an increased risk of developing GDM later in the pregnancy.

T-053

Early Maternal Nutrient Restriction in the Sheep Induces Collagen Accumulation in the Myocardium of Overfed Offspring (F1). Adel B Ghnenis, John F Odhiambo, Peter W Nathanielsz, Stephen P Ford*. *University of Wyoming, Laramie, WY, USA.*

INTRODUCTION: We have shown that exposure to either early maternal nutrient restriction (MNR) or overnutrition/obesity (MO) in sheep predisposes F1 to an adult metabolic syndrome phenotype. Further, MO results in increased fetal left ventricular (LV) wall thickness and fibrosis by day 135 of gestation (dG) and in adult F1 subjected to *ad lib* feeding. In this study, we examined the effects of early MNR on LV wall thickness and collagen content in late gestation and following *ad lib* feeding in postnatal life.

METHODS: Ewes were assigned to either a control diet (CTR: 100% NRC recommendations) or an MNR diet (50% of CTR) from 28 to 78 dG, followed by a CTR diet through term. Subsets of ewes were euthanized at 135 dG (n=8/group), or allowed to lamb. All lambs were fed *ad lib* after weaning at 4 months (m) until necropsy at 8 m (n=8/group). LV tissues were snap frozen in liquid N and stored at -80°C. Collagen was hydrolyzed from LV tissue and content was determined by colorimetry as hydroxyproline equivalents. Data was analyzed by mixed procedures of SAS.

RESULTS: While LV collagen content was similar in MNR and CTR fetuses at 135 dG, LV wall thickness (mm) was greater ($P<0.05$) in MNR than CTR fetuses (7.21 ± 0.19 vs. 5.97 ± 0.15). LV wall thickness remained greater in MNR lambs (17.2 ± 0.3 vs. 14.3 ± 0.2) at 8 m, and LV collagen content was markedly greater in MNR lambs (5.56 ± 0.27 vs. 1.97 ± 0.27µg/mg; (Fig 1; $P < 0.0001$).

CONCLUSIONS: While MNR fetuses exhibited increased LV wall thickness by 135 dG, LV collagen content was similar at that time. In contrast, LV wall thickness and collagen content were markedly elevated by 8 m in overfed MNR vs. CTR F1. These data suggest that as observed with adult MO F1 subjected to a postnatal bout of *ad lib* feeding as adults, overfed MNR F1 have increased capacity for cardiac collagen synthesis compared to CTR F1. This increased myocardial collagen content of overfed MNR offspring would be expected to negatively affect cardiac muscle contractility and function. Supported by NIH INBRE 1P20RR16474.

**Figure(s) will be available online.*

T-054

Prostaglandin Levels in Pregnant Women with and without Hyperemsis Gravidum. Avi Hameroff,[1,2] Victor Mniarji,[1] Ponjeli Talus,[1] Vijaya Nacharaju,[1] Cassandra Charles,[1] Nicole Price,[1] Mudar Dalloul,[1] Ozgul Muneyyirci-Delale*.[1] *[1]SUNY Downstate Medical Center, Brooklyn, NY, USA; [2]Kings County Hospital Center, Brooklyn, NY, USA.*

INTRODUCTION: Nausea and vomiting are common in pregnancy and affect 70 - 85 % of pregnant women. Hyperemesis gravidarum (HG) is the term used to describe more severe nausea and frequent vomiting during pregnancy that may result in weight loss, hospitalization and smaller neonates. It has been shown that levels of hormones can affect how much nausea and vomiting is experienced during pregnancy.

METHODS: An IRB-approved observational cross-sectional study of pregnant women with or without HG seen in two antenatal clinics in Brooklyn, NY was conducted. Multiple pregnancy-related variables were collected and assessed. Plasma prostaglandin levels were assessed using Cayman Chemical Prostaglandin E Metabolite ELISA Kit and compared between the groups. Data were analyzed using two-tailed Student's t-test, Fisher exact test and odds ratio.

RESULTS: Study population of 18 women with single gestations between the ages of 22 and 45 years: 12 with HG and 6 controls without HG. There was no statistical significance difference in demographics between the two groups. Pregnant women who had a history of nausea and vomiting during a prior pregnancy were 10 times more likely to develop HG in their subsequent pregnancies. HG women reported the start of nausea and/or vomiting at approximately 5.8 ± 1.5 weeks of gestation that continued until approximately 22.3 ± 9.5 weeks of gestation. Plasma prostaglandin levels were significantly higher in HG women than in controls (HG: 93.4 ± 19.9 pg/mL, Control: 62.9 ± 34.9 pg/mL, $p = 0.015$).

CONCLUSIONS: Prostaglandin levels were significantly higher in HG women than controls without HG. Prostaglandins serve as important messengers in a wide variety of bodily functions. Our findings suggest that it may be involved in the etiology of HG. Further studies are needed to confirm this hypothesis.

T-055

Severe Vitamin K Deficiency in Pregnancy Presenting with Preterm Labor, Intrahepatic Cholestasis and Hematuria. Maria C Maldonado, Michael S Awadalla, Jay Idler, Welch Robert, Alhousseini Ali*. *Wayne State University, Detroit, MI, USA.*

INTRODUCTION: Severe Vitamin K deficiency is a very rare event in pregnancy in the developed countries. Serious risk factors and adverse outcomes including preterm labor, intrahepatic cholestasis of pregnancy and hematuria need to be carefully evaluated and promptly managed.

METHODS: CASE REPORT

RESULTS: We are reporting a 16 year old G1P0 patient who presented at 24 3/7 weeks with hematuria and preterm labor. Laboratory work up showed Prothrombin Time (PT): 117.8 seconds, Activated partial thromboplastin time (PTT): 80.5 seconds, international normalized ratio (INR): 10.34, Fibrinogen: 622 mg/dL, total bile acids: 29 micromol/L. Vitamin K level was undetectable (<0.1 nMol/L). Coagulation factors levels were within normal limit. With replacement of Vitamin K and administration of fresh frozen plasma, the patient had an arrest of preterm labor at 2 cm cervical dilation and the hematuria resolved. She presented with active labor at 27 1/7 weeks and worsening of intrahepatic cholestasis of pregnancy with increased bile salts level to 93 micromol/L. She delivered a male infant, 1150 grams with Apgar scores 7 and 9. The baby received 0.5 mg of intramuscular vitamin K at delivery. Head ultrasound at delivery showed bilateral grade 3 intraventricular hemorrhage.

CONCLUSIONS: This case demonstrates the importance of evaluating patients with hematuria, preterm labor, and intrahepatic cholestasis of pregnancy for coagulopathy related to Vitamin K or other coagulation factors and the importance of treatment to improve fetal outcomes and prevent serious perinatal complications.

T-056

Interventions for Uterine Atony Prior to Hysterectomy. Audrey A Merriam†,[1] Cande V Ananth,[1,2] Yongmei Huang,[2] Jason D Wright,[1] Mary E D'Alton,[1] Alexander M Friedman*.[1] *[1]Columbia University Medical Center, New York, NY, USA; [2]Joseph L Mailman School of Public Health, New York, NY, USA.*

INTRODUCTION: The objective of this study was to analyze use of interventions for uterine atony performed prior to hysterectomy.

METHODS: Using an administrative database (Premier) that includes drugs, devices, and diagnosis and procedure codes, we identified a cohort of women who underwent hysterectomy in the setting of a delivery hospitalization complicated by uterine atony between 2006-2014. We evaluated medical interventions (misoprostol, methylergonovine, carboprost), uterine tamponade, and uterine artery embolization utilized prior to hysterectomy. The incidence of the various interventions was analyzed temporally and by annualized hospital delivery volume quintile: 1st quintile 4-1309 deliveries per year, 2nd 1310-2187 deliveries, 3rd 2188-2942 deliveries, 4th 2943-4000 deliveries, and 5th 4001-9363 deliveries.

RESULTS: 1,937 patients underwent hysterectomy in the setting of uterine atony. The use of uterine tamponade prior to hysterectomy increased over the study period from 3.6% of cases in 2006-2008 to 21.6% of cases from 2012-2014. Uterine artery embolization increased from 3.6% to 7.6% over the same time period. Rates of embolization and uterine tamponade were highest in the highest delivery volume quintile (9.5% and 17.4%, respectively). Rates of uterotonic agents were similar over the study period. Methylergonovine was the most commonly used medication for treating uterine atony across all hospital volumes, while use of misoprostol varied most. Rates of uterotonic agents were stable over the study period.

**Figure(s) will be available online.*

CONCLUSIONS: Uterine artery embolization and uterine tamponade are increasingly being utilized as interventions prior to hysterectomy for uterine atony. Rates of these interventions vary by hospital volume. Further comparative effectiveness research is needed to characterize the use and efficacy of these interventions.

T-057

The Efficacy of 3rd Generation Cephalosporin Plus Metronidazole versus 3rd Generation Cephalosporin Plus Clarithromycin in Perinatal Outcomes for Women with Preterm Premature Rupture of Membranes. Jong Woon Kim, Yoon Ha Kim*, A Ra Cho, Jong Ho Moon. *Chonnam National University Medical School, Gwangju, Republic of Korea.*

INTRODUCTION: To compare perinatal outcomes of preterm premature of membranes treated with 3rd generation cephalosporin plus metronidazole (regimen A) versus 3rd generation cephalosporin plus clarithromycin (regimen B).

METHODS: A retrospective chart review compared perinatal outcomes in 186 patients with PROM <34 weeks receiving antibiotics regimen A (n=110) versus regimen B (n=76). Ninety-eight patients with PPROM between 25 and 32 weeks of gestation were chosen for comparing changes of the lipid peroxide, the protein carbonyl groups, ORAC values, and interleukin (IL)-6 levels in the maternal venous plasma (regimen A; n=54, regimen B; n=44).

RESULTS: The rates of spontaneous preterm delivery within 2 days after initiation of antibiotic treatment were significantly lower in those receiving regimen B (4/76, 5.3%) than in those receiving regimen A (18/110, 16.4%) (p=0.022). There was no difference in the mean antibiotic-to-delivery interval (regimen A; 11.0 days, regimen B; 11.5 days). There is no difference in the presence of acute histologic chorioamnionitis and funisitis. There is no difference in the rate of neonatal outcomes including respiratory distress syndrome, bronchopulmonary dysplasia, sepsis, intra-ventricular hemorrhage, peri-ventricular leukomalacia, and necrotizing enterocolitis. There was no significant difference in lipid peroxide levels, protein carbonyl formation, ORAC, and IL-6 of the venous plasma before the antibiotics administration, day 3 and day 7 after the antibiotics administration between regimen A and B.

CONCLUSIONS: Our results show that two antibiotics regimens may not effect on the latency period and improvement of neonatal outcomes. And they may not effect on the changes of oxidative stress. Although there was no significant difference in neonatal outcomes, 3rd generation cephalosporin plus clarithromycin regimen may have beneficial effect for short-term prolongation of pregnancy (up to 48 hours) to allow for the administration of antenatal steroids.

T-058

Delivery at Academic Institutions May Improve Cesarean Delivery Rates in Patients with Gastroschisis. Jose R Duncan†,[1] Pranit N Chotai†,[3] Anna K Slaggle†,[2] Eunice Y Huang,[3] Ajay J Talati,[2] Mauro H Schenone*.[1] *[1]University of Tennessee Health Science Center, Memphis, TN, USA; [2]University of Tennessee Health Science Center, Memphis, TN, USA; [3]University of Tennessee Health Science Center, Memphis, TN, USA.*

INTRODUCTION: According to US vital statistic, only 63% of patients with gastroschisis attempt vaginal delivery.

We aim to compare cesarean delivery rates (CDR) in pregnancies with gastroschisis delivered in non-academic institutions vs. those delivered in academic centers.

METHODS: Chart review from 2008 to 2015 was performed. CDR and percentage of attempted vaginal delivery (AVD) were compared among pregnancies with gastroschisis delivered in nonacademic hospitals with those delivered in an academic institution.

Chi-square, Fischer exact and Wilcoxon rank sum were utilized for univariate analysis. Results are presented as median with interquartile ranges and percentages**.** Logistic regression was used to control for birth weights. A p value < 0.05 was considered significant.

RESULTS: We included 93 of 107 cases. Delivery in non-academic centers was associated with increased CDR (30 out of 42 (71.4%) vs. 21 out of 51 (41.2%)) (RR 1.7 (1.2 -2.5)) and lower AVD (16 of 42 (38.1%) vs. 44 of 51 (86.3 %)) (RR 0.44 (0.3-0.7)). After logistic regression, CDR remained different between groups (p = 0.001). See Table 1 for demographics and neonatal outcomes.

	Delivery at academic center	Delivery in non academic center	*p* value
Age (years)	21 (IQR 19-23)	21 (IQR 19-24.5)	0.69
Gestational age (weeks)	36.1 (IQR 34.6-37.2)	36.5 (IQR 35.2-37.4)	0.18
Race (N)			
Caucasian	33 (54.4 %)	35 (85.4 %)	0.007
African American	20 (35.15 %)	4 (9.8 %)	0.008
Hispanic/Latino	6 (10.5 %)	2 (4.9 %)	0.54
Body mass index (Kg/m^2)	28.9 (IQR 26.3-32.1)	29.5 (IQR 26.3-31.7)	0.82
Primigravidas (N)	31 (54.4%)	24 (53.3%	0.92
Hypertensive disorders (N)	8 (16 %)	1 (2.6%)	0.08
Repeat Cesarean deliveries (N)	3 (5.9 %)	1 (2.4 %)	0.77
Breech presentation (N)	1 (2%)	1 (2.4%)	> 0.99
Length of stay (days)	41.5 (IQ 27-69.2)	48 (IQ 30-72)	0.38
Bowel ischemia (N)	5 (8.3 %)	9 (19.2 %)	0.17
Neonatal death (N)	3 (5 %)	1 (2.2%)	0.83

CONCLUSIONS: Delivery at an academic institution may decrease the rate of cesarean delivery in pregnancies with gastroschisis.

T-059

Variation in Endometritis Rates Following Cesarean Section. Joses A Jain†, Cande V Ananth, Zainab Siddiq, Jason D Wright, Mary E D'Alton, Alexander M Friedman*. *Columbia University Medical Center, New York, NY, USA.*

INTRODUCTION: Infection rates for surgical procedures may vary on a hospital-to-hospital basis. This variation may be related to care quality. The objective of this study was to evaluate variation in post-cesarean endometritis rates between hospitals.

METHODS: We used a large administrative hospitalization database, the Perspective (Premier) database, to evaluate hospital-level postpartum infection rates from 2008 to 2009. We limited the study to centers that performed greater than 1,000 deliveries during the study period. We evaluated demographic and hospital factors associated with post-cesarean endometritis, and compared hospital rates of infection.

RESULTS: Among 175,159 women who delivered during the study period at 105 hospitals, 3.5% were diagnosed with post-cesarean endometritis. Endometritis was more common amongst black women than white women (4.4% vs. 2.7% $p<0.01$) and in the Northeast compared to the Midwest, South, and West (4.1% vs. 3.7%, 3.2%, and 3.6%, respectively, $p<0.01$). The rates of infection varied significantly by hospital. The rate of endometritis at the hospital at the 10^{th} percentile of infection rates was 1.4%. The hospital at the 90^{th} percentile was 7.5%. Women delivering in the 90^{th} percentile were 5.5 times as likely to have an infection when compared to those delivering in the 10^{th} percentile. Hospital post-cesarean endometritis rates are demonstrated in **Figure 1** from lowest to highest rates**.**

**Figure(s) will be available online.*

CONCLUSIONS: There is significant variation in post-cesarean endometritis rates among centers. Given that endometritis risk may be secondary to surgical preparation, antibiotic administration, and other factors, this variation may be due differences in care quality. Post-cesarean endometritis rates may be a potentially useful metric for further quality improvement investigation.

T-060

Utilization of Inpatient Psychiatry Consults at an Urban Obstetric Hospital. Nicole R Hall,[1] Emily C Rutledge†,[1] Susan M Ramin,[1] Manju Monga,[1] Mary K Shoemaker†,[1] Lucy J Puryear*.[2] *[1]Baylor College of Medicine, Houston, TX, USA; [2]Baylor College of Medicine, Houston, TX, USA.*

INTRODUCTION: Untreated psychiatric conditions in pregnancy can lead to adverse maternal and fetal outcomes. The consultation-liaison psychiatry model in the inpatient setting addresses acute concerns of inpatients with comorbid psychiatric conditions. The objective of this study was to evaluate the referral and detection rates for psychiatric disorders of inpatients in an urban tertiary care women's hospital.

METHODS: A retrospective chart review was performed of all inpatient psychiatry consults from January 2012 to August 2015. Data extracted included consult indication, psychiatric history, medical and obstetric complications, treatment recommendations and obstetric outcomes.

RESULTS: There were 307 referrals for inpatient psychiatry consults and 19,822 deliveries during the study period. 72% of patients had a psychiatric history and 19% had a history of drug use. 42% of patients were pregnant and the remainder were seen in the postpartum period. The most common referral indications are shown in Table 1.

After consultation, only 8% of patients were diagnosed with no psychiatric illness. The 5 most common diagnoses were depression (17%), anxiety (13%), adjustment disorder (13%), anxiety and depression (9%), and anxiety with adjustment disorder (4%). Psychiatric medications were either initiated or adjusted in 46% of the consults. After initial consultation, ongoing inpatient or outpatient psychiatric treatment was recommened in 87% of patients.

The majority of patients had at least one obstetric (76%) or one medical (65%) complication affecting their pregnancy. The mean gestational age at delivery was 34 weeks 2 days and 56% of neonates were admitted to the NICU after delivery.

Table 1 shows the indicatins for inaptient psychiatry consultation

	No.(%) N=307
Anxiety	115 (37.4)
Depression	73 (23.8)
History of psychiatric disorder	59 (19.2)
Medication recommendations	3 (0.9)
Grief	6 (1.9)
Fetal loss	12 (3.9)
Substance abuse	4 (1.3)
Suicidality	5 (1.6)
Follow up	14 (4.6)
Inappropriate behavior	7 (2.3)
Other	9 (2.9)

CONCLUSIONS: Comorbid psychiatric conditions are common in pregnancy and warrant evaluation for diagnosis and ongoing treatment. Sceening and early identification of mental illness are important for comprehensive obstetric care.

T-061

Management of Breech Presentation Beyond 40 Weeks of Gestation. Hanna Huerter, Isabel Voigt, Frank Louwen. *Johann Goethe-University Hospital, Frankfurt am Main, Hessen, Germany.*

INTRODUCTION: Breech presentation still represents a challenge in counselling patients as far as the mode of delivery is concerned and only a few hospitals in Germany offer women the possibility for a vaginal breech delivery. Especially beyond 40 weeks of gestation there is lack of evidence whether there is still a good chance for a vaginal breech delivery and if this does not increase morbidity and mortality for the mother and her child.

METHODS: We performed a retrospective cohort study through database of all breeches intended to deliver vaginally at the university hospital of Frankfurt from January 2013 until December 2015 (n=390). Only singleton pregnancies where included. To compare vagnial breech deliveries beyond 40 weeks of gestation with those before the estimated date of delivery we divided the collective into two groups: Group A

with intended vaginal breech delivery at ≥ 40+0 weeks of gestation at the time of delivery (n=181) and group B in 37+0 up to 39+6 weeks of gestation (n=209).
RESULTS: In group A 64% (n=115) could deliver vaginally, in 36% (n=66) a caesarean section had to be performed after initially intended vaginal delivery. In group B there were 71% vaginal breech deliveries (n=149) and 29% caesarean sections (n=60). In our statistical analyses we found no significant differences between the two groups. As far as the fetal outcome is concerned (described by fetal pH-value and Apgar Score) no statistically significant differences could be observed.
CONCLUSIONS: According to our data a patient should be offered the option of a vaginal breech delivery even beyond 40 weeks of gestation. Even post term there is no indication to deviate from the initially intended mode of delivery. In this respect pregnancies in breech presentation can be treated equally to those in cephalic presentation.

T-062

High Pelvic Floor Muscle Stiffness Measured by Vaginal Elastometry Is a Risk Factor for Delayed Second Stage of Labour, Instrumental Vaginal Delivery and Pelvic Floor Damage. Dilly OC Anumba*,[1] Siobhan Gillespie,[1] Swati Jha,[1] Shahram Abdi,[1] Jenny Kruger,[3] Xinshan Li.[2] *[1]The University of Sheffield, Sheffield, South Yorkshire, United Kingdom; [2]The University of Sheffield, Sheffield, South Yorkshire, United Kingdom; [3]University of Auckland, Auckland, New Zealand.*
INTRODUCTION: Childbirth is associated with pelvic floor muscle (levator ani, LA) damage (PFMD) in a third of women. In addition to short-term sexual, urinary or bowel symptoms, PFMD results in pelvic organ prolapse and urinary incontinence in 20% of affected women. However the biomechanics, prediction, detection and management of PMFD remain ill-understood. We hypothesised that quantifying PFM stiffness in in a perineal trauma clinic (PTC) may provide insight into the causes and consequences of LA muscle damage.
METHODS: We employed a vaginal elastometer to measure PFM stiffness and assess acceptability in 55 consecutive attendees of a PTC, 12 of who also had MRI to define any LA muscle defects. We explored the association of PFM stiffness with demographics, labour/delivery characteristics, symptoms, and evidence of LA damage on MRI. Eleven women were studied twice to ascertain test-retest reliability.
RESULTS: Raised BMI was associated with reduced PFM stiffness (r= -0.4, P<0.01). Higher PFM stiffness (N/mm) was associated with 2nd stage of labour duration >120min, instrumental vaginal delivery (n=16) vs. spontaneous delivery (n=35) (0.62±0.03 vs 0.50±0.04, P<0.05), and forceps delivery (n=12) vs non-forceps vaginal delivery (n=39) (0.63± 0.04 vs 0.51± 0.04, P<0.05). Women with LA muscle defects (n=7) had higher PFM stiffness than those without (n=5), and those with urinary/ bowel/sexual symptoms (n=13) had lower PFM stiffness (0.57±0.04 vs 0.45±0.04, P<0.05). Combining BMI, PFM stiffness and the Oxford pelvic floor tone score in a regression model was predictive of urinary/bowel/ sexual symptoms (AUC 0.83, 95% CI 0.68 -0.92, P<0.01, sensitivity 75%, specificity 85%).
CONCLUSIONS: Delayed 2nd stage of labour and instrumental vaginal delivery in the antecedent birth is associated with higher PFM stiffness. Elastometry combined with clinical indices may improve prediction of risk of PFMD. Larger studies are required to determine whether high PFM stiffness antenatally is a risk factor for 2nd stage of labour prolongation and/or avulsion injuries, and whether elastometry could prove a useful clinical test.

T-063

Reduced Third Trimester Growth Velocity in Fetuses of a Normal Birthweight Is Associated with Uteroplacental Insufficiency. Teresa MacDonald†,[1,2] Alice Robinson,[1] Lisa Hui,[1,2] Stephen Tong,[1,2] Sue Walker*.[1,2] *[1]Mercy Hospital for Women, Melbourne, VIC, Australia; [2]The University of Melbourne, Melbourne, VIC, Australia.*
INTRODUCTION: Fetal growth restriction is the single biggest risk factor for stillbirth. However 50% of stillbirths in high income countries are *not* small, but born approriate-for-gestational-age (AGA, birthweight>10th centile). Reduced growth velocity in late pregnancy may reflect poor placental function and uteroplacental insufficiency (UPI) in fetuses born AGA. These fetuses may plausibly contribute to "unexplained" stillbirths.
Aim: To determine whether reduced third trimester growth velocity is associated with UPI in AGA fetuses, as evidenced by adaptive fetal Doppler parameters, increased intrapartum fetal compromise and reduced neonatal body fat.
METHODS: 347 nulliparas with uncomplicated pregnancies were recruited to a prospective study of ultrasound examination at 28 (27^{+0}-29^{+0}) and 36w (35^{+0}-37^{+0}). Customised estimated fetal weight (EFW) and cerebroplacental ratio (CPR) were recorded. Customised birthweight centile was calculated; SGA infants were excluded from the analysis. Measures used as evidence of UPI were: 1) Low 36w CPR 2) Umbilical artery (UA) pH<7.15, indicating fetal acidaemia 3) Low neonatal Ponderal Index and body fat percentage (BF%) assessed by skinfolds and/or air displacement plethysmography (ADP) ("Low BF%" if ADP BF%>1SD below the mean). Growth velocity, calculated as EFW and abdominal circumference (AC) centile change per day between ultrasounds, was analysed for each of the outcomes.
RESULTS: 308 fetuses were AGA. EFW growth velocity among AGA fetuses was significantly correlated with all measures of UPI: cerebral redistribution (36w CPR<5th centile, p=0.01), neonatal acidosis (UA pH<7.15, p=0.02), and low BF% (p=0.047). AC velocity also correlated with pH<7.15 (p=0.03) and low BF% (p=0.02). When cut-off thresholds were applied to dichotomise the cohort, a >30 centile fall in EFW between 28 and 36w was associated with a relative risk (RR) of 2.8 for CPR<5th centile at 36w (p=0.03), and a >30 centile fall in AC was associated with a RR of 8.1 for low BF% (p=0.002). A fall of >35 EFW or AC centiles was significantly associated with UA pH<7.15 (EFW-RR=3.51, p=0.03; AC-RR=3.01, p=0.049).
CONCLUSIONS: Reduced growth velocity in AGA fetuses is associated with antenatal, intrapartum and neonatal features of UPI. These fetuses may be an important under-appreciated clinical cohort at increased risk of stillbirth.

T-064

Pre-Conception Blood Pressure and Evidence of Placental Malperfusion. Jacqueline Atlass†,[1] Marie Menke,[1] W Tony Parks,[3] Karen Derzic,[2] Janet Catov*.[2] *[1]Magee Womens Hospital of UPMC, Pittsburgh, PA, USA; [2]Magee Womens Hospital of UPMC, Pittsburgh, PA, USA; [3]Dartmouth-Hitchcock Medical Center, Lebanon, NH, USA.*
INTRODUCTION: Evidence of placental malperfusion is associated with severe preeclampsia, intrauterine growth restriction and preterm birth, perhaps related to maternal vascular health. Pre-pregnancy blood pressure and placental malperfusion are less well characterized.
METHODS: A retrospective case-control study was performed of women with singleton gestations who delivered at Magee-Womens Hospital in 2012 with placental evaluations. Charts from 103 deliveries with placental malperfusion lesions and 107 deliveries without were randomly selected. Subjects were excluded if pre-pregnancy or prenatal visit data were unavailable in the Electronic Medical Record within 3 years of delivery. Overall, 96 women (45%) had pre-pregnancy records (48 with and 47 without malperfusion). Blood pressure, demographic and clinical data were abstracted and compared.
RESULTS: Amongst women with and without malperfusion, no differences in pre-pregnancy systolic (SBP, 114.3 ± 10.6 vs 117.3 ± 12.6 mmHg, p = 0.22) or diastolic blood pressures (DBPs, 71.7 ± 8.2 vs 74.3 ± 10.1 mmHg, p = 0.18) were observed. Early pregnancy SBP (p=0.35) and DBP (p=0.64) were not associated with placental malperfusion (10.0 ± 4.0 and 9.4 ± 4.6 gestational weeks). However, women with placental malperfusion demonstrated a reduction in their pre- to early pregnancy decrease in DBP.
**Figure(s) will be available online.*
Adjusted for race, pre-pregnancy BMI, age, pre-conception interval, and gestational age at the first prenatal visit, the difference in pre- to early pregnancy DBP was significantly less (-1.35 mmHg drop vs -5.6mmg drop, p<0.05) in women with placental malperfusion compared to those without.

CONCLUSIONS: A blunted early gestation drop in DBP may be a risk factor for placental malperfusion, perhaps related to early pregnancy vascular maladaption. Ability of the EMR to provide pre-pregnancy data serves as a novel, untapped opportunity to study the pre-pregnancy state.

T-065

Prenatal Stress and Gestational Weight Gain. MA Kominiarek,[1] W Grobman,[1] E Adam,[2] C Buss,[4] J Culhane,[5] S Entringer,[4] G Miller,[6] H Simhan,[7] P Wadhwa,[3] D Williamson,[8] KY Kim,[9] L Keenan-Devlin,[10] A Borders.[10] *[1]NU, Chicago, IL, USA; [2]NU, Chicago, IL, USA; [3]UCI, Irvine, CA, USA; [4]Universitatsmedizin, Berlin, Germany; [5]CHOP, Philadelphia, PA, USA; [6]NU, Chicago, IL, USA; [7]U Pitt, Pittsburgh, PA, USA; [8]Duke, Durham, NC, USA; [9]NU, Chicago, IL, USA; [10]NorthShore Health System/U of Chicago, Chicago, IL, USA.*

INTRODUCTION: The objective of this study is to evaluate the association between prenatal stress and gestational weight gain (GWG).

METHODS: This was a secondary analysis of a prospective cohort study of women in the Measurement of Maternal Stress Study (MOMS) between 2013-2015 from 4 sites in the US. Participants were ≥18yrs with a singleton, <21wks pregnant, and English speaking without fetal anomalies, progesterone treatment, or corticosteroid use. We compared self-reported responses at 32-35wks to the Life Experiences Survey (LES), a 37-item measure of life changes in a variety of situations, according to GWG (low, met, excessive) categories. Bivariable comparisons and logistic regression analysis were used to estimate the association between LES and the odds of meeting GWG goals.

RESULTS: Of 725 eligible women, 17% were black, 59% white, 19% Hispanic, and 36% had Medicaid-funded prenatal care. Women who met GWG goals were older, had a lower BMI, had higher education and income, and were more frequently married and without gestational diabetes compared to women with low or excessive GWG (all $p<0.04$). GWG did not vary by race with 28% of blacks, 31% of whites, and 26% of Hispanics meeting GWG ($p>0.05$). Exercise and daily servings of vegetables, fruit, dairy, and fish did not vary across the GWG groups ($p>0.05$ for all). Women who met GWG goals had lower mean LES scores (6.7±6.3) compared to women with low (9.0±7.3) and excessive (8.3±7.2) GWG, p=0.005. After adjusting for age, BMI, income, education, marital status and gestational diabetes, there remained a statistically significant inverse relationship between meeting GWG goals and LES scores (aOR 0.97, 95%CI 0.94-0.99).

CONCLUSIONS: Women who met GWG goals have lower stress, as measured by the LES survey. This highlights the potential that interventions directed toward more psychosocial support may also have salutary effects upon GWG, and that such studies should be undertaken.

T-066

Predictors of Antenatal Complications During Expectant Management of PPROM. Kelli Barbour†,[1,2] Christina Herrera,[1,2] Robert Silver,[1,2] Michael Varner,[1,2] Tracy Manuck*.[1,2,3] *[1]Univ of Utah, Salt Lake City, UT, USA; [2]Intermountain Health Care, Salt Lake City, UT, USA; [3]University of North Carolina, Chapel Hill, NC, USA.*

INTRODUCTION: We aimed to identify antenatal risk factors associated with antepartum complications among pregnancies complicated by preterm premature ruptured membranes (PPROM) <34 weeks.

METHODS: This is a retrospective cohort of women with PPROM 20.0-33.6 weeks from 2010-2014. Women with singleton, non-anomalous pregnancies and confirmed PPROM, and >12 hours latency were included. The composite primary outcome included stillbirth, intraamniotic infection and inflammation (III), cord prolapse, or abruption prompting delivery. Risk factors assessed included vaginal bleeding, non-cephalic presentation, regular uterine contractions, and anhydramnios. Data were analyzed by chi-square, t-test, & logistic regression.

RESULTS: 211 women met inclusion criteria. Demographics were similar between women with or without antenatal risk factors. The majority of women were white (62.4%) and married (61.7%). 148 (70.1%) pregnancies had at least one risk factor: 81 pregnancies had vaginal bleeding, 56 had non-cephalic presentation, 67 had contractions, and 31 had anhydramnios. 61 (29.4%) had antenatal complications prompting delivery; of these, there were 0 stillbirths, 36 (17.1%) with III, 5 (2.4%) with cord prolapse, and 23 (10.9%) acute abruptions. The presence of any risk factor was associated with the development of antenatal complications (p=0.032). In analysis of individual risk factors and complications, vaginal bleeding was associated with abruption ($p<0.001$) and III (p=0.037), while non-cephalic presentation was associated with acute abruption (p=0.035) and cord prolapse (p=0.002) (Table 1).

**Figure(s) will be available online.*

In multivariable analyses only the gestational age at PPROM was associated with the development of antenatal complications (aOR 0.86, 95% CI 0.79 0.94).

CONCLUSIONS: Risk factors as a composite and bleeding and non-cephalic presentation as individual risk factors were associated with complications prompting earlier delivery. These data can be used to develop and test models to predict risks of expectant management and need for urgent delivery.

T-067

Increased Proteinuria During Acute Pyelonephritis in Pregnancy. Cindy T Chau,[1] Alex Fong,[2] Rebecca Simon-Freeman,[1] Kenneth K Chan.[2] *[1]University of California, Irvine, Orange, CA, USA; [2]Miller Children's and Women's Hospital, Long Beach, CA, USA.*

INTRODUCTION: There is little published on the quantitative protein spillage in pregnant women with pyelonephritis. The purpose of this study is to quantify proteinuria in pregnancy women with and without acute pyelonephritis, with special considerations for preeclampsia-level proteinuria.

METHODS: Prospectively collected were mean 24-hr urinary protein excretion and urinary protein:creatinine ratio in singleton pregnancies with and without acute pyelonephritis between 20 0/7 and 41 0/7 weeks. Pyelonephritis was diagnosed by at least two of three criteria: Costovertebral angle tenderness, temperature ≥100.4F, and/or positive urine culture. Subjects with hypertension, medical comorbidities affecting renal function, vaginal bleeding, rupture of membranes, or who were hospitalized >3 days were excluded. Student t-test, Mann-Whitney U test, Fisher exact, and chi-square test were used as indicated. Potential confounders were adjusted using analysis of covariance.

RESULTS: Thirty-six pregnant women were enrolled in the study, 20 and 16 with and without acute pyelonephritis, respectively. All urine samples were adequately collected. Maternal age, gestational age, blood pressure, serum creatinine, nulliparity, and BMI were similar between the two groups. All women with pyelonephritis had confirmed positive urine culture. Mean 24-hour urinary protein excretion was significantly higher in pregnant women with an acute pyelonephritis than those without, 417.1 ± 217.0 mg vs. 122.0 ± 30.9 mg, p= <.001. Moreover, a higher proportion of women with pyelonephritis demonstrated proteinuria (>300 mg/24-hours) and protein:creatinine ratio >0.3 (60% with pyelonephritis vs. 0% without, p=<.001). These findings remained statistically significant after adjustment for confounders.

**Figure(s) will be available online.*

CONCLUSIONS: In pregnant women with acute pyelonephritis, urine protein excretion is significantly higher compared to controls, exceeding the threshold for significant proteinuria used for identifying preeclamptic women. This should be taken into account when women are being evaluated for preeclampsia during an acute pyelonephritis episode.

T-068

Is the Use of Prophylactic Antibiotics During Revision of the Uterine Cavity Really Necessary? Myriam Safrai, Yossef Ezra, Michal Lipschuetz, Doron Kabiri*. *Hadassah Medical Center, Jerusalem, Israel.*

INTRODUCTION: The aim of this study was to assess whether the use of prophylactic antibiotics during revision of the uterine cavity indeed reduces the rate of endometritis.

METHODS: We performed a retrospective cohort study which included all women who underwent revision of the uterine cavity following vaginal delivery between 2010 and 2015. The study group consists of all women who underwent revision of the uterine cavity and received prophylactic antibiotic treatment, while the control group consists of all

women who underwent revision of the uterine cavity with no prophylactic treatment. The primary outcome measure was the incidence of postpartum endometritis.

RESULTS: we included 407 vaginal deliveries followed by manual removal of the placenta. Ninety four women (23.8%) were not treated with prophylactic antibiotics, whereas 313 women (77.2%) were treated. Seven women (1.7%) developed endometritis. Six of them had received prophylactic treatment (1.91%) while one woman had not (1.05%), OR=0.55 95%CI [0.065-4.630].

CONCLUSIONS: The use of prophylactic antibiotics was not associated with a significant difference in post-partum endometritis rates in women who underwent revision of the uterine cavity. Based on these results, the use of prophylactic antibiotics during manual removal of the placenta does not appear to be justified, especially since excessive use of antibiotics is known to enhance resistance mechanisms.

**Figure(s) will be available online.*

	Prophylactic antibiotic N=94	No prophylactic antibiotic N=313	P-Value
Maternal age	30.6 ± 4.8	30.5 ± 5.4	0.821
Primiparous	2 (304.%)	84 (30.7%)	<0.999
Term delivery 37-42 week	89 (94.7%)	287 (91.7%)	0.505
Induction	17 (21.5%)	72 (26.3%)	0.463
Epidural	48 (60.8%)	192 (70.1%)	0.133
Prolonge second stage	6 (8.1%)	26 (9.9%)	0.823
Meconium stain	14 (14.9%)	41 (13.1%)	0.731
Vaccum extraction	8 (8.5%)	43 (13.7%)	0.179
Post-Partum Hemorrhage	36 (53.7%)	139 (53.9%)	>0.999
Endometritis	1 (1.1%)	6 (1.9%)	>0.999
Apgar <at 5 min	0	3 (1.1%)	>0.999
pH < 7.1	0	2 (0.9%)	>0.999
Birthweight	3210 ± 549	3233 ± 590	0.187
NICU admission	4 (5.1%)	12 (4.4%)	0.763

T-069

Accuracy of Rapid Group B Streptococcus Polymerase Chain Reaction in Threatened Preterm Labor. Cindy T Chau,[1] Jennifer Duffy,[1] Craig V Towers,[2] Callie Reeder,[2] Kim Fortner,[2] Alex Fong.[3] *[1]University of California, Irvine, Orange, CA, USA; [2]University of Tennessee Medical Center, Knoxville, TN, USA; [3]Miller Children's and Women's Hospital, Long Beach, CA, USA.*

INTRODUCTION: Maternal colonization is the primary risk factor and leading cause of early onset neonatal GBS disease in the United States, with mortality rate of 30% in preterm infants. Standard GBS screening via culture take up to 3 days to obtain results. Real-time polymerase chain reaction (RT-PCR) has been reported to be sensitive and specific for identifying GBS at term. The objective of this study is to evaluate the accuracy of RT-PCR compared to culture for GBS in a large exclusively preterm population.

METHODS: This is a multicenter prospective cohort study performed at Miller Children's and Women's Hospital Long Beach and University of Tennessee Medical Center. Women between 21 6/7 and 36 6/7 weeks with threatened preterm labor or indications for delivery were enrolled. Subjects were excluded if they had GBS bacteriuria, history of neonatal GBS sepsis, or recent antibiotic exposure. Two rectovaginal samples were collected simultaneously: RT-PCR test and standard culture. The sensitivity, specificity, predictive values (PV), and likelihood ratios (LR) of the RT-PCR were calculated using GBS culture as a gold standard reference. 95% confidence intervals were calculated using Wilson scores.

RESULTS: A total of 342 sample pairs were analyzed. All samples yielded valid RT-PCR and culture results. There were 101 culture positive GBS cases identified, yielding a GBS colonization rate of 29.5%. RT-PCR sensitivity was 80.2% while specificity was 97.9%. Positive PV, negative PV, positive LR and negative LR were 94.2%, 92.2%, 38.7, and 0.20, respectively. RT-PCR was able to detect 5 additional cases of GBS undetected by culture, thus conferring an increase in detection rate of 5%.

**Figure(s) will be available online.*

CONCLUSIONS: Due to inadequate sensitivity, RT-PCR should not be used as the sole screening test for GBS in preterm gestation. However, its use as an adjunct to culture should be considered due to its rapid turnaround and potential at identifying some cases otherwise not identified on culture.

T-070

A Scoping Review of Indigenous Longitudinal Studies of Both Pregnancy and Early Childhood. Julie Burrows,[1] Gita Wahi,[2] Sonia Anand,[2] Peter Jones,[3] Kirsty Pringle,[4] Kym M Rae*.[1] *[1]University of Newcastle, Tamworth, NSW, Australia; [2]McMaster University, Hamilton, ON, Canada; [3]Bond University, Gold Coast, QLD, Australia; [4]University of Newcastle, Callaghan, NSW, Australia.*

INTRODUCTION: The concept of developmental origins of health and disease (DOHaD) can be investigated through pregnancy and child cohort studies. Indigenous populations around the world endure many health disparities. This review describes the status of research on Indigenous maternal and child cohort studies, the scope of data collected to date and key health determinants that are common in Indigenous mothers. This review also highlights areas for future research in this field.

METHODS: A keyword search of relevant databases for peer-reviewed literature was undertaken. Exclusion criteria were applied to keep the focus of the review to longitudinal Indigenous pregnancy and mother/child cohort studies employing repeated measure design in both pregnancy and early childhood.

RESULTS: From 76 retrieved articles a total of 4 studies met the inclusion criteria and reported on Indigenous populations of Canada, the United Kingdom, Australia and New Zealand. Measurements investigated included sociodemographic, psychosocial, lifestyle, chronic health and child development. Duration of child follow-up ranged from 16 months to 16 years.

CONCLUSIONS: The number of Indigenous pregnancy and child longitudinal cohort studies employing repeated measures in both pregnancy and early childhood is low. Findings of the studies described in this review raise questions requiring further research; economic, environmental, social and psychosocial factors influencing the development of disease in these populations need to be addressed.

T-071

Maternal Nutrition and Immune Developmental Programming, Role of the Microbiome. Ellen Kraig*,[1] Leslie Linehan,[1] Eirleen Hyun,[1] Lourdes Arteaga-Cortes,[1] Peter Dube,[1] Peter W Nathanielsz,[2] Cun Li,[2] Qunfeng Dong,[3] Xiang Gao,[3] Mark J Nijland.[1] *[1]Univ of TX Health Sci Ctr, San Antonio, TX, USA; [2]Univ of Wyoming, Laramie, WY, USA; [3]Loyola University, Chicago, IL, USA.*

INTRODUCTION: Suboptimal maternal nutrition in pregnancy is associated with intrauterine growth restriction (IUGR), increased neonatal mortality, susceptibility to infection, and a higher incidence of chronic diseases including childhood asthma and diabetes. Many of these complications could be due to common underlying immune deficits elicited *in utero* by inappropriate nutrition. To address this possibility, development of immune competence and the microbiome were examined in an IUGR baboon cohort.

METHODS: A moderate (30%) global maternal nutrient reduction (MNR) was initiated in pregnant baboons and maintained through weaning. MNR offspring were IUGR and exhibited a unique phenotype, notably increased insulin resistance, compared to offspring of control pregnancies (Choi, et al. doi:10.1152/ajpregu.00051.2011). The development of innate and adaptive immunity were measured in these offspring (F1) at 5-6 years of age (post-pubertal), using the following assessments: serum cytokine profiles, blood myeloid and lymphoid cell subset distributions, T cell activation potential, thymic function, and antibody and T cell responses to vaccination.

RESULTS: At the time point analyzed (late adolescence), there were no significant differences in immune competence between IUGR and control F1. We next characterized gut, oral, and vaginal microbiomes that had colonized these cohorts. Microorganisms from the three sites showed distinct profiles, as expected. Moreover, in the female fecal samples, there were several bacterial species that were differentially represented in IUGR vs. control F1. Direct effects of maternal diet on the developing microbiome could have contributed to the endocrine and other systemic changes reported.
CONCLUSIONS: This non-human primate IUGR model offers a unique opportunity to examine consequences of decreased nutrient availability during pregnancy on F1 development. Although immune consequences did not persist into late adolescence, the gut microbiome was shown to be sensitive to MNR, particularly in female F1. We speculate that early skewing in immune development may have affected the microbiota thereby contributing to to childhood autoimmunity (i.e., diabetes) and/or other disorders. [Support: NIH HD072518].

T-072

Effects of Constant Light During Development on Adult Metabolism. Keenan Bates†,[1,2] Omonseigho Talton,[2] Laura Schulz*.[3] [1]*University of Missouri, Columbia, MO, USA;* [2]*University of Missouri, Columbia, MO, USA*.
INTRODUCTION: In adults, circadian disruptions alter metabolism. Constant light exposure *in utero* and during the neonatal period, individually or in combination, disrupts circadian rhythms in rodents and humans. *In utero*, peripheral circadian clocks oscillate with maternal rhythms, such that when the mother is subjected to constant light, both maternal and offspring rhythms are disrupted. The superchiasmatic nucleus and its resulting circadian rhythm develop in the postnatal environment. Constant light during this developmental period, as frequently used in NICUs , can delay the development of normal day-night cycles. We hypothesized that exposure to constant light during these critical developmental periods has a lasting effect on metabolism.
METHODS: To test this, we exposed C57BL/6 mice to constant light (CL) during mating, gestation, and the first four weeks of postnatal life of the offspring. After those four weeks, offspring were maintained on a 12h light:12h dark cycle (LD). Control mice were maintained on LD throughout the study. One cohort of mice was sacrificed for tissue collection at 19 weeks, and the second at 31 weeks, with half the mice from each cohort being challenged with a high fat, high sucrose diet (HFHS) for 8 weeks prior to sacrifice. At 4, 12, 20, and 28 weeks, the chow-fed mice were placed in metabolic cages that recorded activity, food and water consumption, and metabolism for three days. Additionally, mice fed HFHS were placed in the metabolic cages at 30 weeks.
RESULTS: On chow diet, mice exposed to CL during early development were much less active than mice raised in LD at all time points. However, when they were fed HFHS, the activity level of LD mice fell to that of CL, which was not affected by HFHS. The energy expenditure of CL mice was consistently below that of LD, except at 12 weeks. Adult CL males weighed more than LD males and that difference continued when both groups were placed on HFHS. CL males had significantly higher body fat percentage at 4, 12, and 20 weeks. On a chow diet, CL females weighed less than LD females, but on HFHS CL females weighed more than LD controls. At 19 weeks, CL females on chow diet had significantly higher leptin concentrations, and both had significantly higher insulin levels. At 31 weeks, CL males and females on a chow diet had significantly higher leptin levels than LD.
CONCLUSIONS: Constant light exposure during development causes metabolic dysfunction later in life.

T-073

Cardiac-Specific *Akap13* Haploinsufficient Mice Exhibited Sex-Dependent Cardiomyopathy. K Maravet Baig-Ward,[1,2] Stasia Anderson,[3] Szu-Chi Su,[1] James H Segars*.[1] [1]*Johns Hopkins University School of Medicine, Baltimore, MD, USA;* [2]*VCU School of Medicine, Richmond, VA, USA;* [3]*NIH, Bethesda, MD, USA*.
INTRODUCTION: Heart disease can vary in presentation, severity, and outcome contingent upon the sex of the individual. Females often present later and with atypical symptoms. Because of this, a better understanding of the mechanism and progression of heart disease is of utmost importance in women's health research. Previously we showed A-kinase Anchoring Protein 13 (*Akap13*), a known estrogen receptor modulator, to be an essential gene for cardiogenesis. Global loss of *Akap13* caused murine embryonic lethality. Embryos exhibited enlarged hearts and dysregulation of cardiac developmental genes. The objective of this study was to perform cardiac magnetic resonance imaging (MRI) in order to characterize the cardiac-specific *Akap13* haploinsufficient loss of function in an adult murine model.
METHODS: In order to investigate the physiologic role of *Akap13 in vivo*, we generated *Akap13* haploinsufficient mice using an inducible, cardiac-specific Cre-Lox deletion strategy targeted to the guanine nucleotide exchange factor (GEF) domain of *Akap13*. Sequencing and PCR were used to verify the construct *in vitro* and recombination and presence of LoxP sites *in vivo*. The well described Cre-recombinase-expressing mouse model *α-MHC*-MerCreMer (MCM), driven by the *α-MHC* promoter, was used to achieve cardiac tissue specificity. For generation of the conditional model, adult mice at three months of age with heterozygous floxed *Akap13* alleles and expressing *α-MHC*-MerCreMer ($Akap13^{Het\text{-}MCM}$) were administered tamoxifen-laced chow (40mg/kg body weight) for four weeks to induce Cre-mediated excision. For statistical analyses, mean outcomes were compared using a student's t-test with adjustment for multiple comparisons where appropriate. Data were reported as mean ± standard error.
RESULTS: Murine cardiac function was assessed through resting MRI. Female $Akap13^{Het\text{-}MCM}$ mice (n=7) exhibited decreased left ventricular ejection fraction (LVEF) (57.3% ± 2.94) compared to controls (n=7) (control: 65.87% ± 1.01) ($p<0.05$). Notably, no phenotype was seen with male $Akap13^{Het\text{-}MCM}$ mice ($p>0.05$).
CONCLUSIONS: These data showed that cardiac function of female $Akap13^{Het\text{-}MCM}$ mice was significantly lower than controls; females were more affected than males concomitant to *Akap13* disruption. These outcomes suggest a novel, sex-dependent mouse model for sexual disparity research.

T-074

Transcriptomics of Fetal Skeletal Muscles in Response to Chronic Maternal Hypercortisolemia in Late Gestation. Serene Joseph†, Elaine Richards, Maureen Keller-Wood*. *College of Pharmacy, University of Florida, Gainesville, FL, USA*.
INTRODUCTION: An increased incidence of perinatal mortality is observed with chronic cortisol exposure in an ovine model of chronic maternal stress; surviving lambs appear weak at birth. Glucocorticoids are known fetal programming signals and mediate the development of metabolic dysfunction postnatally. Transcriptomic analysis of the skeletal muscle gene expression was undertaken to model the effect of maternal hypercortisolemia on fetal skeletal muscle metabolism and the mediation of adverse pregnancy outcomes.
METHODS: Pregnant ewes were continuously infused with cortisol (1mg/kg/d) from 115 days of pregnancy and euthanized at labor. Transcriptomics was performed using an ovine gene array with labelled cRNA from biceps muscles of fetuses of control (n=6) and cortisol infused (n=6) ewes. Differentially regulated (DR) genes were determined using Bioconductor packages in R software. Pathway inference was analyzed with the Webgestalt program. Real time PCR (qPCR) was used to validate the DR pathways, and test whether changes translate to the diaphragm, essential for neonatal vitality.
RESULTS: 565 genes were DR on the microarray, of which 20% were mitochondrial. Cellular components of the mitochondrial matrix were DR;

thioredoxin interacting protein (TXNIP) was validated by qPCR ($p<0.05$). Processes mediating carbohydrate metabolism in Krebs cycle and oxidative phosphorylation were DR. Pathway analysis indicated insulin signaling is down-regulated; q-PCR further validated decreased expression of SLC2A4, the glucose transporter 4 ($p<0.05$), and increase in suppressor of cytokine signaling (SOCS3) ($p=0.058$). Significantly altered biological processes also included key glucose metabolic pathways in the fetus such as pyruvate metabolism. A key negative regulator of mitochondrial glucose oxidation, pyruvate dehydrogenase kinase 4 (PDK4), which is known to be glucocorticoid–regulated, was the most upregulated on the microarray. qPCR analysis indicated PDK4 was increased with cortisol exposure in diaphragm as well as biceps ($p=0.06$).

CONCLUSIONS: Transcriptomic modeling of the skeletal muscles suggests impairment of glucose uptake and mitochondrial oxidative metabolism of glucose. This suggests a possible role of precocious glucocorticoid exposure in programming the development of metabolic disorders, but also suggests that fetal hypercortisolemia may impact skeletal and diaphragm muscle function at birth.

T-075

Maternal Pre-Pregnancy Body Mass Index (BMI) Predicts Gene Expression in a Novel Human Model. Niraj R Chavan†,[1] Rebecca E Pollack,[2] Leryn J Reynolds†,[3] Brett Dickens,[3] John M O'Brien,[1] Kevin J Pearson*.[3] *[1]University of Kentucky College of Medicine, Lexington, KY, USA; [2]University of Kentucky College of Medicine, Lexington, KY, USA; [3]Carolinas Medical Center, Charlotte, NC, USA.*

INTRODUCTION: Epidemiological and animal research has shown that higher maternal pre-pregnancy BMI is associated with increased risk for pediatric and adult obesity in the offspring. The goal of this pilot study was to evaluate the effects of maternal pre-pregnancy BMI on the fetal programming of adipogenesis, glucose metabolism and inflammatory gene expression in neonates.

METHODS: Foreskin samples were collected and analyzed from a total of 46 non-anomalous singleton, term newborns. Maternal pre-pregnancy BMI was abstracted from medical records. Foreskins were dissected into epidermal/dermal and hypodermal layers. Samples were flash frozen, and RNA was isolated from the epidermal/dermal layer. RNA levels were analyzed using the NanoString Technologies nCounter system. Expression of genes involved in glucose/lipid metabolism and inflammatory response was quantified and normalized to housekeeping genes. The average gene expression levels among infants born to mothers with pre-pregnancy BMI < 25 kg/m^2 (normal weight) ($n = 26$) were compared to those born to mothers with pre-pregnancy BMI ≥ 25 kg/m^2 (overweight and obese) ($n = 20$), using Student's t test.

RESULTS: The mean BMI in the obese cohort was 32 ± 5.3 compared to 21 ± 1.8 kg/m^2 for the normal BMI group ($p<0.001$). Other demographic characteristics were similar between groups. Expression levels of inflammatory stress response and immunomodulation genes - Glutathione Peroxidase 1 ($p = 0.029$) and X-box binding protein 1 ($p = 0.039$), were increased in neonates born to overweight and obese women. These infants were also noted to have a significantly increased expression of Adiponectin receptor 1 ($p = 0.033$) RNA. Finally, the foreskin samples of infants born to overweight and obese women demonstrated increased levels of insulin like growth factor 1 receptor ($p = 0.040$) RNA.

CONCLUSIONS: Genes involved in the inflammatory response and metabolism were differentially expressed in the foreskins from infants born to mothers with a pre-pregnancy BMI ≥ 25 kg/m^2. Further studies are warranted to evaluate if these changes alter protein concentrations and whether these are sustained long-term through epigenetic interactions.

T-076

Ovarian Stimulation Increases the Risk of Fetal Cardiac Defects of Pups Exposed to Severe Maternal Hyperglycemia. Rolanda L Lister,[1] Francine Hughes,[2] Etoi Garrion,[1] Bin Zhou*.[3] *[1]Vanderbilt University Medical Center, Nashille, TN, USA; [2]New York University, New York, NY, USA; [3]Albert Einstein College of Medicine, Bronx, NY, USA.*

INTRODUCTION: To compare the rates of congenital heart defects in mouse pups born to diabetic mothers with and without ovarian stimulation.

METHODS: Hyperglycemia, defined as $\geq$200 mg/dL, was induced in 8 week old CD-1 wild type female mice using a single intraperitoneal dose of 150mg/kg of streptozotocin (STZ). Ovarian stimulation of experimental animals (n=3) consisted of injecting each mouse with pregnant mare serum (PMS) and human chorionic gonadotropin (HCG) 48 hours apart. Control animals (n=4) were not injected. Both stimulated diabetic dams (SD) and non-stimulated diabetic dams (NSD) were mated with normal male CD-1 mice for timed pregnancies. Fetal hearts were extracted at embryonic day 16.5 and histological analysis was performed. Fetal hearts were mounted in frontal orientation sectioned and stained with hematoxylin and eosin and imaged with a high resolution stereomicroscope. Sections were deemed adequate for analysis if both ventricles, atrioventricular valves, the pulmonary and aortic tract were identified. Student t-test were employed to compare the rate of cardiac defects in the SD and NSD groups. P-value ≤ 0.05 was considered significant.

RESULTS: The average litter size was significantly higher in SD dams compared to NSD dams (18.69 ± 1.15 vs 12 ± 2.94; $p=0.015$). The average blood glucose for the SD and NSD did not differ significantly (452 ± 200 mg/dL vs 413 +/- 124 mg/dL; $p= 0.76$). Overall, the rate of cardiac malformations did not differ between the two groups (46%+/-21 vs 26%+/-11; $p=0.16$). However, in severe maternal hyperglycemia (>400 mg/dL), there was a trend toward higher rates of fetal cardiac malformations in the pups born to the SD dams compared to pups born to NSD dams (SD pup cardiac malformations 24/56 ($58\% \pm 4$) vs NSD pup cardiac malformations 12/36 ($27\% \pm 4$).

CONCLUSIONS: In a murine model of severe maternal hyperglycemia, ovarian stimulation may increase the propensity of developing congenital heart defects in their offspring. The underlying mechanism is still elusive. However, this observation may have important clinical and fetal implications for patients who have pre-gestational diabetes and receive assisted reproductive techniques to achieve pregnancy.

T-077

Antenatal Glucocorticoid Exposure and Visceral Fat Effects on Epicardial Fat in Adult Sheep. G Angela Massmann, Won Joon Seong, Jie Zhang, Jorge P Figueroa*. *Wake Forest School of Medicine, Winston-Salem, NC, USA.*

INTRODUCTION: Antenatal exposure to high levels of glucocorticoids (GC) is associated with significant cardiometabolic alterations. Our working hypothesis states that GC alters the development of visceral (V) adipose tissue (AT) which plays a central role in the development of metabolic alterations in the adult. The AT covering the heart is thought to be another site of visceral fat of the heart. The local Renin Angiotensin System (RAS) in fat has important regulatory functions in VAT.

METHODS: Pregnant sheep were treated with two IM doses of betamethasone (Beta, 0.17 mg/kg) or vehicle (V) 24-h apart at 80 days gestation and allowed to deliver at term. Visceral fat was removed in 8 2 mo sheep of each sex who were expose to GC. Omental and perirenal fat was removed under general anesthesia. At 1.8 y of age EAT was harvested from 8 sheep of each sex in each treatment group; Beta (n=8,8), V (n=8,8) and FRB n=8,8). EAT protein was extracted for determining expression levels of the components of the Renin Angiotensin System (RAS) and measured using western blot. Data are expressed as Mean±SEM and were analyzed by ANOVA and two sample t test.

RESULTS: There were no significant effects of GC on any of the three angiotensin receptors (AT1, AT2 or mas) in either sex. In contrast, in exposed (Beta) females angiotensin converting enzyme (ACE) 1 was significantly higher with no change in ACE 2. The ACE1/ACE2 ratio was also higher. VAT ablation had a significant effect on the expression of RAS components in both sexes (‡ $p<0.05$ vs Beta; *$p<0.05$ vs V).

**Figure(s) will be available online.*

CONCLUSIONS: Our data show that exposure to a single course of GC at 0.55 gestation has long-term effects on adipose tissue function. A significant alteration in the expression of component of the RAS in EAT may be an important contributor for the increased risk for developing ventricular hypertrophy in offspring exposed antenatally to GC. Further studies are required to establish if these abnormalities are causally associated with the cardiometabolic alterations present in Beta exposed sheep. Unexpectedly, VAT ablation had significant effects on RAS expression HL 68728 and HD 04784.

T-078

Maternal Antioxidant Treatment May Improve Thermogenesis in Offspring of Hypoxic Pregnancy. A Martin†,[1] B Allison,[2] K Brain,[2] D Giussani,[2] C Ducsay,[3] D Myers*.[1] *[1]U. Oklahoma HSC, Oklahoma City, OK, USA; [2]U. Cambridge, Cambridge, United Kingdom; [3]Loma Linda U., Loma Linda, CA, USA.*

INTRODUCTION: In newborns, perirenal fat (PRF) functions as brown (BA) rather than white (WA) adipose providing non-shivering thermogenesis via Uncoupling Protein 1 (UCP1). We reported (PMID: 18287225) that early-onset hypoxemia (H) from ~40 days gestation (dG) through near term in sheep (~140dG; term 148dG) increased expression of genes governing the BA phenotype in fetal PRF: Deiodinase 1 (DIO1), DIO2, 11β hydroxylase 1 (HSD11B1), PPARγ, PGC1α, PRDM16 and leptin. Here, we determined the effect of late-onset gestational H with and without maternal vitamin C (VC) treatment from 105 to 138 dG to address timing of H and oxidative stress on BA and WA (RIP140, PPARα) genes in PRF in the ovine fetus.

METHODS: Four groups were studied: normoxemia+saline (NS; n=9), N+VC (NVC; n=9); H+S (HS;10% maternal inspired O_2, n=8), H+VC (HVC;n=7)(PMID: 26660546). At 138dG, PRF was collected and mRNA quantified by qRT-PCR.

RESULTS: Maternal PaO_2 was reduced in HS and HVC pregnancy (HS=47±1 vs HVC 46±1 mmHg). This yields fetal PaO_2 values of 11.5±0.6 (H) vs 20.9±0.5 mmHg (N:PMID: 26926316). H (HS) did not alter mRNA for any gene analyzed. In marked contrast, H+VC increased mRNA for all genes except leptin, DIO2 and cyclophilin (CYCLO; housekeeping). Table 1: Effect of H and VC on fetal PRF genes (fg mRNA/50 ng RNA; a 0.05 vs NS; b 0.05 vs HS; c 0.05 vs NVC; mean±SEM; ANOVA with Tukey's post hoc test).

	NS	HS	NVC	HVC
UCP1	38.2 ± 2.2	37.5 ± 3.8	40.6 ± 6.2	142.9 ± 16.9^{a,b,c}
DIO1	2.05 ± 0.6	1.53 ± 0.5	1.30 ± 0.2	7.22 ± 1.6^{a,b,c}
DIO2	0.13 ± 0.03	0.11 ± 0.03	0.06 ± 0.01	0.16 ± 0.04
HSD11B1	0.20 ± 0.03	0.18 ± 0.02	0.11 ± 0.03	0.31 ± 0.06^{c}
LEPTIN	0.20 ± 0.04	0.15 ± 0.02	0.13 ± 0.02	0.16 ±0.01
PPARγ	3.76 ± 0.19	2.8 ± 0.23	2.18 ± 0.13	8.77 ± 0.98^{a,b,c}
PPARα	0.18 ± .007	0.16 ± 0.01	0.22 ± 0.02^{b}	0.06 ± 0.01^{a,b,c}
PGC1α	0.23 ± 0.04	0.18 ± 0.03	0.19 ± 0.02	0.14 ± 0.02^{a}
PRDM16	0.04 ± 0.001	0.03 ± 0.004	0.03 ± .004	0.09 ± 0.02^{a,b,c}
RIP140	0.27 ± 0.01	0.28 ± 0.02	0.31 ± .015	0.15 ± 0.01^{a,b,c}
CYCLO	20.6 ± 0.19	20.8 ± 0.3	20.4 ± .2	20.4 ± 0.1

CONCLUSIONS: Maternal treatment with the antioxidant VC markedly sensitizes fetal PRF towards BA rather than WA tissue in H pregnancy. Supported by *The British Heart Foundation and NIH HD083132.*

T-079

Developmental Programming of the Vasculature: Aortic Caliber (AC) and Distensibility (AD) Are Reduced in Adult IUGR Baboons Offspring (F1) and Show Signs of Earl Aging Changes. Anderson D Kuo†,[1] Cun Li,[2] Peter W Nathanielsz,[2] Geoffrey D Clarke*.[1] *[1]University of Texas Health Science Center, San Antonio, TX, USA; [2]University of Wyoming, Laramie, TX, USA.*

INTRODUCTION: Vascular abnormalities contribute to poor cardiovascular health in adult IUGR (F1). For example AD affects baroreceptor function (PMID: 27122371) and is proposed as a marker to identify individuals at hypertensive risk (PMID: 27686337). We have reported altered cardiac development in IUGR baboons (Cardiac Remodelling in a Baboon Model of Intrauterine Growth Restriction, Kuo, Li, Li, Huber, Nathanielsz, Clarke J. Physiol In Press 2016) and hypothesized impaired aortic growth in IUGR.

METHODS: Pregnant baboons ate *ad lib* (CTL) or 70% *ad lib* who delivered IUGR F1. F1 baboons : IUGR (8Male, 8 female; 5.7 yr; human equivalent 20 yr) and age matched normal birth weight controls (8Male, 8 female; 5.6 yr). We also tested a baboon cohort across the life course from 5 and 23 years - normal life span approx 25 years. 3T MRI was performed to quantify distal descending aorta cross-section. AC was obtained by averaging systolic and diastolic lumen cross-section. AD was estimated by lumen size change with contraction divided by diastolic size and pulse pressure obtained at a separate session after MRI. Life course changes were analyzed by regression analysis.

RESULTS: Normalized AC was higher in CTL vs. IUGR (0.9 ± 0.05 cm^2/m^2 vs. 1.2 ± 0.06 cm^2/m^2, M ± SEM, p = 0.005); no sex or group-sex interaction difference. AD was higher in CTL vs. IUGR (3.7 ± 0.5 vs 1.9 ± 0.3 10^{-3}/mmHg, p = 0.005). No between sex difference or group-sex interaction was seen. No between group differences were seen in pulse pressure (p = 0.6). When IUGR AD was evlauetd agaisnt the life course regression all the IUGR fell below the 95% confidence limits for the aged animals (P < 0.001)

**Figure(s) will be available online.*

Fig. 1 AD in CTL baboons (open) and IUGR (closed) F1 - dashed line 95% confidence limits. p< 0.001 for IUGR vs cTL.

CONCLUSIONS: Decreased normalized AC in our IUGR cohort suggests impaired vascular development persists in adulthood. Additionally, impaired distensibility in IUGR suggests presence of intrinsic vascular pathology.

T-080

Intrauterine Growth Restriction Enhances Hypertension and Markers of Vascular Remodeling in Adult Rat Offspring Fed a High Fat Diet. Blair Dodson,[1] Tom Miller,[2] Yueqin Yang,[2] Baifeng Yu,[3] Erin Zinkhan*.[3] *[1]University of Colorado Denver, Aurora, CO, USA; [2]University of Utah, Salt Lake City, UT, USA; [3]University of Utah, Salt Lake City, UT, USA.*

INTRODUCTION: Intrauterine growth restriction (IUGR) and fetal exposure to a maternal high fat diet (HFD) independently predispose to offspring hypertension in a sex-specific manner. Hypertension and arterial stiffness may be secondary to vascular aging mediators. Advanced glycation end products (AGEs) and their receptors (RAGEs) mediate vascular aging through remodeling. We hypothesized that in a rat model of IUGR, IUGR offspring would have increased blood pressure (BP), AGEs and RAGEs when exposed to a maternal HFD, findings that would persist despite weaning to a regular rat chow.

METHODS: Adult female rats were fed either a regular diet (RD) or a HFD prior to mating through gestation and lactation. IUGR was induced by uterine artery ligation. At weaning, offspring were weaned to either a RD or HFD through postnatal day (PND) 60. For both control (C) and IUGR (I) rats, this study design resulted in 3 diet groups: offspring from dams fed a RD and weaned to a RD (CRR and IRR), offspring rats from dams fed a HFD and weaned to a RD (CHR and IHR), and offspring from dams fed a HFD and weaned to a HFD (CHH and IHH). Tail-cuff blood pressures and aorta protein levels of AGEs and RAGEs were assessed at PND 60 and compared between groups within each sex.

RESULTS: In females, IHH and IHR offspring had increased systolic BP (SBP) and IHH female rats had increased diastolic BP. Concordantly, IHH and IHR females had increased heart mass to body mass (HM:BM) ratios. IHH female rats had increased RAGEs and no change in AGEs. In males, IHH offspring had increased SBP compared to all other groups and increased HM:BM ratio compared to CRR. IHH males had increased AGEs and no change in RAGEs. In both sexes, weaning to a RD normalized AGEs and RAGEs in IHR rats compared to CRR rats. p<0.05.

CONCLUSIONS: IUGR increased BP, cardiac mass, and induced vascular remodeling mediators when combined with a maternal and postnatal HFD. Weaning IUGR rats to a regular diet normalized levels

of vascular remodeling mediators in both sexes without improving blood pressure or cardiac mass in females. We speculate that increased SBP in IUGR rats results from underlying IUGR-induced structural changes to the extracellular matrix that is not normalized by a RD after weaning.

T-081

Changes in the M1/M2 Responses and Epigenetic Markers in Neonatal Monocyte-Derived Macrophages from Women with Pre-Gestational Obesity. Bernardo J Krause,[1] Francisca Cifuentes-Zúñiga†,[1] Viviana Arroyo†,[1] Gustavo Soto-Carrasco,[1] Ricardo Uauy,[1] Paola Casanello,[1,2] Jose Castro-Rodríguez*.[1] *[1]Pontificia Universidad Católica de Chile, Santiago, Metropolitana, Chile; [2]Pontificia Universidad Católica de Chile, Santiago, Metropolitana, Chile.*

INTRODUCTION: Prevalence of obesity is increasing in developing and developed countries, affecting ~30% of women in fertile age. The latter impinges higher risk of developing chronic diseases associated with an altered immune function in the offspring. We aim to determine whether maternal obesity is associated with increased pro-inflammatory response, as well as changes in the DNA methylation profile of key inflammatory genes in neonatal monocyte-derived macrophages.

METHODS: Cord blood samples from 26 newborns of obese (OM) and 25 newborns of lean (control) women were obtained at delivery. Fetal monocytes were isolated by adhesion, cultured and differentiated into macrophages, in which M1 (LPS 100 ng/ml + IFNγ 20 ng/ml) and M2 (IL-4 20 ng/ml) polarization were assayed. The responses were analyzed in terms of mRNA levels for TNFα, IL-1β, IL-12A, IL-12B, IL-10 e IL-4R quantified by qPCR, and the cytokines levels in the culture media. DNA methylation of candidate genes was quantified by CpG-specific pyrosequencing.

RESULTS: Monocytes from children of OM had decreased levels of mRNA for proinflammatory cytokines IL-1β and IL-12B ($p < 0.05$) and no significant changes in the other transcripts assayed. OM monocyte-derived macrophages showed increased levels of mRNA for TNFα, IL-4R and IL-10. The response to LPS/IFNγ was comparable between both groups, characterized by an important induction of TNFα and IL-1β. Control macrophages stimulated with IL-4 showed a decreased expression of inflammatory mediators while OM macrophages had an additional suppression of the anti-inflammatory mediator IL-10 ($p < 0.05$). Changes in IL-1β (in monocytes) and IL-10 (in macrophages) mRNA levels in OM were paralleled by changes in their promoter DNA methylation in freshly isolated fetal monocytes ($p < 0.05$).

CONCLUSIONS: These results suggest that maternal obesity in early gestation induces a basal anti-inflammatory phenotype in neonatal monocyte-derived macrophages, but an unbalanced response to M1 and M2 polarization stimuli, along with epigenetic changes in key inflammatory genes. These changes in neonatal monocytes need to be further analyzed, to determine a potential programming of the fetal immune function by maternal obesity.

T-082

Antenatal Magnesium Sulfate and Ponderal Index From Birth to Age 2 in Preterm Male and Female Infants. Tiffany E Deihl†, Hyagriv N Simhan. *Magee-Womens Hospital of UPMC, Pittsburgh, PA, USA.*

INTRODUCTION: Antenatal magnesium sulfate (Mg) reduces cerebral palsy (CP) in preterm infants. There is biologic rationale for influence of Mg on phenotypes outside the central nervous system. While contributors to infant adiposity are complex, there is known contribution from the intrauterine environment. We investigated the effect of Mg exposure on infant adiposity, measured by ponderal index (PI kg/m^3), from birth to 2 years of age.

METHODS: Secondary analysis of a US RCT of Mg vs placebo among women at 24-31 weeks gestation at high risk for preterm delivery was performed. In the trial, 1095 women were randomized to placebo and 1041 women were randomized to Mg. Neonatal visits were at a mean of 7.5 (SD 7.4), 14.5 (SD 5.5) and 26.0 (SD 3.4) months. After excluding twins and CP, 1030 babies (537 males; 493 females) had complete PI data at birth and followup. Our primary exposure was treatment group and primary outcome was change in PI from birth to age 2. Fetal sex and the 1-way interaction between Mg and sex was considered. Other covariates included race, smoking, marital status, maternal BMI and birth weight.

RESULTS: There was a larger decrease in PI from birth to 2 years in infants exposed to Mg vs placebo (p=0.032); Mg was associated with a 1.53 kg/m^3 larger decrement than placebo. Fetal sex and the 1-way interaction between sex and Mg also had a significant effect on PI change (p=0.013, 0.019); thus, we stratified by sex. Change in PI from birth to 2 years of life in males was not statistically significant (p=0.227) but trended to a greater decrement in males exposed to Mg vs placebo by 0.38 kg/m^3; change in PI from birth to 2 years of life was less in females exposed to Mg vs placebo by 0.75 kg/m^3 (p=0.04).

**Figure(s) will be available online.*

CONCLUSIONS: Antenatal Mg exposure affects the PI trajectory of preterm infants in a sex-specific manner. PI in infancy is associated with obesity and cardiovascular risk in later life. These findings uniquely suggest a sex-specific fetal effect of Mg exposure on a non-neurologic phenotype.

T-083

Chronic Pulsatile Hyperglycemia Does Not Increase Insulin Secretion in Growth Restricted Fetal Sheep. Brit H Boehmer†, Laura D Brown, Stephanie R Wesolowski, William W Hay, Paul J Rozance. *University of Colorado, Aurora, CO, USA.*

INTRODUCTION: Normal sheep fetuses respond to chronic pulsatile hyperglycemia (PHG) with increased glucose stimulated insulin secretion (GSIS) and increased numbers of pancreatic β-cells. Intrauterine growth restricted (IUGR) fetuses have lower insulin secretion and β-cell mass compared to normal fetuses. However, the fetal β-cell response to chronic pulsatile hyperglycemia in IUGR fetuses has not been tested. Therefore, we measured fetal GSIS and β-cell mass in late gestation IUGR sheep after chronic PHG (n = 7 fetuses) or control saline infusions (SAL; n = 7 fetuses).

METHODS: Twin fetal sheep were randomly assigned to either PHG or SAL treatments for one week after placement of fetal intravenous and arterial catheters (~119 dGA). PHG was induced by a constant, basal fetal infusion of 33% dextrose (D33; w/v) designed to achieve a 20% increase in fetal glucose concentrations, plus three 60 min D33 pulses each day at 0900, 1500, and 2100 hrs to achieve an 80% increase in fetal glucose concentrations. Following the chronic infusions GSIS was measured with a square wave hyperglycemic clamp. Pancreatic mRNA and protein were quantified by qPCR and western blot, respectively. Pancreatic sections were analyzed by immunofluorescent staining for insulin in order to calculate β-cell mass.

RESULTS: During the infusion period, daily basal plasma glucose concentrations were 18% greater ($P < 0.001$) in PHG than in SAL fetuses and increased 76% ($P < 0.001$) during the dextrose pulse. Plasma insulin concentrations did not differ between PHG and SAL fetuses during the 7 d infusion period. During the hyperglycemic clamp, GSIS was similar between treatments PHG and SAL fetuses, as was β-cell mass, mRNA expression of insulin, IGF-I and II, IGFBP2, PDX1, GLUT2, and glucokinase, and glucokinase protein expression. Pancreatic GLUT2 protein expression was lower in PHG fetuses ($P = 0.02$).

CONCLUSIONS: These results indicate that, in contrast to normal fetuses, IUGR fetuses have a reduced ability to adapt to PHG showing early development of a degree of metabolic inflexibility.

T-084

Outcomes in the Term Fetal Baboon Pancreas in Response to Challenges of Maternal Under Nutrition and Obesity. Cun Li,[1,3] Ablat Tursun,[1] JunFei Li,[1,2] Peter W Nathanielsz.[1,3] *[1]Texas Biomedical Research Institute, San Antonio, TX, USA; [2]University of Wyoming, Laramie, WY, USA; [3]Xianya School of Medicine, Changsha, Hunan, China.*

INTRODUCTION: Many developmental challenges program U-shaped outcomes. The Harvard Nurses Study, an early programming study, showed adult cardiac outcomes related to birth weight is U-shaped. We evaluated fetal pancreatic insulin, growth and differentiation factors, oxidative stress (OS) and glucocorticoid (GC) receptors (GR) with

immunohistochemistry (IHC) at term in pregnancies in which the mother was 1) moderately nutrient restricted (MNR) or 2) in obese mothers (OB) on a high fat high energy diet.

METHODS: Control baboons ate Purina monkey diet *ad lib* (CTR); MNR mothers ate 70% CTRl through pregnancy; fetuses were IUGR. OB mothers were obese at conception from eating a high fat, high-energy diet (45% energy fat, 4.62% glucose, 5.64% fructose) and unlimited fructose drinks at least nine months before and through pregnancy. Fetuses were retrieved at term C-section. IHC for area stained with image J quantification analyzed by Student's T-test.

RESULTS: Pancreatic insulin was reduced in IUGR and increased in OB fetuses (Fig 1) , presumably due to increased circulating secretagogues. Similarly IGF1 was down in IUGR and up in OB which could account for differences in pancreatic growth. PDX1, important in pancreatic differentiation decreased in IUGR and OB but proportionately more in IUGR. HNF4α was decreased similarly in IUGR and OB. OS is considered a basic mechanism in programming . It is, thus, of interest that nitrotyrosine (NT) was increased similarly in both IUGR and OB as was NDUFV2 and citrate synthase (CS). pGR – Phospho-Glucocorticoid receptor was decreased in both situations.

**Figure(s) will be available online.*

Figure 1. Fetal pancreatic IHC . NT , CS , pGR . Data: percentage fraction of section stained. M + SEM, *p< 0.05.

CONCLUSIONS: Similarities and differences exist in fetal pancreatic outcomes in response to NR and OB which may reflect similarities and differences in diabetic predisposition in later life after these different challenges.

T-085

Central Dopamine "Reward Pathway" Is Upregulated in Offspring of Obese Mothers. Daniela P Laureano,[1,2] Elaheh Mossayebi,[2] Kavita Narwani,[2] Guang Han,[2] Niyati Joshi,[1] Mina Desai,[2] Michael G Ross.[2] *[1]UFRGS, Porto Alegre, Rio Grande do Sul, Brazil; [2]LABioMed at Harbor-UCLA, Torrance, CA, USA.*

INTRODUCTION: The nucleus accumbens (NAc) dopamine pathway mediates reward properties of both drug and non-drug (e.g., food) rewards. Dopamine (DA; catalyzed by tyrosine hydroxylase TH) pathway in NAc plays a major role in reward-motivated behavior and mediates its effects via DA receptors (D1R and D2R). Altered fetal nutrient exposure programs adult offspring with a marked predisposition to metabolic syndrome, neurobehavioral/psychiatric disorders and addiction. As food intake is mediated by both appetite and reward functions, and offspring from maternal obesity/high fat diet (HF) demonstrate hyperphagia,we hypothesized that HF offspring have an upregulated reward pathway. SIRT1 a nutrient sensor and a histone deacetylase is expressed in NAc. We sought to determine if a dysfunctional "reward pathway in HF offspring is mediated via NAc SIRT1 with subsequent activation of downstream SIRT1 target genes.

METHODS: Female mice were fed either a control (10% k/cal) or high fat (HF; 45% k/cal) diet to create maternal obesity prior to mating, and diets continued throughout pregnancy and lactation. At 21 days of age, offspring were weaned to control diet and at 14 months of age were fasted overnight. NAc was dissected from female offspring and protein expression (Western Blot) of SIRT1, TH and D2R was analyzed (values shown as fold change). Offspring food intake and body weight were measured weekly.

RESULTS: HF offspring were heavier at birth and maintained increased body weights as compared to controls (Figure; left panel). Their food intake was increased when measured from weaning at 3 weeks till 48 weeks of age (Figure; right panel). At 14 months, obese HF female offspring NAc protein expression of SIRT1 (1.4-fold; p<0.05) and TH was higher (1.2=fold; p<0.08) with unaltered D2.

**Figure(s) will be available online.*

CONCLUSIONS: Programmed upregulation of SIRT1 may increase TH expression, activating the NAc reward pathway. We propose that programmed DA-mediated reward potentiates hyperphagia, binge eating and addiction predisposition in offspring of obese/HF mothers.

T-086

Ongoing Defects in Cerebellar Development in a Guinea Pig Model of Preterm Birth. Julia C Shaw†,[1,2] Hannah K Palliser,[1,2] Rebecca M Dyson,[3,4] Mary J Berry,[3,4] Jonathan J Hirst*.[1,2] *[1]University of Newcastle, Newcastle, Australia; [2]Hunter Medical Research Institute, Newcastle, Australia; [3]University of Otago, Wellington, New Zealand; [4]University of Otago, Wellington, New Zealand.*

INTRODUCTION: We have previously shown that preterm male guinea pigs exhibit hyperactivity during juvenility compared to those delivered at term[1]. Altered development of the cerebellar GABAergic system is suggested to play an integral role in disorders such as autism and ADHD. We aimed to determine the extent to which cerebellum development is abnormal in our clinically relevant juvenile guinea pig model of preterm delivery and hyperactivity.

METHODS: Guinea pig neonates were delivered preterm by induction of labour (GA62) or spontaneously (GA70). Tissues were collected at corrected PND28. Myelination and neuron number were measured by myelin basic protein (MBP) and neuronal nuclei (NeuN) immunostaining in lobule IX and lobule X of the cerebellum. Relative mRNA expression of $GABA_A$ receptor subunits α6 and Δ in the cerebellum were quantified by PCR.

RESULTS: Myelination was significantly increased in preterm males (n=5) compared to controls (n=5) in lobule IX (p=0.006). In lobule X, preterm females (n=5) had significantly decreased MBP expression compared to controls (n=5, p=0.02). There was no significant effect of preterm delivery on NeuN expression, or the relative mRNA expression of either the $GABA_A$ receptor subunit α6 or Δ within each sex in the cerebellum. Cerebellum-brain weight ratio was not significantly affected at corrected PND28.

CONCLUSIONS: Preterm juvenile males exhibited an over-abundance of myelin, despite no difference in neuronal nuclei expression, suggesting a deficit in their synaptic pruning. A lack of synaptic pruning in the cerebellum is a feature common in autistic models and represents formation of inefficient synaptic connections. Preterm juvenile females were differentially affected by preterm delivery, displaying a lack of myelin. These data provide evidence for the ongoing sexually dymorphic effects of preterm labour on neurodevelopment and supports the use of this animal model to explore developmental mechanisms and clinical therapies.

1. Shaw JC, Palliser HK, Dyson RM, Hirst JJ, Berry MJ. Long-term effects of preterm birth on behavior and neurosteroid sensitivity in the guinea pig. Pediatric research 2016;80:275-83.

T-087

***ZNHIT3*, a New Candidate Gene for Mayer-Rokitansky-Kuster-Hauser (MRKH) Syndrome.** Lawrence C Layman,[1,2] Lacey S Willaims†,[1] Lynn P Chorich,[1] Megan E Sullivan,[1] Hyung-Goo Kim,[1,2] John A Phillips, III,[3] Hugh S Taylor,[4] Alka Chaubey,[5] Michael J Friez.[5] *[1]Med Coll GA, Augusta U, Augusta, GA, USA; [2]MCG, Augusta, GA, USA; [3]Vanderbilt University, Nashville, TN, USA; [4]Yale U, New Haven, CT, USA; [5]Greenwood Genetic Center, Greenwood, SC, USA.*

INTRODUCTION: Mullerian aplasia, known as Mayer-Rokitansky-Kuster-Hauser [MRKH] syndrome, is a common cause of primary amenorrhea, and may be associated with renal agenesis, skeletal, cardiac, and auditory anomalies. The genetic basis for MRKH is only well documented for *WNT4* and *HNF1B,* supported by *in vitro* analyses and family studies. We hypothesize that MRKH is caused by *de novo* or inherited gene mutations in an autosomal dominant fashion. We previously performed whole exome sequencing and found a heterozygous frameshift *ZNHIT3* variant. Point mutations were not seen in other patients, prompting us to determine if intragenic deletions or copy number variants (CNVs) within *ZNHIT3* could be present, and if *ZNHIT3* was expressed in MRKH tissues.

METHODS: Genomic DNA from 50 MRKH patients was used for qPCR for exons 1, 3, and 5 of the five-exon *ZNHIT3* gene, and compared with unaffected family members. Chromosomal microarrays (CMA) were

performed in two patients with whole gene deletions to determine if larger deletions were present. RT-PCR was performed on human RNA from MRKH related tissues.
RESULTS: By qPCR, 5/50 (10%) patients had a heterozygous *ZNHIT3* deletion. Two had exon 5 deletions, and three had deletions of all three exons. No parent had a deletion, but in one case, the father had a duplication. CMAs in two patients demonstrated that both had 1.2 Mb 17q12 deletions containing *ZNHIT3*. RT-PCR showed expression in the uterus, kidney, and heart.
CONCLUSIONS: *WNT4* and *HNF1B* are the only two convincing MRKH genes to date. Although CNVs (17q12, 16p11, 22q11) and variants in other genes (*TBX6, WNT9B, LHX1*, and *RBM8A*) have been identified in MRKH, they were not supported by family studies or by *in vitro* analyses. *ZNHIT3* is a reasonable candidate gene because of: 1) expression in MRKH dependent tissues; 2) identification of an intragenic frameshift variant; 3) the presence of intragenic deletions absent in unaffected family members. Our findings suggest that *ZNHIT3,* within the 17q12 CNV deletion interval, is a promising candidate gene for MRKH that requires serious consideration.

T-088

Are Preterm and Postterm Birth Related? Elise N Erickson, Frances M Biel, Jonathan M Snowden, Leonardo Pereira*. *OHSU, Portland, OR, USA.*
INTRODUCTION: Gestational age (GA) at birth is not normally distributed. The majority of US births occur near term, with 11% < 37 weeks (wk) and only 6% >41wk. The distribution of preterm (PTB) and posterm birth are rarely viewed as being related because early PTB is closely associated with infection or abruption, while postterm birth rarely is. However, a pathologic cause is not determined for many PTBs. Given this heterogeneity in causes of labor, we analyzed a large database, grouped by likely causes of labor. We hypothesize that the distribution of parturients is made up of distinct populations: those with "physiologic" onset of labor and those with pathologic labor triggers (i.e.infection, placental insufficiency, etc).
METHODS: We conducted a retrospective cohort study using linked hospital discharge and vital records for all births (23-42 wk gestation) in California between 2007-10 (N=2,094,220). We excluded cesarean without labor, induction, fetal demise, multiple gestation, noncephalic presentation, placenta previa, prelabor/preterm ruptured membranes and fetal anomalies. The remaining 1,125,951 were categorized into 1 of 3 groups with spontaneous labor: 1) obstetric infection, 2) conditions associated with placental insufficiency, and 3) labor with no known pathology.
RESULTS: Of the remaining labors, 24,963 (2.36%) were in Group 1, 71,784 (6.51%) were in Group 2. The remainder were not affected by these conditions: Group 3, 1,030,756 (91.55%). In Group 3, <0.01% delivered <32 wk. Mean GA (SD) at birth was 39.0 (1.53), 37.12 (2.80) and 39.01 (1.22) for Groups 1,2 and 3 respectively. Skewness and kurtosis of Group 3 were significantly less than Groups 1 and 2.
**Figure(s) will be available online.*
CONCLUSIONS: The distribution of birth by GA is composed of overlapping but distinct groups. In this paradigm, deliveries in Group 3 (no identified pathology) occur in a near normal distribution. This suggests that a large proportion of late PTB (34-37) and postterm (41-42) births are the result of physiologic processes, in contrast with PTB <34wk, which is highly associated with pathologic processes. This interpretation suggests that late PTB and postterm births may be governed by the same genes and epigenetic influences which should prompt future research.

T-089

Prenatal Exposure to Maternal PCOS Associated with Increased Risk of Adult Body Mass Index in Children of Both Genders. Shruthi Mahalingaiah,[1,2] Michael Winter,[3] Ann Aschengrau*.[2] *[1]Boston University School of Medicine, Boston, MA, USA; [2]Boston University School of Public Health, Boston, MA, USA; [3]Boston University School of Public Health, Boston, MA, USA.*
INTRODUCTION: Developmental origins of metabolic syndrome may include prenatal exposure to the hormonal milieu of polycystic ovary syndrome (PCOS) in the mother. The objective of this study was to determine the association of prenatal exposure to a mother with PCOS and adult-onset metabolic syndrome characteristics such as elevated body mass index (BMI), hypertension, and diabetes in the offspring.
METHODS: There were 1,303 mother-child dyads in a cohort study of mothers and children from Cape Cod, Massachusetts originally designed to study health outcomes associated with exposure to tetracholoroethylene (PCE)-contaminated drinking water. Of note, the original study reported no association of prenatal PCE exposure and adult onset benign gynecologic conditions, including PCOS. Seventy-nine of the 1,303 dyads were of PCOS mothers, including 36 dyads with sons and 43 dyads with daughters. The children were born between 1969 and 1983 and both mothers and children completed questionnaires on demographic, lifestyle and health characteristics. Since some offspring were from the same mother, generalized estimating equations were used to account for within-family correlation.
RESULTS: For prenatal exposure to a maternal PCOS environment compared to children born to non-PCOS mothers, the risk ratio (RR) for elevated BMI (≥ 30) was 2.1 (95% CI: 1.3,3.5) in sons and 1.3 (0.7,2.5) in daughters. The RRs for hypertension (for sons or daughters) and diabetes (for daughters) were elevated but not statistically significant. The RR of having at least one of three characteristics associated with metabolic syndrome (e.g. elevated BMI, hypertension and diabetes) in PCOS-exposed vs. unexposed children was 1.6 (1.0,2.4) in sons and 1.2 (0.6,2.3) in daughters; for 2 or more factors the RR was 3.1 (1.1,8.5) in sons and 2.0 (0.5,8.2) in daughters.
CONCLUSIONS: These results suggest that prenatal exposure to the developmental milieu of a PCOS mother may promote characteristics associated with adult onset metabolic syndrome but care must be taken in making firm conclusions about this association because the sample size was small.

T-090

Interdelivery Interval and Indicated Preterm Birth. Annie M Dude†, William Grobman*. *Feinberg School of Medicine, Northwestern University, Chicago, IL, USA.*
INTRODUCTION: Both short and long interdelivery intervals (IDI) have been associated with a preterm delivery (PTD) in the subsequent pregnancy. It remains unknown, however, whether the indications for PTD are similar among women with short and long IDI. We hypothesize that PTD among women with a longer IDI is more likely due to a medical, as opposed to a spontaneous, etiology.
METHODS: This is a case-control study of women with a PTD of a live neonate whose prior birth was at the same institution between 2005 and 2016. Maternal characteristics and delivery outcomes were abstracted from the medical record. PTDs were classified as spontaneous if women delivered due to preterm labor, preterm premature rupture of membranes, cervical insufficiency, or placental abruption. PTDs were classified as indicated if women underwent delivery for fetal indications (including intrauterine growth restriction and oligohydramnios), maternal medical indications, or complications of placentation. IDI was categorized as < 18 months, 18 – 59 months, and 60 months or more. Chi square and t tests were used to compare characteristics of women who had an indicated PTD to those who had a spontaneous PTD. Multivariable logistic regression was used to determine whether IDI remained associated with indicated PTD after adjusting for potential confounders.
RESULTS: Of the 902 women who had a PTD and met eligibility criteria, 219 (24.3%) had an indicated PTD. Compared to women with an IDI of 18 – 60 months (of whom 24.6% had an indicated PTD), women with a

shorter IDI were less likely to have an indicated PTD (18.0%) and women with a longer IDI were more likely to experience an indicated PTD (36.9%; p = 0.001). The relationship between indicated PTD and long IDI persists even when accounting for other factors (Table).
**Figure(s) will be available online.*
CONCLUSIONS: The etiology of PTD varies according to IDI duration, with indicated PTD occurring more commonly with longer IDI.

T-091

Low-Frequency, Damaging Mutations in Hundreds of Genes Are Risk Factors for Endometriosis. Kenneth Ward, Kenneth Ward, Kenneth Ward*. *Juneau Biosciences, Salt Lake City, UT, USA.*
INTRODUCTION: By design, GWAS studies focus on older gene variants, typically those present in greater than 3 % of the population. Recent studies across a range of complex diseases have shown that low frequency, protein-coding variants play an important role in the etiology of many conditions. In this study, we conducted a search for rare exome variants associated with endometriosis using an exome genotyping array and confirmatory whole exome sequencing (WES).
METHODS: 1544 Caucasian patients with surgically confirmed endometriosis were tested for more than 200,000 rare non-synonymous variants (maf<0.005) using the Human Exome Beadchip (Illumina) and allele frequencies compared to the UK and ExAc datasets. Rare variants were selected for further evaluation if they passed the nominal significance threshold (p<0.05) against both the publicly available genotyping datasets from the UK (n=50,000) and the ExAC database(n=33,000). These variants were then tested in 1019 endometriosis subjects and 366 population controls using WES using the Ion Proton Platform (Life Technologies). Mutation burden for each gene was calculated. Association testing was performed using Fisher's exact statistics. Panther software was used to test gene ontologies.
RESULTS: Overall, 1992 rare protein altering variants (1040 predicted to be damaging) in 1703 distinct genes were found to be associated with endometriosis. 96% of the endometriosis subjects carried at least one of these damaging variants. 47% of the endometriosis patients carried more than 3 damaging variants while only 6% of the population controls carried more than four variants. Population controls were not tested for the absence of endometriosis. An enrichment analysis of gene ontology (GO) terms for the 1703 genes identified cell-cell adhesion function as over-represented (p=1.6E-05). No other GO terms showed significant enrichment.
CONCLUSIONS: The multiple genes identified through this study emphasizes the polygenic effect of rare coding variants in the etiology of complex diseases like endometriosis. The relative risk of having endometriosis is significantly higher in women who multiple damaging variants, suggesting that they may serve as a useful predictive or diagnostic markers. The statistically significant enrichment of genes involved with cell-cell adhesion support our previously reported hypothesis that mesothelial barrier integrity plays a role in the pathogenesis of endometriosis [3].

T-092

Effect of Maternal Binge Drinking on the Fetal Circulation. Ana Tobiasz†,[1] Jose Duncan†,[1] Ryan Sullivan,[2] Danielle Tate,[1] Alex Dopico,[3] Anna Bukiya,[3] Giancarlo Mari*.[1] *[1]University of Tennessee Health Science Center, Memphis, TN, USA; [2]University of Tennessee Health Science Center, Memphis, TN, USA; [3]University of Tennessee Health Science Center, Memphis, TN, USA.*
INTRODUCTION: Prenatal ethanol exposure affects the fetal brain with maternal binge drinking of alcohol posing the highest risk. The mechanisms of cerebral damage due to prenatal alcohol exposure are poorly understood. We sought to investigate the effect of prenatal alcohol exposure on fetal blood flow in a baboon model.
METHODS: Pregnant baboons underwent alcohol drinking via orogastric gavage to achieve a blood alcohol concentration of 80mg/dL within 90 minutes. The control group received iso-caloric orange-flavored drink. Flow velocity waveforms of the fetal middle cerebral artery (MCA), umbilical artery (UA), and left ventricular output were obtained immediately before and 120 minutes after gastric infusion of the drink. The MCA PSV and PI, umbilical artery PI and Tei index were calculated. Statistical analysis included the paired t-test.
RESULTS: A total of 10 baboons were included in the analysis. There was a significant decrease in the MCA PSV in the treatment group after alcohol consumption. The Tei index increased post-drink in both the control (mean 0.68 vs 0.96) and alcohol groups (mean 0.72 vs 0.97)

Table 1. MCA and UA Doppler Findings

		Control			Alcohol		
Episode (Days)	**Parameter**	**Pre Mean (St.Er)**	**Post Mean (St.Er)**	***P* Value**	**Pre Mean (St.Er)**	**Post Mean (St.Er)**	***P* Value**
90	MCA PSV	22.72 (2.59)	20.9 (1.93)	NS	23.03 (3.02)	16.09 (1.48)	0.004
	MCA PI	1.84 (0.11)	1.99 (0.22)	NS	1.71 (0.14)	1.89 (0.20)	NS
	UA PI	1.69 (0.99)	2.10 (0.18)	0.04	1.88 (0.32)	2.09 (0.34)	NS
100	MCA PSV	24.22 (1.57)	23.93 (2.64)	NS	26.37 (3.20)	16.92 (1.41)	0.015
	MCA PI	1.98 (0.10)	1.96 (0.05)	NS	1.83 (0.23)	1.75 (0.12)	NS
	UA PI	2.11 (0.16)	2.18 (0.24)	NS	1.95 (0.51)	1.95 (0.02)	NS
110	MCA PSV	28.08 (0.76)	26.84 (2.73)	NS	26.87 (1.02)	18.38 (1.32)	0.029
	MCA PI	1.89 (0.29)	2.00 (0.31)	NS	2.21 (0.18)	1.84 (0.13)	NS
	UA PI	1.88 (0.09)	2.05 (0.08)	0.04	1.78 (0.09)	1.83 (0.13)	NS

CONCLUSIONS: Alcohol exposure in a baboon binge-drinking model alters fetal cerebral blood flow, with no changes in umbilical artery or cardiac indices. This may reflect an alcohol-induced dilation in fetal cerebral blood flow in response to maternal binge drinking.

T-093

Array Comparative Genomic Hybridization Yields Interpretable Results from Fetal Tissue Stored Up to 5 Days at Room Temperature. Neil S Seligman,[1] Philip J Katzman,[2] Anwar Iqbal.[2] *[1]Univ. Rochester Medical Center, Rochester, NY, USA; [2]Univ. of Rochester Medical Center, Rochester, NY, USA.*
INTRODUCTION: Array comparative genomic hybridization (aCGH) detects copy number losses and gains at a higher resolution than routine chromosome analysis. The quality of DNA isolated from unfixed fetal tissue deteriorates gradually over time. This is a particular challenge after intrauterine demise because generation of fetal tissue yields poor quality DNA. We investigated the time window of DNA utility after fetal tissue degeneration.
METHODS: Second trimester male fetal liver, lung, and kidney tissue was harvested from a non-anomalous fetus following elective abortion. Equal aliquots of the 3 tissue types were aggregated and stored at both room temperature (RT; 19-20°C) and refrigeration (4°C). RT and refrigerated samples were submitted for aCGH daily over 5 days both as fresh tissue in Hanks Balanced Salt Solution and formalin-fixed paraffin embedded tissue (FFPE) blocks. Hematoxylin & Eosin (H&E) stained slides were made of each FFPE block. DNA was isolated and checked for quality with the NanoDrop ND-1000. aCGH was performed on the ISCA 4 × 44K v2.0 platform (Agilent Technology Inc. Santa Clara, CA). Male reference DNA was used as control. QC metrics including derivative log ratio (DLR), % labeling, and aCGH results were compared between day 3 through 5 samples.
RESULTS: All samples from days 3-5 yielded DNA that could be analyzed by aCGH. There was no clinically significant copy number variants. DNA concentration ranged from 158-200ng/ul; 260nm/280nm, 260nm/230nm, and DLR ranged from 1.82-1.86, 1.77-2.31 and 0.12-0.23 respectively. There were significant differences only in % labeling between RT (mean 2.24%) and refrigerated specimens (mean 1.85%) (p=0.02)

and in DLR between fixed (mean 0.20) and unfixed tissue (mean 0.16; p=0.04). All fixed tissue retained basophilic staining except RT kidney at 5 days, which had early loss of nuclear staining.

CONCLUSIONS: DNA extracted from fetal tissue kept at RT for at least 5 days can be successfully evaluated by aCHG. Quality indices were largely unaffected by temperature and fixation; small differences in % labeling and DLR were not clinically significant. Further study of aCGH using fetal tissue stored for more than 5 days, to simulate longer periods of intrauterine fetal demise, may be useful.

T-094

Impact of Delivery Route on Neonatal Morbidity and Mortality in Isolated Gastroschisis: A Systematic Review and Meta-Analysis.

Ahizechukwu C Eke,[1] Ashley Hesson,[2] Conisha Holloman,[3] Anna Sfakianaki*.[4] [1]*Johns Hopkins University School of Medicine, Baltimore, MD, USA;* [2]*University of Michigan, Ann Arbor, MI, USA;* [3]*Winnie Palmer Hospital/Orlando Health, Orlando, FL, USA;* [4]*Yale University School of Medicine, New Haven, CT, USA.*

INTRODUCTION: The objective of this paper was to evaluate the impact of delivery route on neonatal morbidity and mortality in cases of isolated gastroschisis.

METHODS: Electronic databases (MEDLINE, Scopus, ClinicalTrials.gov, EMBASE and the Cochrane Central Register of Controlled Trials, AJOL, LILACS and CINAHL) were searched from their inception until October 2016 with the use of a combination of the following text words 'isolated gastroschisis', 'ventral wall defect', 'pregnancy', 'vaginal delivery', 'cesarean section', and 'outcomes'. The pooled results were reported as relative risk (RR) with 95% confidence interval (95% CI).

RESULTS: Twenty two studies including 2,075 neonates with isolated gastroschisis were analyzed: 1150 to vaginal birth and 925 to cesarean birth. After adjusting for confounders, infants delivered via cesarean section were more likely to undergo primary repair of their gastroschisis defect (adjusted OR (aOR) 1.39, 95% CI 1.03–1.87), have Apgar scores of <7 at 5 minutes (aOR 0.39, 95% CI 0.23–0.65) and stayed longer in the hospital than those born vaginally (mean difference (MD) -9.70, 95% CI -11.71 – -7.70). Infants delivered vaginally were more likely to transition to enteral feeds earlier (mean difference (MD) -2.11, 95% CI -3.63 – -0.60) and more likely to survive postnatally (aOR 1.82, 95% CI 1.11–2.96). Infants diagnosed with IUGR antenatally were more likely to be delivered vaginally (aOR 1.24, 95% CI 1.09–1.41). There were no significant differences between route of delivery and development of neonatal sepsis.

**Figure(s) will be available online.*

CONCLUSIONS: Elective cesarean delivery does not improve neonatal outcomes in infants with isolated cases of gastroschisis.

T-095

Prenatal Whole Exome Sequencing in Anomalous Fetuses: Improving Diagnosis, Expanding Mendelian Phenotypes, Identifying Novel Genes, and Identifying Counseling Challenges.

Neeta L Vora,[1] Bradford Powell,[2] Emily Hardisty,[1] Kelly Gilmore,[1] Kate Foreman,[2] Cindy Powell,[2] Debra Skinner,[2] Christine Rini,[2] Karen Weck,[2] Anne D Lyerly,[2] Kim Boggess,[1] Jonathan Berg,[2] James P Evans*.[2] [1]*University of North Carolina at Chapel Hill, Chapel Hill, NC, USA;* [2]*University of North Carolina at Chapel Hill, Chapel Hill, NC, USA.*

INTRODUCTION: We sought to investigate the diagnostic performance of whole exome sequencing (WES) fetuses with sonographic abnormalities who had normal microarray analysis. Given the complexities of analysis and return of results, we sought to understand patient perspectives regarding WES.

METHODS: WES was performed on DNA extracted from chorionic villi, amniocytes, or cord blood in 15 anomalous fetuses and from peripheral blood from their parents (11 additional trios are enrolled and sequencing is pending). Prenatal-specific gene lists and bioinformatics pipelines specific to trio analysis were developed. Parents were consented for the return of 1) diagnostic results in the fetus; 2) medically actionable findings in the parents; 3) carrier status for significant autosomal recessive conditions in which both parents are carriers. Reported variants were confirmed by Sanger sequencing. A mixed-methods assessment with 26 mother-father dyads was completed.

RESULTS: In 7/15 (47%), WES provided a diagnosis or possible diagnosis of the following disorders: osteogenesis imperfecta type 3 (COL1A1), fetal akinesia sequence (MUSK), scalp-ear nipple syndrome (KCTD1), primordial microcephaly-dwarfism syndrome (RTTN); Meckel Gruber Syndrome (TMEM); lymphatic dysplasia (PIEZ01); short rib polydactyly syndrome (DYNC2H1). One additional case revealed a novel candidate gene (MAP4K4) that is embryonic lethal in mice but does not have a human phenotype yet. The average perceived likelihood (5.4/10) that this technique would explain the results was higher than pre-test counseling. Women in the highest income levels scored highest on the pre-sequencing genetics literacy assessment.

CONCLUSIONS: WES has diagnostic utility in fetuses with sonographic abnormalities and normal microarrays. WES can also expand the phenotype of known disorders and has the potential to identify novel genes critical to human fetal development. Challenges related to genetics literacy, diagnostic capability, and variant interpretation must be addressed by highly tailored pre- and post-test genetic counseling.

T-096

Novel Three-Dimensional High-Frequency Ultrasonography for Early Detection and Characterization of Embryo Implantation Site Development in the Mouse.

Mary Peavey†,[1] Corey Reynolds,[2] William Gibbons,[1] Cecilia Valdes,[1] Francesco DeMayo,[4] John Lydon*.[3] [1]*Baylor College of Medicine, Houston, TX, USA;* [2]*Baylor College of Medicine, Houston, TX, USA;* [3]*Baylor College of Medicine, Houston, TX, USA;* [4]*NIEHS, Research Triangle Park, NC, USA.*

INTRODUCTION: Ultrasonography is a powerful tool to non-invasively monitor the development of the human fetus. Although genetically engineered mice have served as valuable *in vivo* models to study embryo implantation and pregnancy progression, such studies require parous mice to be euthanized for phenotypic analysis. To address this issue, our objective is to use three-dimensional (3-D) reconstruction *in silico* of high frequency ultrasound (HFUS) imaging data for early detection and characterization of murine embryo implantation sites and their development *in utero*.

METHODS: Transabdominal high-frequency ultrasound images were obtained, followed by 3-D reconstruction to precisely quantify embryo implantation site characteristics (site number, location, volume and spacing, and embryo viability) and embryonic developmental progression in pregnant C57BL6J/129S mice as early as 5.5 days post coitus (d.p.c.) through to 9.5 d.p.c. using a VisualSonics Vevo 2100 (MS550S, 55MHz) transducer.

RESULTS: Successful and reliable measurements of implantation site number, location, volume and interval spacing were achieved, in addition to confirmation of embryo viability via cardiac activity. A total of 12 dams were imaged with HFUS with approximately 100 embryos examined per embryonic day. In the post-implantation period (5.5 to 8.5 d.p.c.), 3-D reconstruction of the gravid uterus in mesh or solid overlay enabled visual representation *in silico* of the entire horn, including implantation location, number, spacing distances, and site volume.

CONCLUSIONS: Utilization of 3-D HFUS imaging allows for early detection and analysis of post-implantation events in the pregnant mouse with the ability to longitudinally monitor the development of early pregnancy events non-invasively. As genetically engineered mice continue to be used to characterize female reproductive phenotypes, this reliable and non-invasive method can detect, quantify, and characterize early implantation events and will prove to be an invaluable investigative tool for the study of female infertility and subfertility phenotypes based on a defective uterus.

T-097

Midtrimester Fetal Growth Restriction: Who Is at Risk of Remaining Small? Lorene A Temming†, Fayola Fears, Roxane Rampersad, Methodius G Tuuli, George A Macones, Alison G Cahill*. *Washington University in St. Louis, St. Louis, MO, USA.*

INTRODUCTION: When fetal growth restriction(FGR) is diagnosed before viability without a cause, little data exists to identify fetuses at risk for remaining small. We sought to identify maternal factors and sonographic findings associated with a small for gestational age (SGA) and severe SGA neonate in women with isolated FGR at the midtrimester.

METHODS: Retrospective cohort of singleton, non-anomalous pregnancies with FGR found during anatomic survey at 17-22 weeks from 2010-2015. FGR was defined as estimated fetal weight <10th % for gestational age. The primary outcomes for this analysis were SGA and severe SGA, defined as <10th and ≤5th % birthweight for gestational age. Maternal and ultrasound characteristics were compared for those with and without SGA. Receiver operating curve analysis was used to evaluate ultrasound parameters for prediction of SGA and severe SGA.

RESULTS: 437 patients were found with isolated FGR at the midtrimester. Of the maternal characteristics evaluated, only African American race and smoking were associated with SGA and severe SGA neonates. Although growth percentile was not associated with SGA, abdominal circumference (AC) <5% and <10% increased the risk of SGA(aOR 2.78, 95% CI 1.83, 4.21) and severe SGA(aOR 2.28, 95% CI 1.42, 3.67). Similarly, AC ≥10% decreased the risk of SGA and severe SGA. ROC analysis confirmed that AC was a better test than growth % for both SGA(c-statistic 0.673 vs 0.569, p=0.001) and severe SGA(c-statistic 0.653 vs 0.566, p=0.0172)

**Figure(s) will be available online.*

CONCLUSIONS: AC <10th % in the setting of midtrimester FGR more than doubled the risk of SGA. AC was more predictive of both SGA and severe SGA than growth % in these patients. This information can be used to determine which patients are most at risk and counsel patients with isolated FGR at the anatomic survey.

T-098

Lipid Accumulation in the Primate Fetal Liver with Maternal Obesity (MO) May Be Regulated by Novel Epigenetic Mechanisms. Sobha Puppala,[1] Cun Li,[2] Jeremy P Glenn,[1] Amy R Quinn,[3] Jennifer J Palarczyk,[3] Edward J Dick,[1] Peter W Nathanielsz,[2] Laura A Cox.[1] *[1]TBRI, San Antonio, TX, USA; [2]University Wyoming, Laramie, WY, USA; [3]University of Texas Health Science Center, San Antonio, TX, USA.*

INTRODUCTION: The liver is the body's main detoxifying organ and a major site for synthesis, storage and redistribution of metabolites. MO increases risk of offspring (F1) cardiovascular disease (CVD), diabetes and obesity. Mechanisms by which MO predisposes F1 to CVD and metabolic dysregulation are unknown. This study assessed MO impact on primate fetal liver and identified underlying molecular mechanisms.

METHODS: Unbiased hepatic gene and microRNA abundance were quantified in term baboon fetal livers (control, CON = 6, MO = 5) and subjected to network analysis to determine fetal molecular responses to MO. Lipid content (CON = 16; MO = 16) was quantified by Oil Red O.

RESULTS: We identified 933 differentially expressed genes in MO vs CON, 350 up- and 583 down-regulated. Network analysis revealed Wnt/β catenin signaling central to the MO response suggesting that MO impacts fetal liver lipid metabolism. In addition, 53 differentially expressed miRNAs that target Wnt/β catenin signaling pathway genes are inversely expressed with their target genes. Hepatic lipid content was 3-fold greater in MO than CON fetal livers (p=0.02).

**Figure(s) will be available online.*

Fig1. Quantification of lipid content in CON and MO fetal baboon livers. Sections stained with Oil Red O and quantified by stereomicroscopy. Panel A - control fetal liver ; B MO fetal liver. Red indicates lipid.

CONCLUSIONS: MO fetal livers display early indications of metabolic dysregulation/lipid accumulation. Molecular genetic analyses suggest dysregulation is mediated by Wnt/β catenin signaling, a central fatty acid metabolism and lipid storage pathway/ Inverse expression of miRNAs targeting this pathway suggest an epigenetic mechanism responsive to MO. Our findings show that MO has an impact on the fetal liver and predicts a negative impact on F1 metabolic health.

T-099

Left Ventricular Sphericity Index in Fetuses with Congenital Diaphragmatic Hernia. Rachel Rodel†,[1] Michael Zaretsky,[1] Henry Galan,[1] Nicholas Behrendt,[1] Kenneth Liechty,[1] Sonali Patel,[2] Bettina Cuneo*.[1,2] *[1]University of Colorado/Children's Hospital Colorado, Aurora, CO, USA; [2]Children's Hospital Colorado, Aurora, CO, USA.*

INTRODUCTION: Left ventricular sphericity index (LVSI) is an index of ventricular geometry that is independent of gestational age (GA) and is measured by left ventricle (LV) length/width in a 4-chamber long axis view at end diastole. If the LV is slender and under filled, the LVSI is larger. If the LV has normal geometry it is more rounded and the LVSI is smaller. In fetuses with congenital diaphragmatic hernia (CDH), the LV often appears hypoplastic, but the LVSI has not been described in CDH. Our objective was to: 1. characterize LVSI in CHD to determine if there were GA related changes in CDH LVSI; 2. compare CDH LVSI with normal controls; 3. compare LVSI before and after maternal hyperoxygenation (MH) in the third trimester.

METHODS: This is a retrospective review of CDH fetuses and normal controls. CDH patients underwent fetal echoes (FE) in the second trimester and in the 3rd trimester at baseline and after MH. We calculated LVSI at end diastole by measuring the length of the LV from the hinge points of the mitral valve to the LV apex and the width of the LV from the septum to the free wall.

**Figure(s) will be available online.*

MH was performed using 10 liters/minute of oxygen by facemask for 10 minutes. Statistical methods included analysis of variance and calculation of Pearson correlation coefficient.

RESULTS: Nine controls had FE at 25.5±3.54 weeks (w). CDH subjects had initial FE at 25.06±2.33w followed by baseline and MH FE at 34.55±0.52w. Baseline CDH LVSI was significantly higher than control LVSI (2.89±0.68 vs. 2.01±0.15, p<0.0001). CDH LVSI increased as GA progressed from 2.54±0.45 (~25w) to 2.89±0.68 (~34w). LVSI decreased in response to MH, but the difference was not significant (2.89±0.68 v 2.56±0.56).

CONCLUSIONS: These preliminary results suggest that compared to normal controls, the CDH LVSI is larger and increases in the third trimester. The LV assumed a more normal geometry after MH, but whether LVSI can be a surrogate for pulmonary vasoreactivity or a prognosticator for CDH will require further investigation.

T-100

Neonatal Lactic Acid and the Prediction of Severe Brain Injury and Death in Neurologically Depressed Neonates. Christopher Novak†, Hattan Arif, Ernest Graham*. *Johns Hopkins Hospital, Baltimore, MD, USA.*

INTRODUCTION: To determine the predictive ability of neonatal lactate obtained within 24 hours of birth compared to initial neonatal arterial pH and umbilical arterial pH to identify severe neonatal brain injury or death in neurologically depressed infants at birth.

METHODS: This is a retrospective cohort study of all neurologically depressed neonates at birth with suspected hypoxic-ischemic encephalopathy (HIE) that underwent therapeutic hypothermia at our institution from July 2007 to June 2016 and had a neonatal lactate drawn within 24 hours of life. The primary outcome was an abnormal neonatal MRI or death. Logistic regression was performed to estimate the probabilities of the primary outcome given initial neonatal lactate, initial neonatal arterial pH, or umbilical arterial pH. Receiver operating characteristic curves were derived.

RESULTS: There were 89 neonates depressed at birth with suspected HIE that received whole body hypothermia and had a neonatal lactate level drawn within 24 hours of life. An abnormal MRI occurred in 31 and death in 15. This group of 46 (51.7%) neonates was compared to the 43 with a normal MRI. There was no significant difference in nonreassuring FHR prior to delivery, cesarean delivery, gestational age, birth weight, umbilical arterial pH, or initial neonatal arterial pH. The group that experienced the primary outcome had a significantly greater lactate on multivariate regression (OR 1.11±0.06, 95% CI 1.00-1.23; p=.044). Neonatal lactate obtained within 24 hours of birth was moderately predictive of the primary outcome with the optimal cut point of neonatal lactate being

≥6.5 mmol/L. This predicted the primary outcome with a sensitivity of 60.87%, specificity of 69.77%, positive predictive value of 68.29%, and negative predictive value of 62.5%.

	Abnormal MRI or Death (N=46)	Normal MRI (N=43)	*P*
Nonreassuring FHR	36 (78.3%)	27 (62.8%)	0.11
Cesarean delivery	39 (84.8%)	30 (69.8%)	0.09
Gestational age (weeks)	38.4±1.7	38.4±1.9	0.97
Birth weight (gms)	3313±570	3184±618	0.31
Umbilical arterial pH	6.91±0.25	6.92±0.15	0.85
Initial neonatal arterial pH	7.07±0.15	7.11±0.16	0.25
Neonatal lactate (mmol/L)	10.1±7.3	5.9±4.7	0.002*

CONCLUSIONS: Neonatal lactate obtained within 24 hours of birth is superior to initial neonatal arterial pH and umbilical arterial pH in predicting neonatal brain injury or death.

T-101

Modeling of Gene Expression in Newborn Heart Following Chronic Maternal Hypercortisolemia in Late Gestation. Andrew Antolic†, Elaine Richards, Maureen Keller-Wood*. *University of Florida College of Pharmacy, Gainesville, FL, USA.*

INTRODUCTION: In a model of chronic maternal stress, in which pregnant ewes are infused with cortisol (1mg/kg/day) beginning at 115 days of pregnancy (CORT), we have found changes in fetal heart structure and a dramatic increase in fetal perinatal stillbirth. Consistent with this phenotype, transcriptomic analysis of hearts shows an increase in proliferative pathways after 2 weeks of CORT, and shows changes in metabolic pathways in early labor. Recent studies found that CORT significantly decreases fetal mean aortic pressure (MAP) and heart rate (HR), and increases the duration of the P wave and PR interval of the ECG on the day of birth. Therefore, we used microarray to model cardiac gene expression in these same newborns to reveal underlying mechanisms of the dysfunction at birth.

METHODS: Samples from the left ventricle (LV) and septa (SEP) were collected at necropsy from control (n=5) and CORT (n=5) newborns. RNA was extracted and hybridized to an ovine microarray. Differentially regulated genes (DEG) were determined using empirical Bayes moderated t-test. Gene ontology (GO) and KEGG pathway inference were performed using Webgestalt to identify features significantly overrepresented by the DEG.

RESULTS: 166 LV and 61 SEP genes were significantly upregulated, and 220 LV and 124 SEP genes were significantly downregulated by CORT. GO analysis identified SMAD protein complex, GPI-anchor transamidase complex, and pre-autophagosomal structure as over represented cellular structures associated with the DEG in LV; and troponin complex, I band, Z disc, and Ino80 of the chromatin remodeling complex as cellular structures associated with the DEG in SEP. Metabolic pathways, insulin signaling, PPAR signaling, hypertrophic cardiomyopathy, and mTOR signaling were identified as processes associated with the DEG in LV; insulin signaling, adipocytokine signaling, starch and sucrose metabolism, and regulation of actin cytoskeleton were pathways identified in SEP. Among the most highly upregulated DEG at birth in both LV and SEP were Troponin I2, Calmodulin 1 and 2. Only 3 DEG after CORT in the neonate are among the 499 DEG previously identified in CORT fetuses in early labor.

CONCLUSIONS: The pattern of gene expression at birth differed from that of fetuses at the start of labor, and indicate that further dysfunction in cardiomyocyte energetics and calcium handling contribute to the changes in fetal MAP, HR, and ECG seen during labor and delivery.

T-102

Atrial Natriuretic Peptide Regulates the Fetal Cardiomyocyte Cell Cycle. Eileen I Chang†, Natasha N Chattergoon, Samantha Louey, Isa Lindgren, Kent L Thornburg*. *Oregon Health and Science University, Portland, OR, USA.*

INTRODUCTION: The number of cardiomyocytes at birth is related to risks for later heart disease, including heart failure. Atrial natriuretic peptide (ANP) is released from both the atria and ventricles of the fetal heart, and increases as the fetus develops. Circulating ANP is 5-fold higher in the fetus than in the mother. ANP signals the cardiomyocyte by stimulating the ANP receptor "A", a guanylyl cyclase. We have shown that both tri-iodo-thyronine (T3) and ANP suppress cardiomyocyte proliferation in culture. T3 stimulates the cell cycle inhibitor, p21. However the signaling pathways through which ANP regulates the cell cycle is not understood. We hypothesized that ANP ultimately signals similarly to T3.

METHODS: Cardiomyocytes were isolated from non-instrumented, control fetal sheep (n=8) at 135 day gestational age and cultured. ANP (100 nM) was administered for 10 min, 1 hr, and 6 hrs. mRNA levels of p21 (cyclin-dependent kinase inhibitor 1A), PCNA (proliferating cell nuclear antigen), CDK1 (cyclin-dependent kinase 1), and RB1 (retinoblastoma-1) were quantified using real-time PCR and normalized to the abundance of β-actin mRNA. Statistical significance were considered by Kruskal–Wallis one-way ANOVA ($P<0.05$), and Dunn's multiple comparison post hoc test.

RESULTS: The ANP effect was bi-modal. 10 min stimulation caused the mRNA levels for PCNA and CDK1 to increase by approximately 2-fold, and p21 was decreased by 0.5-fold compared to the control ($P<0.05$); these are all associated with increased proliferation. By 6 hr, all the signals are related to cell cycle suppression.

CONCLUSIONS: The acute effect of ANP on late gestation fetal ovine cardiomyocytes is cellular proliferation by promoting DNA replication (s phase) and mitosis (m phase). However, like T3, ANP ultimately signals by stimulating the expression of p21, a powerful cell cycle suppressant of CDK1 (Fig. 1). Both T3 and ANP levels are high at the end of gestation and provides a synergistic influence on heart cell numbers. This suggests that excess levels of ANP earlier in gestation will lead to an under-endowed fetal heart.

**Figure(s) will be available online.*

T-103

A New Method of Predicting a Brain Hemorrhage Risk in Fetal Growth Restriction. Takahiro Minato†,[1,2] Takuya Ito,[1] Naoaki Sato,[1,2] Yoshitaka Kimura,[1,2] Nobuo Yaegashi.[2] *[1]Tohoku University Graduate School of Medicine, Sendai, Miyagi, Japan; [2]Tohoku University Graduate School of Medicine, Sendai, Miyagi, Japan.*

INTRODUCTION: Fetal growth restriction (FGR) is associated with up to 10-to 30-fold increase in the risk of cerebral palsy (CP) at term. Intraventricular hemorrhage is a main factor of CP. Brain blood pressure is controlled by autonomic nerve system. Immaturity of this system is thought to cause failingin autoregulation of the blood pressure against the change in brain perfusion and results in the rupture of a vessel. We examined the association maturation of autonomic nerve system with the brain hemorrhage using FGR model mice.

METHODS: We used ICR pregnancy mice (term 19.0 days) under the approval of Institutional Committee. In 15.5 embryonic day, we tied the ligature at the bottom of the uterine artery and created FGR model fetuses by reducing the placental perfusion. We also created a control group. In 17.5 embryonic day, we measured short term variability (STV) as an indicator of autonomic nerve system maturity with a fetal electrocardiogram. Then we added intermittent hypoxic load by clipping ovarian artery to mimic uterine contraction load at delivery. We examined the association between STV and brain hemorrhage rate in the two groups.

RESULTS: In comparison with the control, the hemorrhage rate in FGR fetus was significantly higher (70.6% vs 92.5% p=0.013). Also the hemorrhage areas per point in FGR fetus were larger than that of control ($1.46mm^2$/point vs $2.50mm^2$/point p=0.018). Regarding the STV, it was significantly lower in FGR fetus than in control group (4.05msec vs 11.43msec p=0.015).

CONCLUSIONS: Immaturity of autonomic nerve system is a risk factor at brain hemorrhage and prone to more severe.
We can measure the degree of autonomic nerve system maturity by using fetal electrocardiogram and predict a risk of brain hemorrhage at delivery. By knowing the risk of brain hemorrhage, we can choose appropriate management of FGR to avoid brain hemorrhage and decrease the incidence of cerebral palsy.

T-104

Exposure to Intrauterine Inflammation Has a Sex-Specific Effect on Gene Expression in the Hippocampus of Exposed Offspring: Potential Mechanisms of Adverse Neurobehavioral Outcomes. Amy G Brown, Natalia M Tulina, Guillermo O Barila, Michal A Elovitz. *Perelman School of Medicine, Philadelphia, PA, USA.*
INTRODUCTION: Exposure to prenatal inflammation is associated with poor neurobehavioral outcomes in offspring. We have previously demonstrated that intrauterine inflammation (IUI) decreases post-natal neurogenesis within the dentate gyrus of hippocampus. The mechanism by which inflammation negatively impacts hippocampal neural cell fate is unknown. These studies were performed to determine the mechanism by which inflammation disrupts hippocampal neurogenesis and to explore sexual dimorphic responses to inflammation-induced brain injury.
METHODS: CD-1 timed-pregnant mice received an intrauterine injection of lipopolysaccharide (LPS, 50ug/100ul) or saline on embryonic day 15 (E15). Pups, born at term, were culled at post-natal day 3 (P3) to a litter of 6-7. On P7, 2 male and female pups from ten LPS- and five saline-exposed dams were euthanized. Hippocampi were surgically dissected and flash-frozen. Changes in gene expression were assessed via QPCR using the Neurogenesis RT^2 Profiler Mouse PCR Array (Qiagen) containing primer-probe sets for 85 different genes related to mouse neurogenesis.
RESULTS: Exposure to IUI significantly altered the expression of 27 genes related to hippocampal neurogenesis ($P < 0.05$). There were nine genes that were commonly enhanced in both sexes in response to LPS. In males, the expression of nine genes was specifically altered and nine genes were uniquely changed in female offspring ($P < 0.05$). These altered genes represent proteins that regulate neuron proliferation, differentiation, histone modification, cell migration and synaptic function. Specifically, members of the Notch signaling pathway and the amyloid beta precursor protein family were elevated in both male and female offspring.
CONCLUSIONS: Our results demonstrate that prenatal exposure to inflammation alters hippocampal gene expression and disrupts neurogenesis. The elevated expression of members of the Notch signaling pathway and amyloid beta precursor protein family suggests a preservation of the neural progenitor pool, resulting in a decline in neurogenesis. Lastly, IUI has a divergent affect on the hippocampi of males and females, suggesting that neurobehavioral phenotypes associated with prenatal exposure to inflammation may be sex-dependent. (RO1HD076032)

T-105

In Utero Oxytocin (OXT) Exposure Alters Gene Expression Associated with Neurotransmitter Secretion and Metabolism in the Perinatal Mouse Brain. Frances Hsieh†,[1] Burton Rochelson,[1] Gopal Kumar,[2] Prodyot Chatterjee,[2] Xiangying Xue,[2] Ilya Kordunsky,[2] Christine Metz.[2] *[1]Hofstra-Northwell School of Medicine, Manhasset, NY, USA; [2]Feinstein Institute for Medical Research, Manhasset, NY, USA.*
INTRODUCTION: Synthetic oxytocin (OXT) is administered to induce and augment labor. When given to non-human neonatal and adult primates and rodents, OXT promotes positive social behaviors. However, little is known about the effects of prenatal OXT exposure on the perinatal brain. Given the behavioral effects of synthetic OXT, we investigated the effect of maternal OXT administration on gene expression patterns in the perinatal mouse brain.
METHODS: Pregnant C57BL/6 mice (10 weeks old, gestational day 18) were given saline (100µl) or OXT (1U/mouse, 100µl) subcutaneously every 30 min for 2 hours; 3 hours later dams (7 per group) and pups, delivered by Cesarean section, were euthanized. DNA and RNA were isolated from fetal tails and brains, respectively. Gender was determined by PCR using *Zfy* and *Ube* gender-specific primers. Fetal brain RNA samples (12 female, 12 male, with RIN values >9.3) were converted to ds-cDNA and then hybridized to mouseWG6v2.0 gene chips (Illumina), scanned (via Illumina HiScan) and analyzed using Genome Studio v2011.1 (Illumina). Gene set enrichment analysis (GSEA) was performed using GSEA software. RT-qPCR was used to confirm notable findings.
RESULTS: Using whole genome expression we found distinct gene expression patterns in perinatal mouse brains following OXT exposure in utero, with an overwhelming majority of genes significantly down-regulated. Female brains exposed to OXT showed significantly more differential expression patterns (OXT vs. saline) when compared to male brains. Differentially regulated pathways shared by males and females include: neuron projection ($p<0.003$ female, $p<0.003$ male), tyrosine metabolism ($p<0.00001$ female, $p<0.002$ male), and neurotransmitter secretion ($p<0.00001$ female, $p<0.0001$ male).
CONCLUSIONS: Prenatal OXT exposure results in the differential regulation of several nervous system genes and pathways in the rodent perinatal brain. Ongoing studies are underway to link gene expression patterns to developmental and/or social behaviors or disease states, and to determine whether these gene expression changes are sustained after the neonatal period.
Supported by the Lax Family Foundation.

T-106

Obstetrics Providers' Perceptions of the Barriers to Diagnosing Preeclampsia (PEC): A Clinical Needs Assessment in Two Low- and Middle-Income Countries (LMIC). Lydia L Shook†,[1] Muchabayiwa F Gidiri,[2] Melanie Peña,[3] Manuel Bousiéguez,[3] Irina A Buhimschi*.[4] *[1]Yale School of Medicine, New Haven, CT, USA; [2]University of Zimbabwe College of Health Sciences, Harare, Zimbabwe; [3]Gynuity Health Projects, Mexico City, Mexico; [4]Nationwide Children's Hospital, Columbus, OH, USA.*
INTRODUCTION: PEC is accountable for 14% of maternal deaths worldwide, with a disproportionate burden on LMIC. An accurate and timely diagnosis of PEC is critical, yet testing can be costly and time-consuming. Breakthroughs in understanding PEC pathophysiology have led to the development of a novel urine-based point-of-care test (POCT) with the potential of being affordable and sustainable. The objectives of this study were to assess the current barriers to diagnosing PEC in resource-limited settings; to assess providers' perceptions of ideal POCT characteristics; and to inform and prioritize future POCT development strategies.
METHODS: Multiple-choice surveys were distributed to obstetrics providers at Parirenyatwa Hospital in Harare, Zimbabwe and at a local health center in Mexico City. Survey questions were based on in-depth group discussions and used a modified discrete choice experiment approach. Survey data were described both qualitatively and quantitatively.
RESULTS: Overall, 24 respondents completed the survey (15 in Harare, 9 in Mexico City). Most respondents (70%) identified as obstetricians or obstetrics trainees. The urine dipstick test was identified as the only test available to evaluate proteinuria at the Harare site, and was the most frequently used test at the Mexico City site (83%). Important barriers to diagnosing PEC in Harare were "cost of testing" and "lack of supplies or staff" whereas in Mexico City, the most commonly identified barriers were "lack of providers' training in diagnosing PEC" and "lack of antenatal care." All respondents chose $10 (USD) or less as the highest affordable cost. 73% of all survey respondents identified that a POCT that avoided false negatives, i.e. a "test to 'rule out' PEC in patients with elevated blood pressure" was preferable to one that avoided false positives. "Reliability" was identified as the most valued test attribute at both sites.
CONCLUSIONS: Development of a POCT for PEC should focus on high sensitivity with an emphasis on reliability and low cost to overcome the barriers identified by obstetrics providers in these LMIC.

T-107

Paclitaxel Promotes Exosomal Expression of TLR8-Activating miR-146a-3p in Chemoresistant Epithelial Ovarian Cancer Cells. Stefan M Gysler†, Mary C Pitruzzello, Melissa J Mulla, Julie A Potter, Ayesha B Alvero, Gil Mor, Vikki M Abrahams*. *Yale University School of Medicine, New Haven, CT, USA.*

INTRODUCTION: Epithelial ovarian cancer (EOC) remains the deadliest of gynecologic malignancies, driven by a high rate of tumor recurrence compounded by acquired chemoresistance to first line therapeutics. Recent studies have demonstrated the ability of EOC cell-derived microRNAs (miRs) to confer chemoresistance via exosomal delivery, though the mechanism is unknown. We and others found specific miRs activate the RNA sensor Toll-like receptor 8 (TLR8) to induce inflammatory responses in cancer and other cell types. Our group also found the TLR/MyD88 pathway is required for EOC chemoresistance. Our objective was to evaluate cellular and exosomal expression of TLR8-activating miRs in response to paclitaxel in chemosensitive (MyD88-) and chemoresistant (MyD88+) EOC cells.

METHODS: The EOC cell lines OCC1 (paclitaxel sensitive, MyD88-) and OCSC1 (paclitaxel resistant, MyD88+) were treated with or without paclitaxel (2μM) for 24-48h. Cellular and exosomal RNA was isolated and expression of TLR8-activating miRs miR-146a-3p, miR-21a-5p and miR-29a-5p was analyzed by qRT-PCR using snU6 as a control. Supernatants were measured for inflammatory IL-8 by ELISA.

RESULTS: Cellular expression of miR-146a-3p, miR-21a-5p and miR-29a-5p was significantly higher in MyD88+ cells compared to MyD88- cells by 5962.5-fold, 4.3-fold, and 5.6-fold, respectively ($p<0.05$). Exosomal expression of miR-146a-3p was significantly 36.1-fold higher in MyD88+ cells compared to MyD88- cells ($p<0.05$). While not significant, exosomal miR-21a-5p and miR-29a-5p were 2.3 and 2.9-fold higher in MyD88+ cells. This correlated with a 95.7-fold higher basal IL-8 secretion in MyD88+ cells compared to MyD88- cells ($p<0.05$). Treatment with paclitaxel significantly upregulated exosomal expression of miR-146a-3p by 1.3-fold in MyD88+ cells ($p<0.05$), while exosomal miR-146a-3p was not altered by paclitaxel in MyD88- cells.

CONCLUSIONS: These results demonstrate differential expression patterns of TLR8-activating miRs in chemoresistant and chemosensitive EOC cells, and that exposure to paclitaxel preferentially upregulates miR-146a-3p in the exosomal compartment of chemoresistant EOC cells. Thus, miR-146a-3p may have a potential role in EOC cell pathology as a mediator of exosomally conferred chemoresistance, and may represent a putative biomarker in the detection of paclitaxel-resistant ovarian cancers.

T-108

Ovarian Cancer Cells Transfer Resistance to Chemotherapy to Other Cells via Exosomes. Mona Alharbi,[1] Richard Kline,[2] Katrina Wade,[2] Jacob Estes,[2] John Hooper,[3] Gregory E Rice,[1,2] Carlos Salomon.[1,2] *[1]The University of Queensland, Brisbane, QLD, Australia; [2]Ochsner Baptist Hospital, New Orleans, LA, USA; [3]Mater Research Institute, University of Queensland, Brisbane, QLD, Australia.*

INTRODUCTION: Hypoxia is a key regulatory factor of cancer progression via multiple processes, including enhanced resistance to chemotherapy drugs. Interestingly, the release of exosomes is higher under hypoxic conditions; however, the potential role of exosomes in chemotherapy resistance in ovarian cancer has yet to be established. We hypothesize that exosomes can induce chemotherapy resistance to neighboring cells.

METHODS: CaOV-3 cells were used as models of ovarian cancer. Cells were cultured under 8% O_2 (normoxia) and 1% O_2 (hypoxia) for 48 hours. Exosomes were isolated from cell-conditioned media by differential and buoyant density centrifugation. Exosomes were characterized by nanoparticle tracking analysis, electron microscopy, and western blot (CD63 and TSG101). Cell migration was assessed by scratch assays using a 96-well plate Wound MakerTM in the presence of 8% or 1% O_2 exosomes. For the chemo drug resistance, cells were incubated in the absence or in the presence of exosomes and with Paclitaxel (0.01-100 μM) or carboplatin (0.01-100 μM) for 48 hours. The effect of chemotherapy drugs on cell apoptosis were determined by quantifying Caspase3/7 using Incucyte.

RESULTS: Exosomes were identified as spherical vesicles, with a typical cup or spherical-shape, with diameters around 100 nm, and positivity for CD63 and TSG101. Hypoxia decreased cell apoptosis compared to normoxia in the presence of Paclitaxel: EC_{50}: 1.74 ± 0.2 μM and 16.21 ± 0.29 μM; IC_{50}: 0.18 ± 0.09 μM and 6.49 ± 0.11 μM for normoxic and hypoxic conditions, respectively; and carboplatin: EC_{50}: 0.33 ± 0.17 μg/ml and 2.67 ± 0.07 μg/ml; IC_{50}: 0.31 ± 0.09 μg/ml and 2.52 ± 0.08 μg/ml for normoxic and hypoxic conditions, respectively. Interestingly, exosomes isolated from cells cultured under hypoxia conditions induce cancer cell invasion and drug resistance in cells cultured under 8% O_2.

CONCLUSIONS: In this study, we suggest that tumor cells use exosome-mediated transfer to communicate with neighboring cells to regulate their response to chemotherapy drugs.

T-109

DNA Copy Number Alteration in Primary Fallopian Tube Carcinoma. Shoko Sakurada,[1] Yoh Watanabe,[2] Yusuke Shibuya,[1] Hideki Tokunaga,[1] Sakae Saito,[3] Jun Yasuda,[3] Hidekazu Yamada,[4] Hitoshi Niikura,[1] Nobuo Yaegashi.[1] *[1]Tohoku University, Sendai, Miyagi, Japan; [2]Tohoku Medical and Pharmaceutical University, Sendai, Miyagi, Japan; [3]Tohoku Medical Megabank Organization, Sendai, Miyagi, Japan; [4]Miyagi Cancer Center, Natori, Miyagi, Japan.*

INTRODUCTION: Primary fallopian tube carcinoma (PFTC) is a rare malignancy and constitutes less than 1% of all gynecologic malignancies. To determine molecular biological characteristics of PFTC, we analyzed DNA copy number alteration (CNA).

METHODS: We analyzed a total of 24 patients with PFTC treated at 2 institutions between October 1998 and December 2015. After IRB approval in each institution, we extracted DNA from cancerous tissue of formalin-fixed paraffin-embedded specimens by microdissection, and examined CNA using OncoScan FFPE assay kit. Genomic Identification of Significant Targets in Cancer (GISTICS) was used to determine the significance of the genomic alterations.

RESULTS: Median patient's age was 55-years (range: 38-85) and FIGO stage distribution was 5 in stage I, 3 in stage II,and 14 in stages III and IV. The most common histological subtype was serous carcinoma (91.6%). CNAs were obtained all 24 patients and 14 high frequency of CNAs (13 gain regions and 1 deletion region) were observed. The deletion on 22q11.23 was more frequently observed in stages III and IV than stages I andII). Moreover gain on 7q33 was significantly frequent in 50-years < patients ($p<0.05$).

CONCLUSIONS: CNAs could analyze in FFPE samples from 20 years ago. CNAs may contributes clinical characteristics of PFTC.

T-110

Gene Expression Patterns in Human Endometrium, Cervix, Sigmoid, and Ileum Suggest Distinct Mucosal-Associated Immune Environments with Potential Impact on Local Susceptibility to HIV Transmission. Shaina Balayan,[1] Sahar Houshdaran,[1] Karen Smith-McCune,[1] Ruth M Greenblatt,[2] Barbara L Shacklett,[3] Juan C Irwin,[1] Linda C Giudice*.[1] *[1]UCSF, San Francisco, CA, USA; [2]UCSF, San Francisco, CA, USA; [3]UC Davis, Davis, CA, USA.*

INTRODUCTION: The mucosae of the female reproductive tract and gut are primary sites of HIV transmission. We evaluated transcriptomes of endometrium and cervix compared to sigmoid and ileum for patterns/pathways relevant to mucosal immune function in uterus versus gut, and potential impact on local susceptibility to HIV transmission.

METHODS: Subject paired samples of endometrium (EBX), cervical transformation zone (CX), ileum (IL), and sigmoid (SIG) were obtained from 5 healthy, normally cycling, HIV-uninfected women in the mid-secretory phase of the menstrual cycle. Total RNA was processed for whole genome microarray. Data analysis included unsupervised principal component analysis (PCA), hierarchical clustering, and differential

expression (≥1.5-fold change, P≤0.05) and pathway analyses (z-score≥2) for the following comparisons: 1. EBX vs SIG; 2. EBX vs IL; 3. CX vs SIG; 4. CX vs IL.
RESULTS: PCA and hierarchical clustering showed samples clustering primarily by organ (uterus, gut) then by tissue (EBX, CX, SIG, IL). Genes related to hormone action (PGR, ESR1, MUC16, DIO2, PAEP, SPP1) were prominent in EBX and/or CX, as well as genes associated with innate and adaptive immune responses (CCL2, CXCR2, CXCL17, TLR5, CD44, IL33). SIG and IL expressed genes essential to intestinal integrity and epithelial barrier function (LTA, DSG2, CLDN7, EPCAM, KRT20, MUC12/13/17). EBX expressed unique immune related genes, as did CX. Uterine tissues showed extensive activation of Biofunctions and Upstream Regulators related to cell movement, growth and proliferation, and cell and tissue development. However, activation of pathways related to infectious diseases was unique to EBX (infection of cells by Retroviridae and RNA virus, viral and HIV infection).
CONCLUSIONS: Gene expression and biofunctional pathway activation patterns in human endometrium suggest a highly active immune environment compared to cervix, sigmoid, and ileum. These findings underscore the potential importance of the upper female reproductive tract as a portal of entry for HIV, and perhaps the endometrium as a site of increased susceptibility to HIV transmission. Support: NIH AI083050-05.

T-111

Side Effect Profile During Treatment of Symptomatic Endometriosis with Norethindrone or Leuprolide Treatment. Ozgul Muneyyirci-Delale,[1,2] Cassandra Charles,[1] Xiaobai Li,[3] Ninet Sinaii,[3] Mudar Dalloul,[1] Pamela Stratton.[4] *[1]SUNY Downstate Medical Center, Brooklyn, NY, USA; [2]Kings County Hospital Center, Brooklyn, NY, USA; [3]NIH Clinical Center, Bethesda, MD, USA; [4]NICHD/NIH, Bethesda, MD, USA.*
INTRODUCTION: Hormonal treatment like norethindrone and leuprolide for endometriosis-associated pain are common and may be long-term approaches to providing symptom relief. In clinical trials of endometriosis-associated chronic pelvic pain, daily calendars are used to gather real-time documentation of side effects that are known to limit use of hormonal therapies. Calendars may provide information about the occurrence of side effects not easily quantified at periodic study visits.
METHODS: Women with surgically-diagnosed, symptomatic endometriosis were randomized to receive 5mg norethindrone (NA) daily or 11.25mg leuprolide (LD) every 12 weeks for 24 weeks in a prospective, double-masked clinical trial. They completed diary calendars beginning one month prior to initiating study treatment throughout the study to report side effects regarding vaginal dryness, headaches, hot flushes, fatigue, anxiety, sleep disorder and depression. Tables by treatment group and phase, and graphing by heat map were used to examine side effects.
RESULTS: 31 women were randomized to each treatment group. Most were Black (82%) and single (66%) with a mean age of 34.1 ± 6.7 years and pelvic pain for 14.3 ± 8.0 years. Hot flashes on LD were the most common side effect, occurring on 47.5% of days with most hot flashes reported as mild (32%). Many fewer days with hot flushes were reported on NA (11.5%) and most were mild (6.8%). Vaginal dryness occurred at similar baseline rates, but was reported on roughly twice as many days for women on NA (4.7%) vs LD (2.8%). The number of days with headaches was similar from 15.1% at baseline to 17.5% on LD while headache frequency decreased on NA from 11.6% to 8.6%. Frequency of fatigue was similar between groups at baseline (1.8% LD, 1.3% NA) and during treatment (7.1% LD, 5% NA). Fewer than 1% of women in either group reported depression, anxiety or sleep disorder during the study.
CONCLUSIONS: The frequency of side effects reported during treatment with either norethindrone or leuprolide was relatively low except for hot flushes. Women on leuprolide reported having hot flushes on more days than on norethindrone which may limit leuprolide use.

T-112

Invasive Growth of Endometrium in SHN Mice: Driven by Novel MMTV Integration Sites? Ralf Lesche, Djork-Arne Clevert, Thomas Zollner, Martin Fritsch. *Bayer Pharma AG, Berlin, Germany.*
INTRODUCTION: Adenomyosis, or endometriosis interna, is defined by the invasive growth of endometrial tissue into the myometrial layer of the uterus. Key symptoms of adenomyosis are pelvic pain, dysmenorrhea, and infertility. A recent prospective study suggests that adenomyosis is a clearly under-recognized condition with a high prevalence in women. The SHN mouse strain, which was originally selected for a high incidence of mammary tumor development, also develops adenomyosis under hyperprolactinemic conditions (Mori & Nagasawa. *Acta Anat* **116:46**, 1983). Since the mouse mammary tumor virus (MMTV) is known to transform tissue by integration into wnt pathway and growth factor genes (Theodorou et al. *Nat Genet* **39(6):759**, 2007), we asked the question whether the integration of the MMTV in yet unidentified novel gene loci in SHN mice may be a driver for the adenomyosis phenotype in this mouse strain.
METHODS: To identify gene loci in which the MMTV virus is integrated, we used the Agilent SureSelect methodology. In short, oligo nucleotide baits for MMTV LTR sequences were designed to enrich for MMTV LTR containing DNA fragments from SHN and other mouse strains for comparison. MMTV integration sites were located by identifying hybrid sequences where one end maps to MMTV LTR and the other to mouse genomic sequences.
RESULTS: In the C57/Bl6 reference genome (built GRCm38), three complete integration sites of the MMTV virus have been identified: chr 4(+):46575144-46585216 (Coro2a gene region), chr 6(+):68242385-68252285, and chr 12(-):92890931-92883867. Using our methodology we confirmed the presence of these MMTV full integration sites at those locations in C57/Bl6 and also in SHN mice. Furthermore, we identified four new integration sites for the full MMTV sequence in the genome of SHN mice, which are not present in C57/Bl6 and other mouse strains for which whole genome sequence information is available. Two of these novel integration sites map to the coding regions of genes and could possibly influence their expression and function. Currently we are sequencing other Swiss mouse strains related to SHN to explore whether these new MMTV integration sites can be seen there.
CONCLUSIONS: We have detected new integration sites of MMTV virus into the genome of SHN mice and we are currently exploring whether those may be causally related to the onset of adenomyosis.

T-113

Novel EP4 Antagonist Demonstrated Significant Effects in Rat Model of Chronic Inflammatory Pain Employing a Dynamic Weight Bearing Readout. Anne-Marie Coelho,[2] Stefan Baeurle,[5] Daryl Walter,[3] Olaf Peters,[4] Markus Koch,[1] Thomas M Zollner,[1] Andreas Steinmeyer,[5] Susan Boyce,[2] Susan Boyce,[2] Jens Nagel*.[1] *[1]Bayer Pharma AG, Berlin, Germany; [2]Evotec AG, Hamburg, Germany; [3]Evotec Ltd, Abingdon, United Kingdom; [4]Bayer CropScience AG, Frankfurt/Main, Germany; [5]Bayer Pharma AG, Berlin, Germany.*
INTRODUCTION: Endometriosis (EMT) is a chronic, hormone-dependent, inflammatory disease, characterized by the presence and growth of endometrial tissue outside the uterine cavity. It is associated with moderate to severe pelvic pain symptoms, subfertility and a marked reduction in quality of life. The pathway leading to PGE2 synthesis is highly up-regulated in EMT and in patients high PGE2 levels were identified in endometriotic lesions. PGE2 is the endogenous, agonistic ligand of EP receptors with potency on the EP4 receptor (EP4) in the low nanomolar range. The EP4 is highly expressed in the ectopic endometrium and is involved in multiple mechanisms of EMT disease progression. EP4 antagonism has the potential to address various treatment paradigms associated with EMT such as chronic pelvic pain, inflammatory pain, proliferation of uterine tissue, and inflammation. Our new compound (Comp A) was identified as a highly potent human EP4 antagonist. *In vitro* assays revealed a high functional potency on EP4 of mouse, rat, and human.

METHODS: SD rats were treated with EP4 antagonist or vehicle. After 1h all of the animals received an intraplantar injection of 50 μL of 100% Complete Freund's Adjuvant (CFA) under anesthesia. The CFA injection induces a robust edema, accompanied by hyperalgesia and allodynia, in the treated paw. The compound was dosed p.o. twice daily. 48 h after the CFA application the animals were placed in a dynamic weight bearing (DWB) apparatus for quantification of spontaneous pain.
RESULTS: Comp A demonstrated very robust effects in *in vivo* studies. Analysis of the DWB test data revealed that spontaneous pain related behaviours were attenuated by compound treatment with values close to the no pain level whilst vehicle-dosed animals adopted a relief posture to protect the CFA affected paw. Effective doses were associated with free exposures in excess of IC50 values obtained in *in vitro* tests.
CONCLUSIONS: The effects induced by the selective EP4 antagonist in a chronic inflammatory pain related model supports the proposed application of EP4 antagonists in addressing the pain and inflammation associated with EMT.

T-114

Possible Role for Mast Cells and PAR-2 Receptor in the Hyperalgesic State of Women with Endometriosis. Bianca De Leo†,[1,2] Arantza M Esnal Zufiaurre,[1] Hilary OD Critchley,[2] Andrew W Horne,[2] Philippa TK Saunders.[1] *[1]University of Edinburgh, Edinburgh, Scotland, United Kingdom; [2]University of Edinburgh, Edinburgh, Scotland, United Kingdom.*
INTRODUCTION: Endometriosis is a chronic inflammatory condition. Symptoms include chronic pelvic pain that has been associated with an abnormal inflammatory state. Immune cells may communicate with neurons to alter pain sensitivity, trigger the transition from acute to chronic pain. There is emerging evidence that MC-nerves interactions may be involved in the stimulation of pain pathways in women with endometriosis. Activation of mast cells (MCs) results in release of inflammatory molecules including the MC-specific protease tryptase. Tryptase can provoke sensitization of nerves via activation of PAR-2 receptor (protease activated receptor 2). The aim of this study was to investigate expression of PAR-2 the peritoneum in women with chronic pelvic pain with/without endometriosis.
METHODS: Tissue biopsies (endometriotic lesions and peritoneum) and peritoneal fluid (PF) were collected from women attending a pelvic pain clinic (n=13 with endometriosis and n=10 with no obvious underlying pathology) and 4 "no pain" control subjects. The expression of PAR-2 was investigated by qRT-PCR and by immunofluorescent co-localization with tryptase (MC marker). Flow cytometry was used to quantify MC number in PF.
RESULTS: PAR-2 mRNA concentrations were similar in the different tissue samples and patient groups. A striking pattern of PAR-2 protein expression was detected in the peritoneal biopsies from women with pelvic pain and endometriosis, including those containing endometriotic lesions. Tryptase positive MCs were detected in the endometriosis sample group. MCs represented <0.2% of the total live CD45+ cells in the peritoneal fluid. MC number did not change between control and pain/endometriosis groups. MC quantification appeared to be higher in the PF of women with grade III-IV endometriosis: but not reaching statistical significance.
CONCLUSIONS: Analysis of peritoneal biopsies has provided, we believe, the first evidence for an increase in immunoexpression of PAR-2, a protease activated receptor, in women suffering from chronic pelvic pain and/or endometriosis. These findings may provide a mechanism by which mast cell-derived factors such as tryptase may alter pain pathways. Further studies are required to determine whether inhibition of PAR- 2 may offer a therapeutic target in women with chronic pelvic pain.

T-115

Abstract Withdrawn

T-116

Dose-Dependent Suppression of Ovulation and Ovarian Activity by Elagolix in Healthy Premenopausal Women. David Archer,[1] Juki Ng,[2] Yi-Lin Chiu,[2] Cheri Klein,[2] Kristof Chwalisz.[2] *[1]Eastern Virginia Medical School, Norfolk, VA, USA; [2]AbbVie, North Chicago, IL, USA.*
INTRODUCTION: Elagolix is an oral gonadotropin-releasing hormone antagonist being developed for treatment of endometriosis-associated pain and heavy menstrual bleeding associated with uterine fibroids. The objective of this study was to assess the effects of elagolix on ovulation, ovarian activity and reserve, and safety in healthy premenopausal women.
METHODS: Upon screening, 163 women were randomized to 1 of 5 elagolix doses in the range studied for endometriosis (100 mg once daily [QD] to 200 mg twice daily [BID]) for 84 days. Ovulation was assessed 3 times weekly based on transvaginal ultrasound measurements of follicle size and serum progesterone. Ovarian activity was assessed using the Hoogland-Skouby 6-point grading scale, and ovarian reserve was estimated based on anti-mullerian hormone (AMH). Endometrial thickness was also measured.
RESULTS: Mean age and weight for these women was ~30 years and 70 kg, respectively. Elagolix suppressed ovulation dose-dependently. Ovulation was least suppressed in the 100 QD dose (22%), similarly suppressed in the 150-200 QD and 100 BID doses (~50%), and further suppressed in the 200 BID dose (~70%).

	Elagolix Dose Group (mg)				
	100 QD N=9	150 QD N=40	200 QD N=35	100 BID N=38	200 BID N=41
No. (%) with ovulation	7 (78)	20 (50)	20 (57)	18 (47)	13 (32)
No. (%) without ovulation	2 (22)	19 (48)	13 (37)	17 (45)	28 (68)
Missing data	0	1 (2)	2 (6)	3 (8)	0

The Hoogland-Skouby grades of 3 (active follicle-like structure) and 5 (ovulation) decreased with higher elagolix dose, consistent with lower ovulation rates and suppression of gonadotropins and ovarian hormones. Serum concentrations of AMH were not affected by elagolix.
The most frequently reported adverse events were headache (25%) and hot flush (23%). The incidence of hot flush appeared to be dose-related. The regimens tested were generally well tolerated by the women in this study, and the adverse event profile remained consistent with that expected for a GnRH antagonist. Mean endometrial thickness decreased for all elagolix doses relative to Screening period. No new or unexpected safety findings were identified in this study.
CONCLUSIONS: Elagolix suppressed ovulation and ovarian activity and decreased endometrial thickness dose-dependently. Ovarian reserve was not affected in these women.

T-117

Rbfox2 Expression Is Upregulated in Stromal Cells of Endometriotic Lesions. Tal Saar,[1] Debra Goldman-Wohl,[2] Iris Eisenberg,[2] Caryn Greenfield,[2] Diana Pruss,[3] Ronit Haimov-Kochman,[1,2] Simcha Yagel,[1,2] Tal Imbar*.[1,2] *[1]Hadassah-Hebrew University Medical Center, Jerusalem, Israel; [2]Hadassah-Hebrew University Medical Center, Jerusalem, Israel; [3]Hadassah-Hebrew University Medical Center, Jerusalem, Israel.*
INTRODUCTION: The role epithelial–mesenchymal transition (EMT) might play in the pathophysiology of endometriosis is unknown. The diversity of mRNA essential for cell differentiation and development is mediated in part by post transcriptional alternative splicing coding for protein isoforms. Rbfox2, an alternative splicing RNA binding protein, plays a major role in controlling EMT and cell invasion.
METHODS: We investigated Rbfox2 and other molecular markers for EMT by immunohistochemistry in different form of endometriotic lesions and normal endometrium. We used tissue blocks from our archived pathology collection. Samples from endometriotic lesions (6) and normal

endometrial tissues from different phases of the menstrual cycle (4) were studied. Immunohistochemistry and immunofluorescence were performed on tissue sections with an antibody specific for Rbfox2. CD-10 was used for identification of stromal cells and pan-keratin for identifying epithelial cells. The slides were examined by an experienced pathologist.
RESULTS: We observed positive staining for Rbfox2 protein expression in the nuclei of stromal cells of endometriosis lesions in: ovarian cysts, connective tissue of the rectal vaginal septum as well as in remote areas of endometriosis such as the appendix as compared to normal stromal cells adjacent to the lesions. Stromal cells from normal control samples of cycling endometrium were also positive for Rbfox2. Cell identity was confirmed using CD10 and pan-keratin immunohistochemistry. Staining for Rbfox2 was less evident in glandular epithelium from normal endometrial tissue and epithelial cells of endometriotic lesions.
CONCLUSIONS: Rbfox2 is expressed in stromal cells of normal cycling endometrium. However, Rbfox2 is upregulated in stromal cells of lesions of endometriosis when compared to normal adjacent stromal cells. This was also confirmed in remote endometriotic tissue including connective tissue of the rectal vaginal septum and the appendix. We suggest that the process of EMT is involved in the pathogenesis of endometriosis. Furthermore, identification of genes regulated by Rbfox2 may provide insight into the development of the disease and potentially identify targets for treatment.

T-118

Aberrant Over-Expression of SIRT1 and K-Ras Reveals a Mechanism for Progesterone Resistance in Women with Endometriosis. Jae-Wook Jeong,[1] Jung-Yoon Yoo,[1] Tae Hoon Kim,[1] Francesco J DeMayo,[2] David P Schamme,[3] Steven L Young,[4] Bruce A Lessey*.[5] *[1]Michigan State University, Grand Rapids, MI, USA; [2]National Institute of Environmental Health Sciences, Research Triangle Park, NC, USA; [3]Greenville Hospital System, Greenville, SC, USA; [4]University of North Carolina, Chapel Hill, NC, USA; [5]Greenville Health System, Greenville, NC, USA.*
INTRODUCTION: Endometriosis is an inflammatory condition associated with progesterone resistance, contributing to infertility and pregnancy loss. SIRT1 has an important role in the regulation of inflammatory cytokine expression and promotes cell survival by cooperating with K-Ras. K-Ras is overexpressed in endometrial stromal cells of women with endometriosis. However, the role of SIRT1 in endometriosis and uterine biology remains unknown. We hypothesize that combined, co-regulated over-expression of SIRT1 and K-Ras mediates progesterone resistance in endometrium.
METHODS: We examined the expression of SIRT1 and K-Ras in eutopic endometrium from women with and without endometriosis. To investigate the molecular mechanism of SIRT1, we examined progesterone regulated genes using ChIP analysis and mice with constitutive activation of K-Ras.
RESULTS: Western blot and IHC analysis revealed expression of SIRT1, whose abundance was significantly higher in the eutopic endometrium from women with endometriosis as compared to women without the disease, in both the proliferative and secretory phases. SIRT1 and K-Ras protein expression levels were strongly and positively correlated in the endometrium of women with endometriosis. In mice engineered to activate K-Ras in progesterone receptor expressing cells, SIRT1 is increased and the expression of progesterone targets genes, including GLI1, are significantly decreased. ChIP analysis demonstrates binding of SIRT1 to the GLI1 promoter, suggesting a direct effect on transcription of this gene.
CONCLUSIONS: Together the data support an effect of K-Ras on SIRT1 expression that, in turn, decreases GLI1 expression. Given the role of GLI1 in the Indian Hedgehog (IHH) pathway, this novel finding suggests a mechanism for the interference in progesterone signaling via inhibition of the IHH pathway in eutopic endometrial stromal cells of women with endometriosis.

T-119

A Familial History of Endometriosis Causes Developmental and Reproductive Anomalies in Male Offspring in an Animal Model. Emily K Secrist†, Henda Nabli, Katherine Costello†, Kelly Gissy†, Kathy L Sharpe-Timms*. *The University of Missouri, Columbia, MO, USA.*
INTRODUCTION: The cause of infertility in women with endometriosis, characterized by growth of uterine endometrial epithelial cells in ectopic locations, remains a vast mystery. While there is evidence of an association between endometriosis and familial, multigenerational infertility, previous studies focused on the effect on female offspring and overlooked potential consequences on male fertility. After noting reproductive dysfunction in females with endometriosis, we have developed a groundbreaking hypothesis that in utero exposure to endometriosis causes multigenerational reproductive anomalies in male fertility. Our objective is to demonstrate infertility in males developmentally exposed to endometriosis as embryos or germ cells within the embryos for translation to human studies.
METHODS: Using an established animal model of surgically induced endometriosis (Endo) and control (Sham) in females (F0 founders), fertility was examined in two subsequent generations of male progeny (F1 and F2). The influence of endometriosis exposure on the male lineage was examined by evaluating litter size and semen analysis to assess sperm density, turbidity, and agglutination when generation of males reached sexually maturity.
RESULTS: F1 and F2 generation male progeny were developmentally exposed (in utero) to endometriosis as embryos (F1) or germ cells within embryos (F2). Data reported as mean ± SEM. Litters from both F1 and F2 males were smaller in the Endo vs Sham groups (F1 = Endo 5.9 ± 1.7 vs F1 Sham 9.3 ± 1.7 pups, P=0.015; F2 = Endo 10 ± 0.3 vs Sham 13 ± 0.7 pups, P=0.030). Similarly, sperm counts from both sexually mature F1 and F2 males were lower in Endo vs Sham groups (F1 = Endo 27 ± 2 x 10^6/mL vs Sham 36 ± 3 x 10^6/mL, P=0.019; F2 = Endo 32 ± 6 x 10^6/mL vs Sham = 66 ± 12 x 10^6/mL, P=0.015). Sperm tended to be more agglutinated in Endo F1 males vs Sham F1 (P=0.070); no difference was found between F2 Endo and Sham agglutination. Turbidity was greater in F1 Shams (15 ± 1 x 10^6/mL) vs Endo (12.0 ± 1 x 10^6/mL; P=0.040), but no difference was found in the F2 generation.
CONCLUSIONS: Our data support a familial history of endometriosis resulting in developmental and reproductive anomalies in male offspring in a rat model which have never reported. These results indicate a need for studies of male infertility in men developmentally exposed to endometriosis. (NICHD R21HD080763 to KST).

T-120

TGM2 Is Highly Expressed and Active in Endometriosis Where It Mediates Pro-Fibrotic and Pro-Inflammatory Effects. Fernando Martinez Estrada,[1] Maik Obendorf,[2] Stefanie Mesch,[2] Oliver M Fischer,[2] Cemsel Bafligil,[1] Manman Guo,[1] Christian Becker,[3] Krina Zondervan,[3] Catherine Shang,[3] Stephen Kennedy,[3] Siamon Gordon,[4] Thomas M Zollner,[2] Udo Oppermann*.[1] *[1]University of Oxford, Oxford, United Kingdom; [2]Bayer AG, Berlin, Germany; [3]University of Oxford, Oxford, United Kingdom; [4]University of Oxford, Oxford, United Kingdom.*
INTRODUCTION: Macrophages are abundant in lesions and the peritoneal cavity of endometriosis patients. However macrophage activation profiles are ill defined. M2 or alternative activated macrophages are elicited by Th2 cytokines and support pro-fibrotic networks leading to increased collagen deposition. Transglutaminase 2 is a versatile and robust M2 macrophage marker, able to crosslink extracellular matrix proteins driving deposition in a variety of fibrotic models. Here we investigate TGM2 expression, activity and effects of its inhibition in monocytes, macrophages and lesions in endometriosis patients.
METHODS: Blood, plasma, peritoneal fluid (PF), lesions and eutopic endometrium were collected at the Endometriosis Clinic of the John Radcliffe hospital from informed and consenting donors. Cells were isolated with Ficoll and negative monocyte isolation kits. FACS and Histology on FFPE tissues for TGM2 were performed using the mouse IgG1 Zedira A033 antibody. Enzymatic assays involving cadaverin deposition were from Zedira.

RESULTS: TGM2 mRNA is higher in monocytes and PF cells in endometriosis patients, compared to patients with peritoneal pain but endometriosis free. FACS staining of peritoneal macrophages confirms increased expression in endometriosis. Soluble protein and activity are higher in the PF of patients. TGM2 protein is also detectable in eutopic and ectopic endometrium where it is highly constrained to the lesion area. Several inhibitors for human and mouse Tgm2 were evaluated, 3 active compounds with diverse action modes, were further investigated *in vitro*. M1 and M2 macrophage activation assays show that interfering with Tgm2 alters the ability of cells to respond to immune polarizing stimuli. *In vivo* experiments show that Tgm2 inhibition skews inflammatory responses such as Zymosan induced peritonitis, without affecting pain response. Tgm2 inhibition was monitored by *ex vivo* analyses of TG activity.
CONCLUSIONS: We conclude that TGM2 is highly expressed and active in endometriosis. Interfering with the enzyme may provide new ways of controlling M2 macrophage dependent inflammation and fibrosis.

T-121

Endometriosis Alters Expression of Genes Modulating Anxiety, Depression and Pain in the Brain. Tian Li,[1] Ramanaiah Mamillapalli,[1] Sheng Deng,[2] Hao Chang,[2] Zhong-wu Lu,[1] Xiao-Bing Gao,[1] Hugh S Taylor*.[1] *[1]Yale School of Medicine, New Haven, CT, USA; [2]Yale School of Medicine, New Haven, CT, USA.*
INTRODUCTION: Chronic pelvic pain often debilitates women with endometriosis and is associated with anxiety and depression. Although these symptoms suggest that the involvement of nervous system, the underlying changes in brain remain unknown.
METHODS: Endometriosis was induced in 9 weeks old female C57BL/6 mice by suturing donor mouse endometrium into the peritoneal cavity. Sham surgeries were performed on control mice. Behavioral tests (hot plate, open field and tail suspension tests) were performed every two weeks to determine pain, anxiety, and depression. After twelve weeks, mice were sacrificed and collected the amygdala, hippocampus, insula and cerebral cortex of brain. RNA was extracted from each part for microarray analysis and qRT-PCR. Tissue from each part was fixed in 4% paraformaldehyde for immunohistochemical staining.
RESULTS: Open field test showed that endometriosis mice spent less time and traveled less distance at 6, 8, 10 and 12 weeks after surgery while tail suspension test showed significantly longer immobility time for these mice compared to sham group. Duration in the hot plate test was significantly shorter for endometriosis mice indicating persistent depression and pain hypersensitivity. Microarray analysis revealed that 2410, 931, 837, 567 genes were up-regulated while 2114, 665, 612, 500 genes were down-regulated in insula, amygdala, hippocampus and cerebral cortex, respectively, in endometriosis mice compared to sham mice. Six of identified genes chosen from top ten up- or down-regulated genes and validated. The levels of anxiety mediating genes Lcn2 and Nptx2 were significantly increased and decreased respectively in the amygdala tissue in endometriosis mice relative to sham mice. In the insula, levels of Gpr88 and Glra3 involved in anxiety and pain respectively, increased significantly in endometriosis group compared to sham group, whereas the levels of Lct and Serpina3n, involved in pain, decreased significantly.
CONCLUSIONS: Pain, anxiety and depression were induced by endometriosis results changes in gene expression in the brain associated with these behaviors. Brain modulation may underlie pain sensitization reported in women with endometriosis.

T-122

History of Pharmacologic and Surgical Interventions Among Canadian Women Presenting with Symptomatic Uterine Fibroids. Ally Murji,[1] Philippe Y Laberge,[2] Sukhbir S Singh,[3] Nicholas Leyland,[4] Joshua Polsky,[5] Roy Jackson,[6] Claude Fortin,[7] Angelos Vilos,[8] Barry Sanders,[9] Aubrey Uretsky,[10] John A Thiel,[11] Diego Garzon,[12] Alain Lamontagne,[12] George Vilos*.[8,13] *[1]Univ of Toronto/Mt. Sinai, Toronto, ON, Canada; [2]Univ Laval, Québec, QC, Canada; [3]Ottawa Hospital Research Inst., Ottawa, ON, Canada; [4]McMaster Univ/Hamilton Health Sciences, Hamilton, ON, Canada; [5]Windsor Regional Hospital, Windsor, ON, Canada; [6]Romich Group, White Rock, BC, Canada; [7]Centre de Gynécologie et de Maternité de LaSalle, Montreal, QC, Canada; [8]London Health Sciences Center, London, ON, Canada; [9]Univ of British Columbia, Vancouver, BC, Canada; [10]Univ of Alberta/Misericordia Community Hospital, Edmonton, AB, Canada; [11]Univ of Saskatchewan, Saskatoon, SK, Canada; [12]Allergan plc, Markham, ON, Canada; [13]Western Univ, London, ON, Canada.*
INTRODUCTION: The **CA**nadian women wi**Th** **U**terine fibroids [UF] **RE**gistry (CAPTURE) is the first registry worldwide designed to collect real-world data about UF burden, management, and outcomes.
METHODS: This is a multicenter, prospective, observational cohort study intending to enroll 1000 premenopausal adult women with symptomatic UF at ≥12 Canadian clinical practice sites. Women will be followed up to 2 years.
RESULTS: The first 461 women enrolled in CAPTURE had a mean age of 43.3 ± 6.9 years and BMI of 26.4 ± 6.2 kg/m^2. At the baseline visit, patients were most interested in treatment options (69.4%), obtaining information (54.7%), and gaining symptom control (50.8%). 16.3% of women were interested in maintaining fertility and 10.6% wanted to get pregnant. In the 3 months prior to baseline visit, 60.0% had been treated with medication for UF-related symptoms; the most frequent were ulipristal acetate (53.4%), iron (43.6%), nonsteroidal anti-inflammatories (25.1%), tranexamic acid (18.9%), and combined hormonal contraceptives (12.0%). At baseline, 21.2% of women had previously undergone UF-related procedural intervention(s); myomectomy (46.5%) and uterine artery embolization (13%) were most common. Time since prior procedural intervention was <1 year for 17.3%, 1 to <3 years for 23.6%, 3 to <5 years for 21.3%, and ≥5 years for 37.8%.
CONCLUSIONS: To date, data have indicated that Canadian women referred for treatment of symptomatic UF have varying expectations for management of UF. Many women had a history of medical and procedural intervention(s) for UF.

T-123

Urinary Estrogen Metabolites and Antioxidant System Activity in Premenopausal Women with Uterine Fibroids. Larisa V Suturina,[1] Leonid F Sholohov,[1] Darya V Lizneva,[1,2] Lyubov I Kolesnikova.[1] *[1]Scientific Center of Family Health and Human Reproduction Problems, Irkutsk, Russian Federation; [2]Augusta University, Augusta, GA, USA.*
INTRODUCTION: The data regarding estrogen metabolism disturbances and its associations with uterine fibroids growth remains limited and controversial. The main hypothesis of this study were: (a) 2/16α-OHE1 ratio and antioxidants, involved in estrogen metabolism, are not similar in premenopausal women with and without uterine fibroids, and (b) proliferative active urine estrogen metabolite 16-OHE1 correlates with uterine fibroid size.
METHODS: We examined 63 untreated women with fibroids and 31 healthy women without fibroids, comparable in BMI and age (33,57±0,53 and 32,19±0,59 years, respectively). All women were recruited at the outpatient department of Scientific Center of Family Health and Human Reproduction, Irkutsk, Russian Federation (2010-2014). Data collection included anthropometry/vital signs, gynecologic exam, pelvic U/S, blood and urine samples. Concentrations of 2-OHE1 and 16α-OHE1 were measured in urine samples using a commercially available competitive, solid-phase enzyme-linked immunoassay (ESTRAMET, ImmunaCareCorp.). The ratio of 2/16-OHE1 was computed from the

concentrations of 2-OHE1 and 16 α-OHE1. Reduced and oxidized glutathione were detected fluorometrically (Shimadzu RF-1501). For statistical analysis we used U-test and Pearson's correlation with p<0,05.
RESULTS: It was shown that 2/16α-OH-E1 ratio was significantly decreased in premenopausal women with uterine fibroids compare to controls (1,13±0,16 vs 2,01±0,21, pU=0,001) due to lower levels of proliferative neutral 2-OH-E1 (12,50±2,09 vs 30,29±2,84, pU=0,002). Reduced glutathione level was also decreased in women with fibroids compare to the group of healthy women (pU=0,002). Interestingly that the increase of proliferative active 16α-OH-E1 metabolites in women with uterine fibroids positively correlated with the largest fibroid nodule size (p=0,003).
CONCLUSIONS: Uterine fibroids are associated with compromised glutathione system activity and disturbances of estrogen metabolism, the most significant in women with largest fibroid nodule more than 50 mm in diameter.

T-124

Effect of RhoA Pathway Inhibitors and Activators on the Interaction of a Kinase Anchoring Protein 13, AK Chantel I Washington†,[1] Paul H Driggers,[1] Minnie Malik,[2] James H Segars*.[1] *[1]Johns Hopkins University, Baltimore, MD, USA; [2]USUHS, Bethesda, MD, USA.*
INTRODUCTION: Vitamin D deficiency may play an important role in fibroid development. Vitamin D treatment of human leiomyoma cells inhibits cell growth, reduces expression of extracellular matrix proteins and reduces F-actin formation. We previously reported that AKAP13, a Rho-guanine nucleotide exchange factor (GEF) that activates RhoA, is overexpressed in fibroid cells and increases F-actin nucleation. Our work suggested that AKAP13 interacts directly with the vitamin D receptor (VDR) and represses ligand-dependent activity in fibroid cells through its GEF domain. The aim of this study was to extend our previous findings by testing the effect of RhoA pathway inhibitors and activators on the interaction of AKAP13 and VDR.
METHODS: HEK293T and immortalized human fibroid cells (P51F) were transfected with a vitamin D response element Luciferase (Luc) reporter. To examine the effects of RhoA pathway activation on Luc activity, we transiently transfected cells with the VDR expression construct in the presence or absence of increasing amounts of RhoAQL, a constitutively active mutant of RhoA. Cells were treated with $1\alpha,25(OH)_2D3$ (D3) or vehicle control, lysed 18hrs later and assayed for luciferase activity. To examine the effects of RhoA pathway inhibition, in HEK293T cells, expression vectors encoding AKAP13 and VDR were transfected in the presence or absence of increasing amounts of expression vector for C3 transferase, an inhibitor of RhoA. Cells were treated with D3 or vehicle control, lysed 18hrs later and assayed for luciferase activity.
RESULTS: Co-transfection of VDR with increasing concentrations of RhoAQL revealed a ligand-dependent, dose responsive repression of Luc activity, with up to an 80% reduction in Luc activity. Co-transfection of VDR and AKAP13 resulted in a 53% reduction in ligand-dependent Luc activity. Transfection of C3 transferase enhanced ligand-dependent Luc activity up to 33%.
CONCLUSIONS: These results suggest that the RhoA signaling pathway may play a key role in AKAP13 mediated VDR repression. Additionally, this data further validates our previous findings that the GEF-domain of AKAP13 is essential for the repression of VDR activity in fibroid cells.

T-125

Dimished DNA Repair Capacity in Stem Cells from Human Uterine Fibroids Compared to Adjacent Myometrium Leads to Compromised Genomic Integrity and Increased Tumorigenesis. Lauren Prusinski†*, Qiwei Yang, Michael Diamond, Ayman Al-Hendy. *Augusta University, Augusta, GA, USA.*
INTRODUCTION: Uterine fibroids (UFs), benign myometrial tumors, negatively impact female reproductive health, but the mechanism by which they arise is not yet elucidated. Somatic mutations in *MED12* gene, detected in ~85% of sporadic human UFs, are currently thought to arise in myometrial stem cells (MSCs) converting them into UF tumor-initiating cells. Defective DNA repair increases the risk of somatic mutations that can lead to tumorigenesis, suggesting that additional mutations arising in fibroid stem cells (FSCs), unable to be repaired properly due to impaired DNA repair capacity, ultimately further tumor growth and development. We aimed to analyze and compare the DNA repair system in the human $Stro1^+/CD44^+$ MSC and FSC populations isolated from patients affected by UFs.
METHODS: Human fibroid (F) and adjacent myometrial (MyoF) tissues from reproductive age women (N=7) undergoing hysterectomy for treatment of UF were enzymatically digested to obtain single-cell suspensions. Magnetic beads were then used to select MyoF and F cells positive for both Stro1 and CD44 surface markers (MyoF+/+ and F+/+, respectively). Quantitative PCR was performed on both F+/+ and MyoF+/+ cells for 10 genes pivotal to cellular DNA repair and homologous recombination (HR) pathways.
RESULTS: By qRT-PCR, F+/+ cells from 5/7 human samples demonstrated significantly ($p<0.05$) decreased (fold change <0.9) expression of 10 HR-related genes compared to their MyoF+/+ control cells from adjacent tissue; 2/7 showed similar decreases in 5/10 genes. These deregulated genes, *BRCA1, RAD1, RAD17, RAD18, RAD50, RAD51, RAD51AP1, RAD51B, RAD52, and XRCC2* are important in mammalian cells for sensing and repairing chromosomal double-strand breaks by HR, a pathway protective against tumorigenesis suggesting their impairment may be involved in UF development. Further characterization of these and other DNA repair-related genes in human F+/+ and MyoF+/+ cells isolated from F/MyoF tissues is currently underway in our laboratory.
CONCLUSIONS: Our data suggest that impaired DNA repair capacity, specifically the homologous recombination pathway, in human fibroid stem cells contributes to UF development. Further studies are needed to reveal early changes in myometrial and/or fibroid stem cells leading to UF development and their possible contribution to the ethnic disparity of this disease. Support: R01 HD046228-12.

T-126

Abundance of Fungal Species in the Gravid Vaginal Microbiome. Brett Tortelli†, Ping Liu, Justin Fay*. *Washington University, St. Louis, MO, USA.*
INTRODUCTION: The vaginal microbiome has been demonstrated to play an important role in vaginal health and reproductive outcomes. Distinct bacterial communities have been found associated with various aspects of reproductive health. However, the contributions of fungal taxa to the vaginal microbiome and the relationship between fungal and bacterial communities are often not known and could be important to reproductive health. Prior studies have reported a prevalence of *Candida spp.* greater than 60% based on PCR-based sequencing whereas culture based methods indicate a prevalence closer to 20%, and higher in pregnant women. However, both of these approaches are unable to quantify the abundance of *Candida* or other fungi in relation to bacterial abundance and composition. Both prevalence and abundance are important for developing a clear model of how fungi contribute to the vaginal microbiome and reproductive health.
METHODS: Genomic DNA was extracted from vaginal swabs collected from pregnant women. Samples were subjected to PCR based ribosomal (16S) sequencing to quantify bacterial species and internal transcribed spacer (ITS) sequencing to quantify fungal species. Shotgun metagenomic sequencing was also completed along with quantitative PCR (qPCR) to determine the relative abundance of fungi to bacteria.
RESULTS: Sequencing of the ITS region indicated that *Candida spp.* were present in the majority of samples and not associated with bacterial communities. However, both shotgun metagenomic sequencing and qPCR indicate that the *Candida* community is rare (<1%) compared to the bacterial community, with the exception of samples from women with noted candidiasis.
CONCLUSIONS: *Candida* and other fungal species are not abundant members of the gravid vaginal microbiome. Because the incidence of *Candida* and other fungi depend on the sensitivity of method used to detect them, methods that estimate relative abundance will be important to associating fungi with reproductive health and outcomes.

T-127

Effect of Gender on the Innate Immune Response in Septic Mice. Noor Mohd Nasri†,[1,2] Julia Zollner,[1] James Leiper,[3] Mark Johnson*.[1] *[1]Imperial College London, London, United Kingdom; [2]Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia; [3]Imperial College London, London, United Kingdom.*

INTRODUCTION: Sepsis is a major health problem and associated with a high mortality rate in and out of the intensive care setting and a massive septic insult in this polymicrobial infection has shown a negative impact on the innate immunity system.

METHODS: Male and female CD1 mice (25 to 45 g, 8-10 weeks) were used. All mice were rendered to septic by caecal ligation puncture (CLP), and survival was compared after 5 days. Caecum is isolated, ligated (70% from the end), and punctured twice (21G needle). A laparotomy was performed without ligation in the sham group. Following the operation, animals were monitored using temperature probes to determine the onset of sepsis and to enable euthanasia at a defined and humane endpoint. Blood and lung tissue were collected for the flow cytometry analysis at 3 and 6 hours after sepsis induction. All data were analysed by ANOVA with repeated measures followed by Bonferroni post-tests correction test. A p value of < 0.05 was considered significant. Data was analysed using GraphPad PRISM software (V.5).

RESULTS: All sham-operated male and female mice survived the entire time course of the experiment. The mortality of this CLP experiment was more than 75% five days post-CLP in male CLP as compared to 50% in female CLP. Using log-rank analysis, we detected a significant difference in survival between male and female in sham and CLP group during sepsis ($p<0.005$). The fall in temperature was more marked in female than male mice, between 4 to 6 hours ($p<0.01$), at 9 hours ($p<0.05$) and at 20 hours ($p<0.001$). Interestingly, in the blood, the number of neutrophils and $LY6C^{low}$ monocytes were significantly increased in male CLP compared to female CLP ($p<0.01$). In the lung, the neutrophils count in the female CLP was slightly increased compared to male CLP, however, the $LY6C^{low}$ monocyte count in the male CLP and sham groups was slightly increased when compared to the female CLP.

CONCLUSIONS: In this study, an exaggeration of the innate immune response, for example, activation and migration of neutrophils and monocytes from the blood to the remote organ such as lung. Furthermore, to our knowledge this is the first report implicating a gender-based differential neutrophil and monocyte response during sepsis.

T-128

Application of Thrombelastography to Monitor the Change of Coagulation Function in Patients of Recurrent Spontaneous Abortion with Different Times Miscarriages Before and After Pregnancy. Danyang Kang, Yue Hou, Qiaoni Yang†, Qiushi Wang†, Chong Qiao*. *ShengJing Hospital, Shenyang, China.*

INTRODUCTION: The occurrence of recurrent spontaneous abortion(RSA)is associated with maternalprothrombotic state, which means that patients with RSA have more serious hypercoagulable state than other healthy women in childbearing years. Therefore, people with RSA are at increased risk of coagulation dysfunction. The thrombelastography (TEG) can measure whole blood clotting to reflect the blood coagulation function .We want to know whether there are differences in coagulation function among patients with different number of miscarriages before and after pregnancy according to TEG ,so that we can make more detailed plan to guideanticoagulant therapy of different times abortions. **Objective:** To explore the change of the TEG in patients with RSA in different number of miscarriages.

METHODS: Selected 126 cases of patients with RSA as the research objectS, in which there are 101 cases of pregnant patients and 25 of non-pregnant patients to compare TEG changes between two groups of patients.Selected 101 with RSA as the research object, in which there are 52 cases of patients with two times miscarriages , 27 cases with three times miscarriages and 22 cases with greater than or equal to four times miscarriages to compare TEG changes between three groups of patients.

RESULTS: (1)MA values of patients with greater than or equal to four times miscarriages, which were significantly increased than patients with two or three times miscarriages.; (2)Angle values of pregnant patients were(66.39±5.175)°,which were significantly increased than non-pregnant patients(64.16±4.967)°($P<0.05$).

CONCLUSIONS: Coagulation function of RSA patients is associated with pregnancy and abortion times . Increased abortion times and pregnancy state of RSA patients show more obvious hypercoagulable state.TEG can found changes of the blood coagulation function early and sensitivity ,which may provide better guidance for anticoagulant managements.

T-129

Elevated Maternal Testosteronemodulates Synthesis of Long-Chain Polyunsaturated Fatty Acids, Leading to Offspring Deficiency. Kathirvel Gopalakrishnan†, Sathish Kumar. *University of Texas Medical Branch, Galveston, TX, USA.*

INTRODUCTION: Testosterone (T) levels are elevated in PCOS and preeclampsia pregnancies who often deliver small-for-gestational age babies. Studies in rats and sheep, confirms that elevated T during pregnancy indeed leads fetal growth restriction and increased risk for adult diseases. However, how maternal androgens cause fetal growth restriction is not clear. Since long chain polyunsaturated fatty acid (LC PUFA) of the n-3 and n-6 series are crucial for fetal growth and health, we assessed if maternal fatty acid metabolism is altered in mothers with elevated T and examined its impacts on offspring LC PUFA status.

METHODS: Pregnant SD rats were injected with vehicle or T propionate (0.5 mg/kg/day from gestation day 15-19 to increase plasma T levels twofold, similar to that observed in preeclampsia. On gestation day 20, triglyceride levels were analyzed by ELISA and fatty acids in the maternal and fetal serum were analyzed through LC-MS. mRNA expression by qRT-PCR for enzymes involved in fatty acid synthesis and transport were quantitated in placenta and maternal liver.

RESULTS: Placental weight and birth weight of pups were significantly reduced by T treatment. Maternal serum LC PUFA concentrations were altered following T exposure with significant decrease in both n-3 (-33%) and n-6 (-72%) fatty acids. Similar to their mothers, there were significantly lower concentrations of n-3 (-40%) and n-6 (-60%) fatty acids in serum of T fetuses. Elevated T decreased triglyceride levels in liver of dams (control: 60± 5.5, T: 35± 1.9 mg/dl) and fetuses (control: 32± 2.8, T: 26± 2.5 mg/dl) but increased in placenta (control: 28± 3.1, T: 45± 7.1 mg/dl). The mRNA expression of enzymes involved in fatty acid synthesis were upregulated in the liver of T dams - acetyl-CoA carboxylase alpha (2.5-fold), hormone-sensitive lipase (2-fold), delta 5 desaturase (4-fold) and fatty acid elongase (7-fold) and hepatic lipase (7-fold). T placenta showed only upregulation of lipoprotein lipase (2-flod). The expression of fatty acid transporters (fabp4) was upregulated by 4-fold in T placenta.

CONCLUSIONS: These data suggest that elevated maternal T concentrations decreases maternal and fetal n-6 and n-3 PUFA concentrations despite enhanced hepatic synthesis and increased placental fatty acid transporters. The offspring of T mothers are deficient in essential LC PUFAs, which may have long-term consequences for their development.

T-130

Mitogen-Activated Protein Kinases Mediate Leptin-Induced Proliferation of Ovine Uterine Artery Endothelial Cells During the Follicular phase of the Ovarian Cycle and Late Pregnancy in Sheep. Vladimir E Vargas†,[1,2] Maja Okuka,[1] Rosalina Villalon Landeros†,[2] Gladys E Lopez,[2] Jing Zheng,[2] Ronald R Magness*.[1,2] *[1]Univ. South Florida, Tampa, FL, USA; [2]Univ. of Wisconsin, Madison, WI, USA.*

INTRODUCTION: During the follicular phase and pregnancy estrogen levels and uterine blood flow (UBF) are elevated mediated via uterine angiogenesis and vasodilation. Leptin plays a role in the control of endothelial function, and angiogenesis via its OB-Rb receptor. Recently, our lab showed: 1) leptin treatment did not result in significant cell proliferation in luteal phase ovine uterine artery endothelial cells (UAECs), however it significantly increased cell proliferation in follicular UAECs and pregnant (P-UAECs) sheep; and 2) both OB-Ra/OB-Rb proteins are expressed in NP-UAECs (luteal and follicular) and P-UAECs.

However, little is known regarding the signaling mechanism(s) involved in leptin-stimulated UAEC proliferation. Leptin binding to the OB-Rb receptor activate the ERK1/2 mitogen-activated protein kinase (MAPK) pathway to stimulate angiogenesis in vascular endothelial cells (ECs). We **hypothesized** that one or more of the most well studied MAPK pathways (i.e. ERK1/2, p38, and JNK) play a role in the enhanced P-UAECs and follicular UAECs proliferation, but not luteal phase UAECs, in response to leptin treatment under *in vitro* conditions.

METHODS: Fully validated passage 4 UAECs obtained from P-UAECs and NP-UAECs (n=4) sheep were treated with leptin 1ng/ml for 0 (Untreated basal), 0.25, 0.5, 1, 2, 4, 12, and 24 hr. The effect of leptin on P-UAECs and NP-UAECs activation of ERK1/2, p38, and JNK MAPK pathways protein phosphorylation was evaluated by Western blotting.

RESULTS: Compared to untreated basal controls, Luteal UAECs ERK1/2, p38, and JNK MAPK phosphorylation state throughout the time course were unaltered in response to leptin treatment. Phospho-JNK was unaltered in P-UAECs and Follicular NP-UAECs, phospho-ERK1/2 reached maximum activation by 0.25, while phospho-p38 peaked at 0.25, 12 and 24hr in response to leptin vs. untreated basal controls.

CONCLUSIONS: Consistent with our hypothesis, leptin stimulates proliferation of P-UAECs and follicular NP-UAECs, but not Luteal UAECs, and activates the ERK1/2 and p38, but not JNK MAPK pathways. These data suggest that leptin activation of the specific MAPK pathways are key for regulating angiogenesis in preparation for the increase UBF during the periovulatory period and pregnancy.

T-131

Echocardiography in Obese versus Non-Obese Pregnant Women. Jessica McPherson,[1] Melissa Caughey,[2] Patricia Chang,[2] Nathan Howell†,[3] Zarina Sharalaya,[2] Thomas Ivester*.[1] *[1]University of North Carolina at Chapel Hill, Chapel Hill, NC, USA; [2]University of North Carolina at Chapel Hill, Chapel Hill, NC, USA; [3]University of North Carolina at Chapel Hill, Chapel Hill, NC, USA.*

INTRODUCTION: Obese pregnant women are at increased risk of cardiac dysfunction. Echocardiographic parameters in pregnancy are not well defined. The aim of this study was to estimate differences in echocardiographic findings in a cohort of obese versus non-obese pregnant women.

METHODS: A prospective cohort of pregnant women without known cardiac dysfunction were recruited to undergo routine echocardiogram (ECHO) antenatally (34 weeks gestation) and 5 months postpartum. Select echocardiographic findings in obese (body mass index (BMI) ≥ 30kg/m^2) women were compared to non-obese women. Multivariable linear regression was used to adjust for potential confounders.

RESULTS: Of 237 women enrolled, 219 had complete data and were included in the current study. There were 64 (29%) obese and 155 (71%) non-obese women. After adjusting for diabetes, hypertension, and smoking, obese women had similar ejection fraction, fractional shortening, and tricuspid regurgitant jet velocity. Obese women had greater atrial diameter and left ventricular mass.

Echocardiography value (mean±SD)	Non-obese (BMI <30kg/m^2) N=155	Obese (BMI ≥30kg/m^2) n=64	β regression coefficient (adjusted for diabetes, hypertension, smoking)	P-value
Ejection fraction (%)				
Antenatal	57±5	57±5	0.1	0.9
Postpartum	59±5	59±6	0.7	0.4
Left atrial diameter (cm)				
Antenatal	3.4±0.3	3.6±0.3	0.2	<0.01
Postpartum	3.1±0.4	3.4±0.3	0.3	<0.01
Left ventricular mass (g)				
Antenatal	141±27	161±28	19.4	<0.01
Postpartum	119±25	144±31	20.8	<0.01
Fractional shortening (%)				
Antenatal	33±7	32±8	-0.01	1.0
Postpartum	34±6	35±6	0.5	0.6
Tricuspid regurgitant jet velocity (m/s)				
Antenatal	1.9±3.6	2.1±1.9	0.10	0.2
Postpartum	1.8±3.3	1.9±3.1	0.06	0.4

CONCLUSIONS: Obese pregnant women do not exhibit increased major markers of cardiac dysfunction on ECHO during routine examination antenatally and postpartum.

T-132

Increased Fraction of Cardiac Output Toward Uterine Artery in Maternal Compromise in *Papio Spp.* Natalia Schlabritz-Loutsevitch*,[1] Maria Chavez,[2] Anand Cholia,[1] Daniella Pino†,[1] Gary White,[2] Marcel Chuecos†,[1] Saloni Cholia†,[1] James Maher.[1] *[1]Texas Tech University HSC at the Permian Basin, Odessa, TX, USA; [2]University of Oklahoma, Norman, OK, USA.*

INTRODUCTION: Maternal vascular remodeling plays a central role in pregnancy development. Local (spiral artery) and central (maternal cardiovascular system) vascular beds undergo physiological changes that start in early gestation. Maternal cardiac output (CO) has been suggested as an index of fetal growth and maternal vascular resistance- as a screening tool for pre-eclampsia. Non-human primates - baboons (*Papio spp*) have a type of placentation that is relatively similar to humans, however these species do not develop pre-eclampsia. The aim of this study was to evaluate pregnancy-driven blood flow distribution toward uterine artery (UtA) as a fraction of maternal CO in *Papio spp.*

METHODS: Five non-pregnant and five pregnant baboons near term underwent ultrasound examination as previously described (Ultrasound Obstet Gynecol. 2005 Sep;26(3):252-7). The absolute blood flow was calculated using GE algorithm: QA (in ml/min) = V (in cm/s)×πr2×60 s/min; where QA is the arterial flow, V is the time-averaged mean velocity, and r is the radius of the vessel. Data were analyzed using the Mann-Whitney U-test.

RESULTS: The absolute and weight-adjusted UtA blood flow was increased in pregnant, compared to the non-pregnant, animals, the ratio UtA/CO was higher in two animals with advanced reproductive age and cardiac pathology (higher number of pregnancies and vegetation on the aortic valve).

ID	P	Weight (Kg)	UtA, blood flow		Aorta, blood flow		Fraction
			ml/min	ml/min/kg	ml/min	ml/min/kg	
1	N	13.8	53.94	3.91	Na	na	na
2	N	18.15	100.81	5.55	1718	94.65	5.87
3	N	23.7	83.92	3.54	2360	99.57	3.5
4	N	29.9	31.99	1.07	1338	44.75	2.39
5	N	22.3	52.92	2.37	2492	111.75	2.12
6	Y	15	86.14	5.74	2281	152.07	3.78
7	Y	15.7	149.72	9.54	4635	295.22	2.2
8	Y	16.6	164.22	9.89	1035	62.35	**15.87**
9	Y	18.9	175.25	9.27	4824	255.24	3.6
10	Y	23.1	148.4	6.42	1855	80.30	**8**

CONCLUSIONS: The increase in the UtA/CO ratio could be a compensatory mechanism, ensuring fetal nutrient supply in compromised maternal conditions.

T-133

Remodeling and Altered Biomechanics of the Mouse Abdominal Aorta During and After Pregnancy. Aaron Gelinne†, Nga Ling Ko, Liam John, Lucia Brown, Stephen Brown, George Osol*. *Larner College of Medicine, University of Vermont, Burlington, VT, USA.*

INTRODUCTION: A number of studies have described remodeling accompanied by altered biomechanical properties of smaller arteries during pregnancy, however, large vessel remodeling also plays a vital role in hemodynamics and has not been studied extensively to date. We hypothesized that pregnancy will induce significant adaptive changes in aortic caliber and in the composition of the vascular wall that favor accommodation of increased cardiac output and augmented uteroplacental flow.

METHODS: Infrarenal abdominal aortas from age-matched non-pregnant (NP; n=7), late pregnant (LP; n=7) and 30 days post-partum (PP30; n=6) B6 mice were dissected and cannulated. Intraluminal pressure was adjusted using a pressure-servo system under no-flow conditions. Step-wise pressurization (10 to 150 mmHg) was performed in a relaxing solution containing 100 μM papaverine and 1 μM diltiazem while using a video dimension analyzer to measure lumen diameter and wall thickness. Distensibility was expressed as the % increase in lumen diameter relative to that measured @ 10 mmHg and used to calculate the elastic modulus (*E*).

RESULTS: Compared to the NP (706 ± 8 μm) control group, aortic luminal diameter was significantly ($p<0.05$) increased in both LP (836 ± 14 μm) and PP30 (889 ± 16 μm) mice. Distensibility was reduced in LP (90 ± 4%) mice and returned to NP (108 ± 2%) values in PP30 (108 ± 3%) mice ($p<0.05$). There were no significant differences in wall thickness or *E* between treatment groups.

CONCLUSIONS: (1) Absent changes in blood pressure, the gestational increase in abdominal aortic lumen diameter would predict an approximate doubling of volume flow, and thereby accommodate the well-documented increase in cardiac output characteristic of mammalian pregnancy. (2) Reduced distensibility in LP vessels would facilitate perfusion of the uteroplacental circulation by minimizing the Windkessel effect which occurs primarily in the thoracic aorta. These adaptations, which function in a coordinated manner to alter maternal systemic hemodynamics in normal pregnancy, may be compromised in preeclampsia, which is associated with both reduced expansive (outward) remodeling and further increases in arterial stiffness.

T-134

Pre Pregnancy Hemodynamics and Changes During Pregnancy in Women Who Develop Recurrent Hypertensive Disease. Kylie Cooper†,[1] Carole McBride,[1] Gary Badger,[2] Ira Bernstein.[1] [1]*University of Vermont, Burlington, VT, USA;* [2]*University of Vermont, Burlington, VT, USA.*

INTRODUCTION: Prior preeclampsia is a risk factor for recurrent hypertensive disease (RPIH) in pregnancy and predisposition may include baseline hemodynamic status. We evaluated cardiovascular function both pre pregnancy and in the third trimester in women with a history of preeclampsia; comparing those who developed RPIH to those who did not.

METHODS: 21 women with a history of preterm preeclampsia were recruited prior to pregnancy and underwent assessment of arterial stiffness, cardiac output, plasma volume and sympathetic responsiveness both pre pregnancy and in the third trimester. Vascular compliance was assessed pre pregnancy using a volume challenge. Comparisons of both time points as well as change over time were made. Statistical analysis was by paired t-test and $p<0.05$ accepted as significant.

RESULTS: 10 women had no hypertension and 11 women developed RPIH. RPIH recurrence was 52%. Risk of recurrent preeclampsia was 38% (8/21) with 6 developing preterm disease. Pre pregnancy, women with RPIH had lower plasma volume per BMI ($p=0.03$), increased diastolic blood pressure ($p=0.003$), beta sympathetic responsiveness ($p=0.03$), and pulse wave velocity ($p=0.04$). A trend toward increased cardiac output response to volume loading was also noted ($p=0.05$). In the third trimester, RPIH women had lower plasma volume per BMI ($p=0.005$). There were no significant differences between the groups with regard to changes from pre pregnancy to third trimester.

CONCLUSIONS: Women with a history of preeclampsia who develop recurrent hypertension have evidence of a less compliant vascular system with increased tone and responsiveness prior to pregnancy that persists into the third trimester. Given that we observed no difference in longitudinal changes between groups these observations support the hypothesis that risk for development of RPIH lies in the pre pregnancy cardiovascular characteristics that become maladaptive in the setting of pregnancy.

T-135

Enriched H_2S Biosynthesis *via* Selective CBS Upregulation Is Associated with Endometrial Angiogenesis in Women. Thomas J Lechuga†, Bansari A Patel, Nicole A Nguyen, Hong-hai Zhang, Dong-bao Chen*. *University of California Irvine, Irvine, CA, USA.*

INTRODUCTION: Angiogenesis is a key mechanism for endometrium regeneration and turnover during the menstrual cycle and pregnancy in women. Hydrogen sulfide (H_2S) has been shown to be potent proangiogenic factor. H_2S is biosynthesized by cystathionine β-synthase (CBS) and cystathionine γ-lyase (CSE). The objective of the current study is to determine if H_2S biosynthesis is associated with human endometrial changes during the menstrual cycle and pregnancy.

METHODS: Human endometrium tissues were obtained from hysterectomies from women who were postmenopausal, premenopausal in the secretory and proliferative phases of the menstrual cycle, and late pregnancy (8-10 per group). Expression levels of CBS and CSE mRNA and protein were analyzed by real-time qPCR and immunoblotting, and H_2S was measured by methylene blue assay. Semi-quantitative immunofluorescence microscopy using specific antibodies of CD31, CBS, and CSE was used to assess endometrial angiogenesis and cellular localization and levels of CBS and CSE proteins in endometrium, microvessels, and glands.

RESULTS: CBS mRNA and protein and H_2S production was significantly greater in premenopausal women compared to postmenopausal women ($P<0.05$). CSE was expressed but did not significantly alter among different groups. During pregnancy, CBS protein was highly localized in endometrial epithelial cells, microvessels, and glands, in association with significantly increased angiogenesis as determined by increased vessel number, diameter, and length ($P<0.05$).

CONCLUSIONS: Enriched H_2S biosynthesis via selective CBS upregulation is associated with endometrial angiogenesis during the menstrual cycle and pregnancy in women (supported by NIH RO1 HL70562).

T-136

Patient and Provider Evaluation of a Postpartum Patient Navigation Program to Improve Postpartum Care Among Publicly Insured Women. Fengling Hu†, Angelina M Strohbach†, Noelle G Martinez†, Nadia Hajjar, Melissa A Simon, Lynn M Yee*. *Northwestern University Feinberg School of Medicine, Chicago, IL, USA.*

INTRODUCTION: Navigating New Motherhood (NNM) was a postpartum patient navigation program established to provide logistical and personal support to publicly insured women following delivery. After NNM completion, we performed a comprehensive, 360° program evaluation to integrate stakeholder assessments and guide future expansion.

METHODS: All NNM participants who returned for care (N=180 of 218) completed the Patient Satisfaction with Interpersonal Relationship with Navigator (PSN-I) scale. 18 provider stakeholders (navigators, nurses, clinic coordinator, medical assistants, physicians, social worker, breastfeeding peer counselor, and front desk staff) underwent semi-structured interviews to gauge program satisfaction, perceived outcomes, and ideas for improvements. Interview transcripts were analyzed by constant comparative method.

RESULTS: In this population of largely low-income, minority (49.5% non-Hispanic black and 32.6% Hispanic) women, participants were highly satisfied with NNM; PSN-I scores averaged 42.6 of 45 (SD=4.3). Provider stakeholders offered consistently positive program feedback, expressing satisfaction with NNM execution and outcomes. Stakeholders noted that navigators worked around them without inhibiting clinic workflow and eased clinic administrative burdens. The most common perceived outcomes included increases in: postpartum attendance, contraception uptake, breastfeeding counseling, depression screening, quality of postpartum appointment, continuity of care, patient satisfaction, and patient support. Perceived program outcomes differed by stakeholder role, though most stakeholders strongly emphasized seeing increased continuity of care and contraception uptake. All providers believed the program should be sustained long-term in all or almost all of its entirety. Regarding areas for improvement, suggestions included: introducing the navigator earlier in the prenatal period, educating the navigator to better answer clinical questions, and increasing physician-navigator communication despite the program's ability to function independently of physician involvement.

CONCLUSIONS: A postpartum patient navigation program can perceivably improve patient support and patient clinical care with workflow improvement and minimal burden to clinicians, though improvements can be made to further magnify benefits to patients.

T-137

Increased Vaginal Gram-Negative Bacterial Diversity in Third Trimester of Pregnancy in NHP (Non-Human Primates). Natalia Schlabritz-Loutsevitch*,[1] Nithya Mudaliar,[2] Abdul Hamood,[2] James Maher,[1] Gary White,[3] Gary Ventolini.[1] *[1]TTUHS-PB, Odessa, TX, USA; [2]TTUHSC, Lubbock, TX, USA; [3]Oklahoma State University, Oklahoma, OK, USA.*

INTRODUCTION: The composition of vaginal microbial community is important for pregnancy maintenance. Decreased diversity of vaginal microbiome in third trimester of human pregnancy is associated with the preterm birth. NHP have been used as a model of pregnancy-related research for decades, being especially crucial for development of therapies, counteracting effects of human teratogens. The understanding of bacterial changes in pregnancy in NHP is critical for data interpretation and analyses. We and others reported decreased presence of *Lactobicilli* in baboons (Papio spp), compared to human vaginal milieu, however, the reports regarding pregnancy-related changes in these species are sparse.

METHODS: Vaginal swabs were taken from 5 pregnant and 5 non-pregnant baboons (Papio spp) at the end of gestation. The specimens were evaluated for the presence of colony forming units [CFU].

RESULTS: The gram-negative bacterial CFU were increased in pregnant animals (n= 26) compared to non-pregnant (n=9) and included spp., which are probably *Achromobacter, Staphylococcus spp., Diphteroids,* etc., including novel subspecies.

CONCLUSIONS: Increase vaginal bacterial diversity in pregnancy might be universal evolutionary phenomenon, which is independent on presence of *Lactobacilli spp.*

T-138

Placental Vascular Endothelial Growth Factor165b Expression in Women with Uncomplicated Pregnancy. Jayasri Basu, Valmiki Seeraj, Samantha Gonzalez, Carolyn M Salafia, Aruna Mishra, Enyonam Agamasu, Magdy Mikhail. *Bronx Lebanon Hospital Center, Bronx, NY, USA.*

INTRODUCTION: Vascular endothelial growth factor (VEGF) is a potent mediator of angiogenesis. VEGF-A gene can produce 6 mRNAs resulting in 6 isoforms of VEGF containing 121, 145, 165, 183, 189 and 206 amino acids. $VEGF_{165}$ is commonly present in different human tissues. Recently a $VEGF_{165b}$ has been identified. While $VEGF_{165}$ is proangiogenic, $VEGF_{165b}$ competitively inhibits $VEGF_{165}$ action by binding to the same receptor VEGF-R2, and inhibits receptor phosphorylation and downstream intracellular signalling. During human pregnancy, VEGF expression is detected in trophoblast cells but the role of VEGF in the placenta is not well understood. In this study, we have examined the placental expression of $VEGF_{165b}$ in normal women throughout gestation.

METHODS: In an IRB approved study, placentas were obtained from normal pregnant women who underwent elective abortion or term delivery. Tissues were collected within 30 minutes of the procedures and dissected in saline to identify chorionic villi without associated decidua. Cytotrophoblast $VEGF_{165b}$ expression was assayed using ELISA kit DY3045 (R&D Systems, Minneapolis, MN). Samples were grouped by trimester, and non-parametric tests considered $p<0.05$ as significant.

RESULTS: $VEGF_{165b}$ protein expression was detected throughout gestation. The median $VEGF_{165b}$ expression was highest in the 2nd trimester. Significant differences in $VEGF_{165b}$ expression were found among the three groups ($p<0.0001$). There was significant positive correlation between $VEGF_{165b}$ expression and gestational age (GA) in days in the first trimester (rho=0.327, $p<0.001$); in the 2nd and 3rd trimesters, the correlation was negative but insignificant.

Groups	N	$VEGF_{165b}$ (pg/100 mg tissue) Mean Rank
1st Trimester (7 - 12 wk GA)	101	78.11
2nd Trimester (12^{+}-$23^{6/7}$wk GA	56	180.90
3rd Trimester (37-42 wk GA)	74	118.60

CONCLUSIONS: Our findings of $VEGF_{165b}$ protein expression in 231 chorionic villi samples suggest that it may have a regulatory role in human pregnancy. $VEGF_{165b}$ is reported to be down regulated in renal carcinoma. Hence, it may be suggested that our finding of $VEGF_{165b}$ protein expression in placental tissues could be a physiological phenomenon during placental development to restrain overexpression of VEGF that could lead to pregnancy complications. Currently our group is examining the balance between $VEGF_{165}$ and $VEGF_{165b}$ expression throughout human gestation.

T-139

Temporal Expression of Genes Involved in Placental Tryptophan Metabolism in Chorionic Villus Tissues. Padma Murthi,[1,2] Stacey Ellery,[2,3] Hayley Dickinson,[2,3] Miranda Davies-Tuck,[2,3] Jan J Erwich,[4] David Walker,[2,3] Euan M Wallace,[2,3] Peter R Ebeling.[1] *[1]School of Clinical Sciences, Monash University, Clayton, VIC, Australia; [2]Hudson Institute of Medical Research, Clayton, VIC, Australia; [3]Monash University, Clayton, VIC, Australia; [4]University Medical Centre, University of Groningen, Groningen, Netherlands.*

INTRODUCTION: Fetal growth is dependent on substrate supply, which is dependent on substrate transport and its regulation by the placenta. An important placental function is the uptake of tryptophan and its metabolism to serotonin and kynurenine metabolites, which are essential for increased protein synthesis, fetal neuronal growth, and immune function. Whether these particular processes are involved early in gestation has not been fully elucidated. We hypothesised that genes in the tryptophan metabolic pathway are expressed in human first trimester chorionic villus biopsies (CVB).

METHODS: This is a retrospective case-control study conducted in CVBs archived from 2004-2009 at the University Medical Centre of Groningen, The Netherlands. CVBs were performed between 10.1 and 12.4 weeks of gestation. Further clinical and demographic data were collected at birth. cDNA was generated from 83 tissues. Relative mRNA expression of tryptophan metabolic pathway genes was assessed using Fluidigm single-cell DNAseq and TaqMan chemistry (Thermo Fisher Scientific). Data were analysed using Mann-Whitney test.

RESULTS: Enzymes that are involved in tryptophan catabolism including, TPH1, IDO1, TDO1; serotonin receptor, HTR5B; and serotonin transporter SLC6A mRNA were detected in all CVB samples. The expression IDO1 was negatively correlated with gestation ($p>0.01$, $r^2=-0.27$). There were no associations of early gene expression with the sex or birth weight of offspring.

CONCLUSIONS: This is the first study to detect gene expression for tryptophan catabolic enzymes TPH1, IDO1, TDO1; serotonin receptor, HTR5B; and serotonin transporter SLC6A mRNA in human placenta samples <12-weeks gestation. Findings support our hypothesis that tryptophan plays a role in placental metabolism from early in gestation. The fate of tryptophan in the 1st, 2nd and 3rd trimesters of pregnancy is now under investigation.

T-140

Could Gonadotrophin-Releasing Hormone Receptor Antagonists Be Repurposed to Treat Ectopic Pregnancy? Lisa L Campbell†,[1] Natalie J Hannan,[2] Mohamed A Bedaiwy,[3] Nicola Gray,[1] Stephen Tong,[2] Andrew W Horne*.[1] *[1]University of Edinburgh, Edinburgh, Scotland, United Kingdom; [2]University of Melbourne, Melbourne, VIC, Australia; [3]University of British Columba, Vancouver, BC, Canada.*

INTRODUCTION: Tubal ectopic pregnancy (EP) affects 1-2% of all pregnancies and is potentially life threatening. Until two decades ago, EP was often diagnosed late, necessitating emergency surgery. Now, transvaginal ultrasound and serum hCG measurement enable early diagnosis, permitting medical treatment with systemic methotrexate in selected women. There is, however, a need to develop a more effective, targeted and less toxic treatment than methotrexate for EP. We have shown that trophoblast cells at EP implantation sites express gonadotrophin-releasing hormone receptor (GnRHR). To assess if GnRHR could be a potential new treatment target in EP, we examined the effects of GnRHR inhibition on trophoblast function in-vitro.

METHODS: Three GnRHR antagonists in current clinical use (ganirelix, cetrorelix and degarelix, with short, medium and long half-lives, respectively) were used to investigate effects of GnRHR antagonism on trophoblast cell hCG production, proliferation and migration in three trophoblast cell lines, and compared to methotrexate.

RESULTS: All three drugs significantly inhibited JEG-3 hCG production (choriocarcinoma trophoblast model for hCG secretion). Medium and high dose cetrorelix inhibited cell proliferation and migration in first trimester trophoblast cell lines Swan71 and HTR8/svneo (extra villous trophoblast models). Multi-dosing (consistent with the half-life and stability of cetrorelix) or a combination of cetrorelix and methotrexate, significantly inhibited proliferation compared to methotrexate alone.

CONCLUSIONS: GnRHR antagonism reduces hCG production, proliferation and migration in trophoblast cell lines. Future work will examine the action of these GnRHR antagonists in primary trophoblast cells and animal models to examine if GnRH antagonists could be repurposed for the treatment of EP.

T-141

The NALP3 Inflammasome Mediates LPS Effects on IL-1β Secretion by Placental Hofbauer Cells (HBCs). Seth Guller*, Zhonghua Tang, Vikki M Abrahams, Gil Mor. *Yale School of Medicine, New Haven, CT, USA.*

INTRODUCTION: HBCs are placental macrophages located between the syncytium and fetal capillaries, a critical site for the protection against microbes migrating from the mother to the fetus. Our previous research indicates, that although HBCs are generally considered M2 (anti-inflammatory/pro-angiogenic) macrophages, they are exquisitely sensitive to the pro-inflammatory actions of LPS. Given the importance of IL-1β in promoting inflammation, and the demonstrated role of the Nalp3 inflammasome in generating mature IL-1β from pro-IL-β in non-placental macrophage cell lines, our goal was to use siRNA technology to directly test the role of the Nalp3 in mediating HBC inflammatory response to LPS.

METHODS: HBCs isolated from normal term placenta (n=5) were treated for 16 h with and without Nalp3 siRNA or scrambled RNA (Dharmacon). Cells were then treated for 8 h with 1 ng/ml LPS and levels of secreted IL-1β, TNF-α, and IL-6 were measured by ELISA. Levels of Nalp3 and pro-IL-1β in cell extracts were measured by Western blotting and normalized to HSP90 levels.

RESULTS: LPS treatment significantly enhanced HBC IL-1β secretion by 1500-fold from 1 pg/ml to 1500 pg/ml. Treatment of HBCs with Nalp3 siRNA (L+NALP3), but not scrambled RNA (L+Scrambled), suppressed Nalp3 levels 72% and significantly inhibited the LPS-induced increase in IL-1β secretion 69% ($P<0.05$). The LPS-mediated increase in pro-IL-1β and secreted TNF-α, IL-6, and IL-8 were not significantly affected by treatment with Nalp3 siRNA**.**

**Figure(s) will be available online.*

CONCLUSIONS: Our results indicate that the Nalp3 inflammasome specifically modulates the post-translational effects of LPS treatment on the secretion of IL-1β by HBCs. This suggests that the interaction of bacterial LPS, HBCs, and the Nalp3 inflammasome drives an IL-1β-dependent perivascular inflammatory cascade.

T-142

The Placental Microbiome in Intrauterine Growth Restricted Pregnancies. Men-Jean Lee,[3] Michelle Wang†,[1] Yula Ma,[2] Xiuliang Bao,[1] Inga Peter,[1] Luca Lambertini,[2] Jianzhong Hu*.[1] *[1]Icahn School of Medicine, New York, NY, USA; [2]Icahn School of Medicine, New York, NY, USA; [3]University of Hawaii, JABSOM, Honolulu, HI, USA.*

INTRODUCTION: Intrauterine growth restriction (IUGR) is associated with an increased risk for perinatal morbidities and fetal programming. Pathological IUGR is associated with uteroplacental insufficiency that results in the inability of the fetus to achieve its growth potential. The placenta is known to be a sensor of the intrauterine environment and serves as a barrier between mother and fetus. Although the human placenta is considered a sterile environment, recent microbiome studies reveal diverse commensal placental microbiota as well as pathogenic flora found in intrauterine infection. Therefore, we tested whether IUGR is associated changes to the placental microbiome.

METHODS: Total DNA samples were extracted from placentas from 20 IUGR and 20 AGA (appropriate for gestational age) pregnancies. The placental microbiome was surveyed using bacterial 16S rRNA sequencing. R-package [Vegan] was used to compare the overall microbiota diversity and the LEfSe method to find differential taxa features associated with IUGR.

RESULTS: Placenta microbiota screening demonstrated signals from a diverse range of flora including *Proteobacteria*, *Fusobacteria*, *Firmicutes* and *Bacteroidetes*. The overall microbiota dissimilarities (beta-diversity) were not significantly different by IUGR status. The Shannon index suggested no significant difference in alpha-diversity between IUGR and AGA placentas. At the taxa level, the placenta microbiota of IUGR patients had significantly higher prevalence of *Bacteroidetes* phyla, *Desulfovibrio* and *Neisseria* genus, and lower levels of *Lactobacillus and Bifidobacterium* genus. The IUGR samples showed significantly lower *Firmicutes*/*Bacteroidetes* ratio compared to AGA samples.
**Figure(s) will be available online.*
CONCLUSIONS: Distinctive placenta microbiota patterns, particularly the loss of potential beneficial *Lactobacillus* were found in placentas from IUGR pregnancies. Our results suggest that the placental microbiome is a biomarker for placental and fetal health.

T-143

Trophoblasts Derived from Preeclamptic iPSCs Do Not Up-Regulate ITGA1 in Response to High Oxygen Over Time. Rowan M Karvas†,[1] Ying Yang,[3] Toshihiko Ezashi,[3] Schust Danny,[2] R Michael Roberts,[3,4] Laura C Schulz*.[1,2] *[1]MU, Columbia, MO, USA; [2]MU School of Medicine, Columbia, MO, USA; [3]MU, Columbia, MO, USA; [4]MU, Columbia, MO, USA.*
INTRODUCTION: Human placentation is an invasive process that involves not only navigating the maternal decidua, but also invasion into the myometrium and remodeling of the spiral arteries by trophoblast. The efficiency of invasion by the trophoblast cells depends on their ability to change their adhesion proteins with each new layer of tissue invasion. An adhesion protein critical for invasion into the deepest layers is integrin alpha1 (ITGA1). Preeclampsia (PE) is a pregnancy disease that is characterized by shallow invasion with reduced remodeling of the spiral arteries. Analysis of placental beds from women diagnosed with PE showed no upregulation of ITGA1- the reason for this is currently unknown. If trophoblasts derived from iPSCs from PE and control placentas replicate this defect, then the underpinnings of the inability to respond to an oxygen signal can be studied in an actively differentiating cell.
METHODS: Cell lines H1, MRuci3-7 (control), and MRuciB-1 (PE) were maintained at both 20% and 5% Oxygen and treated with BMP4 (10ng/mL)+A83-01 (1mM)+PD713074 (0.1mM), termed BAP treatment, to induce trophoblast differentiation. Cells were grown on Matrigel coated coverslips and fixed at days 2, 4, 5, 6, and 8 of BAP treatment. IF staining against ITGA1, hCGb, and KRT7 was performed on all slides. 3, 20x regions were chosen per slide and total image intensity of ITGA1 was measured using Cell Profiler software.
RESULTS: Embryonic stem cell line H1 expresses more ITGA1 in response to 20% oxygen at days 6 (11,917.34 $\pm$ 566.44 SEM arbitrary units) and 8 (16,218.55$\pm$1023.59 SEM arbitrary units) of BAP treatment compared to 5% exposure (6 day- 6,362.6$\pm$133.61 SEM; 8 day-6881.3$\pm$102.01 SEM arbitrary units; ttest $p<0.005$). MRuci3-7 showed a significantly greater upregulation of ITGA1 over time in 20% vs. 5% oxygen (2-way ANOVA oxygen X days, $p<0.0026$). MRuciM-4 did not significantly upregulate ITGA1 in response to high oxygen.
CONCLUSIONS: Previous studies have shown that exposure to high oxygen environments triggers upregulation of ITGA1 and this was recapitulated in our BAP-iPSC model. ITGA1 expression is a uselful marker to understand impaired response to oxygen signals in PE trophoblasts.

T-144

Loss of Programmed Cell Death 4 Associates with the Progression of Gestational Trophoblastic Disease. Hui-Juan Zhang*,[1] Ya-Xin Wang,[1] Jiu-Ru Zhao,[1] Ramkumar Menon,[2] Yuan Liu.[1] *[1]International Peace Maternity and Child Health Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, Shanghai, China; [2]The University of Texas Medical Branch at Galveston, Galveston, TX, USA.*
INTRODUCTION: Gestational trophoblastic disease (GTD) encompasses a range of trophoblast derived disorders. The most common type of GTD is hydatidiform mole (HM). Most of HMs are benign whereas some of HMs can further develop into gestational trophoblastic neoplasia (GTN), including invasive HM and choriocarcinoma. However, the exact molecular mechanisms of etiopathogenesis and development of GTN largely remain unknown. Programmed cell death 4 (PDCD4) is an important tumor suppressor, and down-regulation of PDCD4 has been observed in many cancers. Till now, the roles of PDCD4 in the pathogenesis of GTD have not been determined. In this study, we aimed to investigate the functions and regulatory networks of PDCD4 in the progression of GTD.
METHODS: Fresh and formalin-fixed, paraffin-embedded trophoblastic tissues were collected. Expression of PDCD4 in trophoblast cells and tissues was examined by immunohistochemistry, qRT-PCR and Western blotting. Migration and invasion of choriocarcinoma cells were analyzed by Transwell tests post siRNA transfection. Downstream genes of PDCD4 were screened by PCR array and verified by western blotting.
RESULTS: We discovered that the mRNA and protein expressions of PDCD4 was significantly repressed in HM tissues than in normal first trimester placental tissues, and almost loss of expression in invasive HM. Consistently, PDCD4 was suppressed in JAR and JEG-3 choriocarcinoma cells compared with normal trophoblastic cells. We also found that silencing of PDCD4 significantly increased the migration and invasion capabilities of JAR and JEG-3 cells. Furthermore, we proved that PDCD4 repressed the migration and invasion of choriocarcinoma cells by down-regulation of MMP-3, MMP-8 and up-regulation of TIMP-2.
CONCLUSIONS: Our results suggested PDCD4 could be a potential valuable diagnostic and prognostic marker for GTD.

T-145

MicroRNA Signature in Progression of Gestational Trophoblastic Disease. Jiu-Ru Zhao, Hui-Juan Zhang*, Ya-Xin Wang, Yue-Ying Xu, Wei-Bin Wu. *International Peace Maternity and Child Health Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, Shanghai, China.*
INTRODUCTION: Gestational trophoblastic disease (GTD) encompasses a range of trophoblast derived disorders. The most common type of GTD is hydatidiform mole (HM). Most of HMs are benign whereas some of HMs could further develop into malignant gestational trophoblastic neoplasia (GTN), including invasive HM and choriocarcinoma. Till now, the exact molecular mechanisms of etiopathogenesis and development of GTN largely remain unknown. We hypothesized that the aberrant expression of microRNA (miRNA) played roles in GTN such as in the initiation and progression of other human cancers. We aimed to determine the profiling of miRNA in the progression of GTD, and to investigate the effects of related miRNAs on choriocarcinoma cells.
METHODS: Fresh and formalin-fixed, paraffin-embedded (FFPE) trophoblastic tissues, choriocarcinoma cells were used. The experiments were conducted including miRNA array screening (MAS), RT-qPCR, Western blot, etc.
RESULTS: By MAS, we identified 134 upregulated and 119 downregulated miRNAs in benign HM tissues compared with GTN. For validation, miRNAs were tested by RT-qPCR in 25 benign HM and 13 GTN fresh tissues, and in 35 benign HM and 21 GTN FFPE tissues. The cut-off value for fold change is more than 5. Six miRNAs, including miR-370-3p, miR-371a-5p, miR-518a-3p, miR-519d-3p, miR-520a-3p and miR-934, were proved to be differently expressed in benign HM and GTN tissues. Moreover, we discovered miR-371a-5p and miR-518a-3p were significantly increased in JAR, JEG-3 and BeWo

choriocarcinoma cells compared with normal primary trophoblastic cells. Functional analysis further proved that miR-371a-5p and miR-518a-3p could promote proliferation, migration and invasion of choriocarcinoma cells.Additionally, we demonstrated that miR-371a-5p was negatively related to its predictive target genes *BCCIP*, *SOX2* and *BNIP3L* protein expressions, while miR-518a-3p was negatively related to its predictive target genes *MST1* and *EFNA4* protein expressions.
CONCLUSIONS: The results presented here may offer new clues to GTD genesis and develop, and may provide diagnostic biomarkers as well as new therapy targets for GTN.

T-146

Redox-Sensitive Transcription Factor NRF2 Promotes Human Trophoblast Differentiation by Inducing miR-1246. Sribalasubashini Muralimanoharan,[1] Carole R Mendelson*.[1,2] *[1]UT Southwestern Med Ctr, Dallas, TX, USA; [2]UT Southwestern Med Ctr, Dallas, TX, USA.*
INTRODUCTION: Dysregulation of human trophoblast invasion and differentiation with placental hypoxia can result in preeclampsia (PE), a devastating hypertensive disorder of pregnancy. The *hCYP19A1/ aromatase* gene, which is highly induced when human cytotrophoblasts (CytT) fuse to form syn-cytiotropho-blast (SynT) in primary culture, requires transcription factor GCM1 and is prevented by hypoxia (2% O_2). Mouse studies indicate that both Gcm1 and the Wnt/β-catenin pathway are crucial for chorionic branching and SynT formation and form a positive feedback loop. Using miRNA microarray, we characterized miRNAs that are significantly decreased during differentiation of CytT to SynT in primary culture, target hCYP19A1, WNT receptor FZD5, and GCM1, and are aberrantly expressed in placentas of PE women. In this study, we characterized miR-1246, which is markedly induced during SynT differentiation and predicted to target components of the β-catenin destruction complex (GSK3β, AXIN2) and JARID2, which silences developmen-tally regu-lated genes.
METHODS: CytT from mid-gestation human placenta were cultured in 2% or 20% O_2 for 0-72 h to analyze expression of miR-1246 and its targets during SynT differentiation and effects of O_2 tension. Placentas from women with PE and gestationally-matched normotensive controls also were studied.
RESULTS: miR-1246 was induced >200-fold during differentiation of CytT to SynT, while predicted targets, GSK3β, AXIN2 and JARID2, were significantly decreased. However, when CytT were cultured in 2% O_2 for 36 h, induction of miR-1246 was blocked, whereas predicted targets were increased. miR-1246 was significantly decreased in PE placentas, compared to controls. To study mechanisms underlying the profound induction of miR-1246, we investigated the role of the redox-regulated transcription factor, NRF2, which has putative binding sites upstream of the *miR-1246* coding sequence. Intriguingly, NRF2 mRNA levels were profoundly upregulated during SynT differentiation and significantly reduced by hypoxia and in PE placentas. Moreover, siRNA-mediated knockdown of NRF2 in cultured trophoblasts markedly reduced expression of miR-1246 and caused upregulation of JARID2.
CONCLUSIONS: These novel findings suggest that redox-sensitive NRF2 may promote human SynT differentiation by inducing miR-1246, which targets components of β-catenin destruction complex and JARID2 and is dysregulated in PE.

T-147

Acquisition of an Endothelial-like Fate in Differentiating Trophoblast Stem Cells and Vascular Mimicry at the Placentation Site. Masanaga Muto†, Damayanti Chakraborty†, Regan L Scott†, Michael J Soares*. *University of Kansas Medical Center, Kansas City, KS, USA.*
INTRODUCTION: Hemochorial placentation is characterized by the development of trophoblast cells specialized to interact with uterine and fetal vascular beds. These specialized trophoblast cells arise from a trophoblast stem (TS) cell population possessing the capacity to differentiate into multiple trophoblast cell lineages. Among the differentiated trophoblast lineages are cells that acquire an endothelial-like cell phenotype. In this investigation, we examine the differentiation of TS cells and their acquisition of a pseudo-endothelial cell fate.
METHODS: Trophoblast cell differentiation was investigated in rat blastocyst-derived TS cells. Transcriptomes of TS cells in the stem state and following eight days of differentiation were determined by RNA sequencing (RNA-seq). Bioinformatic and pathway analyses were performed. Transcript expression profiles were validated by qRT-PCR. Expression patterns of select endothelial cell-markers identified from the RNA-seq analysis were examined by immunocytochemical analyses of rat placentation sites.
RESULTS: RNA-seq analysis yielded robust differences in transcript profiles for TS cells in the stem state versus differentiating cells. The stem state was characterized by the expression of transcripts previously shown to be critical for self-renewal and inhibition of differentiation. The differentiation phenotype was characterized by transcript signatures consistent with acquisition of known differentiated trophoblast cell lineages and a striking endothelial-like phenotype. The endothelial-like phenotype included RNAs encoding cell adhesion proteins (Cdh5, Esam), regulators of coagulation (Thbd, Tfpi, Procr), and vasoregulatory factors (Adm, Pgf, Vegfa). CDH5 and TFPI were specifically localized to endovascular invasive trophoblast cells lining uterine spiral arteries.
CONCLUSIONS: Precise transcript profiles were defined for stem state and differentiating trophoblast cells. The profiles reflect the capacity of TS cells to differentiate into multiple trophoblast lineages, including acquisition of an endothelial-like cell fate. The results demonstrate the experimental value of the in vitro TS cell model system and its potential for elucidating regulatory mechanisms controlling differentiation. (Supported by NIH grants: HD020676 and HD079363).

T-148

Trophoblast Dependent Secretion of Stannocalcin-1 and Interleukin-8 by Endothelial Cells and Their Role as Possible Mediators of Spiral Artery Remodeling. Arwa Esmail†, Alexa Bishop, Judith E Cartwright, Guy S Whitley*. *St George's University of London, London, United Kingdom.*
INTRODUCTION: Extravillous trophoblasts invade into and remodel the maternal spiral arteries (SA) replacing the endothelial cells (EC) and vascular smooth muscle cells (VSMC). The mechanism has not been completely elucidated. Using a 3D vascular spheroid model we have shown that trophoblast conditioned medium (TCM) stimulates the expression of a number of genes including interleukin 8 (IL8) and stanniocalcin-1 (STC-1). IL8 is an inflammatory cytokine that has been associated with angiogenesis while STC-1 is a widely expressed glycoprotein implicated in tumour angiogenesis. The role these two factors have in SA remodelling and how they may interact with each other has not been investigated.
METHODS: The trophoblast cell line SGHPL-4 was grown in 3D culture and after 72h the TCM harvested. An angiogenic protein array was used to determine the components of the TCM. The human umbilical vein endothelial cell line SGHEC-7 was stimulated with TCM and the secretion of IL8 and STC-1 determined by ELISA. Identification of pathways activated by TCM and responsible for the increased secretion of IL8 and STC-1 were investigated using pharmacological inhibitors. The effect of recombinant IL8 and STC-1 on VSMC migration was determined by time-lapse microscopy.
RESULTS: TCM significantly stimulated the secretion of both IL8 and SCT-1 by endothelial cells ($p<0.5$). TCM contains a number of growth factors and cytokines including TGFβ, HGF, VEGF and IL1β. Recombinant IL1β significantly stimulated IL8 but not STC-1 secretion by endothelial cells. IL1β stimulation of IL8 secretion was significantly inhibited following inhibition of p38MAPK ($p<0.001$). IL8 was significantly stimulated following activation of protein kinase C ($p<0.05$). IL8 in combination with STC-1 stimulate VSMC migration.
CONCLUSIONS: TCM stimulates the secretion of IL8 and STC-1 by endothelial cells. They may act together to stimulate vascular smooth muscle cell migration; an important process in the remodelling of maternal spiral arteries.

T-149

Changes in the Expression of Calcium Channels in Placentas Complicated with Preeclampsia or Fetal Growth Restriction According to the Administration of MgSO4. Hyun-Hwa Cha,[1] Jae Ryoung Hwang,[3] Suk-Joo Choi,[2] Soo-young Oh,[2] Cheong-Rae Roh*.[2] *[1]Kyungpook National University Hospital, Kyungpook National University School of Medicine, Daegu, Korea; [2]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea; [3]Sungkyunkwan University School of Medicine, Samsung Medical Center, Seoul, Korea.*

INTRODUCTION: Plasma membrane Ca-ATPase (PMCA) is the major calcium channel involved in Ca^{2+} efflux pathway and sarcoendoplasmic reticulum Ca^{2+} ATPase (SERCA) is responsible for Ca^{2+} sequestration to endoplasmic reticulum (ER). In this study, we aimed to check the changes of expression calcium channels including plasma membrane Ca-ATPase (PMCA) and sarcoendoplasmic reticulum Ca^{2+} ATPases (SERCA-2) in placentas from pregnancies complicated by preeclampsia (PE) or fetal growth restriction (FGR) according to the administration of MgSO4.

METHODS: Pregnant women were recruited according to the following 2 groups: (1) normal pregnancies (n=11), (2) women with PE or FGR (n= 43). Then we subdivided PE or FGR group according to antenatal MgSO4 exposure: (2A) women with PE or FGR who had MgSO4 exposure (n=29), and (2B) women with PE or FGR who did not have MgSO4 exposure (n=14).The placental expression of PMCA and SERCA-2 was assessed by using western blot according to the treatment MgSO4 exposure and gestational age at delivery. To corroborate using in vitro experiment, we examined the change in expression of PMCA and SERCA-2 according to the treatment of MgSO4 under hypoxia mimicking condition ($CoCl_2$treatment) in BeWo cells.

RESULTS: Overall, there was no difference in the expression of PMCA or SERCA-2 in placenta from PE or FGR compared to control. And we found that the exposure of MgSO4 did not affect the placenta expression of PMCA and SERCA. However, the expression of PMCA was significantly increased in placenta from PE or FGR beyond 36 weeks of gestation. In vitro study, we observed that the treatment of MgSO4 increase the expression of PMCA and SERCA in BeWo cell. Treatment with $CoCl_2$ significantly increased the expression of PMCA but decreased the expression of SERCA-2 in BeWo cells.

CONCLUSIONS: Antenatal exposure of MgSO4 in PE or FGR could not affect the expression of PMCA and SERCA.

T-150

The Effects of Periconceptional Maternal Under Nutrition on Mouse Placental Development. Gerialisa Caesar†,[1,2] Lauren Parmeley†,[1] Laura Schulz*.[1,2] *[1]University of Missouri-Columbia, Columbia, MS, USA; [2]University of Missouri-Columbia, Columbia, MS, USA.*

INTRODUCTION: Maternal undernutrition has detrimental effects on fetal development and adult health. The placenta plays a crucial role in fetal development, and may be programmed by maternal nutrition in early pregnancy. For example, women who were exposed to the Dutch Hunger Famine during the first trimester and received an adequate diet in later pregnancy showed increased placental weight at delivery compared to control mothers. Male offspring of these women were observed to have increased incidences of obesity, diabetes and cardiovascular disease as adults. Similarly, placentas from ewes fed a 50% undernourished diet during early-mid gestation were larger than normal at birth. Previously, we found mouse dams fed 50% of *ad libitum* calorie intake from d1.5 to d11.5 had smaller placental weights, with labyrinth sparing at d11.5. However when food was returned to normal levels in the latter part of pregnancy, placentae from caloric restricted mothers were indistinguishable from controls at d18.5, indicating the ability to recover from the adverse intrauterine environment. We test the hypothesis that the critical period during which maternal nutrient restriction early in pregnancy may alter the placenta later in pregnancy occurs prior to d1.5.

METHODS: Periconceptually is a period of oocyte selection and maturation, and two rounds of DNA methylation reprogramming. To test this, mice were fed either 50% of ad libitum consumption levels (n=6) or ad libitum (n=5) from -3 weeks of pregnancy until d11.5. Both treatment groups were fed ad libitum from d11.5 to d18.5. At d18.5, placentae mice were sacrificed and placentae were collected to examine placental morphology and gene expression. Image J software was used to quantify junctional, labyrinth and total zone areas in 3 placentae/dam, as well as maternal and fetal blood space areas.

RESULTS: There were no significant differences in placental weights, efficiency, junctional and labyrinth zones between dietary groups. Real-time RT-PCR was used to measure relative transcript levels. To compare mRNA levels, ΔC_t were analyzed by Students' t-test, with results averaged from 3 placentae per dam to obtain n=1. Expression of placental trophoblast markers and lipid transporters were similar in in both treatment groups.

CONCLUSIONS: These findings suggest that periconceptual undernutrition does not cause overgrowth of the mouse placenta near term.

T-151

Mechanisms Underlying Cell-Free DNA Release by Mouse Placental Explants. Mark Phillippe*, Sharareh Adeli. *Massachusetts General Hospital, Boston, MA, USA.*

INTRODUCTION: Research from my laboratory has demonstrated that cell-free DNA (cfDNA) is progressively released from mouse placental explants over time in culture; however, the mechanisms underlying cfDNA release are unclear. These studies sought to test the hypothesis that release of cfDNA by placental tissue is associated with oxidative stress induced cellular apoptosis.

METHODS: Placentas were harvested from pregnant (gd 15-18) CD-1 mice and placed into 6-well plates contained 2 mL media (45% DMEM/45% Hams F12/10% FBS + pen/strep) and cultured at 37°C for up to 21 hours in incubators containing oxygen at 8% or 21%. Some cultures contained Q-VD-OPh (50 μM; caspase inhibitor), necrostatin-1 (10 μM; inhibitor of necroptosis) or LPS (250 ng/mL; proinflammatory mediator that induces apoptosis). Media and placentas were collected at 0, 6 and 21 hours. After centrifugation at 8,000 x g, the cfDNA was extracted from the media using a DNA isolation kit (Roche-Applied Science), and quantified using a Nanodrop DNA spectrophotometer then reported as ng DNA per mg tissue. Cell death was quantified using the Cytotox LDH assay (Promega) on the media. Tissue homogenates were used to quantify caspase activity (Caspase Glo 3/7 assay (Promega)) and for BAX expression (BAX ELISA kit (MyBioSource)).

RESULTS: CfDNA levels released under physiologic conditions (8% O2) were not significantly different from explants cultured in ambient oxygen (21% O2). At 21 hours, cfDNA release by explants cultured with LPS was significantly higher than media alone (225.2 ± 40.8 ng/mg tissue vs. 166.0 ± 39.5, $p < 0.001$); whereas, cfDNA release was significantly lower with the addition of the caspase inhibitor (Q-VD-OPh) (141.2 ± 34.2, $p < 0.01$). The cell death (Cytotox LDH level) increase in the explants paralleled cfDNA release. Necrostatin-1 had no effect on cfDNA release and did not significantly decrease LDH. Caspase activity (Caspase Glo 3/7 data), which significantly increased by 21 hours (242 ± 94 percent control), was further increased by LPS (342 ± 115) and inhibited by Q-VD-OPh (70 ± 39) (all $p < 0.05$). The pro-apoptotic BAX protein expression in the placental explants increased by 74% at 21 hours.

CONCLUSIONS: These *in-vitro* studies have confirmed increasing cfDNA release by mouse placental tissue in parallel with increasing cell death. Classic caspase-mediated apoptosis appears to play a role in these events; whereas necroptosis does not. (Funded by the Burroughs Welcome Fund-Preterm Birth Initiative).

T-152

Computational Modeling of Murine Uteroplacental Blood Flow Using 3D Microct Imaging and Contrast-Enhanced Ultrasound Suggests Spiral Artery Number Is a Major Hemodynamic Regulator. Mabelle Lin†,[1] Jessica F Herbert†,[2] Terry K Morgan,[2] Alys R Clark*.[1] *[1]University of Auckland, Auckland, New Zealand; [2]Oregon Health & Science University, Portland, OR, USA.*

INTRODUCTION: Elevated maternal angiotensinogen expression (20% increase in transgenic (TG) dams versus wild-type (WT) controls) inhibits uterine spiral artery growth and branching as measured by 3D

microCT at day 16.5. TG dams have faster uteroplacental blood flow flux rates (measured by microbubble-enhanced ultrasound), relatively reduced plasma volumes, and develop pregnancy-induced hypertension. Pups and placentas from TG dams are smaller, but labyrinth capillary density is similar in TG dams and controls. We hypothesized that differences in spiral artery structure may drive differences in uteroplacental blood flow independent of maternal plasma volume and blood pressure.

METHODS: We used quantitative 3D microCT measurements of the uterine spiral arteries and stereological assessments of the placental capillary labyrinth to parameterize a computational model of uterine hemodynamics at d16.5. The model incorporated spiral artery number, length, lumen diameters, and the conductivity of blood into the labyrinth as a function of capillary density. The model was then compared to mean microbubble ultrasound measurements of uteroplacental blood flow in a second cohort of WT and TG mice.

RESULTS: TG dams had fewer spiral arteries with slightly reduced lumen diameters compared with WT controls, which the model predicted would account for a 4.6-fold increase in vascular resistance. To carry the same volumetric flow, the TG vasculature would require an additional 19 mmHg of driving pressure, which was reflected in telemetry measured MAPs of 85 mmHg in WT dams compared with 110 mmHg in TG mice at day 16.5. Our model predicted a 0.7-10.5 second range in WT spiral artery delay time of microbubble reappearance kinetics, but only 0.4-4.1s delay in TG dams. This compared favorably with the microbubble measurements of 3-10s in WT and 0-2s in TG mice. The faster uteroplacental flux rates in TG dams was primarily due to a reduced number of spiral arteries.

CONCLUSIONS: Our computational model predicts that the number and diameter of spiral arteries feeding a placental lobule may be a major driver of blood flow rate, but not volume. Interestingly, the WT group showed an increased variability in spiral artery delay times, but the adaptive significance of this variability requires further study.

T-153

Placental-Specific Extracellular Vesicle Sorting by Multiparametric High-Resolution Flow Cytometry. Mayu Morita, Pam Canaday, Jessica Hebert, Terry Morgan. *OHSU, Portland, OR, USA.*

INTRODUCTION: The ability to monitor the placenta *in vivo* from early gestation to term is limited and there is immense interest in developing new methods to perform "liquid biopsies" of maternal blood to test for placental dysfunction. Fragments of the placenta are released into the maternal blood stream as early as 6 weeks' gestation. Concentrations of these extracellular vesicles (EVs) appear to be related to placental size and pregnancy outcomes. These lipid encapsulated particles contain protein, RNA, and DNA, which are suitable for –omics research. Progress in the field has been limited, however, by the lack of placental-specific EV isolation methods. To address this need, our group has developed a new high resolution flow cytometry (HRFC) sorting method that can reliably identify, quantitate, and purify cell-specific submicron-sized EVs.

METHODS: We employed a modified *FACSAria* sorting machine for HRFC. Submicron-sized polystyrene beads (100, 160, 200, 240, 300, 500, 900nm) were used as sizing and sorting efficiency controls. Placental EVs isolated from *in vitro* preparations of first trimester explants were used as a positive tissue control. Male (n=10) and non-pregnant female (n=10) plasma and antibody isotypes served as negative controls. A panel of cell-specific antibodies (e.g. PLAP, Annexin, CD9, CD41) were used to identify and sort cell-specific EVs in maternal plasma (n=38; 6-12 weeks'). Sorted placental EVs were characterized by electron microscopy, *Nanocyte*, proteomics (comparing sorted beads from plasma—hitchhikers—to different sized EVs sorted from maternal blood), and miRNA by qRT-PCR analysis.

RESULTS: Cell-specific subsets of EVs can be sorted to a high level of purity (>95%). Exosome-sized PLAP positive EVs were sorted from 100ul of plasma yielding 10^7/ml. Protein and total RNA yields were 1.0 ug and 0.25 ug per 10^5 EVs, respectively. Proteomic analysis revealed similar profiles to published placental EV data without albumin or immunoglobulin contamination. Placental targets were enhanced 2 orders of magnitude compared with plasma alone. Characteristic miRNAs were also identified in these sorted EVs.

CONCLUSIONS: HRFC provides a means to characterize, count, and isolate placental-specific EVs from maternal plasma for –omics research.

T-154

Maintenance of Fatty Acid Oxidation in Placentas of Obese Women: A Role for Peroxisomes. Virtu Calabuig-Navarro†, Judi Minium, Perrie O'Tierney-Ginn. *CWRU, Cleveland, OH, USA.*

INTRODUCTION: Obesity is associated with impaired placental mitochondrial function. Although, fatty acid oxidation (FAO) occurs mainly in the mitochondria (~95%), peroxisomes also contribute to this process. How their role in placental FAO is affected by maternal obesity is largely unknown. We measured the mitochondrial vs peroxisomal component of FAO *in vitro,* in trophoblasts isolated from lean and obese mothers.

METHODS: FAO was measured in isolated trophoblasts collected at term c/s delivery in healthy lean (BMI: 22.1±3.2 kg/m^2, n=3) and obese (37.7±1.5 kg/m^2, n=3) women, following treatment with ^{3}H-Palmitate (PA,100 μM). We used etomoxir (200μM), a specific and irreversible inhibitor of carnitine palmitoyl transferase 1, to block the entry of FA into the mitochondria, revealing the peroxisomal component of FAO. We measured mRNA expression of D-bifunctional protein (DBP), peroxisomal carnitine O-octanoyltransferase (COT) and peroxisomal biogenesis factor 3 (PEX3) -key genes in peroxisomal FAO-, and cytochrome B (CYTB) a marker of mitochondrial number, in placenta by PCR. One sample t-test was used to assess the effect of etomoxir treatment vs untreated control. Student's t-test was used to assess differences in gene expression between lean and obese groups. P <0.05 was considered statistically significant.

RESULTS: ^{3}H-PA oxidation was not different in trophoblast of lean (57±7 nmol/mg/h) compared to obese (39±13 nmol/mg/h) mothers. Etomoxir had a greater inhibitory effect on FAO in trophoblast cells from lean compared with obese women (93±1 % vs 82±2 %, P<0.05).

**Figure(s) will be available online.*

Placental mRNA expression of COT and DBP was increased by 115% and 31%, respectively, while CYTB was decreased by 34% in obese compared to lean women (P<0.05).

CONCLUSIONS: The smaller inhibition of FAO in trophoblasts of obese compared to lean women, and the higher mRNA expression of genes regulating peroxisomal FAO, suggest a greater peroxisomal contribution to FAO in placentas of obese women. Directing FAs to peroxisomes may be an alternative mechanism to compensate for impaired mitochondrial number/function, thus maintaining the critical FAO capacity of placentas of healthy obese women.

T-155

Baboon Placental Endocannabinoid Responses to Maternal High Fat Diet. Marcel Chuecos,[1] Cun Li,[2,3] Stacy Martinez,[1] Kushal Gandhi,[1] Cezary Skobowiat,[4] Maira Carrillo,[1] Moss Hampton,[1] Suraparaju Raju,[1] Gary Ventolini,[1] Peter Nathanielsz,[2,3] Natalia Shlabritz-Loutsevitch*.[1] *[1]TTUHSC-Permian Basin, Odessa, TX, USA; [2]University of Wyoming, Laramie, WY, USA; [3]SNPRC, San Antonio, TX, USA; [4]The Ludwik Rydygier Collegium Medicum, Nicolaus Copernicus University, Bydgoszcz, Poland.*

INTRODUCTION: The endocannabinoid system (ECS) is essential for fetal development and pregnancy maintenance. We described decreased fetal ECS tone in naturally obese non-human primates and in human pregnancy. This decrease was paradoxically associated with increased ECS tone, described in obese non-pregnant individuals. The **goal of this study** was to evaluate placental expression of ECS receptors CB1R and CB2R in an experimental model of a maternal high fat diet.

METHODS: Baboons (*Papio spp*) were fed a diet of 45% fat (HFD; n=11) while controls (CTR; n=9) ate 12% fat for at least 9 months prior to conception. The placenta was collected at term via cesarean section and CB1R and CB2R expression were evaluated using immunohistochemistry, western blot, and RT-PCR methods.

RESULTS: CB2R expression was increased in villi and decidual tissues of male fetuses of HFD fed mothers.

Table 1. CB1R and CB2R placental protein expression (histoscore) in male fetuses

	n	M (SEM)	n	M (SEM)	p	ES
CB1R						
Villi	4	54.54 (2.73)	4	59.83 (6.49)	0.77	-0.53 (-1.93–0.92)
Decidua	3	46.88 (10.27)	5	45.26 (3.03)	0.45	0.14 (-1.31–1.56)
CB2R						
Villi	4	89.78 (7.22)	5	100.4 (1.48)	0.086	-1.09 (-2.56–0.5)
Decidua	4	62.65 (12.17)	6	85.14 (5.75)	0.088	-1.21 (-2.62–0.29)

**Figure(s) will be available online.*

CONCLUSIONS: Increased CB2R expression is consistent with the pattern of inflammation associated with MO, thus it provides the pharmacological target for placental interventions in MO.

T-156

Role of Renin-Angiotensin System Activation in a Rat Model of Placental Insufficiency and Pregnancy-Induced Hypertension. Eugenia Mata-Greenwood, LeeAnna Sands, Daliao Xiao, Lubo Zhang, Blood Arlin. *Loma Linda University, Loma Linda, CA, USA.*

INTRODUCTION: Activation of the Renin-Angiotensin system (RAS) has been described in several pregnancy complications such as preeclampsia. Our goal was to assess RAS activation in the Brown Norway rat that is known to have placental insufficiency.

METHODS: BN and Lewis (LW, control) rats were assayed at non-pregnancy (NP) and pregnancy days 8, 13, 17 and 20 (P8, P13, P17, P20) for the plasma levels of Angiotensin II and 1-7 by EIA, and for renal and placental expression of RAS members via immunoblotting and real-time PCR. In addition, BN rats were treated with an angiotensin II receptor 1 inhibitor (ATR1), Losartan (10 mg/kg/day i.p.); and LW rats were treated with a low dose of Angiotensin II (2 ng/day via osmotic minipump) at P13-P18. At day 18, rats were assayed for systemic blood pressure, proteinuria, uteroplacental blood flow (assayed with microspheres) and pregnancy outcomes.

RESULTS: BN rats had significantly higher levels of renal angiotensin converting enzyme (ACE) at all stages and higher ACE2 expression at NP and P9 stages compared to LW rats. Concordantly, BN rats had higher Angiotensin II plasma levels than LW at all times tested. Both rat strains showed an increase in plasma Angiotensin 1-7, with LW having significantly higher levels at P17 and P20. The renal expression of ATR1 was higher in P17 BN rats than P17 LW rats, and that of ATR2 and the MAS receptor were decreased at P13 and P17 compared to LW. Similarly placental expression of ATR1 was increased while ATR2 and MAS was decreased at day 17 in BN rats compared to LW. Losartan-treated BN rats showed an increased uteroplacental blood flow compared to controls (0.36 ± 0.06 vs. 0.83 ± 0.1 solvent vs. Losartan in ml/min/g, $p < 0.05$). Losartan also lowered mean arterial blood pressure (102 ± 7 vs. 62.4 ± 5.7 mmHg, solvent vs. Losartan respectively, $p < 0.05$), and improved fetal outcomes (fetal and maternal weight increases). Angiotensin II-treatment did not induce proteinuria or changes in mean arterial blood pressure in LW, but it decreased uteroplacental blood flow (0.45 ± 0.02 vs. 0.23 ± 0.01 ml/min/g, solvent vs. Ang II, $p<0.01$), and pregnancy outcomes (fetal, placental and maternal weight gain).

CONCLUSIONS: RAS activation has an important role in BN and LW pregnancy phenotype, including regulation of maternal blood pressure, placental insufficiency and fetal growth. We conclude that the role of RAS depends on the genetic background.

T-157

Effects of Tributyltin on Placental Cytokine Production. Yuko Arita,[1] Michael Kirk,[1] Neha Gupta,[1] Ramkumar Menon,[2] Darios Getahun,[3] Morgan R Peltier*.[1] *[1]Winthrop University Hospital, Mineola, NY, USA; [2]UTMB-Galveston, Galveston, TX, USA; [3]Kaiser Permenante Southern California, Pasadena, CA, USA.*

INTRODUCTION: Tributyltin (TBT) is a persistent pollutant and suspected endocrine disruptor. It is detectable in nearly 100% of placental samples but its effects on placental function are poorly understood. Also unknown are the potential interactions that this compound may have with infectious agents to compromise placental functions. Therefore, we evaluated the effects of TBT on production of steroids, cytokines and other biomarkers by placental explants cultures in the presence and absence of bacterial stimulation.

METHODS: Placental explant cultures were established from 8 women undergoing elective Cesarean Section at term but prior to the onset of labor. Cultures were treated with 0, 0.5, 5, 50, 500 or 5000 nM TBT in the presence and absence of 10^7 CFU/ml heat-killed *E. coli* for 24 hr. Conditioned medium was then harvested and concentrations of placental steroids (P_4, T, and E_2) as well as biomarkers of inflammation (IL-1β, TNF-α, IL-10, IL-6, sgp130 and HO-1), oxidative stress (F_2-IsoP) and neurodevelopment (BDNF) were quantified using immunoassays. Viability of the cultures was ascertained using a variant of the MTT assay.

RESULTS: At the highest concentration tested, TBT significantly reduced viability of both unstimulated and bacteria-stimulated placental cultures. Under basal conditions, TBT increased P_4 slightly but had little or no effect on T or E_2 production. IL-1β, IL-6, IL-10, and F_2IsoP were enhanced by TBT to varying degrees but no effect of TBT on HO-1 production was detected. BDNF production was reduced and sgp130 production enhanced at the highest dose. For bactera-treated cultures, TBT had similar effects on steroid production, slightly increasing P_4 but having no effect on E_2 or T production. However, TBT significantly reduced IL-1β, sgp-130, F_2-IsoP, and BDNF production but enhanced TNF-α and IL-6 production with little or no effect on HO-1 and IL-10 secretion.

CONCLUSIONS: TBT alters placental steroidogenesis, increasing P_4 production, but has minimal effect on downstream steroids. TBT also enhances the production of inflammatory biomarkers such as IL-1β, TNF-α, IL-10, and IL-6. Inhibition of sgp-130 for bacteria-treated cultures suggests that this compound may also cause an overall increase in bioactive IL-6 which has previously been associated with adverse neurodevelopmental outcomes.

T-158

Elevated Biomarkers of Ageing in Placentas of Advanced Maternal Age Women. Katie J Stephens†, Samantha C Lean†, Mark R Dilworth, Alexander EP Heazell, Rebecca L Jones*. *University of Manchester, Manchester, United Kingdom.*

INTRODUCTION: In the UK 21.5% of infants are born to women of advanced maternal age (AMA, ≥35 years). AMA mothers are at high risk of stillbirth and fetal growth restriction. Placental dysfunction is evident in AMA women[1]. The AMA placental phenotype at term resembles that of post-term pregnancies including increased syncytial nuclear aggregates and aberrant trophoblast turnover; suggesting accelerated placental ageing in AMA women. We hypothesise that features of placental ageing (oxidative stress, inflammation and mitochondrial/telomere dysfunction) are elevated in placentas from AMA women and contribute to placental dysfunction.

METHODS: Placentas were compared between a) AMA women with uncomplicated pregnancies and a matched group aged 20-30 years and b) AMA women with appropriately grown and small for gestational age (SGA) infants (n=15/group). Placental markers of ageing (cytokine levels, oxidative stress, mitochondrial DNA content and telomere length) were investigated using qPCR, ELISA and immunohistochemistry.

RESULTS: Placentas from AMA women had elevated protein concentrations of pro-inflammatory cytokines, IFN-γ, TNF-α, IL-8 and IL-1α ($p<0.01$), compared to those from younger women. There was increased placental IFN-γ and TNF-α ($p<0.001$) and reduced anti-inflammatory cytokines IL-1Ra, IL-4 and IL-10 ($p<0.01$) in AMA women with a SGA infant versus those with a normal outcome. Elevated oxidative DNA damage ($p<0.05$) and increased total anti-oxidant capacity ($p<0.05$) were detected in placentas from AMA women versus younger controls. Increased mitochondrial DNA content was apparent in placentas of AMA women, but only those from female infants ($p<0.01$). AMA had no effect on placental telomere length.

CONCLUSIONS: These studies have identified biomarkers of ageing in the placentas of AMA women, including oxidative stress and inflammation. Both are known to adversely affect placental function,

thus providing potential mechanistic links between AMA and placental dysfunction. Moreover, the changes in oxidative stress and inflammatory markers detected in the placenta are concordant with those evident in the circulation of AMA women at 36 weeks gestation[2]. Together these observations support the hypothesis that AMA is associated with placental ageing and provide potential avenues for studies to reduce stillbirth and FGR in this high risk cohort.

1) Lean *et al.* (2014) *Plac* 35(9):A77; 2) Lean *et al.* (2016) *Reprod Sci* 23:199Ai.

T-159

Advanced Maternal Age as an Independent Risk Factor for Adverse Pregnancy Outcomes: A Systematic Review and Meta-Analysis. Samantha C Lean†, Hayley Derricott, Rebecca L Jones, Alexander EP Heazell*. *Institute of Human Development, University of Manchester, Manchester, United Kingdom.*

INTRODUCTION: Advanced maternal age (AMA; ≥35 years) is associated with a range of pregnancy complications including stillbirth and fetal growth restriction. Previous systematic reviews have omitted many of these pregnancy outcomes and lack mechanism, causation or maternal commodities associated with advanced age. We hypothesise that AMA increases risk of stillbirth and other pregnancy complications independently of parity, maternal comorbidities and use of assisted reproductive therapies (ART).

METHODS: A contemporary literature research was conducted include cohort and case-control studies; births from any countries; full text and English language. Studies reported data on one or more co-primary outcomes (stillbirth or fetal growth restriction (FGR)) and/or secondary outcomes (neonatal death, abruption, preeclampsia, low birth weight, very low birthweight, neonatal acidosis, preterm birth, NICU admissions and gestational diabetes mellitus (GDM)) in AMA mothers (≥35 years) and a control population (<35 years). The effect of age on pregnancy outcome was investigated by random effects meta-analysis and meta-regression. Where possible, data were split by parity. Stillbirth rates were correlated to rates of maternal diabetes, obesity, hypertension and use of ART between maternal age groups.

RESULTS: Out of 1940 identified titles; 63 cohort studies and 12 case-control studies were included in the meta-analysis. AMA increased the risk of stillbirth (OR 1.75, 95%CI 1.62 to 1.89) with a population attributable risk of 4.7%. There was no association between parity or the incidence of stillbirth and the prevalence of obesity, diabetes or hypertension in AMA mothers and despite an apparent negative association between rate of stillbirth and use of ART in mothers ≤40 years suggesting an independent effect of maternal age. Similar data trends were seen for risks of FGR, neonatal death, NICU unit admission restriction and GDM.

CONCLUSIONS: Stillbirth is associated with AMA; the strength of this relationship increases with maternal age. This relationship is not wholly explained by parity, maternal co-morbidities and use of ART. As stillbirth and FGR are mediated by placental dysfunction we propose that this may mediate the association between AMA and adverse pregnancy outcome. Further prospective studies are now needed to directly test this hypothesis to establish the cause of stillbirth.

T-160

Testosterone Contributes to Angiotensin II-Induced Hypertension and Associated Pathophysiology. Amar More†, Jay Mishra†, Gary Hankins, Sathish Kumar. *University of Texas Medical Branch, Galveston, TX, USA.*

INTRODUCTION: Hypertension is the leading cause of cardiovascular diseases, and angiotensin II (ang II) is one of the major components of the mechanisms that contribute to the development of hypertension. However, the precise mechanisms for the development of hypertension are unknown. Our recent study shows that ang II-induced vascular contraction depends on androgen status, with elevated androgen levels contributing for exaggerated vasoconstriction. This led us to investigate the contribution of androgens to hypertension caused by ang II.

METHODS: Ang II was infused for 28 days via subcutaneous miniosmotic pump (120 ng/kg per minute) to 10-week-old intact, castrated and castrated with testosterone replaced (testosterone propionate, 90 mg s/c pellet) Wistar rats. Progressive changes in blood pressure (non-invasive CODA), cardiac function (echocardiography), heart weight, cardiac BNP mRNA levels, and vascular reactivity (wire myography) were assessed.

RESULTS: Ang II infusion increased arterial pressure in males with intact testes and testosterone replaced castrated males. Castrated males showed less blood pressure and ang II infusion did not increase blood pressure in these animals. Ang II infusion induced left ventricular hypertrophy, increased heart-to-body weight ratio and BNP mRNA expression, indicators of cardiac hypertrophy, in intact and testosterone replaced castrated males. Castration alone had no effect on left ventricular size, heart weight and BNP mRNA level but minimized the increase in these parameters caused by ang II. Ang II-induced hypertension was associated with an increased contractile response of mesenteric arteries to phenylephrine and ang II in intact and testosterone replaced castrated males; these increases were prevented in castrated rats. Ang II infusion caused endothelial dysfunction in the mesenteric artery, as determined by the dilatory effect of acetylcholine. Ang II infusion to castrated males did not alter acetylcholine- and sodium nitroprusside-induced relaxations.

CONCLUSIONS: This is the first study to demonstrate a novel role whereby testosterone contributes to development and maintenance of ang II-induced vascular dysfunction, hypertension and cardiac hypertrophy. Identifying agents that prevents androgen-mediated upregulation of ang II-induced hypertension could be useful for treatment of hypertension and associated cardiovascular diseases.

T-161

Maternal and Fetal Fetuin-A Levels in Pregnancies Complicated by Preeclampsia. Ana Tobiasz†, Jose Duncan†, Laura Detti, Luis Gomez*. *University of Tennessee Health Science Center, Memphis, TN, USA.*

INTRODUCTION: Fetuin-A is a known marker for metabolic syndrome and insulin resistance. Its association with pregnancy complications is conflicting. Previous work has indicated both increased and decreased maternal levels associated with the condition, as well as direct affects on trophoblast cell viability. The association with fetal levels and preeclampsia has not previously been described. Our objective is to determine if elevated maternal or fetal fetuin-A is associated with preeclampsia.

METHODS: Cross-sectional analysis of women presenting to labor and delivery who delivered. Subjects were included if the gestational age was 34 weeks or greater and diagnosed with a hypertensive disorder of pregnancy. Maternal blood was collected at the time of admission and umbilical artery and vein samples were collected after delivery. Serum concentrations of fetuin-A were measured by ELISA. Statistical analysis included the t test, Chi square, and Fisher's Exact as appropriate. A $p<0.05$ indicated significance.

RESULTS: Thirty-seven subjects were included. Maternal fetuin-A levels were decreased in subjects with preeclampsia. Fetal fetuin-A levels were not different between groups. Table 1 shows the study outcomes. Maternal and fetal fetuin-A levels differed in subjects with preeclampsia (462.23±175.82 vs 665.64±253.60;p=0.0003); there was no difference in control subjects (667.94±201.27 vs 569.74±177.76;p=0.25). Using a cut-off of 600μg/mL, more subjects with preeclampsia had decreased maternal fetuin-A levels than controls.

Table 1. Maternal and Fetal Fetuin-A Levels in Subjects versus Controls

	Maternal		**Fetal**	
	Preeclampsia (25)	**Control (12)**	**Preeclampsia**	**Control**
Fetuin-A (mean± SD)	462.23± 175.82	667.94± 201.27	665.64± 253.60	569.74± 177.77
	P=0.003		*P*=0.183	

Table 2. Prevalence of Decreased Fetuin-A Levels in Subjects versus Controls

	Variable	Preeclampsia (n=25)	Control (n=12)	*P* vlaue	Odds Ratio (CI)
Fetal	Fetuin-A <600	11 (44%)	9 (75%)	*P*=0.038	0.2717(0.048-1.221)
	Fetuin-A ≥600	14 (56%)	3 (25%)		
Maternal	Fetuin-A <600	19 (76%)	5 (42%)	*P*=0.027	4.433(1.02-19.27)
	Fetuin-A ≥600	6 (24%)	7 (58%)		

CONCLUSIONS: Maternal fetuin-A levels at the time of delivery are decreased in women with preeclampsia. The difference between maternal and fetal fetuin-A levels are greater in women diagnosed with preeclampsia as compared to healthy controls. Our study suggests that fetuin-A plays a role in preeclampsia.

T-162

The Circulating Levels of Estradiol-17b and Progesterone Are Reduced in Women with Preeclampsia. Jiayi Wan,[1] Ke Zeng,[1] Yongxiang Yin,[2] Min Zhao,[2] Qi Chen.[3] *[1]Wuxi No 2 People's Hospital, Wuxi, Jiangsu, China; [2]Wuxi Women's Hospital, Wuxi, Jiangsu, China; [3]Fudan University, Shanghai, China.*

INTRODUCTION: Preeclampsia, a pregnancy specific disorder is characterised by systemic endothelial cell activation and exaggerated inflammation. During pregnancy, levels of both estrogen and progesterone are increased. In animal models, inhibition of estrogen production results in pregnancy loss, suggesting that estrogen may have a role in the maintenance of healthy pregnancy. In addition, estrogen is also involved in regulation of cardiovascular adaptation during pregnancy. Studies have suggested that estrogen and progesterone play an important role in the pathogenesis of preeclampsia. However, the profiling of estrogen and progesterone in preeclampsia is controversy. In this study we investigated the serum levels of estradiol-17b and progesterone in women with preeclampsia taking into account the time of onset and severity status.

METHODS: Blood samples were collected from 87 women with preeclampsia at the time of onset and 74 gestation-matched normotensive pregnancies. The serum levels of estradiol-17b (E2) and progesterone were measured using ELISA kit following the manufacturer's instructions.

RESULTS: The serum levels of E2 and progesterone were significantly reduced in women with preeclampsia compared to normotensive pregnancies (p=0.0001 and p=0.021, respectively). We then divided the study population into early and late onset or severe and mild preeclampsia, the reduced levels of E2 and progesterone in each subgroup were significantly reduced compared to each gestation-matched normotensive pregnancy. However, the levels of E2 and progesterone were not significant different between early and late onset preeclampsia (p=0.448). In addition, the levels of E2 and progesterone were also not significant different between severe and mild preeclampsia (p=0.068).

CONCLUSIONS: In this large sample size study, we demonstrate that the levels of sex hormone, estrogen and progesterone are significantly reduced in preeclampsia at presentation regardless the time of onset and the severity of preeclampsia. Our data may suggest the reduction of sex hormone levels with an impairment of placental steroidogenesis in preeclampsia.

T-163

Risk Factors for Preterm and Term Pre-Eclamptic Pregnancies Complicated by an SGA Neonate- A Population Based Study. Dikla Akselrod†,[1] Neta Ben-Shalom Tirosh†,[2] Moshe Stavsky†,[2] Tal Refaeli-Yehudai†,[2] Paz Dorit†,[2] Majdi Imtirat†,[2] Shirley Greenbaum†,[2] Limor Besser†,[2] Offer Erez*.[2] *[1]Faculty of Heralth Sciences Ben Guirion University of the Negev, Beer Sheva, Israel; [2]Soroak University Medical Center, Faculty of Heralth Sciences Ben Guirion University of the Negev, Beer Sheva, Israel.*

INTRODUCTION: The association between PET and small for gestational age (SGA) is not straightforward since both syndromes can develop independently. Therefore, the objectives of this study were to explore the association between different risk factors and perinatal outcomes to the ominous combination of pre-term and term PET + SGA.

METHODS: A retrospective population- based cohort study including all singleton deliveries. The study population was divided into four groups: 1) Preterm PET+SGA (n=591); 2) spontaneous preterm delivery (n=23,707); 3) term PET + SGA (n=1,869); 4) term delivery (n=272,236). Generalized estimating equations (GEE) multivariable models were used for the identification of independent risk factors for PET+ SGA.

RESULTS: Among those who delivered pre-term, women with PET + SGA had higher rates of chronic hypertension (HTN), history of PET, history of SGA neonate, nulliparity , labor induction, cesarean section and non-reassuring fetal heart rate than the comparison group (p<0.001 for all comparisons (.Among those who delivered at term, women with PET + SGA had a lower mean maternal age, higher rate of chronic HTN , history of PET, history of SGA, assisted reproductive treatments, nulliparity, labor induction, breech presentation , instrumental delivery, CS (p=0.001(and non-reassuring fetal heart rate (p<0.001 for all comparisons (. Moreover, neonates of women with pregnancies complicated by preterm and term PET + SGA had a higher rates of one minute low Apgar score , antepartum fetal death and total perinatal mortality (p<0.001 for all comparisons. After adjustment for cofounding factors, chronic HTN (aOR=5.468), history of PET (aOR=3.073) and nulliparity (aOR=3.017), were all independent risk factors(p<0.001(for pre-term PET + SGA. While the independent risk factors for PET+SGA at term (p<0.001) were maternal age (aOR=1.04), chronic HTN (aOR=4.976), history of PET (aOR= 2.566) and nulliparity (aOR= 14.368).

CONCLUSIONS: Chronic HTN, history of PET and nulliparity were independent risk factors for term and pre-term PET + SGA. Maternal age was an independent risk factor for this combination only at term.

T-164

Biomarker Discovery for Preeclampsia Using Newly Established Global Metabolomic Analysis. Yasuhiro Kurosawa,[1] Daisuke Saigusa,[2] Maiko Wagata†,[2] Masatoshi Saito,[1] Nobuo Yaegashi,[1] Junichi Sugawara*.[2] *[1]Tohoku University Graduate School of Medicine, Sendai, Miyagi, Japan; [2]Tohoku University, Sendai, Miyagi, Japan.*

INTRODUCTION: Global metabolomics (G-Met) is a cutting edge technology to discover biomarkers for various diseases. However, the quality of metabolomics largely depends on the instrumentation and protocol for normalization. In this study, we applied a newly established protocol for G-Met to elucidate dynamic metabolomic changes in plasma from preeclamptic patients.

METHODS: Retrospective case control study was conducted using plasma samples corrected between 2008 to 2011. Protocol was approved by ethics committee in Tohoku University Graduate School of Medicine (2014-1-44). Test subjects consisted of 10 patients with normal pregnancies, 9 and 5 patients with preeclampsia and gestational hypertension, respectively. Plasma samples were processed by UHPLC-QTOF/MS and LC-FTMS analysis and data normalization was performed using automated liquid-handling system and quality markers to compensate intra- and inter- batch differences (PLoS One 2016). Multivariate and statistical analysis was performed by principal component analysis and feature extraction by S-plot using analysis software (Quantbolome).

RESULTS: We obtained 5,272 plasma metabolites with relative quantification data from all samples. 254 potential biomarker candidates were extracted by multivariate analysis between preeclampsia and normal pregnancies, such as Carnitines, uric acid, and diacylglycerol.
CONCLUSIONS: In the present study, we discovered potential biomarker candidates for preeclampsia by newly established metabolomic systems. Targeted metabolomics should be conducted for the validation of candidates in a large-scale cohort study.

T-165

Abnormal Angiogenic Gene Expression in the Decidua and Placenta in a Mouse Model of Preeclampsia. Angelina M Seffens†,[1] Carrie J Shawber,[1] Xinjing Xu,[1] Robin L Davisson,[3] Jennifer L Sones,[2] Nataki C Douglas*.[1] *[1]Columbia Univeristy Medical Center, New York, NY, USA; [2]Louisiana State University, Baton Rouge, LA, USA; [3]Weill Cornell Medical College, New York, NY, USA.*
INTRODUCTION: Abnormal placentation can result in preeclampsia (PE). Angiogenesis in the uterine decidua is essential for embryo implantation and proper placentation. Abnormal expression of angiogenic genes from VEGF, Notch, Angiopoietin (Ang), and Ephrin signaling pathways has been observed in human PE. We hypothesize that angiogenic signaling is disrupted in the decidua and placenta in PE pregnancies, with a decrease in pro-angiogenic genes and increase in anti-angiogenic genes. We utilize BPH/5 mice, a non-primate rodent model that spontaneously develops a PE-like phenotype, to characterize changes in angiogenic genes at the maternal-fetal interface in early gestation.
METHODS: Intrastrain timed matings of BPH/5 and C57BL/6 (C57) control mice were established to assess gene expression in implantation sites at embryonic day (E) E.5 and placentas at E10.5. We used quantitative RT-PCR to assess changes in mRNA expression. The sample size was n=5 at E5.5 and n=3 at E10.5. Samples were run in triplicate. Unpaired t test was used to compare relative mRNA expression with $P<0.05$ for statistical significance.
RESULTS: At E5.5, expression of pro-angiogenic VEGFA and Dll4 was increased while expression of pro-angiogenic EphrinB2 was decreased in BPH/5 pregnancies as compared to controls.
**Figure(s) will be available online.*
Expression of pro-angiogenic VEGFR1, VEGFR2, Notch1, and Tie2 was decreased in BPH/5 pregnancies, as was expression of anti-angiogenic Ang2 and the Notch effector, Hes1. At E10.5, placental expression of anti-angiogenic sVEGFR1, more commonly known as sFlt1, and pro-angiogenic Jagged1, Ang1 and EphB4 was significantly increased in BPH/5 pregnancies.
CONCLUSIONS: These data suggest that disrupted signaling via VEGF, Notch, Ang and Ephrin pathways contributes to abnormal decidualization and placentation in BPH/5 pregnancies. Increased sVEGFR1 implicates abnormal VEGF signaling as a contributor to the BPH/5 PE-like model.

T-166

Recurrence Rates of Preeclampsia After Postpartum Evaluation in the Past 20 Years. Eva G Mulder†, Chahinda Ghossein-Doha†, Fleur EM Froeling†, Marc EA Spaanderman*. *Maastricht University Medical Center, Maastricht, Netherlands.*
INTRODUCTION: Preeclampsia (PE) and related fetal complications are one of the leading causes of maternal and fetal morbidity and mortality. PE is mostly superimposed upon pre-existing cardiovascular and metabolic risk factors. Recurrence rates vary between 6 and 65%, depending on the population studied. Efforts to reduce recurrence disease and to increase awareness for the associated (often modifiable) risk factors have been implemented in clinical practice in the past decades. Whether these strategies effectively resulted in less maternal disease and fetal complications is unknown. We assessed recurrence rates of PE and related fetal complications in the past 20 years in women admitted for postpartum evaluation.
METHODS: In this observational study, 752 women who had their first pregnancy complicated by PE were admitted to a postpartum cardiovascular and metabolic evaluation in Maastricht University Medical Center between 1996-2012. All women were counseled on personal risk factors and received state of the art preventive advice based on their risk profile. All women were sent a questionnaire between June 2015 and June 2016 about obstetric outcomes of subsequent pregnancies. We divided the women in three subgroups based on year of their second delivery 1) 1996-2004; 2) 2005-2009; and 3) 2010-2016. We analyzed differences in recurrence rates of PE, and fetal complications (small for gestational age, placental abruption, perinatal death) in the three time intervals using chi-square, with the first time-interval as the reference group.
RESULTS: In total, 467 women (62%) responded to the questionnaire. The non-responders differed from the responders by a higher prevalence of overweight, dyslipidemia and insulin resistance at evaluation. Two third of the responders had a second pregnancy, and the overall recurrent rate of PE was 24%. Of women who delivered between 1996 and 2004, PE recurred in 28%, compared to recurrence rates of 20% in 2005-2009 and 23% in 2010-2016 (*P*-value .425). Prevalence of fetal complications decreased significantly over time (22%, 19% and 9% respectively; *P*-value .028). Maternal age and prevalence of cardiovascular and metabolic risk factors at non-pregnant evaluation did not differ between groups.
CONCLUSIONS: Recurrence rates of PE did not decrease in the past 20 years. However, fetal outcomes improved substantially over time. Efforts to improve preventive strategies are still needed to reduce recurrence risk of PE.

T-167

Placental Underperfusion and Its Clinical Associations. Carole A McBride†,[1] Brenda L Waters,[1] Erin A Morris,[1] Gary J Badger,[1] Ira M Bernstein*.[1] *[1]UVM, Burlington, VT, USA; [2]UVM, Burlington, VT, USA; [3]UVM, Burlington, VT, USA.*
INTRODUCTION: Placental underperfusion (PU) is associated with intrauterine growth restriction (IUGR), preeclampsia, and fetal mortality. We sought to examine the relationship between PU, prepregnancy hemodynamics, and maternal hypertension status.
METHODS: Fifty-four nulliparous and 21 prior preeclamptic women were evaluated prepregnancy (PP) and at 12-14 weeks gestation (EP). At both time points, plasma volume corrected for lean body mass (PV), blood pressure (MAP), pulse wave velocity (PWV), uterine artery pulsatility (PI) and resistance (RI) indexes, and cardiac output (CO) were evaluated. Body composition was measured using DEXA prior to pregnancy. At delivery, placentas were collected and analyzed for evidence of PU and deliveries were characterized by pregnancy associated hypertension (PAH) diagnosis. Relationships between PU and physiologic measures were analyzed by PAH status. Data are presented as mean ± SD.
RESULTS: Of 74 placentas examined, 27 (36%) showed evidence of underperfusion. PU occurred in 34.8% of normotensive women (n=46), 42.9% of those with gestational hypertension (n=14), 0% of term preeclampsia (n=6), and 62.5% with preterm preeclampsia (n=8). For all women, PU was strongly associated with IUGR (+PU=33% vs -PU=4%: $p<0.001$) and lower birth weight percentile (+PU=27% vs -PU= 60%; $p< 0.001$). PU was less common in term preeclampsia than other PIH diagnoses ($p<0.02$). PU was also associated with lower EP PV (+PU= 69±11 vs -PU 75±9 mL/kg; p= 0.04) and higher uterine PI (+PU= 1.73±0.53 vs -PU= 1.46±0.40; p=0.03) and RI (+PU= 0.74±0.53 vs –PU= 0.70±0.08; p= 0.05). PU was not associated with parity. Within normotensive women (age 31±4 years, BMI=23±4.8 kg/m^2), PU was associated with decreased PP CO (+PU= 4.1±1.2 vs -PU= 4.8±1.2 L/min; p= 0.04) and lower PV (+PU= 62.1±7.1 vs -PU= 67.1±7.2mL/kg; p=0.03). For PAH (age 30±5 years, BMI= 28.8±6.0 kg/m^2), PU was associated with increased PP serum creatinine (+PU= 0.68±0.07 vs -PU= 0.60±0.07mg/dL; p= 0.007), and higher PP MAP (+PU= 100±7 vs -PU= 93±8 mmHg; p= 0.02).
CONCLUSIONS: PP hemodynamics and EP uterine artery remodeling play an important role in the development of placental underperfusion. Underperfusion, which often occurs in conjunction with PAH, appears less common in term preeclampsia than with other PAH diagnoses.

T-168

Gender Imbalance Confounds Meta-Analysis of Pre-Eclampsia Microarray Studies of the Placental Transcriptome. Justyna Dopierala†, Gordon CS Smith, D Stephen Charnock-Jones*. *University of Cambridge, Cambridge, United Kingdom.*

INTRODUCTION: Several meta-analyses have been performed of the placental transcriptome in pre-eclampsia (PE). None of them, however, takes sex into account, indeed, some previous meta-analyses identified Y chromosome genes as differentially expressed in PE. We hypothesized that failure to account for feto-placental sex could lead to incorrect conclusions from such studies.

METHODS: We developed a method to identify the sex of samples from published PE microarray studies. We compared standard meta-analysis of these studies and an approach where sex was taken into account. Finally, we compared the placental transcriptome associated with PE separately for males and females.

RESULTS: A total of 39 studies were publically available, but only 8 met our inclusion criteria. Sample sex was identified in 6 of those. While cases were quite well balanced: 33/70 (47%) were male, there was a sex bias in controls: 37/96 (38%) were female ($\chi 2$ test: P=0.094). Using a standard meta-analysis (not sex corrected), we found apparent differential regulation (FDR<$5x10^{-5}$) of genes in PE which included 8 Y chromosome genes (CD24P4, DDX3Y, EIF1AY, EIF4A1P2, KDM5D, RPS4Y1, UTY & USP9Y) and 3 X chromosome genes known to escape X inactivation (XIST, STS and FHL1). 91% and 96% of up- and down-regulated genes respectively, remained significant when gender was accounted for, but all but two Y chromosome pseudogenes and all X chromosome genes lost their significance when gender was taken into account. When we performed meta-analysis stratified by fetal sex, PE datasets showed different placental molecular profiles for males and females. Of the 500 most significantly up-regulated genes in the two groups, only 54% overlapped between males and females. The equivalent figure for down-regulated genes was 48%. Over 20% of the non-overlapping up- and down-regulated genes showed a male to female rank difference >1,000 and two genes had a rank difference of >10,000: CRHR1-IT1 (ranked 205 in males and 16,280 in females) and C2orf88 (ranked 380 in males and 11,022 in females).

CONCLUSIONS: (1) Feto-placental sex is an important factor that should be taken into account when performing integrative analysis of microarray data, and biases could also arise from failure to match for other demographic and obstetric characteristics; (2) male and female PE have a different molecular profile; (3) well-designed, large scale, one-platform or RNA-seq study could address these issues.

T-169

The Impact of Low Dose Aspirin on Markers of Placental Disease – Results of the TEST Multicentre RCT. F Mone,[1] C Mulcahy,[2] P McParland,[1] M Culliton,[3] P Downey,[3] O Maguire,[4] P Clarke,[3] A Stanton,[5] F Breathnach,[2] J Morrison,[2] S Daly,[2] J Higgins,[2] A Cotter,[2] E Tully,[2] P Dicker,[2] F Malone,[2] F McAuliffe*.[1] *[1]National Maternity Hospital, Dublin, Ireland; [2]Rotunda Hospital, Dublin, Ireland; [3]National Maternity Hospital, Dublin, Ireland; [4]St. Vincent's University Hospital, Dublin, Ireland; [5]Royal College of Surgeons in Ireland, Dublin, Ireland.*

INTRODUCTION: The aim was to determine the impact of low dose aspirin 75mg once daily from 11-weeks on; (i) placental histopathology; (ii) PAPP-A and PLGF; (iii) urine albumin creatinine ratio (ACR); and (iv) fetal growth.

METHODS: This is a secondary analysis of the multicenter TEST Study where 546 low risk nulliparous women were randomised to one of three arms; (i) routine aspirin, (ii) no aspirin, (iii) aspirin based on a positive first trimester Fetal Medicine Foundation pre-eclampsia screening test. Serum PAPP-A, PLGF and urinary ACR was assessed prior to starting aspirin and 9-weeks following aspirin commencement. Fetal growth was assessed through ultrasound fetal abdominal circumference assessment (AC) in all trimesters. Placental histopathology was performed and categorised using a novel classification system. Aspirin and non-aspirin taking groups were compared. This study was carried out by Perinatal Ireland and the HRB Mother and Baby Clinical Trials Network in Ireland.

RESULTS: Assessment of placental pathology showed no differences in terms of either gross findings; fetal-placental weight ratio; 7.7 (+/- 2.3 S.D) vs. 7.3 (+/- 2.4 S.D) (p=0.545), cord hypercoiling 0.8% vs. 1.9% (p=0.76) or histopathological sub-categories of maternal vascular malperfusion (p=0.3), fetal vascular malperfusion (p=0.5), villitis (p=0.9) or delayed maturation (p=0.7) between those on aspirin and controls. There was no signifiant difference between time-points on assessment of the PAPP-A (p=0.10), PLGF (p=0.40) and ACR (p=0.13) and nor in terms of the fetal AC trajectory, at the time of all three trimester assessments (p=0.66).

CONCLUSIONS: Aspirin does not appear to have a significant impact on fetal growth nor major serum, urinary or histopathological markers of placental disease in low-risk nulliparous women.

T-170

Amyloid Precursor Protein Products Are Associated with Vessel Stiffness and Hypertension in Subsequent Pregnancy. Carole A McBride†, Erin A Morris, Ira M Bernstein*. *UVM, Burlington, VT, USA.*

INTRODUCTION: Increasing evidence suggests Amyloid Precursor Protein (APP) products may be associated with cardiovascular disease (CVD), playing a role in vascular inflammation and vessel stiffness. We sought to determine whether plasma sAPPα and sAPPβ are associated with hemodynamic measures linked to vascular dysfunction or the development of preeclampsia (PE) when measured prior to pregnancy.

METHODS: We evaluated 31 women with a history of prior preterm PE and 64 nulliparas, prepregnancy, in the follicular phase. Measures included pulse, blood pressure, cardiac output (CO), CO response to volume challenge, brachial flow mediated vasodilation, and popliteal pulse wave velocity (PWV). Additionally we measured APP alpha and beta as well as uric acid, hemoglobin, and dDimer. Statistical analysis was performed using Pearson correlation coefficients and t-tests, with p<0.05 accepted for significance.

RESULTS: Women were young, (31±4 yrs) healthy, (BMI 25.5±5.8 mg/kg^2) and normotensive (mean arterial pressure 90±9 mmHg) at prepregnancy evaluation. Increased sAPPα was associated with high uric acid (r=0.204 mg/dL; p=.05), increased pulse (r=0.257 bpm; p=.01), increased CO response to volume challenge (r=0.210 L/min; p=.04), faster PWV (r=0.246 m/sec; p=.02), sAPPβ was associated with faster pulse (r=0.244bpm; p=.02), increased response to volume challenge (r=0.238 L/min; p=.02), increased d-Dimer (r=0.379; p<.001). History of PE was not associated with sAPPα or sAPPβ. All women (n=95) delivered singleton gestations; 10 developed with preterm PE, 7 term PE, 21 had non-PE hypertension (HTN), and 57 had normal pregnancies. Women who developed any hypertension had higher sAPPα levels prior to pregnancy than other women (mean preterm PE= 0.98±0.44, term PE= 0.80±0.35, HTN= 0.78±0.38, normal= 0.66±0.35 ng/mL; p=.002 for normal vs. all others). Levels of sAPPβ were similar between groups.

CONCLUSIONS: Both sAPPα and sAPPβ were associated with reduced vessel compliance, including faster PWV, and increased CO response to volume challenge. We observed increased uric acid and ddimer, supporting previous reports of underlying inflammation observed in PE. It is significant that prepregnancy levels of sAPPα differ between women who develop hypertension from those who do not, with the highest levels seen in women who develop preterm preeclampsia. Further studies are needed to elucidate the function of sAPPα and its role in cardiovascular disease and both term and preterm PE.

T-171

The Placental Expression of HLA-G, HLA-C, and HLAF in Severe Preeclampsia and Preterm Labor. Rinat Hackmon, Lakmini Pinnaduwage†, Jianhong Zhang, Dan E Geraghty, Stephen J Lye, Caroline E Dunk*. *OHSU, Portland, OR, USA; University of Toronto, Toronto, ON, Canada; Fred Hutchinson Cancer Research Institute, Seattle, WA, USA; University of Toronto, Toronto, ON, USA; Mount Sinai Hospital, Toronto, ON, Canada.*

INTRODUCTION: Human pregnancy is one of the most interesting examples of immune tolerance seen in mammalian biology. A key-organ, the placenta, is the single organ tissue expressing simultaneously each of the non-classical MHC class I antigens - HLA- F, G and C. Interestingly,

activated lymphocytes express HLA-F on their cell-surface. We recently proposed a inhibitory KIR model of HLAF/C complex in early placentation. We hypothesized that the immune inflammatory mediated - preeclampsia and preterm labor, may show a distinct expression of non classical HLA.

METHODS: Immunohistochemistry, q-PCR, and western blot were used from placentas with term CS not in labour, with term in labour, with severe preeclampsia, and with preterm delivery. Placental EVT explants and Swan-71 cells were used to assess HLA-F and HLA-C. We performed immunohistochemistry of serial sections of placenta.

RESULTS: HLA-C is weakly expressed in the EVT of the preterm and term non laboring C section placentae, HLA-C staining of EVT and placental villi increased with the onset of labor and vaginal delivery. In preeclampsia the EVT which showed a shallow invasion HLA-C was slightly increased in intensity. HLAG was strongly expressed in the cytoplasm of EVT of the term placenta and all preeclampsia but reduced in the preterm EVT. In the term non labor placenta HLA-F was expressed by the EVT throughout the decidua at a moderate level, while in preeclampsia HLA-F expression was was increased in the distal EVT at the front of the invasive edge. HLA-C, mRNA and protein levels remained consistent across gestation but significantly increased in laboring term and preterm placentas.

CONCLUSIONS: 1.The increased EVT expression of HLA-C and G in term- parturition and in severe preeclampsia show similar pattern that support that both are inflammatory responses mediated by non classical-HLA expression. 2.The significant increase of HLA-F expression in severe preeclampsia and its presence in term placentas may indicate the immune activity of the trophoblast. 3.The significant high levels of HLA-C m-RNA in labor may indicate a role in parturition.

T-172

cAMP Rescues the Negative Regulatory Effects of TNF-α on Endothelial Cx43 Gap Junction Function and Protects Cell Permeability. Bryan C Ampey†,[1] Amanda C Hankes†,[2] Ian M Bird,[3] Ronald R Magness*.[4] *[1]University of Wisconsin-Madison, Madison, WI, USA; [2]University of Wisconsin-Madison, Madison, WI, USA; [3]University of Wisconsin-Madison, Madison, WI, USA; [4]University of South Florida, Tampa, FL, USA.*

INTRODUCTION: Pregnancy is not only a state of vasodilation but also increased inflammation. Rises in uterine blood flow are associated with increases in vasodilation, which are associated with gap junction (GJ) connexin (Cx) 43 protein expression. Recently, we demonstrated that Cx43 function is required for Ca^{2+}-mediated NO production in uterine artery endothelial cells from pregnant sheep (P-UAEC). We have also shown that Cx43 function is improved in response to cyclic nucleotide-mediated S365 Cx43 phosphorylation, most likely because of net movement of newly synthesized Cx43 to the plasma membrane. However,in hypertensive diseases of pregnancy such as preeclampsia, pro-inflammatory cytokines (TNFα) are known to be further elevated and disrupt GJ function and decrease cell-cell contact (monolayer integrity) by disrupting junctional proteins. Therefore, we hypothesize that cAMP and to a lesser extent cGMP will rescue and/or protect the loss of Cx43 function in response to patho-physiologic levels of TNFa.

METHODS: To measure GJ communication, P-UAEC were grown on chamber slides, treated with 10 ng/ml TNFα (1 hr) followed by 1 μM and 1mM of either 8 Br-cAMP or –cGMP (30 min), scraped at several sites with a razor, incubated with 0.05% Lucifer Yellow and tetramethylrhodamin dextran, and viewed by fluorescent microscopy**.** To measure monolayer integrity, P-UAEC were grown on 96-well plates that measure monolayer resistance using an alternating current to determine monolayer integrity. Cells were pretreated with 1 μM or 1mM 8-Br-cAMP or -cGMP (30 min) followed by an addition of 10ng/mL TNFα (25 hrs).

RESULTS: TNFα-mediated reduction in GJ communication was fully recovered ($P<0.05$) by 1mM 8-Br-cAMP (4.5-fold) but only partly rescued by 8-Br-cGMP (2-fold). Endothelial cell monolayer integrity function was correspondingly improved by 8-Br-cAMP and 8-Br-cGMP alone, but only 1 mM 8-Br-cAMP delayed and significantly improved monolayer integrity in P-UAEC treated with TNF-α within 15 hours ($P<0.01$).

CONCLUSIONS: Together, these results indicate that Cx43 GJIC and P-UAEC monolayer integrity can be, respectively "recovered" and "protected" from destructive pro-inflammatory cytokines such as TNFα via cAMP, but not so much by the cGMP signaling pathway.

T-173

Differences in Peripheral Guanylate-Binding Protein-1 Concentrations During Healthy and Preeclamptic Pregnancies. Joost HN Schuitemaker,[1,2] Thomas IFH Cremers,[3] Mariëlle G van Pampus,[4] Sicco A Scherjon,[5] Marijke M Faas*.[2,5] *[1]IQ Products BV, Groningen, Netherlands; [2]University Medical Center Groningen, Groningen, Netherlands; [3]University of Groningen, Groningen, Netherlands; [4]Onze Lieve Vrouwe Gasthuis, Amsterdam, Netherlands; [5]University Medical Center Groningen, Groningen, Netherlands.*

INTRODUCTION: Guanylate-Binding Protein-1 (GBP-1) plays a role in the regulation of angiogenesis. Previously it has been shown that increased levels of proinflammatory cytokines, like TNF-α and IFN-γ, induce the secretion of GBP-1 from endothelial cells. Therefore, we hypothesized that the plasma levels of GBP-1 would be increased during pregnancy and even further during preeclampsia (PE).

METHODS: Peripheral plasma samples from 22 non-pregnant women, 25 healthy, 48 severe early-onset PE and 7 severe late-onset PE pregnancies were collected during the third trimester. In these plasma samples GBP-1 was measured by ELISA. In randomly taken biopsies of the chorionic villi from 13 healthy pregnancies, 9 severe early-onset PE and 6 severe late-onset PE pregnancies GBP-1 mRNA was determined by qPCR.

RESULTS: The GBP-1 plasma concentration was significantly higher during pregnancy (mean 169 pg/ml ± 32 pg/ml SEM) compared to non-pregnant women (mean 81 pg/ml ± 22 pg/ml SEM) (Mann Whitney, $p<0.001$). The GBP-1 concentration of the severe early-onset pregnancies (mean 55 pg/ml ± 6.6 pg/ml SEM) and those with severe late-onset PE (mean 42 pg/ml ± 12 pg/ml SEM) were comparable (Mann Whitney, $p=0.518$), but both were significantly decreased as compared to healthy pregnancies (Mann Whitney respectively $p<0.001$ and $p<0.01$). In the chorionic villi biopsies GBP-1 mRNA was detectable, but there was no difference in mRNA levels between the different groups.

CONCLUSIONS: In line with our hypothesis, GBP-1 levels were increased in pregnancy. However, GBP-1 levels were decreased during preeclampsia as compared to healthy pregnancy. Based on the GBP-1 mRNA levels it is likely that the placenta is able to be a source of GBP-1. During healthy pregnancies the placenta might be the source of the higher levels of GBP-1, but it is unclear why the GBP-1 levels in PE pregnancies are significantly lower. More research is needed to get insight into mechanisms behind this observation.

T-174

First Trimester T Helper Cell Subsets, Th1/Th2 and Th17/Treg Cell Ratio Levels May Predict Preeclampsia. Maria D Salazar Garcia†,[1] Yuvon Mobley,[2] Jennifer Henson,[3] Michael Davies,[2] Nayoung Sung,[1] Annie Skariah,[1] Svetlana Dambaeva,[2] Alice Gilman-Sachs,[2] Kenneth Beaman,[2] Charles Lampley,[3] Joanne Kwak-Kim*.[1] *[1]Rosalind Franklin University of Medicine and Science, Vernon Hills, IL, USA; [2]Rosalind Franklin University of Medicine and Science, North Chicago, IL, USA; [3]Mount Sinai Hospital, Chicago, IL, USA.*

INTRODUCTION: Preeclampsia affects 4–6% of all pregnancies and is consider the first cause of maternal death in developed countries. Although the etiology of preeclampsia remains unknown, researchers have suggested that immunological alterations in the early placental microenvironment may participate in the origins of preeclampsia. The aim of this study was to investigate the association between peripheral blood immune effectors and the development of preeclampsia and to evaluate their use as predictors of preeclampsia in early gestations.

METHODS: We performed a prospective cohort study in 189 pregnant women recruited from Mount Sinai Hospital in Chicago, IL. Peripheral blood was collected between 5-16 weeks of gestation (mean ± SD, 10.5±2.6). Intracellular cytokine analysis and immunophenotype were performed by flow-cytometry. Patients were followed up until delivery and clinical data was collected. 104 patients lost follow-up having 85 patients as final analytical sample.

RESULTS: A total of 9 women (10.5%) presented preeclampsia. Patients with preeclampsia had significantly higher percentage of $CD3^+CD4^+TNF\alpha^+$ T helper 1 cells (45.3±11.5 vs 37.1±8.5, *P*=0.009) and $CD3^+CD4^+IL17^+$ T helper 17 cells (2.4±1.3 vs 1.6±1.1, *P*=0.043) when compared to those of patients without preeclampsia. $CD3^+CD4^+CD25+CD127^+$ Treg cells (5.7±1.2% vs 7.0±1.6%, *P*=0.016) were significantly lower in patients with preeclampsia when compared to those without preeclampsia. Patients with preeclampsia had significantly higher TNFα/IL-10 ratio (43.8±10.3 vs 34.3±7.9, *P*=0.001) and Th17/Treg ratio (0.4±0.3 vs 0.2±0.1, *P*=0.002) when compared to those of patients without preeclampsia. The logistic regression predictive model combining Th1, Treg and Th17 cell percentages and TNFα/IL-10 and Th17/Treg ratios had the best performance with an area under the curve of 0.847, sensitivity of 88.9% and specificity of 89.9% (95%CI 0.7-0.9).
CONCLUSIONS: First trimester Th1, Treg and Th17 cell percentages and TNFα/IL-10 and Th17/Treg ratios may predict preeclampsia. A large scale study is warranted to confirm these findings.

T-175

CD40 Inhibitor Is a Novel Translational Treatment for Inflammatory Modulation in Endometriosis. Alessandra J Ainsworth†,[1] Chandra C Shenoy†,[1] Ye Zheng,[1] Abu Osman*,[2] Khashayarsha Khazaie,[2] Gaurang S Daftary.[1] *[1]Mayo Clinic, Rochester, MN, USA; [2]Mayo Clinic, Rochester, MN, USA.*
INTRODUCTION: Ectopic implants in endometriosis are commonly associated with inflammation and fibrosis. We have shown that the TGF-β regulated Sp/KLF transcription factor KLF10 is associated with human endometriosis. Moreover, KLF10 is associated with predominantly inflammatory disease progression and minimal scarring. Here we show that KLF10 regulates a critical mechanism mediated by CD40/CD154 that links T- and B-cell mediated immune responses and its response to targeted therapy.
METHODS: 8-week old wildtype (wt) and Klf10-/- mice were treated with DMSO or CD40-inhibitor (CD40i) by daily IP injections (N=7 mice/group). 1wk after initiation of treatment, endometriosis was surgically induced by suturing 0.5 mm everted uterine segments onto parietal peritoneum. The resultant phenotype was assessed at 3wks by morphometry, immunofluorescence and mesenteric lymph node and peritoneal lavage flow cytometry.
RESULTS: Klf10-/- mice treated with CD40i had an average lesion size of $11.6mm^2$ and fibrosis score of 22 compared to $14.3mm^2$ and 13 respectively in those treated with vehicle control. Peritoneal fluid lavage and draining lymph nodes were assessed for localized inflammation. Compared to wt and vehicle treated Klf10-/- mice, CD40i treated Klf10-/- mice had decreased cell counts of total FoxP3+ and activated CD25+, FoxP3+ T-regulatory (T-reg) cells as well as increased dysfunctional RORγt+, FoxP3+ T reg cells. There were no changes in PD1+; ICOS+, FoxP3+ or CD44+, FoxP3+ cells. There were decreased CD11b+ myeloid cells and myeloid-derived suppressor cells. There were decreased cell counts of PDL1 and PDL1+, CD11b+, CD11c+ in both wt and KLF10-/- mice treated with CD40i compared to vehicle. There were no changes in inflammatory monocytes or resident macrophages.
CONCLUSIONS: KLF10 epigenetically activates both CD40 and its ligand CD154. CD40 on T-cells activates CD154 on B-cells and thereby mediates a critical acquired immune response pathway. Loss of KLF10 results in inflammation and progression of endometriosis through dysregulation of this pathway. This pathway is amenable to targeted pharmacological therapy using CD40i. CD40i diminished activation of T-reg cells to modify the local immune infiltrate and response. This novel anti-inflammatory therapy is safe, efficacious and translationally relevant as it arrests disease progression by targeting a key inflammatory disease mechanism.

T-176

Reduced CD200 Expression Contributes to Altered Th1/Th2 Cytokine Production in Placental Trophoblasts from Preeclampsia. Jie Xu†, Yang Gu, David F Lewis, Yuping Wang*. *LSUHSC-Shreveport, Shreveport, LA, USA.*
INTRODUCTION: CD200 and CD200R tolerance-signaling molecules play an important role in regulating immune system by suppression of inflammatory cytokines and by modulation of T-cell function. CD200 expression was reduced in placental villous tissue from spontaneous abortion. However, trophoblast (TC) CD200 and CD200R expression has not been studied in preeclampsia (PE). This work was undertaken to determine if reduced CD200 and CD200R expression occurs in placental TCs from PE and to test our hypothesis that downregulation of CD200 expression leads to altered TC Th1/Th2 cytokine production.
METHODS: TCs were isolated from normal (n=12) and PE (n=12) placentas and incubated with DMEM supplemented with 5%FBS for 3 days. Total cellular protein and culture medium were collected at the end of incubation. CD200 and CD200R expression was determined by Western blot analysis. Production of Th1 (sTNFR1, IL-6, IL-8) and Th2 (IL-10) cytokines was measured by ELISA. The role of CD200 in Th1 and Th2 cytokine production was determined by transfection of CD200 siRNA in TCs from normal placentas (n=6). Data was presented as mean±SE (pg/μg protein for cytokine production) and analyzed by unpaired and paired t-test. Statistical significance is defined as $p<0.05$.
RESULTS: 1) Relative CD200 expression was significantly reduced in TCs from PE vs. normal placentas: 0.43±0.05 vs. 0.73±0.12, $p<0.05$; CD200R expression was not significantly different between the two groups; 2) Th1 cytokine production of sTNFR1 (4.51±0.65 vs. 2.99±0.34), IL-6 (4.27±0.82 vs. 2.08±0.28), and IL-8 (40.22±7.45 vs. 22.16±3.28) were significantly increased, $p<0.05$, and Th2 cytokine IL-10 production (0.23±0.03 vs.0.58±0.05) was significantly decreased, $p<0.01$, by TCs from PE vs. normal placentas; 3) TCs transfected with CD200 siRNA produced significantly more sTNFR1 (5.21±0.64 vs.4.35±0.61), IL-6 (2.02±0.38 vs.0.71±0.22) and IL-8 (32.03±10.19 vs. 20.64±7.86), $p<0.05$, but significantly less IL-10 (0.40±0.03 vs. 0.53±0.04), $p<0.05$, than control cells.
CONCLUSIONS: Downregulation of CD200 expression is associated with increased Th1 and decreased Th2 cytokine production by TCs from PE placentas. Inhibition of CD200 expression by CD200 isRNA results in increased Th1 and decreased Th2 cytokine production by placental TCs. These findings suggest that reduced CD200 expression may contribute to imbalanced Th1/Th2 cytokine production by placental TCs and reduced immune tolerance at maternal-fetal interface in PE.

T-177

A Case of Recurrent Posterior Reversible Encephalopathy Syndrome. Moayad Turkistani, Rana Alamoudi, Emad Alkhotani, Abdulrahim Ali Rouzi*. *King Abdulaziz University, Jeddah, Makkah, Saudi Arabia.*
INTRODUCTION: Posterior reversible encephalopathy syndrome, is characterized by headache, confusion, seizures and visual loss. It may occur due to malignant hypertension, eclampsia and some medical treatments. The objective was to report a case of recurrent posterior reversible encephalopathy syndrome after post-partum eclampsia.
METHODS: A 22-years old, T3, P0, A0, L3 woman from Burkina Faso, presented to our ER with headaches, decrease level of consciousness, and convulsions after delivering at home. She was unregistered in our hospital and she did not have proper antenatal care. Her first delivery was spontaneous vaginal delivery at full term. The second delivery was emergency C/S due to eclampsia with posterior reversible encephalopathy syndrome at 30 weeks of gestation. On examination she was unconscious with blood pressure of 220/120. She was intubated and transferred to the intensive care unit. Investigation showed hemoglobin of 8.9 g/dL and evidence of HELLP syndrome. She was diagnosed with posterior reversible encephalopathy syndrome by CT scan of the brain.
RESULTS: She was extubated on the third day after admission and recovered completely with appropriate medical care. She was discharged home one week after admission to be followed in the out-patients clinics.
CONCLUSIONS: Posterior reversible encephalopathy syndrome may recur in subsequent pregnancy.

T-178

Preeclampsia Is an Independent Risk Factor for Surgical Site Infection (SSI) Following Cesarean Delivery After Labor. Kara M Rood,[1] Mark A Klebanoff,[2] Emily A Oliver†,[1] Mark B Landon,[1] Irina A Buhimschi,[2] Catalin S Buhimschi*.[1] *[1]The Ohio State College of Medicine, Columbus, OH, USA; [2]Nationwide Children's Hospital, Columbus, OH, USA.*

INTRODUCTION: Preeclampsia may increase the host susceptibility to infection through heightened systemic oxidative stress, dysregulation of pro-inflammatory cascades and alternations of maternal innate immune response to microbial invasion. We hypothesized that, in laboring women, PE is an independent risk factor for post-cesarean SSI.

METHODS: This was a secondary analysis of analysis using data from Maternal-Fetal Medicine Units Network (MFMU) Cesarean Registry (1999-2002). Patients included in this analysis had a singleton viable pregnancy and a cesarean delivery following labor from 24 to 42 weeks gestational age (GA). A multivariable logistic regression model was used to control for gestational age, race, BMI at delivery, smoking, limited prenatal care, length of labor, length of rupture of membranes, pre-gestational diabetes, hypertensive diseases, physical health assessed using American Society of Anesthesiologists' established categories, PPROM and chorioamnionitis.

RESULTS: In women who labored the rate of SSI was 9.9% (2,585 of 25,986). The adjusted Odds Ratio (OR) for SSI among patients who had preeclampsia (n=2521) was significantly increased (95% CI=1.15-1.54, p=0.0002).

Risk Factors	OR (95% CI)	P value
Preeclampsia	1.33 (1.15-1.54)	0.0002
Gestational HTN	1.22 (0.98-1.53)	0.0766
HELLP	1.53 (0.84-2.77)	0.1628

The increased risk of SSI was specifically associated with a diagnosis of preeclampsia and not to other hypertensive disorders [i.e., gestational hypertension (n=1028), HELLP (n=134)].

CONCLUSIONS: In laboring women undergoing a cesarean delivery, preeclampsia is a risk factor for SSI independent of other hypertensive diseases and well-recognized risk factors for infection morbidity.

T-179

2-Cell Embryos Are More Sensitive Than Blatocysts to AMPK-Dependent Suppression of Anabolism and Potency/Stemness by Commonly Used Fertility Drugs, a Diet Supplement and Stress. Alan Bolnick,[1] Mohammed Abdulhasan,[1] Brian Kilburn,[1] Mindie Howard,[2] Alexandra Shamir,[3] Omar Pasalodos,[1] Jing Dai,[1] Elizabeth Puscheck,[1,4] Daniel Rappolee*.[1,5] *[1]Wayne State University, Detroit, MI, USA; [2]EmbryoTech Labs, Haverhill, MA, USA; [3]University of Utah, Salt Lake City, UT, USA; [4]Wayne State University, Southfield, MI, USA; [5]Wayne State University, Detroit, MI, USA.*

INTRODUCTION: Drugs such as Metformin (Met) or diet supplements (DSs) such as BioResponse-3,3'-Diindolylmethane (BRDIM) are used to improve fertility and diabetes. Aspirin (Asa) is often used for analgesia and as an anti-inflammatory drug. BRDIM, Asa and Met have therapeutic effects through AMPK activity but at clinically relevant doses decrease anabolism, potency, and cell growth immediately and have delayed toxicity for cultured 2-cell mouse embryos. This study tested whether Met, Asa or DS BRDIM induced AMPK-dependent decrease in anabolism assayed by pACC ser79P, potency loss assayed by Cdx2 and Oct4, and decrease cell growth, and whether 2-cell embryos are more sensitive>blastocysts for these outcomes.

METHODS: Culture post-thaw mouse zygotes to 2-cell embryos and test effects after 1hr AMPK agonists' (Met, Asa, BRDIM, control hyperosmotic sorbitol) exposure on AMPK-dependent loss of phosphorylation of acetyl coA carboxylase pACC ser79P) by quantitative immunofluorescence. Test post-thawed cultured blastocysts for increased pACC ser79P and decreased oct4. Confirm AMPK-dependence by reversing potency loss in 2-cell or blastocysts with AMPK inhibitor compound C (CC). Test whether Met+Asa or DS BR-DIM decrease growth rates blastocysts counting cells.

RESULTS: Asa, Met, BRDIM and sorbitol increased pACC ser79P ~20-30fold in 2-cell embryos but ~3-6-fold in blastocysts. We showed before that these stresses caused a 40-85% Oct4 protein loss in 2-cell embryos that was ~60-90% reversible by co-culture with CC. However, Oct4 loss in blastocysts was 30-50% but reversibility was similar at 50-90% with CC. We showed that pharma and a DS arrested cell growth at the 2-cell stage and are now testing for a lower diminished growth in blastocysts.

CONCLUSIONS: The data suggest that AMPK-dependent drugs and DSs decrease anabolism and potency more at the 2-cell>blastocyst stage. We now test if cell proliferation is diminished at the 2-cell>blastocyststage and whether greater affects are due to higher AMPK or substrateamounts.

T-180

Early Endocrine Gene Expression in 8-Cell Human Embryos. Amy M Lee†,[1] Dimitri Loutradis,[2] Peter Drakakis,[2] Charalampos Theofanakis,[2] Thomas L Toth,[1] Ann A Kiessling*.[3] *[1]Massachusetts General Hospital, Boston, MA, USA; [2]University of Athens, "Alexandra" Maternity Hospital, Athens, Greece; [3]Bedford Research Foundation, Bedford, MA, USA.*

INTRODUCTION: Little is known about gene signaling in early developing embryos. Our objective is to elucidate patterns of early hormone gene expression in 8-cell human embryos.

METHODS: RNAs extracted from a pool of fresh 8-cell stage, morphologically normal human embryos were linearly amplified and hybridized to an Agilent 60-mer whole human genome microarray platform. Of the complete 43,477 element data set, 280 individual genes were identified as hormones or hormone receptors by Gene Ontology, Reactome, and DAVID. This dataset was compared with published datasets of the same Agilent microarray platform for lines of human embryonic stem cells (hESCs) and lines of human fibroblasts before (fibro) and after induced pluripotency i(PSCs). Selected microarray elements were verified by independent qPCR analysis. Statistical analysis was performed by Chi-square tests.

RESULTS: Of the 280 genes examined, half of the hormone/receptor genes were detected at low levels (<500 fluorescent units) in the 8-cell embryo. This is fewer than in the hESCs, the human fibroblast, or the iPSC (P<0.0001). High-level detection (>5,000 fluorescent units) was similar in all the cell lines P=N/S).

Cell type	Number of Gene Microarray Signals (Total= 280 genes)		
	Low Expression (<499 fluorescent units)	Moderate Expression (500-5000 fluorescent	High Expression (>5001 fluorescent units)
8 Cells	156 (55%)	68 (24%)	22 (8%)
hES	200 (71%)	44 (16%)	22(8%)
i(PSCs)	204 (73%)	42 (15%)	18 (6%)
Fibro	207 (73%)	40 (14%)	24 *9%)

Several genes variable have expression between probes, which may represent circadian expression. Thyroid hormone receptor and thyroid hormone receptor associated proteins were detected at high levels specifically in the 8-cell embryo. Oxytocin gene was detected 100-fold higher in the 8-cell embryo than in the other cell lines.

CONCLUSIONS: At the 8-cell stage, embryo gene expression appears highly active for hormones-related genes. Robust expression of thyroid receptors suggests a novel role in the developing embryo. Oxytocin expression could potentially play a role in embryo development and migration.

T-181

Enhancement of Human Sperm Motility by Novel Recombinant Endo-β-Galactosidases. Toshiaki Shibata,[1] Tomoya Akama,[2] Kiyohiko Angata,[3] Michiko Fukuda,[3] Kazuhiro Sugihara,[1] Naohiro Kanayama.[1] *[1]Hamamatsu University School of Medicine, Hamamatsu, Shizuoka, Japan; [2]Kansai Medical University, Hirakata, Osaka, Japan; [3]National Institute of Advanced Industrial Science and Technology, Tsukuba, Ibaraki, Japan.*

INTRODUCTION: We have previously shown that polylactosamine in semen is a decapacitation factor1. Polylactosamine is hydrolyzed by endo-β-galactosidase (EBG) and increases motility when added to human

sperm. Treatment of human sperm with EDG induces sperm motility signal transduction through Ca^{2+} and cAMP influx. The receptor that interacts with polylactosamine in human sperm is FGFR2. Therefore, there is an adjustment mechanism for sperm motility at the molecular level. Furthermore, we have reported that polylactosamine in the semen is involved in sperm motility, fertility, and embryonic development. Recently, we cloned a novel EDG from Bacteroides fragilis (Akama, Angata and Fukuda et al; unpublished). We report here the activity of recombinant EBGs for assisted reproductive technologies.

METHODS: *B. fragilis* EBGs were cloned, produced and purified by Akama et al., as follows. EDG was purified from the culture medium of EDG-producing *C. freundii*, as described previously. We then sequenced the EDG N-terminal amino acids. Subsequently, we identified the cDNA of *B. fragilis* genome in the Genbank database. The open-reading frame DNA sequence of *B. fragilis* EDG was amplified by PCR and ligated into an *E. coli* expression vector. The recombinant EDG was then purified. Changes in human sperm motility were measured after treatment with purified EDG, using the Computer-Aided Sperm Analysis system.

RESULTS: The *B. fragilis* genome had six open reading frames homologous to the isolated EDG sequence. Large-scale synthesis of recombinant EDG enzyme was successful using four of the six *B. fragilis* sequences. We confirmed that at least one of the recombinant proteins had EDG activity being able to degrade polylactosamine or keratan sulfate (unpublished). When human sperm was treated with the four recombinant EDGs, all recombinant EDGs significantly elevated the sperm motility. These results are similar to our previous data obtained when human sperm was treated with EDG purified from *C. freundii*.

CONCLUSIONS: All four novel recombinant *B. fragilis* EBGs had activity on human sperm to elevate human sperm motility. Future studies toward clinical application will include examination of sperm motility activation and improving fertility.

T-182

Aberrant Expressions of Transmembrane Chloride Ion Channels in Endometriosis. Jeong Sook Kim†,[1] Ji Hyun Park,[1] Jae Hoon Lee,[2] Minkyung Kim,[2] Bo Hyon Yun,[2] Joo Hyun Park,[1] Seok Kyo Seo,[2] Young Sik Choi,[2] SiHyun Cho*,[1] Byung Seok Lee.[1] *[1]Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea; [2]Yonsei University College of Medicine, Seoul, Republic of Korea.*

INTRODUCTION: This study aimed to introduce the Na^+–K^+–$2Cl^-$ cotransporter (NKCC-1/2) and Chloride channel-3 (CLC-3), transmembrane chloride channels in endometrium, and evaluate the functions of those chloride channels in endometriosis.

METHODS: We performed the quantitative RT-PCR and Western blot of NKCC1/2, CLC-3 respectively. It allowed to compare the expressions of mRNA and protein levels of those transmembrane chloride channels between control (n=18) and endometriosis (n=21) group. After siRNA transfection in endometrial cells and Ishikawa cell, migration assay of each cell was done.

RESULTS: We performed the quantitative RT-PCR and Western blot of NKCC1/2, CLC-3 respectively. It allowed to compare the expressions of mRNA and protein levels of those transmembrane chloride channels between control (n=18) and endometriosis (n=21) group. After siRNA transfection in endometrial cells and Ishikawa cell, migration assay of each cell was done.

CONCLUSIONS: We demonstrate that there are the increased expressions of NKCC 1/2 and CLC-3 in endometriosis. Moreover, migration cell number was decreased when we transfect each transmembrane chloride channel siRNA in endometrial cell and Ishikawa cell. These data indicate that NKCC 1/2 and CLC-3 had a strong relationship of endometrial cell migration. Especially, NKCC 1 and CLC-3 expression levels showed a positive relationship of ovarian cyst size in endometriosis.

T-183

The Role of G-CSF Treatment in Recurrent Miscarriage on the Expression of FOXP3, VEGF, VEGF-R2 and C-KIT in First Trimester Pregnancy Specimens. Fabio Scarpellini,[1] Marco Sbracia,[2] Avenir Balili.[3] *[1]CERM, Rome, Italy; [2]CERM, Rome, Italy; [3]State University of Albania, Tirana, Albania.*

INTRODUCTION: We used successfully G-CSF in the treatment of Recurrent Miscarriage, as well as in recurrent implantation failure. However, there not data on the mechanism of action of G-CSF on pregnancy. In order to assess the effects of G-CSF treatement on decidual immunocells and trophoblast we conducted an immunohistochemical study for the expression of FoxP3, VEGF, VEGF-R2 and c-kit in first trimester pregnancy specimens.

METHODS: The study was conducted on tissue specimens of decidua and trophoblast of 8 abortive first trimester pregnancies obtained from 8 women with recurrent pregnancy loss treated during the pregnancy with G-CSF. These pregnancies aborted since the embryos showed a chromosomal aneuploidy assessed by trophoblast kariotyping. Controls were 10 specimens, obtained from 10 spontaneous abortions and 10 specimens obtained from women underwent first trimester voluntary pregnancy terminations Immunohistochemistry was performed on tissue sections to assess FoxP3, VEGF, VEGF-R2, c-kit, with commercially available monoclonal antibodies, and nn avidin-biotin-peroxidase detection system was used.

RESULTS: In the decidua of women with recurrent pregnancy loss treated with G-CSF a significant increase in the number of cells positive to Foxp3 with respect to controls was observed (HSCORE 167 ± 46 vs 79 ± 24: $P<0.01$). VEGF expression in trophoblast of specimens of women treated with G-CSF was statistically significant higher than controls (HSCORE 156 ± 39 vs 70 ± 19:$P<0.01$) VEGF-R2 expression in trophoblast of specimens of women treated with G-CSF was statistically significant higher than controls (HSCORE 148 ± 37 vs 81 ± 28:$P<0.01$). The c-kit expression in trophoblast of specimens of women treated with G-CSF was statistically significant higher than controls (HSCORE 1417 ± 34 vs 72 ± 21:$P<0.01$).

CONCLUSIONS: Our data showed that G-CSF administration in pregnant women with recurrent fetal loss increases the amount of Treg cells in decidua and the VEGF, VEGF-R2 and c-kit expression on trofoblast. These findings show that G-CSF treatment acts on both trophoblast and maternal immune system.

T-184

MicroRNA-27b Mimic Inhibits VEGF B and VEGF C in Human Endometrial Stromal Cells. Beverly G Reed†, Bruce R Carr, Ruth A Word, Patricia T Jimenez*. *University of Texas Southwestern Medical Center, Dallas, TX, USA.*

INTRODUCTION: MicroRNAs are small non-coding RNAs that regulate gene expression through inhibition of transcription and/or translation. We have previously shown that MicroRNA 27b (miR-27b) is hormonally regulated in human endometrium; Specifically, miR-27b is decreased with both estradiol and with the endocrine disruptor Bisphenol A (BPA). Our objective was to identify potential important targets of miR-27b in human endometrium.

METHODS: Endometrial tissue was obtained after informed consent from reproductive-aged women undergoing hysterectomy for benign indications without hormonal exposure for three months. Human endometrial stromal cells from the proliferative phase were serum deprived for 24 hours prior to a 48-hour transfection with miR-27b mimic and microRNA mimic negative control/vehicle. Potential targets of miR-27b were identified by TargetScan and biological plausibility. Candidate gene expression was analyzed by RT-qPCR.

RESULTS: VEGF B expression was significantly decreased by miR-27b mimic (Control 1.02 vs miR-27b mimic 0.74, $p=0.0113$). In addition, VEGF C expression also was significantly decreased (Control 1 vs miR-27b mimic 0.83, $p=0.05$). Other predicted targets (VEGF A, ERa, FOXO1, and FOXO3), were not affected by overexpression of miR-27b in these non-decidualized cells.

CONCLUSIONS: These findings suggest that VEGF B and VEGF C are targets for miR-27b in human endometrial stromal cells. As estradiol increases during the menstrual cycle, miR-27b is downregulated thereby facilitating estrogen-induced upregulation of VEGFs to stimulate angiogenesis during the proliferative phase. The results indicate that hormonal alterations and disruptors may lead to dysregulation of miR-27b and its targets required for successful endometrial development. Studies are ongoing to determine the effect of mir27b inhibitor on the selected targets.

T-185

Network Biology of Menstrual Cycle to Understand the Key Drivers of Endometrial Receptivity. Patricia Sebastian-Leon,[1] Ana Conesa,[2] Vicente Arnau,[3] Jose Remohí,[1] Antonio Pellicer,[1] Carlos Simon,[1,4] Patricia Diaz-Gimeno*.[1] *[1]Valencia University, Valencia, Spain; [2]CIPF, Valencia, Spain; [3]Valencia University, Valencia, Spain; [4]Technological Park, Valencia, Spain.*

INTRODUCTION: Biomarkers prioritization in transcriptomics studies has been typically designed using differential expression analysis that consider genes as independent entities. Weighted Gene Correlation Networks (WGCN) give us the opportunity to understand gene cooperation as part of a biological system where genes are interconnected and working together to perform functions.

The main objective of this work is to analyze menstrual cycle from this perspective to prioritize biomarkers based on their co-expression evolution.

METHODS: Transcriptomics for 238 endometrial receptivity genes (Díaz-Gimeno et al., 2011) from 523 patients among the menstrual cycle was modeled. Samples were classified using LH peak and K-means unsupervised classification. Scale-free WGCN were performed on each stage to analyze co-expression changes and associated functions using KEGG pathways database.

RESULTS: WGCN showed a different network structure along menstrual cycle (Figure 1).

**Figure(s) will be available online.*

In receptive profile, 127 connections involving 94 genes were specific of endometrial receptivity showing a dysregulation in other phases (Figure 2).

**Figure(s) will be available online.*

Main functions involved in these specific relationships included complement and coagulation cascade; FoxO signaling pathway and HTLV-I infection disease pathway.

CONCLUSIONS: Even if the same genes are implicated in menstrual cycle changes, differences among stages bring out when co-expression relationships are analyzed. This approach provides predictive network models that give rise to Network Medicine, providing a deeply understanding of the process that will generate new holistic and realistic biomarkers.

T-186

Oxytocin Activates Pro-Inflammatory Pathways in Decidualised Human Endometrial Stromal Cells. Camilla West†, Sung Hye Kim†, Shirin Khanjani, Aylin Hanyaloglu, Phillip Bennett, Vasso Terzidou*. *Imperial College, London, United Kingdom.*

INTRODUCTION: Successful implantation is dependent on the acquisition of a receptive endometrium as well as the development of a high-quality, competent embryo. A characteristic of early implantation is high-levels of the pro-inflammatory T-helper (Th)-1 and cytokines such as interleukin-6 (IL-6) and interleukin-8 (IL-8). Indeed, it has recently been shown that local endometrial injury augments an inflammatory response and this results in a higher rate of successful embryo implantation in women undergoing IVF. Thus, pharmacological modulation of the inflammatory response in the endometrium during implantation could be a potential therapeutic avenue for women who suffer from recurrent implantation failure. Oxytocin (OT) and the OT antagonist Atosiban have both been shown to induce inflammatory pathways in human amnion however the inflammatory effects of OT and Atosiban in the endometrium have not been explored.

METHODS: Human endometrial stromal cells (HESCs) were isolated from endometrial biopsies taken from women undergoing IVF treatment. HESCs were decidualised for 72 hours with 8-Bromoadenosine 3',5'-cyclic monophosphate (8-bromo-cAMP) and medroxyprogesterone-17 acetate (MPA) prior to stimulation with OT (10nM or 100nM) or Atosiban (100nM, 1μM or 10μM). Activation of inflammatory pathways (namely NF-κB) was assessed via Western blot and cytokine gene expression was assessed via RTQ-PCR.

RESULTS: HESCs treated with OT for 30 minutes showed significant activation ($p=<0.05$) of NF-κB phospho-p65 but in contrast HESCs treated with Atosiban elicited a significant decrease in levels of phospho-p65 ($p=<0.05$). Additionally, HESCs treated for 2 hours with OT induced the expression of IL-6, IL-8, CXCL1 and CCL5 in a dose-dependent manner (of which IL-6 and IL-8 were significantly upregulated with 100nM OT ($p=<0.05$)). HESCs treated with Atosiban failed to induce a significant increase in any of the four cytokines examined.

CONCLUSIONS: Together, our data here show that HESCs respond to OT and initiate the activation of pro-inflammatory p65 and induce the expression of pro-inflammatory cytokines. Atosiban acts in an opposing manner reducing levels of activated p65 and does not initiate the expression of pro-inflammatory cytokines. To our knowledge, this has not previously been shown and could represent a novel use of OT in controlling inflammatory responses in the endometrium.

T-187

The Calcium-Permeable Mechanosensitive Piezo1 as Cellular Sensor in Human Endometrial Epithelial Cells. Aurélie Hennes†,[1] Katharina Held†,[1,2] Katrien De Clercq†,[1] Luc Meeuwis,[3] Christel Meuleman,[3] Thomas Voets,[2] Joris Vriens*.[1] *[1]KU Leuven, Leuven, Belgium; [2]KU Leuven, Leuven, Belgium; [3]University Hospital Leuven, Leuven, Belgium.*

INTRODUCTION: Embryo implantation is defined by many crucial interactions between the developing blastocyst and the receptive endometrium that allow for an enhanced endometrial decidualization and successful implantation. To date, a complete understanding of this process is lacking and it remains unclear how signals can be detected by endometrial epithelial cells and transmitted towards the stromal bed. Recently, ion channels such as the epithelial sodium channel (ENaC) in combination with voltage-dependent calcium channels (VDCC) were proposed as important signal mediators during embryo implantation (Ruan et al. Nature Medicine, 2012). Here, we aim to investigate the functional expression of other ion channels in the endometrial epithelial cells as candidate sensors.

METHODS: Human endometrial epithelial cells (HEEC) were isolated from endometrial biopsies obtained during the luteal phase of the menstrual cycle. qRT-PCR was used to assess the mRNA expression levels of several ion channels. Functionality was assessed via Ca^{2+} microfluorimetry and whole-cell patch clamp experiments.

RESULTS: Expression and functional analysis provided no evidence for the presence of VDCC in HEEC. Moreover, Ca^{2+} microfluorimetry experiments showed that application of the ENaC activator, trypsin, induces transient calcium influxes, independent of the presence of extracellular calcium in HEEC. In addition, the trypsin-induced calcium influx could not be blocked by the VDCC-blockers (nifedipine and amiloride). In contrast, HEECs showed high mRNA levels of the mechanosensitive ion channel piezo1 and functional evaluation with different piezo1 activators such as Yoda1 and mechanical stimulation, provided strong evidence for the functional expression of piezo1 in HEECs.

CONCLUSIONS: Our data provides evidence for the high functionality of the mechanosensitive ion channel piezo1 in human endometrial epithelial cells. We therefore hypothesize that this channel might be a key player in the signal transduction process between the blastocyst and the endometrium during embryo implantation.

T-188

Improvement of the Endometrial Receptivity Signature Reveals a Possible Maternal Origin of Biochemical Pregnancies. Patricia Diaz-Gimeno,[1] María Ruiz-Alonso,[2] Patricia Sebastián-León,[1] Vineeta Singh,[2] Antonio Pellicer,[1,3] Diana Valbuena,[2] Carlos Simón*.[1,2,3,4] *[1]University of Valencia/INCLIVA, Valencia, Spain; [2]S.L, Valencia, Spain; [3]Valencia University, Valencia, Spain; [4]Stanford University School of Medicine, Stanford, CA, USA.*

INTRODUCTION: Endometrial Receptivity Analysis (ERA) was developed by our group as a predictive method to diagnose the localization of the Window Of Implantation (WOI) in the evaluation of the endometrial factor (Diaz-Gimeno *et al.* 2011). Here, a new ERA 2.0 version has been retrained and tested against the ultimate goal that is pregnancy outcome finding interesting cues for the maternal origin of biochemical pregnancies.

METHODS: This is a cohort prospective study for ERA gene expression to retrain the original predictor model ERA 1.0. Machine learning predictors using co-training and stacking strategy with SVM and KNN models were designed. Systematic training set (n= 523), followed by a validation set (n= 321) was used to detect the WOI variability in the population. The pregnancy outcome associated with the different receptive signatures (n = 228) was compared using a Fisher exact test.

RESULTS: In the ERA 2.0, the endometrial receptivity gene profiling was further subdivided in four signatures with higher sensibility and specificity. The accuracy of ERA 2.0 with 95% of confidence interval was 0.9694 (0.951, 0.982) for KNN, and 1 (0.993, 1) for SVM. The reproductive outcome of ERA 2.0 profile compared to ERA 1.0 reveals a curated receptive signature (RRR) with the highest ongoing pregnancy rate in terms of live birth, and a late receptive (LR) signature with a potential high risk of biochemical pregnancy.

**Figure(s) will be available online.*

CONCLUSIONS: Our results demonstrate that the personalized WOI in humans is not functionally homogenous. It has a central period where the highest ongoing pregnancy rate is achieved and a late period implicated in high risk for biochemical pregnancies.

Funding: This work was supported by the EU: FP7-PEOPLE-2012-IAPP grant SARM, No. 324509, and Igenomix, SL.

T-189

Growth Differentiation Factor 9 Induces Granulosa Cell Proliferation via Inhibition of the Expression of AMH Type II Receptor. Akira Iwase*, Satoko Osuka, Bayasula Bayasula, Sachiko Takikawa, Tomohiko Murase, Tomoko Nakamura, Maki Goto, Fumitaka Kikkawa. *Nagoya University Graduate School of Medicine, Nagoya, Aichi, Japan.*

INTRODUCTION: TGF-β superfamily including AMH and GDF-9 plays a key role in folliculogenesis. GDF-9, one of the oocyte-derived factors, is involved in the folliculogenesis via its effect on granulose cells, of which mechanism is not fully understood. We investigated the effects of GDF-9 on receptor of AMH, which suppress the development of early-stage follicles.

METHODS: We evaluated gene expression of AMH type II receptor (AMHRII) in immortalized human nonluteinized granulosa cells we recently established (HGrC1) using quantitative RT-PCR, following stimulation by bone morphogenetic proteins (BMPs), GDF-9, FSH, HCG, forskolin, estradiol (E2), progesterone(P) and cAMP. We also evaluated gene expression of AMH type I receptor (ALK2/3/6) in HGrC1 stimulation by GDF-9. AMH-induced phosphorylation of Smad1/5/8 was analyzed after GDF-9 pretreatment.

RESULTS: The expression of AMHRII under stimulation of GDF-9, not BMPs, FSH, HCG, forskolin, E2, P or cAMP, was reduced to one tenth of the control level. The phosphorylation of Smad1/5/8 induced by AMH was reduced after GDF-9 pretreatment. GDF-9 induced cell proliferation of HGrC1.

CONCLUSIONS: Our data suggests that GDF-9 might promotes the recruitment and development of early-stage follicles via regulation of AMH action on granulosa cells with GDF-9-reduced expression of AMHRII.

T-190

Melatonin Supplementation Improves Fetal Outcomes in a Mouse Model of Advanced Maternal. Samantha C Lean†, Mark R Dilworth, Alexander EP Heazell, Rebecca L Jones*. *University of Manchester, Manchester, United Kingdom.*

INTRODUCTION: Advanced maternal age (AMA; ≥35 years old) is associated with increased risk of fetal growth restriction (FGR) and stillbirth. Our studies found aspects of placental dysfunction and oxidative stress in these pregnancies[1]. We previously developed a mouse model of AMA which mirrors the FGR, late stillbirth and placental dysfunction that occurs in human AMA pregnancies. We hypothesized that treatment with melatonin, a potent antioxidant, would improve fetal outcomes in AMA mouse pregnancies.

METHODS: Young (8-12wk) and aged (AMA;38-41wk) C57Bl6/J (C57) virgin mice were mated with C57 males (10-16wk). At E12.5, dams were randomised to receive either 0 (vehicle) or 5μg/ml melatonin in drinking water (n=6-7/group). At E17.5 placentas and fetuses were harvested for anthropometric measurements. Placental system A amino acid transport was assessed in pregnant mice following maternal ^{14}C-MeAIB tail vein injection. All statistics were by Kruskal-Wallis test with Dunn's multiple comparisons.

RESULTS: As previously observed, at E17.5 AMA mice (vehicle) had lower fetal weight ($p<0.005$), increased placental weight ($p<0.01$), reduced fetal:placental weight (FW:PW) ratio ($p<0.01$) and reduced anthropometric measures ($p<0.05$) compared to young mice (vehicle), and suffered 3 late fetal deaths. Melatonin treatment removed the effects of AMA on fetal anthropometric measures and reduced the effects on fetal weight and FW:PW ratio ($p<0.05$), although placental weight remained increased ($p<0.01$). No late fetal losses occurred in melatonin-treated AMA mice. Melatonin treatment had no significant effects on young pregnancy outcomes. Preliminary data suggests uni-directional maternofetal clearance of ^{14}C-MeAIB was reduced in AMA mice and is unaffected by melatonin treatment.

CONCLUSIONS: AMA negatively affects pregnancy outcome in C57 mice resulting in late fetal deaths, increased placental weight, and growth restricted offspring. Melatonin treatment appears to eliminate or alleviate most of the effects of AMA on pregnancy outcome. This is likely due to its antioxidant properties, but this is yet to be investigated. These data support the hypothesis that aging-related oxidative stress contributes to the negative effects of AMA on pregnancy outcome and provides promise for antioxidants as a future therapy in AMA pregnancies. This work was funded by Tommy's the baby charity.

[1]Lean *et al.* (2014) Placenta 35(9):A77, [2]Lean *et al.* (2015) Repro Sci 22(1):79A.

T-191

Exercise Ameliorates the Oocyte Defects Associated with Impaired Fertility in Homozygous *PolG* Mitochondrial Mutator Mice. Christine E Faraci†, Jonathan L Tilly, Dori C Woods. *Northeastern University, Boston, MA, USA.*

INTRODUCTION: While a number of factors accompany poor egg quality, an accruing body of evidence strongly supports that mitochondrial dysfunction in oocytes from aged women is a key contributor to infertility. To study the impact of severe mitochondrial mutations on oocyte quality we used the well-characterized 'mtDNA mutator mouse' (PolG), which harbors a genetic defect in the proofreading subunit of the mtDNA polymerase-gamma, resulting in a rapid accumulation of mtDNA mutations that lead to an accelerated aging phenotype.

METHODS: Oocyte quality was analyzed in C57Bl/6 female mice homozygous for the PolG mutation (POLG) at 3, 6, 7, 8, and 9 months of age. Cumulus oocyte complexes were isolated following superovulation, and denuded oocytes were counted and assessed for stage of development (*i.e.* germinal vesicle stage, metaphase II (MII)), and analyzed by confocal microscopy for proper formation of meiotic spindles, chromosome distribution, and mitochondrial localization. Additionally, 3-month old (m.o.) POLG female mice were subject to forced treadmill exercise (3 x

week, 45 min; rate = 15m/min) until 8 months of age (endurance exercised; END), or left sedentary (SED). All oocytes were collected and assessed for the endpoints described above and scored for quality.

RESULTS: The number of ovulated oocytes declines steadily in PolG-SED with age, with no viable ovulated oocytes obtained at 9 months. By 7 months, the yield of oocytes declined by approximately 73% as compared to wild type, with 50% of all MII oocytes exhibiting defects in spindle assembly, chromosomal segregation and/or mitochondrial distribution. By comparison, POLG-END have improved oocyte yield at 8-9 m.o. and, strikingly, 86% of MII oocytes demonstrated normal spindle formation, chromosomal segregation, and mitochondrial distribution, similar to oocytes of 4-5 month old wild-type mice.

CONCLUSIONS: Accelerated mitochondrial mutational rates have a negative impact on female fertility. The fertile period in PolG-SED was abbreviated, with a demonstrated decline in both quantity and quality of oocytes by 7 months.Exercise had an ameliorative impact, delaying the decline of both oocyte quantity and quality.We are currently investigating the molecular mechanisms underlying the impact of exercise on the POLG oocyte phenotype, including effects on mitochondrial mutational loads and the potential contributions of distinct mitochondrial subpopulations to the oocyte aging process.

T-192

Hormone-Dependent Chemotaxis and Homing of Innate Lymphoid Cells in the Context of Pregnancy. Christine Lamb†, Damián O Muzzio†, Kristina M Hilz†, Laura N Castro†, Marek Zygmunt*. *University of Greifswald, Greifswald, Germany.*

INTRODUCTION: Innate Lymphoid Cells (ILCs), recently discovered immune cells that belong to the innate immune system, have been shown to play an important role in gut, lung and skin homeostasis, but their role in reproduction still needs to be evaluated.

ILCs are known to express the chemokine receptors CCR4, CCR6 and CCR10 which have been shown to be crucial for general localization of ILCs on tissue barriers. Whether ILCs are recruited to the uterus from the periphery or originate in situ from precursors remains unknown. Our aim is to study the homing mechanisms of ILCs during murine pregnancy.

METHODS: To assess the expression of CCR4, CCR6 and CCR10 on ILCs in murine lymphoid organs, we collected the spleen, thymus, uterus-draining lymph nodes and Peyer's Patches from non-pregnant and pregnant BALB/c mice. To further investigate the effect of hormones in this process, we stimulated isolated murine splenocytes with different concentrations of estrogen and progesterone.

The role of chemotaxis and chemokine ligands in homing of ILCs was analyzed using a migration assay focusing on CCL4, CCL20 and CCL28.

RESULTS: Our work shows that levels of CCR4 and CCR10 rise within the first week of pregnancy (p<0,05), whereas CCR6 reaches its maximal expression at day 14 of murine gestation (p<0,05).

**Figure(s) will be available online.*

This was mostly similar in all compared organs. We found a significant decrease of ILCs' percentage in bone marrow (p<0,001) as well as of levels of the integrin α4β7 in peripheral organs in pregnant mice (p<0,05).

**Figure(s) will be available online.*

CONCLUSIONS: We showed that ILCs undergo changes in their homing behavior during pregnancy.

The decrease of ILCs in bone marrow and of α4β7 in peripheral organs could indicate an adaptation of the ILCs' compartment as well as a regulation of the proportion of pro-/anti-inflammatory cytokines during pregnancy.

T-193

Excess Glucose Induces Trophoblast Inflammation Through HMGB1 Activation of Toll-Like Receptor 4. Kathleen R Heim†,[1] Julie A Potter,[1] Christina S Han,[2] Vikki M Abrahams.[1] *[1]Yale University, New Haven, CT, USA; [2]UCLA, Los Angeles, CA, USA.*

INTRODUCTION: Diabetes affects ~1-2% of pregnancies worldwide, and poor glycemic control in pregnancy increases the risk for preeclampsia and other complications. We previously found that hyperglycemic levels of glucose induced a trophoblast anti-angiogenic and pro-inflammatory profile by elevating the secretion of sEndoglin, sFlt-1, IL-8 and IL-1β. The IL-1β response to excess glucose was mediated by upregulation of the damage associated molecular pattern (DAMP), uric acid, which in turn activated the Nalp3 inflammasome. Another DAMP - high-mobility group box-1 (HMGB1) - activates Toll-like receptor 4 (TLR4). The objective of this study was to determine the role of HMGB1 and TLR4 in the trophoblast response to hyperglycemia.

METHODS: Human first trimester trophoblast cells (Sw.71) were exposed to glucose doses mimicking normoglycemic (5mM) and hyperglycemic (10mM) conditions, either alone or in the presence of the TLR4 antagonist, LPS-RS (10μg/ml), or the HMGB1 inhibitor, glycyrrhizin (200μM). Trophoblast were also treated under normoglycemic conditions (5mM) with or without recombinant (r) HMGB1 (1μg/ml). After 48-72hrs supernatants were collected and measured by ELISA and bioassay for the inflammatory cytokines: IL-8 and IL-1β; the anti-angiogenic factors: sEndoglin and sFlt-1; and the DAMPs: HMGB1 and uric acid.

RESULTS: LPS-RS significantly inhibited excess glucose induced trophoblast secretion of IL-8 by 60.1±10.8%; uric acid by 37.5±13.9%; and IL-1β by 27.5±14.1% ($p<0.05$). Excess glucose induced sEndoglin and sFlt-1 was not reduced by LPS-RS. Excess glucose significantly increased trophoblast secretion of HMGB1 by 1.6±0.3-fold compared to normoglycemic levels ($p<0.05$). Under normoglycemic conditions, treatment of trophoblast with rHMGB1 significantly increased IL-8 secretion by 1.6±0.3 fold and IL-1β secretion by 1.3±0.2 fold ($p<0.05$). Under hyperglycemic conditions, the presence of the HMBG1 inhibitor, glycyrrhizin, significantly inhibited excess glucose-induced trophoblast secretion of IL-8 by 19.1±4.2% ($p<0.05$), but did not reduce the IL-1β response.

CONCLUSIONS: Our findings suggest that hyperglycemic levels of glucose trigger a sterile inflammatory IL-8 response in the trophoblast through endogenous HMGB1 activation of TLR4. Excess glucose-induced IL-1β is also TLR4 mediated, however, HMGB1 and uric acid may not be the only DAMPs involved.

T-194

Evaluation of B Cell Subsets in Women with Recurrent Pregnancy Losses and Implantation Failure. Annie M Skariah†,[1] Maria D Garcia†,[1] Wenmin Qin†,[1] Joanne Kwak-Kim*,[1,2] Alice G Sachs,[2] Alejandra Comins-Boo†.[1] *[1]Chicago Medical School at Rosalind Franklin University of Medicine and Science, North Chicago, IL, USA; [2]Chicago Medical School at Rosalind Franklin University of Medicine and Science, North Chicago, IL, USA.*

INTRODUCTION: A significant proportion of women with recurrent pregnancy losses (RPL) or repeated implantation failure (RIF) have autoimmune abnormalities, which may suggest dysregulated B cell and its subpopulations.

METHODS: This is a prospective case-control study of women with RPL and RIF. Peripheral blood B cell subsets, NK cell levels and cytotoxicity and Th1/Th2 ratios were analyzed by flow cytometry. Autoantibodies including antinuclear antibodies, anti-thyroid antibodies, anti-ovarian antibodies and anti-phospholipid antibodies were analyzed by ELISA. Controls are healthy fertile women. Statistical analysis was made by student t- test, Mann Whitney test and Spearman's rho correlation test.

RESULTS: Women with RPL/RIF had significantly higher CD19+ B cells%, (13.8 ± 3.85 vs. 9.8 ± 3.08, P<0.05) and naive B cells (74.7± 7.8 vs. 61.5 ± 8.95, P<0.05) as compared with those of controls. Contrarily, non-switched memory B cells and switched B cells were significantly decreased in RPL/RIF women (8.17 ± 1.36 vs. 18 ± 9.7, P<0.05 and 11.42 ± 5.55 vs 16.9 ± 3.8, P<0.05) as compared with those of controls. No significant differences were present in double negative (DN) memory B cells between the two groups. A positive correlation was present between switched memory B cells and double negative B cells (r=0.557, P= 0.016). Negative correlations were present between naïve B cells and non-switched memory B cells (r= -0.698, P = 0.001), and switched memory B cells (r= -0.638, P <0.005). 55% women with RPL/RIF have at least 1 autoimmune abnormality. No correlation was present between CD19+ B cell/subsets and autoimmunity in women with RPL/RIF. No correlations were present between CD 19+ B cell % or its subsets and NK cell number, cytotoxicity and Th1/Th2 ratio.

CONCLUSIONS: In women with RPL/RIF, B cell subpopulations are dysregulated as compared with those of normal fertile women, which is not correlated with autoimmune profile.

T-195

Comparing Pain from Fertiloscopy and Laparoscopy for the Diagnosis of Infertility. Kathryn S Merriam†,[1] Lara Aboulhosn,[1] Paul B Marshburn,[1] Rebecca S Usadi,[1] Michelle L Matthews,[1] Megan Templin,[2] Bradley S Hurst*.[1] *[1]Carolinas Medical Center, Charlotte, NC, USA; [2]Carolinas Medical Center, Charlotte, NC, USA.*

INTRODUCTION: The primary objective of this study was to determine if fertiloscopy is less painful than laparoscopy by comparing amounts of intra-operative and post-operative pain medications required by patients undergoing the two procedures for diagnosis and/or treatment of infertility. Additional objectives were to compare surgical time, cost, and time to conception.

METHODS: This study was a retrospective chart review including records from July 1, 2010 to December 31, 2014. Subjects were undergoing outpatient surgery at a teaching hospital. There were 96 total participants with 50 in the fertiloscopy group, women who underwent fertiloscopy for diagnosis and/or treatment of infertility, and 46 in the laparoscopy group, women who underwent laparoscopy for the same purpose. Outcomes included intra-operative and post-operative pain medication requirement, surgical time, and cost of the procedure. Narcotic pain medication use was converted into Morphine equivalents. The time to conception with natural conception, assisted reproductive technology (ART), or ovulation induction (OI) with intrauterine insemination (IUI) was recorded. The data was analyzed using T-Test, ANOVA, and chi squared tests.

RESULTS: Table 1. Comparison of the Mean Values of Study Outcomes

Outcome	Fertiloscopy (n=40)	Laparoscopy (n=56)	P-Value
Intra-op Pain Med (Morphine Equivalent units)	12.1	16.3	0.015
Post-op Pain Med (Morphine Equivalent units)	3.1	5.7	0.04
Surgeon OR Time (mins)	47.6	63.3	0.0003
Total OR Time (mins)	75.7	102.0	<0.0001
Cost (USD)	18,920	23,610	<0.0001
Time to natural conception (mos)	13.2 (n=13)	11.7 (n=11)	0.61
Time to conceptions with OI IUI (mos)	2.5 (n=1)	3.7 (n=5)	0.77
Time to conception with ART (mos)	7.3 (n=6)	6.7 (n=7)	0.83

CONCLUSIONS: Fertiloscopy was found to be less painful than laparoscopy for the diagnosis and/or treatment of infertility, as patients who underwent fertiloscopy required significantly less intra-operative and post-operative narcotic pain medication than those who underwent laparoscopy. Additionally, fertiloscopy was found to have significantly less surgical time and was significantly less costly than laparoscopy. Both seemed comparable in terms of the time to natural conception or conception with the use of OI IUI or ART.

T-196

Hypochlorous Acid Reversibly Inhibits Caspase-3: A Potential Regulator of Apoptosis. Roohi Jeelani, Inga Sliskovic, Sasha Mikhael, Faten Shaeib, Mili Thakur, Husam Abu-Soud*. *Wayne State University School of Medicine, Detroit, MI, USA.*

INTRODUCTION: Loss of apoptotic regulation is observed in several human diseases including many gynecological cancers. Caspase-3, a cysteine-aspartate protease is one of the main regulators of apoptosis pathway. Interestingly, many of these pathological conditions are also associated with inflammation and higher myeloperoxidase (MPO) activity. However, the mechanistic link between caspase-3 and MPO activity is still unclear. Here, we examined whether hypochlorous acid (HOCl), exogenously added, or generated by MPO/chloride/hydrogen peroxide (H_2O_2) system can modulate the caspase-3 activity both including in mice oocyte.

METHODS: Acetyl-Asp-Glu-Val-Asp p-nitroanilide was used as a chromogenic substrate for caspase-3 by following the increase in absorbance at 405 nm, 25°C, pH 7.0. Addition of dithiothreitol (DTT) was used to monitor recovery of caspase-3 activity. Metaphase II cumulus oocytes (n=160) were exposed to 0, 10, and 100 μM HOCl for 30 minutes. Apoptosis kit (ApopTag Fluorescein In Situ Apoptosis Detection Kit) was utilized to detect HOCl-mediated apoptosis. The apoptosis signal was detected using confocal microscopy using DAPI, Alexa Flour 488 (green) with emission wavelength of 358 and 461mm, 596 and 613 nm respectively.

RESULTS: Caspase-3 activity showed a dose dependent decrease with a complete loss of activity at ~7 μM HOCl. Subsequent addition of DTT caused a complete or partial recovery of caspase-3 activity, for the sample treated with 10 or 50 μM of HOCl, respectively, indicating that the inactivation involved the oxidation of the Cys-thiol group in its active site. Accumulation of HOCl generated by MPO in the presence of caspase-3 not only inhibits caspase-3, but also inhibits MPO. Plotting the remaining activity of both caspase-3 and MPO as a function of increasing H_2O_2 concentration showed specificity of lower HOCl concentrations to the inhibition of caspase-3. Treatment of metaphase-II mouse oocytes with 100 μM of HOCl showed apoptosis as compared to no apoptosis in control oocytes or those treated with 10 μM of HOCl, however through mitochondrial damage and not through caspase-3.

CONCLUSIONS: MPO generated HOCl modulates caspase-3 activity through a reversible post-translational modification of the protease, and may play an important physiological role in regulating apoptosis. Potential therapeutic targets can be developed to target and inhibit HOCl to prevent this inhibition.

T-197

Body Mass Index Modulates Anti-Mullerian Hormone Response After Ovarian Stimulation Treatment. Sanne B Overdijkink†,[1] Maria PH Koster,[1] Esther B Baart,[1] Fatima Hammiche,[1] Joop SE Laven,[1] Regine PM Steegers-Theunissen*.[1,2] *[1]Erasmus MC, University Medical Center, Rotterdam, Netherlands; [2]Erasmus MC, University Medical Center, Rotterdam, Netherlands.*

INTRODUCTION: During in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI) treatment, efforts are being made to obtain the highest amount of qualitative oocytes. We hypothesize that poor nutritional status, in particular low folate intake and high body mass index (BMI), may cause hypomethylation of the Anti-Mullerian hormone (AMH) gene resulting in increased expression and ovulatory dysfunction. The aim of this study was to investigate whether BMI is associated with AMH levels in women undergoing IVF/ICSI treatment.

METHODS: We included 163 women who underwent IVF/ICSI treatment. Blood samples were taken at cycle day 2 (CD2) prior to ovarian hyperstimulation treatment and on the day of human chorionic gonadotropin administration (HCG day). Serum AMH and red blood cell (RBC) folate levels, as measure of long-term folate status, were determined at both time points. BMI on CD2 was categorized as lean (BMI<25) or overweight (BMI≥25).We used linear regression analysis to assess the association between BMI and log-transformed AMH levels, while adjusting for age and RBC folate levels on CD2. For the associations with AMH levels at HCG day, we additionally adjusted for baseline AMH (at CD2).

RESULTS: At CD2 and HCG day, mean serum AMH was higher in overweight compared with lean women (5,9 vs. 5,3 μg/L;p=0,157 and 4,3 vs. 3,3 μg/L;p= 0,048, respectively)(figure).

**Figure(s) will be available online.*

RBC folate on CD2 was significantly lower in overweight compared with lean women (1435 vs. 1057 nmol/l; p=0.01). After adjusting for potential confounders, BMI was positively associated with AMH at HCG day (β=0.28 95%CI=0.04-0.52); p=0.02), but not at CD2.

CONCLUSIONS: Overweight women undergoing IVF/ICSI treatment have higher AMH levels before, but especially after ovarian

hyperstimulation treatment compared with lean women, implying that BMI affects AMH response. These results suggest AMH is not only a marker for the oocyte reserve, but can also be considered a marker of excessive oxidative stress induced by a poor nutritional status.

T-198

The Impact of Race and Ethnicity on Infertility Diagnosis Among Haitians, African Americans, and Caucasians Seeking Infertility Care. Roxane Handal-Orefice†, Melissa Pritchard†, Joseph Politch, Wendy Kuohung*. *Boston University School of Medicine, Boston, MA, USA.*

INTRODUCTION: Several studies have examined the impact of race on infertility diagnosis and treatment outcomes, but few have looked at different ethnicities/nationalities within a given race. Boston Medical Center, an urban safety-net hospital with a large Haitian and African American patient population, is uniquely positioned to address the impact of ethnicity within race on fertility diagnosis. We hypothesized that etiology of infertility would differ between Haitians and African Americans although both groups share the same race, and also from Caucasian women seeking infertility care.

METHODS: We conducted a retrospective chart review of all Haitian, black American, and white American women seeking infertility care at BMC between January 2005 and July 2015. The ICD-9 diagnoses of infertility (including subgroups) and PCOS were used to select the cohort of patients using our clinical database. Infertility diagnoses were assigned as determined by a combination of physician reports, clinical history, and fertility testing of each patient. The data was stratified by race-ethnicity as determined by place of birth and language in order to evaluate the different etiologies of infertility among white Americans, black Americans, and Haitian women seeking infertility treatment. The data was analyzed in STATA using t-tests and ANOVA analyses.

RESULTS: A total of 560 charts were reviewed. Infertility was confirmed in 99 black American, 111 Haitian, and 87 white American women. Black American women had a higher frequency of infertility due to anovulation/PCOS (56.6%) compared to Haitian women (26.1%, $P<0.05$). Whites had a significantly lower frequency of tubal factor (6.9%) than either American blacks (18.2%) or Haitians (25.2%, $P<0.05$). Haitians had a significantly higher frequency of uterine factor (20.7%) than either American blacks (7.1%) or whites (9.2%, $P<0.05$). In Haitian women, infertility was multifactorial, with anovulation (26%), tubal factor (25%), and uterine factor (21%) contributing almost equally to their infertility.

CONCLUSIONS: Etiology of infertility differs among different ethnicities within a race as well as among races. Studies examining infertility causes and outcomes in different races need to specify ethnicity/nationality as well as this may affect study results.

T-199

An Updated Meta-Analysis Evaluating the Effect of Progesterone (P) Luteal Support on Live Birth After Ovulation Induction (OI) and Intrauterine Insemination (IUI). Katherine A Green†,[1] Jessica R Zolton†,[1] Sophia MV Schermerhorn†,[2] Alan H DeCherney,[1] Micah J Hill*.[1,3] *[1]Eunice Kennedy Shriver, NICHD, NIH, Bethesda, MD, USA; [2]Uniformed Services University of the Health Sciences, Bethesda, MD, USA; [3]Walter Reed National Military Medical Center, Bethesda, MD, USA.*

INTRODUCTION: P luteal support after OI/IUI is controversial due to conflicting literature. Our previous meta-analysis of randomized control trials (RCTs) suggested higher pregnancy and live birth rates with P support only in gonadotropin (GND) induced cycles, but was limited to just 2 RCTs utilizing GNDs. With 5 new published RCTs on luteal support in OI/IUI cycles, the goal of this study was to expand the sample size and update the meta-analysis with these recent publications.

METHODS: A systematic review of PubMed and Embase literature searches was conducted for RCTs evaluating P support after OI/IUI. OI was completed with clomiphene citrate (CC), GNDs, or CC plus GNDs. All studies used vaginal routes of P luteal support. Outcomes included clinical pregnancy rate (CPR) and live birth rate (LBR). The meta-analysis was completed on a per-patient, intent-to-treat basis. Random effects models were used for combining studies with clinical heterogeneity or I^2 >25%; otherwise, fixed effects models were used.

RESULTS: Ten trials were identified that met inclusion criteria, providing 2,434 and 1,027 patients for the analysis of CPR and LBR, respectively. Over all types of OI medications, patients who received P support had a higher CPR (RR 1.37, 95% CI 1.14-1.66) and LBR (RR 1.56, 95% CI 1.11-2.2) compared to those without P support. A sub-group analysis revealed that this effect persisted only in patients undergoing OI with GNDs (CPR: RR 1.67, 95% CI 1.24-2.24, and LBR: RR 1.63, 95% CI 1.13-2.34). In GND cycles, live birth increased from 10% to 16% with P support, an absolute increase in 6% per cycle with a NNT of 16 patients for 1 additional live birth. There was no difference in the likelihood of pregnancy for patients undergoing OI with CC alone or CC plus GNDs.

CONCLUSIONS: Level I RCT data demonstrate that P luteal support improves both clinical pregnancy and live birth rates in patients undergoing OI with gonadotropins. These data strengthen the concept that there may be physiologic differences in luteal function after OI with gonadotropins compared to CC and that the former group may benefit from P supplementation.

T-200

Can Embryo Transfer Simulation Improve the Learning Curve for REI Fellow Training? Justin D Pilgrim†,[1,2] Micah J Hill,[2] James H Segars,[3] Alan H DeCherney,[1] Ryan J Heitman*.[5] *[1]NICHD, Bethesda, MD, USA; [2]Walter Reed, Bethesda, MD, USA; [3]Johns Hopkins, Baltimore, MD, USA; [4]Madigan, Tacoma, WA, USA.*

INTRODUCTION: Medical simulation training has become ubiquitous throughout OBGYN residency training. Simulation training has demonstrated improved outcomes in obstetrical emergency and gynecologic surgical training. ASRM has developed a high-fidelity embryo transfer trainer. In 2014, we developed a low cost embryo transfer (ET) simulation trainer, which our prior studies suggest accurately mirrors the feel and technique of TVUS guided embryo transfer. Our objective was to compare the pregnancy rate of fellows trained on the ET simulator versus fellows prior to the ET simulator.

METHODS: A retrospective analysis of pregnancy rates of fellows in the 2 years pre-simulator (2012-2013) versus those trained on the ET simulator (2014-2015). The primary outcome was pregnancy, defined as an elevated serum quantitative hCG, as events post-implantation were not considered to be affected by the ET technique. Individual fellow pregnancy rates and collective pregnancy rates were calculated and the learning curve for embryo transfer was calculated on individual and collective rates per increments of 10 ETs. Fellows were considered proficient when pregnancy rates exceeded 40% per transfer. Both groups of fellows were required to have 30 real patient "mock" transfers prior to live ET.

RESULTS: A total of 12 REI fellows were analyzed, 6 pre-ET trainer and 6 post-ET trainer. Pregnancy rates were 31% in the initial 10 ET per fellow pre- simulator versus 46% post-simulator (P=0.03). 0/6 fellows had pre-trainer pregnancy rates >40% in their first 10 ET (Table 1); whereas, 4/6 fellows had pregnancy rates >40% in their first 10 post-trainer ETs. The average number of ETs to obtain >40% pregnancy efficiency was 27 ETs pre-trainer versus 15 ETs post-trainer (P=0.03). Pregnancy rates were similar in the two groups after 20 ETs and eventually collective terminal pregnancy rates were >50% after 40 ETs.

CONCLUSIONS: Embryo transfer simulation improved REI fellow pregnancy rates in their first ten transfers and lead to a more rapid ET proficiency compared to fellows no trained with the simulator. These data suggest value in adopting ET simulation, even in programs with a robust history of live ET in fellowship training.

T-201

Ectopic Pregnancy Rate Does Not Correlate with the Number of Retrieved Oocytes or Estradiol Levels in Fresh Autologous IVF Cycles. Mohamad Irani†, Vinay Gunnala†, Zev Rosenwaks, Steven D Spandorfer*. *Weill Cornell Medicine, New York, NY, USA.*

INTRODUCTION: It has been suggested that increased oocyte yield and the supraphysiologic hormone levels may increase the rate of ectopic pregnancy (EP) in autologous IVF cycles. In the present study, we aim to determine whether oocyte yield and peak estradiol levels correlate with the incidence of EP in IVF.

METHODS: It is a case-control study. Patients who achieved pregnancy following autologous fresh IVF cycles between January 2004 and May 2013 were included. Exclusion criteria were the following: Patients achieving biochemical pregnancy, history of tubal disease, and previous ectopic pregnancy. Group A includes patients who had an ectopic pregnancy, whereas group B encompasses patients who had an intrauterine pregnancy following autologous fresh IVF. A sample size of 1248 (78 in group A and 1170 in group B) was deemed necessary to detect a difference of 2 retrieved oocytes with 5% level of significance and 80% power. Values were expressed as mean ± SEM. χ^2 test, t-test, and Fisher's exact test were used as appropriate.
RESULTS: A total of 7671 patients who achieved pregnancy following autologous fresh IVF cycle were included. 110 patients (1.4%) had an ectopic pregnancy. There was no significant difference in the number of retrieved oocytes (12.4 ± 0.5 vs. 11.7 ± 0.1; p=0.2) or peak estradiol level (1760 ± 71 vs. 1709 ± 8.9 pg/mL; p=0.4) between group A (n=110) and group B (n=7561) respectively. There was no significant difference in the number of stimulation days (9.5 ± 0.1 vs. 9.6 ± 0.1; p=0.4), total dose of gonadotropins (3245 ± 165 vs. 3018 ± 32 IU; p=0.39), number of fertilized oocytes (7.2 ± 0.3 vs. 7.1 ± 0.1; p=0.9), number of transferred embryos (2.9 ± 0.1 vs. 2.8 ± 0.1; p=0.9), day of embryo transfer (15.4% vs 15.4% were day 5; p=0.9), or endometrial thickness on the day of trigger (10.1 ± 0.7 vs. 10.5 ± 0.1 mm; p=0.7) between group A and group B respectively. Patients in group A had comparable BMI (23.7 ± 0.4 vs. 23.6 ± 0.1 kg/m^2, respectively; p=0.9, respectively) and age at retrieval (36.4 ± 0.3 vs. 36 ± 0.1 years, respectively; p=0.34) to patients in group B.
CONCLUSIONS: Contrary to previously published reports, the number of retrieved oocytes and estradiol levels do not appear to be associated with an increase in the rate of ectopic pregnancy in women undergoing fresh IVF cycles.

T-202

Characterization of Embryo-Derived Exosomal miRNAs: Implications on Endometrial Receptivity. Hayden Homer,[1] Anusch Yazdani,[1] Gregory E Rice,[1,2] Carlos Salomon*.[1,2] [1]*The University of Queensland, Brisbane, QLD, Australia;* [2]*Ochsner Baptist Hospital, New Orleans, LA, USA.*
INTRODUCTION: Approaches for non-invasive embryo selection would be a major advance that would increase efficiency and reduce both cost and risks associated with Assisted Reproductive Treatments. Exosomes are a particular subtype of extracellular vesicles (EVs) that are secreted from a wide range of cells, including placental and endometrium cells. The aim of this study was to characterize the exosomes and their miRNA content in embryo-conditioned media.
METHODS: Embryo-conditioned (ECCM) used to culture embryos was obtained from the Queensland Fertility Group *In-vitro* fertilization embryology laboratory. Exosomes were characterised using electron microscopy, western blot (CD63 and TSG101), and size distribution (NanoSight). Total exosomal RNA was isolated by miRNAeasy (Qiagen) according to manufacturer's' instructions. Illumina TrueSeq Small RNA kit was used to construct a small RNA library. The resulting sequencing FASTQ file was analysed using miRDeep2, a program specifically designed to identify both known and novel microRNA's. Gene target identification for miRNAs was performed using the CyTargetLinker application in Cytoscape. A total of 3 miRNA gene target databases (MicroCosm, miRTarBase and TargetScan) were allocated to Cytoscape for analysis.
RESULTS: The exosome fractions displayed particle sizes ranging from 30 to 150 nm in diameter (with mean of 89 ± 58 nm). The presence of exosomal markers CD63 and TSG101 was confirmed. A total of 207 miRNA were identified in exosomes. The top 20 high abundance miRNA were: hsa-miR-22-3p, hsa-miR-21-5p, hsa-miR-143-3p, hsa-miR-10b-5p, hsa-miR-10a-5p, hsa-miR-221-3p, hsa-let-7i-5p, hsa-miR-27b-3p, hsa-let-7f-5p, hsa-let-7a-5p, hsa-miR199a-3p, hsa-miR-199b-3p, hsa-miR-181a-5p, hsa-miR-423-5p, hsa-miR-26a-5p, hsa-miR-3168, hsa-miR-100-5p, hsa-miR-30a-5p, hsa-miR-21-3p and hsa-miR-424-5p. A total of 240 genes were identified to be regulated by at least two of the top 20 miRNAs, and are detected within at least two miRNA-gene target databases.
CONCLUSIONS: We suggest that exosomes released by the embryo may be used to identify a predictive biomarker from spent media, and therefore, at no risk to the embryo, would be a powerful non-invasive innovation.

T-203

Intra-Follicular C-Type Natriuretic Peptide (CNP) Levels: New Biomarker of Follicle Growth and Gamete Maturation in Humans. Julia A Dias†,[1] Cynthia Dela Cruz,[1] Luiza C Lima†,[1] Maíra Casalechi†,[1] Maria T Pereira†,[1] Inês K Cavallo†,[1] Adelina M Reis,[2] Fernando M Reis*.[1] [1]*Universidade Federal de Minas Gerais, Belo Horizonte, MG, Brazil;* [2]*Universidade Federal de Minas Gerais, Belo Horizonte, MG, Brazil.*
INTRODUCTION: C-type natriuretic peptide (CNP) is a member of the natriuretic peptide family that binds to the cell membrane receptor NPR2 and signals through the second messenger cGMP. Previous studies in mice suggested that CNP stimulates preantral and antral follicle growth but inhibits meiotic resumption of oocytes. Preliminary data in humans have suggested that ovarian CNP levels may decrease after the preovulatory LH surge. Despite the compelling evidence from mouse studies that CNP is a key paracrine regulator of oocyte maturation, its correlation with ovulation induction in humans is unknown.
METHODS: Following IRB approval and written informed consent, follicular fluid samples were collected prospectively from 46 women during oocyte retrieval for in vitro fertilization. All samples were immediately mixed with a protease inhibitor cocktail, chilled in ice, centrifuged at 4°C and stored at -80°C. CNP levels were measured by enzyme immunoassay. The assay sensitivity is 0.01 ng/ml and there is no cross-reaction with other natriuretic peptides. Data were analyzed with Spearman's rank correlation coefficient.
RESULTS: CNP was detectable in all follicular fluid samples, at concentrations ranging from 0.07 to 0.47 ng/ml. CNP levels correlated directly with the number of preovulatory follicles ($r = 0.361$, $p = 0.016$) and the number of oocytes retrieved ($r = 0.371$, $p = 0.013$) and inversely with the proportion of mature oocytes at metaphase II ($r = 0.386$, $p = 0.035$). **Figure(s) will be available online.*
CONCLUSIONS: The present results indicate that intra-follicular CNP is a novel biomarker of ovarian response to gonadotropin stimulation and oocyte maturation in humans. Moreover, these findings corroborate the experimental evidence for a critical role of CNP in the paracrine stimulation of follicle growth, while protecting oocytes from early meiotic resumption.

T-204

Embryo Euploidy in Relation to Morphology, Embryo Sex, and Birth Outcomes. Ange Wang†, Jonathan Kort†, Lynn Westphal*. *Stanford University School of Medicine, Stanford, CA, USA.*
INTRODUCTION: Few studies have investigated whether morphological parameters are associated with embryo ploidy. The aim of this research was to assess the relationship of both embryo morphology and embryo sex with embryo ploidy, and to investigate birth outcomes from transfer of euploid blastocysts.
METHODS: This is a retrospective cohort study of patients who underwent in vitro fertilization with preimplantation genetic screening on day 5/6, at an academic medical center from 2010-2015. Using a multivariate logistic regression model, we studied euploidy rates in relation to morphological parameters, embryo sex, biopsy day, and blastocyst cohort size. Among euploid embryos transferred, we used separate logistic regression models to investigate morphological parameters in relation to positive hCG, clinical pregnancy, and live birth.
RESULTS: A total of 1,559 embryos from 316 cycles and 233 patients (mean maternal age = 37.8 +/- 4.2 years) were included in the analysis. Six hundred and twenty-eight blastocysts (40.3%) were found to be euploid. Expansion, inner cell mass (ICM), and trophectoderm grade were significantly associated with embryo ploidy in bivariate models controlling for maternal age, while embryo sex, biopsy day, and blastocyst cohort size were not associated with embryo ploidy. In a multivariate logistic regression model incorporating all the significant parameters, maternal age, higher grade of expansion, and better quality trophectoderm remained significantly associated with increased embryo euploidy, but ICM grade

was no longer significant. Blastocyst sex was not associated with maternal age, expansion, or ICM in a multivariate model, though male embryos were found to be associated with higher trophectoderm scores. A total of 103 euploid blastocysts were transferred on day 6 after day 5 PGS. Among these euploid transfers, morphological parameters, embryo sex, and maternal age were not associated with pregnancy and birth outcomes (positive hCG, clinical pregnancy, and live birth) in univariate logistic regression models.

CONCLUSIONS: To our best knowledge, this is the first study to examine morphology and embryo sex in relation to birth outcomes for euploid embryos. Our findings suggest that while maternal age and some morphological parameters (expansion, trophectoderm grade) are associated with euploidy, transfer of euploid embryos results in similar pregnancy and live birth rates regardless of morphological parameters, embryo sex, or maternal age.

T-205

No Increased Cardiovascular Disease Risk in Women with High Postmenopausal Androgen Levels: The Rotterdam Study. Cindy Meun†,[1] Oscar H Franco,[2] Klodian Dhana,[2] Loes Jaspers,[2] Taulant Muka,[2] Bart CJ Fauser,[3] Maryam Kavousi,[2] Joop SE Laven*.[1] *[1]Erasmus University Medical Centre, Rotterdam, Zuid-Holland, Netherlands; [2]Erasmus University Medical Centre, Rotterdam, Zuid-Holland, Netherlands; [3]University Medical Centre, Utrecht, Netherlands.*

INTRODUCTION: Polycystic ovary syndrome (PCOS) is the most common cause of hyperandrogenism (HA). In PCOS, HA seems to be particularly associated with metabolic disturbances that potentially increase the risk for cardiovascular disease (CVD) later in life. However, currently the association between PCOS and cardiovascular disease is unclear. We aim to assess the association between high androgen serum levels during postmenopausal life and the risk for atherosclerosis and CVD.

METHODS: 2784 women aged >55, included in the Rotterdam Study, were assessed and divided into tertiles based on testosterone, sex hormone binding globulin, dehydroepiandrosterone and androstenedione serum concentrations. Cox regression was used to assess the association between high androgen levels and coronary heart disease, heart failure and stroke. Moreover, logistic and linear regression were used to assess the relationship between high hormone levels and coronary artery calcium score, carotid intima media thickness and the prevalence of atherosclerotic carotid plaque.

RESULTS: A high free androgen index (FAI: Testosterone X 100 / SHBG)) is associated with a lower risk for atherosclerotic cardiovascular disease [HR (95%CI): 0.759 (0.590-0.976)]. High DHEA and androstenedione levels are associated with a lesser carotid intima media thickness; [β (95%CI): -0.007 (-0.013 ; -0.001)] and [β (95%CI): -0.006 (-0.012 ; -0.001]. High levels of DHEA were also associated with a lower coronary artery calcium score [β (95%CI): -0.258 (-0.379 ; -0.136].

CONCLUSIONS: Persistent postmenopausal hyperandrogenism is not associated with an increased risk for CVD. Moreover, high levels of the free androgen index after menopause seem to protect women from atherosclerotic cardiovascular disease.

T-206

Patient-Provider Communication Around Menopause-Related Symptoms and Quality of Life. Timothy DV Dye,[1] Margaret Demment,[1] Christopher Morley,[2] Miriam Weber,[1] Ollivier Hyrien,[3] Ivelisse Rivera,[1] Morgan Pratt,[2] James Woods*.[1] *[1]University of Rochester, Rochester, NY, USA; [2]SUNY Upstate Medical University, Syracuse, NY, USA; [3]University of Rochester, Rochester, NY, USA.*

INTRODUCTION: A substantial care gap exists in women's experiences of menopause-related symptoms (MRS) and treatment for those symptoms. The range of symptoms, their sometimes non-specific, ambiguous manifestation, and stigma all contribute to this gap. Reducing this gap requires improved communication between patients and providers around MRS, for which women may be reluctant to mention and providers reluctant to ask. This study describes the experience of a sample of women at the menopause transition in discussing MRS with providers.

METHODS: A total of 82 non-pregnant women age 45-64 without past surgical history of oophorectomy or history of breast/endometrial cancer were invited via EPIC's MyChart messaging to join a study examining patient-provider communication around menopause. Women were administered the Greene Climacteric Scale (GCS) and the Utian Quality of Life Questionnaire (UQOL), and were also asked if they had spoken with their providers about their menopause-related quality of life (mQOL) and their MRS. Bivariate mean component quality of life scores were compared by whether or not the woman had spoken with the provider about MRS or mQOL.

RESULTS: Overall, 56.1% of women discussed MRS with their providers, and 51.2% discussed mQOL. None of the UQOL and GCS component scores significantly related to discussing MRS. Only the GCS Depression score was statistically significantly associated, with women with worse depression symptomatology more likely to discuss mQOL with providers ($p<.01$). The only specific symptom significantly associated with talking with providers about MRS was sweating at night ($p<.01$) though a range of individual specific items relating to mood and vasomotor symptoms were significantly associated with talking with provider about mQOL.

CONCLUSIONS: With the exception of depression, women experiencing MRS and diminished mQOL were not more likely to discuss their experience with providers than their less-symptomatic counterparts. Interventions are necessary to help improve patient-provider communication around women's experience of MRS and mQOL to help reduce the treatment gap and improve well-being during menopause specifically related to initiating conversations around MRS.

Support: Pfizer Independent Grants for Learning & Change (IGLC).

T-207

Ovarian Stimulation Is Safe and Effective in Many Patients with GYN Malignancies. Mary Ellen Pavone*,[1] Molly B Moravek,[2] Rafael Confino,[1] Susan C Klock,[1] Angela K Lawson,[1] Kristin N Smith.[1] *[1]Northwestern University, Chicago, IL, USA; [2]University of Michigan, Ann Arbor, MI, USA.*

INTRODUCTION: It is estimated that 21% of gynecologic cancers affect women in the reproductive age group. Standard treatment for many gynecologic cancers often includes removal of the ovary and/or uterus. For these reproductive aged women diagnosed with these cancers, fertility preservation may be of upmost importance. The safely and efficacy of ovarian stimulation for oocyte or embryo cryopreservation within this group of women is largely unknown.

METHODS: This is a retrospective cohort study of all women diagnosed with primary GYN malignancies or malignancies with metastasis to the reproductive tract who contacted the fertility preservation patient navigator to discuss fertility preservation options. Patients were then divided into 2 groups: those who chose to undergo ovarian stimulation and those who did not. Demographics were obtained on all patients, as well as IVF cycle outcomes, time to next treatment, cancer recurrence and mortality.

RESULTS: 67 patients contacted the fertility preservation patient navigator, of which 22 underwent ovarian stimulation and 45 did not. Average age and type of cancer was not significantly different between the groups. Number of days to next cancer treatment in the ovarian stimulation group was 49d, while in the no stimulation group it was 21d ($p=0.36$, NS). There were a total of 2 deaths, 1 in the stimulation group, and 1 in the no stimulation group. The patients who underwent stimulation had a rage of 3-25 oocytes retrieved. No patients in the stimulation group were cancelled because of failure to respond. There were no procedure related complications.

CONCLUSIONS: Time to next treatment was not statistically different between our groups. It appears that in selected patients with GYN malignancies, ovarian stimulation for oocyte or embryo cryopreservation is safe, with reasonable stimulation outcomes and no difference in long term outcomes.

T-208

Characteristics and Experiences of Women Who Have Undergone Oocyte Cryopreservation at an Academic Center. Sanaa H Suharwardy†, Meera Shah†, Lynn M Westphal*. *Department of OB/GYN, Palo Alto, CA, USA.*

INTRODUCTION: Fertility preservation with oocyte cryopreservation is increasingly used to help circumvent reproductive aging for both medical and elective indications. However, little is known about patient motivation, knowledge or attitudes toward oocyte cryopreservation, or reproductive outcomes of women who pursued this treatment.

METHODS: We administrated a secure, confidential online survey to women who underwent oocyte cryopreservation at a single academic institution from 1999 to 2016 and performed a retrospective chart review of women who returned to use their frozen oocytes.

RESULTS: To date, 93 patients have completed the survey. The average age of patients undergoing oocyte cryopreservation and completing the survey was 35.4 and 38.7 years, respectively. Most women were Caucasian (58%), single (70.5%), and chose to undergo fertility preservation because they were not in a relationship (60%), while 14% reported delaying childbearing for professional reasons. On average, patients spent $10,466 per cycle and 41% reported this as a moderate to significant financial burden requiring financial sacrifice. At our institution, 424 patients have undergone oocyte cryopreservation, of which 18 patients (4%) have come back to use their frozen oocytes. Among women who returned to use their frozen oocytes, 28% used donor sperm due to lack of a partner. In patients who underwent an embryo transfer, the live birth rate was 31% (5/16). Among women who completed the survey, 21% spontaneously conceived after undergoing oocyte cryopreservation. Of the patients who have not tried to conceive, nearly 50% cite the lack of a suitable partner, while 25% cite career/personal goals as the rationale for not yet starting a family. Most women were well informed about the risks of pregnancy at an advanced maternal age and stated they would only consider using their oocytes up to age 43. Nearly all, 93%, of women were happy with their decision and would do it again.

CONCLUSIONS: Patient survey responses provide insights into motivations and attitudes about fertility preservation. A significant financial burden is a concern for women pursuing fertility preservation, supporting the importance of advocating for increased insurance coverage. Few women have returned to use their oocytes, primarily due to a lack of a partner; however, donor sperm appears to be a viable and well-used option for women who are ready to begin family building.

T-209

Mesenchymal Stem Cells Derived from the Human Placenta (PMSCs) Express Neuronal Stem/Progenitor Markers Nestin and SOX2, and Could Differentiate into Neuronal Cells In Vivo. Yuping Wang*,[1] Yang Gu,[1] Xiaohong Lu,[2] David F Lewis.[1] *[1]LSUHSC-Shreveport, Shreveport, LA, USA; [2]LSUHSC-Shreveport, Shreveport, LA, USA.*

INTRODUCTION: Mesenchymal stem cells (MSCs) are the most widely employed for cell therapy due to their renowned regenerative and immune-regulatory properties. Placental is the richest source of MSCs in the human tissues. In this study, we aimed to investigate neurogenic property of placenta-derived MSCs (PMSCs) to test the hypothesis that PMSCs could differentiate into neuronal lineage cells.

METHODS: Fresh placentas were collected immediately after delivery from normal term pregnancies. MSCs were isolated by enzymatically digestion of placental villous tissues with trypsin and DNAse. PMSCs were characterized by flow cytometry and immunofluorescent staining using antibodies specifically for MSCs, stem/progenitor cells, and neuronal progenitor cells. To test PMSC neurogenic differentiation potential, cells were transfected with AAV-GFP, and GFP-labeled PMSCs were implanted into mouse brain. C57BL/6J mice were used. Euthanasia was performed 4 weeks after PMSC transplantation. Brain tissue was fixed and sectioned. GFP-positive PMSCs were then evaluated under confocal microscopy.

RESULTS: PMSCs not only expressed MSC markers such as CD73 and CD90, stem cell/progenitor cell markers such as CD133 and Oct-4, but also expressed neural stem/progenitor cell markers nestin, SOX2, and vimentin, and astrocyte progenitor cell marker CD44. Brain tissue section analysis showed that GFP positive cells were present in different brain regions including striatum, cortex and substantial nigra, etc. Moreover, some of engrafted PMSCs exhibited fully differentiated dendrites, axons and dendritic spines. We have transplanted GFP labeled PMSCs into brain tissue in C57BL/6J mouse with different ages, from young to aged, and have followed up to more than two months. No observable side effects such as limp or neural dysfunction were noticed and no death occurred in the study mice.

CONCLUSIONS: PMSCs exert neurogenic potential. These cells could migrate within the brain and have the ability to differentiate into neuronal lineage cells. It is expected that the neurogenic potential of PMSCs could make the placenta an important valuable source of MSCs in stem cell therapy and personalized medicine in the treatment of brain injury and neurodegenerative disorders.

T-210

Novel p63-Expressing Epithelial Cells from Normal Human Endometrium. Shaina Balayan,[1] Fatima Barragan,[1] Sahar Houshdaran,[1] Joseph Rabban,[2] Juan C Irwin,[1] Linda C Giudice*.[1] *[1]UCSF, San Francisco, CA, USA; [2]UCSF, San Francisco, CA, USA.*

INTRODUCTION: P63 is expressed by stem/progenitor populations in various epithelia. In adult uterus, p63 is expressed in ectocervical epithelium basal and suprabasal cells, endocervical subcolumnar reserve cells. In cycling endometrium p63 expression is restricted to scattered intraepithelial and periglandular cells whose physiological significance is currently unknown.

METHODS: Primary endometrial (EBX), endocervical (ECC), and ectocervical (CX) cultures were established on Matrigel with defined keratinocyte serum-free medium (KSFM). Total RNA was processed for whole genome microarray, including primary endometrial epithelial (eEC) and stromal fibroblast (eSF) cultures as controls. Data analysis included principal component analysis (PCA), hierarchical clustering, and differential expression (≥1.5-fold change, $p \leq 0.05$). EBX cultures were treated with small molecule inhibitors of TGFBR kinase, and gamma secretase.

RESULTS: Extended EBX primary culture resulted in emergence and selection of a rare but highly proliferative and migratory, morphologically distinct, epithelial cell population with a molecular phenotype distinct from epithelial cultures from endo- and ecto-cervix, and endometrial luminal/glandular cells. Compared to endometrial luminal/glandular cells, the novel cell population showed increased expression of p63 (*TP63*), and an epithelial-mesenchymal phenotype coexpressing vmentin and basal keratins (*KRT5, 6, 14*). TGB beta receptors (*TGFBR1, 2*), and Notch pathway (*NOTCH1, JAG1*) were prominent, but normal endometrial luminal/glandular genes (*KRT18*, *MUC1*, *MUC16* and *MMP7*) were downregulated. Immunolocalization showed nuclear p63, co-expression of cytoskeletal keratin 5 and vimentin, low/absent keratin 18, and no E-cadherin reactivity, in contrast to polarized endometrial luminal/glandular epithelial cultures. Inhibition of TGF beta signaling induced pericellular/junctional localization of E-cadherin, and Notch pathway inhibition increased expression of keratin 18.

CONCLUSIONS: p63-expressing cells from human endometrium have the potential to acquire in vitro discrete features of polarized endometrial epithelium through intervention of TGF beta and Notch signaling pathways, suggesting a potential role as a stem/progenitor pool and/or a pre-luminal/glandular epithelium transitional phenotype.

Support: NICHD/NIH NCTRI P50 HD 055764-09 (L.C.G.).

T-211

***In Vitro* Derivation of Precursor Granulosa Cells from Human Pluripotent Stem Cells.** Alisha M Truman†, Jonathan Tilly, Dori Woods. *Northeastern University, Boston, MA, USA.*

INTRODUCTION: Stem cell derived germ cells have been identified and offer new avenues for modeling the ovary, but an exogenous source of functional cells of the somatic lineage remains elusive. Pluripotent stem cells, capable of multi-lineage differentiation, posit a new and intriguing possibility for the generation of *in vitro* derived cells of granulosa-like

ovarian lineages. An exogenous source of steroid producing cells would provide therapeutic use in restoring the hypothalamic-pituitary-gonadal axis in individuals who have lost it and provide the critical somatic cell component to modeling ovarian cellular interactions *in vitro*. Here, we propose a model of directed differentiation in which we specify somatic precursor cells that are capable of proliferation and differentiation into pre-granulosa and granulosa-like cells *in vitro* and potentially *in vivo*.

METHODS: Human embryonic stem cells (WA09, WiCell) were maintained in feeder free conditions and subjected to 2-D directed differentiation. Cells were plated and treated with GSK3 inhibitor (GSK3i, CHIR99021, 10μM) to induce mesendodermal lineage via WNT signaling. Further treatment with fetal growth factor (bFGF, 100ng/ml) and retinoic acid (1μM) was utilized to induce cells of a gonadal/renal lineage, and subsequent treatment with Notch activators, Jagged 1 (1μg/ml), a ligand for notch receptors, and resveratrol (50μM), a compound shown to induce notch signaling, to increase the incidence of potential granulosa-like cells. Cells were subject to quantitative RT-PCR to assess gene expression throughout differentiation, with *FOXL2* serving as a marker for pre-granulosa cells.

RESULTS: Forty-eight hours of treatment with a GSK3i resulted in an average 521.9±11.2 -fold increase in brachyury expression at day two, indicating successful induction of mesendoderm lineage. Treatment with GSK3i followed by bFGF and retinoic acid resulted in a peak of *FOXL2* expression at 6 days of differentiation with maintained increased expression over controls after 10 days. Combined treatment with notch activation resulted in an increase in *Foxl2* expression peaking at day 6 with a 3.1-4.5 fold increase, respectively.

CONCLUSIONS: This strategy indicates that a step-wise differentiation from hESCs through mesoderm and notch activation can increase the production of putative pre-granulosa cells which can be isolated and used in *in vitro* studies and theoretically *in vivo*.

T-212

Intrauterine CXCL12 Therapy for Asherman's Syndrome. Gulcin Sahin Ersoy, Masoumeh Majidi Zolbin, Ramanaiah Mamillapalli, Irene Moridi, Hugh Taylor. *Yale School of Medicine, New Haven, CT, USA.*

INTRODUCTION: We have previously shown that delivery of bone marrow derived stem cells (BMDSCs) to mice improved reproductive performance in Asherman's Syndrome (AS). BMDCs express CXCR4 which modulates cell migration. We aimed to determine whether the migration of BMDSCs during endometrium repair is enhanced by CXCR4's ligand, stromal derived factor (SDF-1 or CXCL12) in AS resulting in improved reproductive performance.

METHODS: To assess the stem cell trafficking to AS, 8-weeks-old irradiated female C57BL/6J mice received unfractionated BM cells from mice expressing green fluorescent protein (GFP). Subsequently, AS (n=20) or a sham control (n=20) surgery was performed. Groups were divided and received one of 4 treatments: PBS, intrauterine CXCL12, subcutaneous AMD3100 or CXCL12 + AMD3100 injections. Uterine stem cell engraftment was measured by immunofluorescence. To eliminate the effect of the irradiation on uterine stem cell recruitment we also conducted the identical experiments on mice that were not irradiated. In addition, 45 non-irradiated mice were used to determine the pregnancy outcome.

RESULTS: After uterine injury we demonstrate that CXCL12 augmentation increased BMDSC engraftment and ADM3100, blocked stem cell recruitment

**Figure(s) will be available online.*

CXCL12 reduced, while AMD3100 increased fibrosis compared to AS induced mice (p=0.015 and p=0.042). Asherman's mice had smaller litters and took a longer time to conceive comparing to sham group (p=0.002 and p=0.012). CXCL12 treatment led to improved fertility and litter size while ADM3100 treatment reduced fertility and litter size

**Figure(s) will be available online.*

CONCLUSIONS: CXCL12 increased stem cell recruitment, improved fertility and increased litter size in mice with experimental AS. CXCL12 may be useful in the treatment of AS and other related uterine disorders.

F-001

Comparison of Latency Antibiotic regimen for Preterm Premature Rupture of Membranes. Juliana Sung†,[1] Angela Rugino,[3] Ann Lal,[2] Jean R Goodman.[2] *[1]Loyola University Medical Center, Maywood, IL, USA; [2]Loyola University Medical Center, Maywood, IL, USA; [3]Loyola University, Maywood, IL, USA.*

INTRODUCTION: The primary objective of the study is to determine if substituting azithromycin for erythromycin affects the latency period for patients admitted with PPROM.

METHODS: This retrospective cohort study was performed at Loyola University. Study participants were accrued through the medical record from October 2012 to February 2016. Inclusion criteria were: women admitted for PPROM at ≥ 24 weeks gestation and < 34 weeks gestation, received latency antibiotics, and were without signs of labor or infection. Exclusion criteria were administration of antibiotics other than those in the study groups, cerclage and known fetal genetic or congenital anomalies. Latency antibiotics were either ampicillin/amoxicillin + erythromycin, erythromycin group, or ampicillin/amoxicillin + azithromycin, azithromycin group. A policy change in PPROM antibiotic regimen was undertaken at our institution in November 2014, substituting azithromycin for erythromycin. Basic patient demographics were obtained. Outcome information was collected, including latency period, length of stay, gestational age at delivery and neonatal outcomes. Statistical analysis was performed using Excel and Open Epi. Chi square and t-test were used for categorical and continuous variables, respectively. $p<0.05$ was considered significant.

RESULTS: 46 patients were in the erythromycin group and 15 patients were in the azithromycin group. Patients in the azithromycin group were significantly younger; no other differences between the groups, including gestational age on admission, were noted. There were no differences between the groups in latency period, 5.8 days versus 7.9 days. There were no differences in the gestational age at delivery, 31.6 weeks versus 31.3 weeks. There were no differences in the rates of vaginal delivery, maternal length of stay, or infections. There were no differences in neonatal length of stay, sepsis or neonatal death.

CONCLUSIONS: We recommend the use of azithromycin with ampicillin/amoxicillin for patients admitted with PPROM.

F-002

Quantification of Exosomes in Cervico-Vaginal Fluid from Term and Preterm Pregnancies. Rachel M Tribe,[1] Vikash Mistry,[1] Vyjayanthi Kinhal,[2] Gregory Rice,[2,3] Carlos Palma,[2] Natasha L Hezelgrave,[1] Evonne C Chin-Smith,[1] Andrew H Shennan,[1] Carlos Salomon*.[2,3] *[1]King's College London, London, United Kingdom; [2]The University of Queensland, Brisbane, QLD, Australia; [3]Ochsner Baptist Hospital, New Orleans, LA, USA.*

INTRODUCTION: Exosomes are a subtype of extracellular vesicle released into extracellular compartments through exocytosis. Exosomes can contain a range of signalling molecules (including protein, microRNAs, mRNA and non-coding RNA) and influence the activity of neighbouring or distal cells. There is a growing interest into the signalling role of exosomes in pregnancy, but little is known of their presence or bioactivity in cervico-vaginal fluid (CVF). The aim of this study was to determine whether exosomes could be detected in CVF from low risk pregnant women and whether exosome abundance was altered in pregnancies associated with birth <37 weeks of gestation.

METHODS: A prospective cohort of pregnant women (n=80) provided cervico-vaginal fluid (between 11 and 20 weeks) and the pregnancy outcomes obtained. Exosomes were isolated from CVF by differential buoyant density gradient and characterized by nanoparticle tracking analysis (NTA) using The NanoSight NS500. A retrospective stratified study design was used to quantify exosomes present in CVF from normal (n=46, delivery >37 weeks) and PTB (n=34, delivery <37 weeks). Patients were also classified in low and high risk of PTB based on previous history of spontaneous preterm birth/PPROM/late miscarriage or cervical surgery.

RESULTS: NTA showed particles between 30-800 nm present in CVF of all groups. Interestingly, the the particles between 30-100 nm were significantly higher in all groups compared to <35nm and >125nm

particles. Exosomes were identified as spherical vesicles of ~100 nm and positive for proteins CD63, TSG101, and CD81. The number of total exosomes were ~-2-fold and 1.7-fold higher in low-risk and high risk women who had PTB compared to women classified as low risk who delivered after 37 weeks.
CONCLUSIONS: Exosomes are the predominant subtype of extracellular vesicles in CVF. We suggest that the quantification of exosomes and knowledge of the content may aid identification of women at risk of spontaneous PTB.

F-003

Expression of CPPED1 in Human Trophoblasts Is Associated with Timing of Term Birth. Antti M Haapalainen,[1,2] Minna K Karjalainen,[1,2] Steffen Ohlmeier,[3] Julia Anttonen,[1,2] Tomi A Määttä,[1,2] Annamari Salminen,[1,2] Mari Mahlman,[1,2] Ulrich Bergmann,[3] Kaarin Mäkikallio,[4,5] Marja Ojaniemi,[1,2] Mikko Hallman,[1,2] Mika Rämet.[1,2,6] *[1]University of Oulu, Oulu, Finland; [2]Oulu University Hospital, Oulu, Finland; [3]University of Oulu, Oulu, Finland; [4]Oulu University Hospital, Oulu, Finland; [5]Turku University Hospital, Turku, Finland; [6]University of Tampere, Tampere, Finland.*
INTRODUCTION: Understanding of timing of human parturition is incomplete. Therefore, we carried out proteomic analyses of full term placentas from uncomplicated pregnancies to identify protein signatures associated with the onset of spontaneous delivery.
METHODS: Protein and RNA were from the spontaneous and elective term placentas. For proteomics, two-dimensional difference gel electrophoresis with fluorescence dyes and MALDI-TOF/TOF mass spectrometry were used. The significant associations with spontaneous births were determined using Student's t-test or Mann-Whitney *U* test, as appropriate. Single-nucleotide polymorphisms (SNPs) located in the vicinity of the genes regulated in spontaneous term delivery were assessed for association with gestation age (GA) in 342 infants at term.
RESULTS: We show that the levels of ten proteins either increase or decrease at spontaneous labor, and additionally may localize within functional regions of placenta. One of them is newly characterized CPPED1 shown to involve in blocking cell cycle and suppressing tumor growth *via* PI3K/AKT1 signaling pathway. In our placental proteomics, the amount of CPPED1 decreased at spontaneous delivery. Additionally, two intronic single-nucleotide polymorphisms (SNPs) of *CPPED1* associated with the length of pregnancy ($p < 6.5 \times 10^{-4}$). Both of these suggested a role of CPPED1 in the initiation of the term delivery. Consequently, CPPED1 was shown to be regulated at the transcriptional level ($p = 0.6 \times 10^{-4}$) and located in the villous and extra villous trophoblast as well as in decidual trophoblast of human placenta. We did not see changes in the phosphorylation of AKT1 and FOXO1 of Pi3K/AKT1 pathway.
CONCLUSIONS: We postulate that the functions regulated by CPPED1 in trophoblasts at the choriodecidual interphase have a role in the induction of term labor, but independently of AKT1.

F-004

Placenta-Derived Exosomes Profile During Term and Preterm Birth: Understanding the Signal of Human Parturition. Christopher L Dixon,[1] Vyjayanthi Kinhal,[2] Carlos Palma,[2] Kechichian Talar,[1] Rheanna Urrabaz-Garza,[1] Carlos Salomon,[2] Ramkumar Menon*.[1] *[1]The University of Texas Medical Branch, Galveston, TX, USA; [2]The University of Queensland, Brisbane, Australia.*
INTRODUCTION: Despite decades of research, the mechanism responsible for human parturition remains elusive. Exosomes are membrane-bound nanovesicles that transport molecular signals between cells, and are released from a wide range of cells, including the human placenta and placental membranes. The aim of this study was to test the hypothesis that the exosomal profile present in maternal is associated with signal of human parturition.
METHODS: Plasma samples were collected from group 1: term not-in labor (TNIL); group 2: term in labor (TL), group 3: preterm premature rupture of membranes (pPROM); and group 4: preterm birth (PTB). Exosome were isolated by differential buoyant density centrifugation and characterised by morphology, enrich of exosomal proteins and size distribution by electron microscopy, western blot and nanoparticle tracking analysis, respectively. The exosomal protein profile was analysed by Liquid Chromatography (LC)/ Mass Spectrometry (MS) LC-MS/MS on a 5600 Triple TOF mass spectrometer (AB Sciex, Framingham, U.S.A.).
RESULTS: Exosomes were identified as spherical vesicles, with a typical cup-shape and diameters around of 100 nm and positive for enrich exosomal proteins CD63 and TSG101. We did not find different in the physical properties of isolated exosomes between the groups. The total number of exosomes (exosomes/ ml plasma) present in maternal circulation was significantly lower in PROM (4.5×10^{11}) compared to TNIL (5.6×10^{11}; $p<0.05$), TL (5.9×10^{11}) and PTB (6.2×10^{11}). Placental exosomes (PLAP+) were significantly higher (~4,5-fold) in PTB and TL compared to TNL and pPROM. MS/MS analysis identified over 200 different exosomal proteins involved in development, immune response, and cell-to-cell communication.
CONCLUSIONS: We postulate that homeostatic imbalances produced by exosomal signaling during gestation might disrupts the maintenance of pregnancy resulting in labor related changes.

F-005

Uterine Tissue Orientation and Stiffness Influence Cervical Tissue Stretch. M Perez†,[1] AR Westervelt†,[1] J Vink,[2] R Wapner,[2] G Gallos,[3] M House,[4] K Myers*.[1] *[1]Columbia University, New York, NY, USA; [2]CUMC, New York, NY, USA; [3]CUMC, New York, NY, USA; [4]Tufts Medical Center, Boston, MA, USA.*
INTRODUCTION: Uterine growth during pregnancy is associated with geometric heterogeneity and asymmetric uterine stretch, which have the potential to affect the mechanical load and stretch on the cervix. Using 3D finite element (FE) simulations, we sought to define how the uterine geometry and tissue mechanical properties influence the load and stretch of the cervix in pregnancy.
METHODS: We built a baseline FE model (Trelis 15.1) using measurements of uterine diameter and thickness, cervical diameter, length, and angle obtained from ultrasound scans (G8 Voluson E8) of a 35 y/o patient at 25 weeks gestation. The uterus and cervix were modeled as a Neo-Hookean elastic material, and the membranes as an Ogden material. Dimensions of the transverse inner diameter (ID), anterior-posterior ID, and longitudinal ID were varied. Simulations of uterine stiffness were run with baseline geometry using values derived from previously reported tissue mechanical tests. Intrauterine pressure (IUP) was applied at contraction magnitudes in all cases for comparative purposes, and then the cervical stretch at the internal os was evaluated.
RESULTS: For uterine orientations investigated, the percentage of cervical tissue stretch above a 1.05 threshold ranged from 44-61% (Fig. 1). With differing tissue stiffness, little difference can be seen in the cervical tissue stretch (Fig. 2).
**Figure(s) will be available online.*
CONCLUSIONS: While the percentage of internal os tissue stretch varied modestly across uterine orientations, the stretch distribution was influenced. The anatomical location of maximum cervical stretch shifts depending on uterine orientation. Little relationship was found between the uterine tissue stiffness and the internal os tissue stretch.

F-006

Leukocyte Invasion of the Labouring Uterus Is Upregulated by Leukocyte and Uterine Activation. Han Lee†, Xin Fang, David M Olson*. *University of Alberta, Edmonton, AB, Canada.*
INTRODUCTION: Leukocytes invade the uterus at delivery in all tested mammalian species. Our data has demonstrated that leukocyte migration to a standard chemotactic stimulus increases as the leukocytes are collected closer to term of pregnancy. We hypothesized that this phenomenon is due to increased sensitivity of leukocytes to a standard signal, and greater secretions of chemoattractant in the uterus or fetal membranes, as pregnancy advances. Our objective was to test this in both the mouse uterus and human fetal membranes. We also hypothesized that both mouse and human chemoattractants increase as gestation progresses.
METHODS: Peripheral blood was collected from pregnant women at multiple points from 30 weeks of gestational age to term not in labour

(TIL) and term in spontaneous labour (STL). Leukocytes were isolated using an erythrocyte aggregation agent. Fetal membranes of women were collected at TIL or STL, and whole mouse uterus was collected daily over the last 4d of gestation. Chemotactic factors were isolated via tissue homogenization and density centrifugation (each pooled samples, n = 6). In a modified Boyden chamber, leukocytes were migrated across a polycarbonate filter (3 μm pores) in response to these factors. Flow cytometry was used to characterize the number and phenotype of chemoattracted leukocytes. Multiplex analysis and real-time quantitative RT-PCR was used to measure the expression of known cytokines in the mouse uterus. Statistical analysis: one-way ANOVA, $P < 0.05$.

RESULTS: Human granulocytes from pregnant women exhibited greater migratory activity to both human and mouse chemoattractant as gestation increased ($n = 6$, $r = 0.36$, $P < 0.05$). Increased abundance of neutrophil chemoattractants (MIP-2, KC, G-CSF) and pro-inflammatory mediators (IL-1β, IL-6) were detected in mouse uterine extracts as labour progressed.

CONCLUSIONS: Granulocyte migration to a standard chemoattractant increased as gestation advanced. Increased secretion of local chemoattractants was evident in both human fetal membranes and in mouse uterine extracts. This system offers direction for studying the underlying mechanisms of leukocyte invasion, and a better understanding of leukocyte invasion of the uterus could ultimately lead to new diagnostic and therapeutic measures for those at risk for preterm birth.

F-007

A Novel Quantitative Framework for the Prioritization of sPTB Candidate Genes. Haley R Eidem†, Antonis Rokas*. *Vanderbilt University, Nashville, TN, USA.*

INTRODUCTION: Studies of a single data type lack power to identify genetic risk factors involved in spontaneous preterm birth (sPTB). Furthermore, such studies often impose hard thresholds on p-values, fold changes, and other variables, introducing bias and increasing the chance of missing potentially interesting genes. To facilitate the unbiased integration of heterogeneous omics data that better capture key sPTB genetic risk factors, we have developed a novel quantitative framework based on Harrington and Derringer's desirability functions for the prioritization of sPTB candidate genes.

METHODS: We employ user-driven multicriteria optimization desirability functions to translate key variables across studies and data types (e.g., p-value, fold change) into common [0, 1] scales and combine these scales via geometric mean to create an overall desirability index (DI) for the genes in each study. After ranking genes by DI within single data types, genes are again ranked across data types, allowing us to integrate genomic, transcriptomic, and epigenomic data from heterogeneous sPTB studies and identify the most desirable candidate genes.

RESULTS: We created a software program, integRATE, that enables automated prioritization of sPTB candidate genes using heterogeneous data types obtained directly from GEneSTATION (http://genestation.org), our database of sPTB omics data, and/or uploaded by the user. integRATE also allows for the intersection of relevant biological data including tissue specificity and gene coexpression networks. To test the validity of our integRATE software and desirability-based approach, we interrogated 6 sPTB studies (2 RNA-seq, 2 microarray, 1 proteomics, 1 tissue specificity), resulting in the generation of numerous sPTB candidate genes. Among the candidates with the highest overall DI were *IGF2BP3* (an insulin-like growth factor binding protein), *IL1RL1* (an interleukin receptor), *PEG10* (a maternally imprinted gene), and *PAPPA2* (a pregnancy-associated metalloproteinase).

CONCLUSIONS: Our novel quantitative framework and software, integRATE, allows for the prioritization of promising sPTB candidate genes as targets for further functional analysis and streamlines the integration of complex omics data types. This work is supported by the March of Dimes Prematurity Research Center Ohio Collaborative Transdisciplinary Scholar program.

F-008

Potential Role for Cytokines in Adverse Pregnancy Outcomes (APOs) in a Rat 2-Hit Stress Model. Barbara SE Verstraeten†,[1,2] J Keiko McCreary†,[3] Hans Verstraelen,[2] Gerlinde AS Metz,[3] David M Olson*.[1,4] *[1]U Alberta, Edmonton, AB, Canada; [2]Ghent U, Ghent, Belgium; [3]U Lethbridge, Lethbridge, AB, Canada; [4]U Alberta, Edmonton, AB, Canada.*

INTRODUCTION: Maternal stress and inflammatory mediators interact to affect the birth process. In our 2-hit stress model parental (F0) dams receive both psychological and inflammatory stressors in late gestation. Together, but not alone, they increase APOs, mainly preterm birth. Since stress effects are transgenerational, **we hypothesize** that, in uteri of F0 rats and their F1 offspring, two prenatal stress hits increase the mRNA abundance of Interleukin (Il)*1a*, *Il1b*, IL-1 receptor antagonist (*Il1rn*), *Il6* and *Il10* more when combined than either does alone.

METHODS: F0 dams were exposed to psychological (swimming/restraint) and/or immune stress (IL-1β, 5μg/kg/day i.p.) on gestational days 12-18 and 17-delivery, respectively. F0 and F1 rats were split into: no stress/saline (NS/S), stress/saline (S/S), no stress/IL-1β (NS/IL) and stress/IL-1β (S/IL), n=3-7/group. mRNA abundance in F0 (weaning) and F1 (adult virgin) uteri was evaluated by qRT-PCR for genes of interest and housekeeping gene Cyclophilin. One-way ANOVA with post-hoc testing, $p<0.05$.

RESULTS: In F0 animals S/IL exposure increased the mRNA abundance of *Il1rn* and *Il1b* compared to NS/S offspring ($p<0.05$). Upregulation of *Il6* and *Il10* was evident in S/IL vs both NS/S and S/S ($p<0.05$). In F1 offspring *Il1a* expression decreased >10-fold in the 2-hit group as compared to S/S and NS/IL offspring ($p<0.05$), approximating the level observed in the NS/S group, which itself was significantly lower than in S/S animals ($p<0.05$). Downregulation of *Il1rn* abundance in S/IL in contrast with S/S offspring was noted as well ($p<0.05$). The lowest expression of *Il1b* was observed in the NS/IL group vs S/S ($p<0.01$) and S/IL ($p<0.05$). *Il6* and *Il10* were not differentially expressed, though showed a similar trend towards normalisation in S/IL animals.

CONCLUSIONS: Two hits markedly stimulate cytokine gene expression in F0 whereas a single prenatal stressor increases mRNA abundance in F1 offspring only. These data support our proposal that stressors accumulate to increase one's stress or allostatic load. The intriguing observation of downregulation after two hits in F1 suggests an accommodation to this augmented load. Placing these dams into the vulnerable condition of pregnancy may reveal important information regarding perinatal resilience or lack thereof. Supported by Research Fund Flanders, CIHR.

F-009

Comparative Exosomal Profile Analysis Between Maternal and Fetal Compartments During Term and Preterm Human Parturition. Ramkumar Menon,[1] Carlos Salomon*.[2] *[1]The University of Texas Medical Branch, Galveston, TX, USA; [2]The University of Queensland, Brisbane, United Kingdom.*

INTRODUCTION: Timing and initiation of labor are well orchestrated by signals communicated between the fetal and maternal compartments; however, how these signals are communicated is not completely understood. The aim of this study was to compare the exosomal profile between maternal and fetal compartments (i.e. Maternal plasma (MP), Amniotic fluid (AF) and umbilical Cord blood (CB)) from women with different signal of parturition.

METHODS: Samples (MP, AF and CB) were collected from group 1: term not-in labor (TNIL); group 2: term in labor (TL), group 3: preterm premature rupture of membranes (pPROM); and group 4: preterm birth (PTB). Exosome were isolated by differential buoyant density centrifugation and quantified by Nanoparticle Tracking Analysis (NanoSight™) using quantum dots coupled with CD63 or PLAP antibodies. The association in the exosomes concentration between different compartments was assessed using 2-way ANOVA, with the variance partitioned between compartment (i.e. MP, CB or AF) and condition (i.e. TNIL, TL, pPROM and PTB. Multiple regression analyses of 3 continuous variables (i.e. dependent variable: Exosomes; independent variables: compartments and condition) was also used.

RESULTS: A significant ($p<0.05$) association between the concentration of total exosomes between MP and CB was identified (slope = 0.096 ± 0.038) and this association was independent of the condition. No significant association was seen between MP and AF, or AF and CB ($P>0.05$). The concentration of exosomes normalised by ml of plasma or fluid was higher in MP compared to CB and AF and independent of the condition. Interestingly, in PTB the ratio PLAP/exosomes was significantly higher ~6.8-fold and ~63-fold in AF compared to CB and MP, respectively.
CONCLUSIONS: This study identified association of the levels of exosomes through different maternal and fetal compartments. Therefore, we suggest that signals originating from the placenta and placental membranes might indicate their physiologic status and functional contributions during pregnancy and labor and delivery.

F-010

Gestational Tissue Inflammatory Biomarker Phenotype at Term Labor: A Systematic Review. Emily E Hadley†,[1] Lauren Richardson†,[1] George Saade,[1] Maria R Torloni,[2] Ramkumar Menon*.[1] [1]*University of Texas Medical Branch, Galveston, TX, USA;* [2]*Federal University of Health Sciences, Sao Paulo, Brazil.*
INTRODUCTION: Term labor is characterized by inflammatory overload in feto-maternal tissues initiated by signals associated with fetal organ maturation and placental membrane senescence. Despite large numbers of individual studies on changes in inflammatory biochemicals linked to human parturition, the profile in each compartment is not clear. A better understanding of inflammatory biomarker profiles help to understand their contributions to labor. This systematic review investigated the inflammatory biomarker profiles of intrauterine compartments at term labor.
METHODS: A systematic review of studies on inflammatory biomarkers in human term parturition, in English from 1980-2015, in 3 electronic databases was performed. Selection of studies, data extraction and quality assessment was performed in duplicate by 2 independent reviewers.
RESULTS: A total of 3,712 studies were identified, 177 were selected for full text evaluation, 173 were included in the final review.
**Figure(s) will be available online.*
Each tissue expresses a unique set of biomarkers at time of term labor, but there is significant overlap between tissue types. All tissues (amnion, chorion, placenta, decidua, and myometrium) had the following biomarkers in common at the time of term labor: IL-6, IL-8, IL-1β, COX-2, PGE-2, TNF-α, MMP-9 and hCAP18.
**Figure(s) will be available online.*
CONCLUSIONS: We report common and unique inflammatory biomarkers in feto-maternal compartments at time of labor. Unique biomarkers have localized functions whereas a higher load of common inflammatory markers in gestational tissues signifies a harmonious functional role in parturition. Feto-maternal signals that can increase these common markers should be the focus of studies to understand the mechanism initiating human labor.

F-011

Risk Factors for Group B Streptococcal Colonization among Pregnant Women in West Virginia. Paul Dietz*,[1] Eric Coughlin†,[1] Dara Sebold,[2] Byron C Calhoun.[1] [1]*West Virginia University-Charleston, Charleston, WV, USA;* [2]*Charleston Area Medical Center, Charleston, WV, USA.*
INTRODUCTION: Group B streptococcus (GBS) colonization increases risk for preterm labor, premature rupture of membranes, neonatal sepsis, and other potential adverse outcomes. The objective of this study was to identify risk factors of GBS colonization in pregnant women.
METHODS: Retrospective observational study of patients receiving prenatal care with universal swabbing for GBS (May 11 2019-February 9, 2013) at a tertiary care center clinic. The following variables identified in the literature were included in a backwards logistic regression model to predict a positive GBS result: maternal age, gravida, racial identity, marital status, tobacco usage, illicit drug us, infections, and diabetes.
RESULTS: Of the 619 patients who met our inclusion criteria of GBS testing at 24-42 weeks, 153 (24.7%) tested positive for GBS. A majority of the women were single (403; 65.1%), obese (362; 58.5%) and of White racial identity (516; 83.4%). There was high tobacco use (297; 48.0%). Results of the logistic regression model revealed the following significant predictor of GBS, racially identify of either African American, Asian, or Other were 2.2 times more likely to be positive for GBS (95% CI 1.4-3.5; p=0.001) than Whites, single marital status 1.6 times (95% CI 1.0-2.4; p=0.030), and obesity 1.5 times (95% CI 1.0-2.4; p=0.049).
CONCLUSIONS: It is important for clinicians to identify patients who may be at risk for GBS.

F-012

The Vaginal Microbiota Composition at First Admission in Korean Pregnancy Women. Young-Ah You†,[1,2] Eun Jin Kwon†,[1,2] Soo Yeon Park,[1] Mi Hye Park,[1] Young Ju Kim.[1,2] [1]*Ewha Womans University, Seoul, Korea;* [2]*Ewha Womans University, Seoul, Korea.*
INTRODUCTION: The vaginal microbiome in pregnancy is important to both maternal and neonatal health outcomes. The vaginal microbiota composition changes during pregnancy, dominating one or two species of Lactobacillus. We aimed to examine the vaginal microbiota composition at first admission and to find the association between the microbiome and pregnancy outcomes in Korean pregnancy women.
METHODS: DNA was isolated in vaginal fluid of 65 pregnant women at first admission, using the Quiagen mini kit, and we characterized the vaginal microbiota of pregnant women, using MiSeq sequencing of 16S rRNA gene amplicons. The clustering characteristics were compared using the Chi-squared test or t-test. In addition, hierarchical clustering in the R package was applied to identify the groups of samples that have similar bacterial compositions. Statistical significance was considered present when the probability value (P) was less than 0.05.
RESULTS: This analysis was performed in 65 pregnant women with the vaginal samples at first admission. Fifty pregnant women were preterm delivered and fifteen pregnant women were term delivered. Hierarchical clustering analysis of bacterial species from the all pregnant vaginal microbiome communities revealed 5 major groups that reflect vaginal bacterial community state types (CSTs) previously defined. The most commonly observed CST in Korean pregnant women was CST I (L. crispatus), followed by CST III (L. iners), CST II (L. gasseri), and CST V (L. jensenii). CST IV was characterized by reduced Lactobacillus spp. and increased proportion of bacterial species associated with bacterial vaginosis including Prevotella spp., Clostridium spp., Atopobium spp., and Megasphaera. Notably, L. sakei and L. algidus were significantly decreased in vaginal fluid of preterm delivered women ($p < 0.05$).
CONCLUSIONS: This work suggests that the variation of community composition in vaginal fluid at first admission is useful to indicate pregnancy outcomes. This result gives an implication that future studies should be designed to explore the relationship between the vaginal microbiome and pregnancy outcomes.
Funding: Korea Health Technology R&D Project through the Korea Health Industry Development Institute (grant number: HI14C0306).

F-013

Cytokine Profile in Women with Cervical Insufficiency. Stephany Monsanto†,[1] Silvia Daher,[2] Erika Ono,[2] Karen Pendeloski,[2] Evelyn Trainá,[2] Rosiane Mattar,[2] Chandra Tayade*.[1] [1]*Queen's University, Kingston, ON, Canada;* [2]*Universidade Federal de São Paulo, São Paulo, SP, Brazil.*
INTRODUCTION: Cervical ripening is a crucial process for completion of normal pregnancy and labor. Cervical insufficiency (CI) is a condition where gradual premature cervical ripening leads to prolapse and eventual rupture of the amniotic membrane, usually resulting in midtrimester pregnancy loss or preterm birth. CI develops in the absence of noticeable symptoms and the cause is unknown. Diagnosis relies on clinician experience and pregnancy history, making prevention unfeasible, especially in primiparous women. Current treatment consists of surgical suturing of the cervix (cerclage), which carries some risks and is sometimes ineffective. Cytokines are the regulatory molecules of the immune system. Pregnancy complications like spontaneousabortion and preterm birth have been associated with aberrant levels of inflammatory

cytokines. The goal of this project was to evaluate the role of cytokines in the development of CI, and the impact of cerclage on the cytokine profile of women with CI.

METHODS: We recruited two groups of women between 12-20 weeks of pregnancy (Outpatient Clinic, Obstetrics Department at UNIFESP, Sao Paulo, Brazil): Group 1 included women with CI referred for cerclage (n=36), and Group 2 included women with no maternal or fetal disorders (n=19). Blood and vaginal fluid were collected by resident or doctor in turn, with our supervision. A second set of samples was collected from CI patients 2-22 weeks after surgery. Blood was collected in serum vacutainers and processed within two hours to separate serum and store it at -80C. Vaginal fluid was collected with a sterile plastic Pasteur pipette, diluted in 500uL sterile PBS and stored at -80C. Serum and vaginal fluid were analysed using an 11-plex cytokine array (Eve Technologies, Calgary, AB, Canada).

RESULTS: Preliminary analyses revealed higher levels of GM-CSF and TNF-α in vaginal fluid from CI patients compared to control patients. These differences disappeared after cerclage surgery. In CI patients, vaginal fluid levels of IL-6 and MCP-1 decreased after cerclage, but levels were not significantly different from control patients.

CONCLUSIONS: Our preliminary data suggests CI patients had higher levels of certain proinflammatory cytokines than normal subjects. Cerclage decreased levels of certain cytokines in these patients. Further analyses are in progress.

F-014

Racial Disparity in *Ureaplasma Parvum* Induced Inflammatory Responses. Liping Feng*,[1] Alex Antonia,[2] Amy Murtha,[1] Dennis Ko.[2] *[1]Duke University School of Medicine, Durham, NC, USA; [2]Duke University School of Medicine, Durham, NC, USA.*

INTRODUCTION: Preterm birth is a leading contributor to maternal and neonatal morbidity and mortality. *Ureaplasma. Parvum* (*U. parvum*) is gaining recognition as an important pathogen for preterm birth. Research findings indicate that it is the microbial/host interaction rather than *U. parvum* presence that triggers preterm delivery. These findings indicate an inter-individual variation in host-U. parvum traits among pregnant women. The current study aims to investigate the profile of inflammatory response in cells with different genetic background when they are exposed to *U. parvum*.

METHODS: The availability of a vast panel of Lymphoblastoid Cell Lines (LCLs) from different ethnic groups (available through the HapMap project) allowed us to assess the profile of cytokine/chemokine expression when exposed to *U. parvum*. LCLs are both easily maintained and a reliable genetic source, with a somatic mutation rate of only 0.3%. To ensure diverse genetic backgrounds, LCL cell lines used were from 6 Caucasians and 6 Africans. Cultured LCLs (4×10^4) were exposed to *U. parvum* (4×10^5 colony forming units [CFU]) for 24h. Cell death was measured by flow cytometry using 7-Aminoactinomycin D (7AAD). Forty cytokines and chemokines were measured by Luminex Multiplex Assay.

RESULTS: Cell death was not observed under the treatment conditions in all LCLs. *U. parvum* exposure induced significantly more pro-inflammatory cytokines G-CSF and IFNg in LCLs from Africans compared to LCLs from Caucasians. Conversely, the anti-inflammatory cytokine interleukin 1Ra (IL1Ra) was up-regulated by *U. parvum* exposure in LCLs from Caucasians but not from Africans.

CONCLUSIONS: Our findings demonstrate a stronger pro-inflammatory response and a reciprocal weaker anti-inflammatory response in LCLs from Africans compared to LCLs from Caucasians. G-CSF is associated with *Ureaplasma* infection of placenta tissues in a recent *in vivo* study and IFNγ is critical for innate and adaptive immunity against infections. Interestingly, the levels of G-CSF, IFNγ and IL-1Ra are all associated with SNPs and under significant genetic influence. These findings further suggest the inter-individual variation in host-*U. parvum* traits. The influence of genetic variation on the expression of G-CSF, IFNγ and IL-1Ra induced by *U. parvum* infection deserves further investigation.

F-015

Colonization of the Cervicovaginal Space with *Gardnerella vaginalis* Leads to Inflammation and Cervical Remodeling *In Vivo*. Luz-Jeannette Sierra†, Amy G Brown, Guillermo O Barila, Michal A Elovitz*. *Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA.*

INTRODUCTION: While treatment of Bacterial Vaginosis (BV) does not appear to reduce the risk of spontaneous preterm birth (SPTB), associations between this condition and SPTB remain. Advances in microbiology have demonstrated that the clinical syndrome of BV can actually be induced by a variety of microbes. The most common of these bacteria is *Gardnerella vaginalis*. We hypothesize that overgrowth of *G. vaginalis* in the cervicovaginal space may induce changes to the cervical epithelial barrier and alter cervical function as a mechanism by which it may lead to SPTB. The objective of this study was to evaluate the effects of *G.vaginalis* colonization of the murine CV space on local inflammatory pathways and on the cervical epithelial barrier.

METHODS: CD-1, timed-pregnant, mice received an intravaginal inoculation of *G.vaginalis* ($5X10^8$ CFU/ml, ATCC 14019) on embryonic day 12 (E12). On E18, the mice were sacrificed and cervicovaginal fluid (CVF), amniotic fluid (AF), cervix, uterus, and placentas were collected. Genomic DNA was isolated from the CVF, placenta and uterus and QPCR was performed to confirm colonization. IL-6 and soluble e-cadherin (SE-cadherin) ELISAs were performed on the CVF. Intrauterine inflammation was assessed in the AF via ELISA (IL-6). RNA was extracted from the cervices and QPCR was performed to evaluate the following targets: IL-8, IL-1β, TNF-α, Tff-1, SpinK-5, HAS-1 and LOX.

RESULTS: *G.vaginalis* successfully colonized the CV space and was not detected in the placenta or uterus. Colonization increased IL-6 levels in CVF ($p=0.0007$) and in AF ($p=0.0008$). SE-cadherin was enhanced ($p<0.0001$) in CVF in response to *G vaginalis* colonization. Cervical expression of IL-1β, IL-8 and TFF-1 were enhanced ($p=0.01$, $p=0.02$, and $p=0.03$ respectively). All other targets were not significantly altered.

CONCLUSIONS: This study demonstrates the feasibility of mimicking the human CV microbiota in a pregnant mouse model. Notably, these results show that CV colonization, or disruption of the normal CV microbiota, can induce CV inflammation, cervical remodeling, breakdown of the cervical epithelial barrier and fetal inflammatory responses. The ability of *G.vaginalis* to induce these molecular, immune and cellular changes suggests that this bacterium likely plays a pathogenic role in SPTB in which cervical remodeling is the initiating event. (MOD Prematurity Center at PENN).

F-016

Immunological Changes in the Choriodecidua, Placenta and Amnion in Preterm Deliveries Secondary to Chorioamnionitis. Sivatharjini P Sivarajasingam†,[1] Ananya Das,[1] Bronwen R Herbert,[1] Maria F Fais,[1] Natasha Singh,[1] Nesrina Imami,[2] Mark R Johnson*.[1] *[1]Chelsea and Westminster Hospital, Imperial College London, London, United Kingdom; [2]Imperial College London, London, United Kingdom.*

INTRODUCTION: The choriodecidua (CD) is a highly immunologically active, yet largely overlooked gestational tissue of research. Previous studies have demonstrated a significant increase in macrophage infiltration in CD in days prior to labour, which precedes changes in the myometrium. Better understanding of the immunological changes of the CD in context of the surrounding tissues' immunology, may help identify a potential target for therapy.

METHODS: Matched samples (CD, amnion, placenta) were collected from patients who underwent non-labouring preterm caesarean deliveries (n=14) and labouring preterm caesarean deliveries due to chorioamnionitis (CA) (n=11). Samples were stored at -80^0C. Protein lysates were generated and Bio-Plex cytokine assays (19-plex) were undertaken on 3 separate plates. Data was analysed using GraphPad prism, normality was assessed via D'Agostino & Pearson omnibus testing. Unpaired t-test and Mann-Whitney test were used for parametric and non-parametric data respectively.

RESULTS: Inflammation indicated by high levels of cytokines/chemokines was globally raised across all 3 tissues in CA

**Figure(s) will be available online.*

, but on whole less significantly in placenta. Comparing CD to amnion, the level of inflammation was most pronounced in CD. IL-1β ($p<0.05$), CCL20 ($p<0.0001$) and IL-8 ($p=0.0001$) were the most significantly raised cytokines in amnion, CD and placenta respectively.

CONCLUSIONS: Our data concur with findings that preterm labour (PTL) due to infection is characterised by an influx of neutrophils, as CCL20, a chemoattractant of dendritic cells may contribute to a neutrophilia via recruitment of T helper cells such as Th17. Furthermore, IL-8 which is also a potent chemoattractant of neutrophils may play an additional role and both may be useful biomarkers of PTL. Immunological changes in CA peak in the CD, followed by those observed in amnion, indicating that changes in the CD may be the trigger in PTL.

F-017

Progesterone Prevents Preterm Birth by Suppressing the Enhancement of Uterine Contractility in Mice with Chronic Dental *Porphyromonas gingivalis* Infection. Haruhisa Konishi,[1] Hiroshi Miyoshi,[1] Yuko Teraoka,[1] Satoshi Urabe,[1] Hisako Furusho,[2] Mutsumi Miyauchi,[2] Takashi Takata,[2] Yoshiki Kudo.[1] *[1]Hiroshima University, Hiroshima, Japan; [2]Hiroshima University, Hiroshima, Japan.*

INTRODUCTION: Progesterone (P4) plays an essential role in the maintenance of pregnancy by promoting uterine quiescence, however, this mechanism has not been less understood. We previously demonstrated that mice with dental *Porphyromonas gingivalis* infection (*P.g* mice) were useful as an animal model for chronic inflammation-induced preterm birth. In *P.g* mice, the average gestational period was 2 days shorter and the uterine contractility was significantly enhanced. The aim of this study was to investigate whether P4 prevented preterm birth and to determine the effect of P4 on uterine contractility.

METHODS: *P.g* mice were injected subcutaneously with (*P.g* +P4 mice) or without (*P.g* mice) 1mg P4 daily at day 15.5-18.5 of gestation. At first we observed these gestational period. Secondly, the contraction of the myometrium at day 18.0 of gestation was recorded in tissue organ bath systems and analyzed. Thirdly, we examined the mRNA expressions of contractile associated proteins so-called CAPs (oxytocin receptor, connexin 43) and ion channels (L-type Ca^{2+} channel and P2X7 receptor; a purinergic receptor) in the myometrium at day 18.0 of gestation using real-time PCR.

RESULTS: The average gestational period was 20.4 days in *P.g* +P4 mice (n=4) and 18.3 days in *P.g* mice. The average intensity of spontaneous uterine contraction was reduced by 40% in *P.g* +P4 mice, compared to *P.g* mice. The concentration-response curve for oxytocin turned right and the EC_{50} was 1.3 nM in *P.g* mice and 2.2nM in *P.g* +P4 mice, demonstrating that sensitivity to oxytocin was markedly decreased by P4 treatment. The treatment with P4 significantly reduced the enhancement of the expression of oxytocin receptor, connexin 43, L-type calcium channel and P2X7 receptor in the myometrium by 73%,57%,78% and 50 %, respectively($P < 0.001$; $n = 8$).

CONCLUSIONS: P4 prevented preterm birth by suppressing the enhancement of CAPs expressions and reducing uterine contraction in chronic inflammation-induced preterm birth mouse model.

F-018

Prognostic Capacity of Cervicovaginal Fluid Acetate-Glutamate Ratio for Risk of Preterm Delivery within Two Weeks of Presentation with Symptoms of Preterm Labor. Emmanuel Amabebe†, Steven Reynolds, Victoria Stern†, Graham Stafford, Martyn Paley, Dilly Anumba. *University of Sheffield, Sheffield, United Kingdom.*

INTRODUCTION: Decreased cervicovaginal fluid (CVF) acetate appears a suitable "rule-out" marker for imminent preterm delivery (PTD) or delivery within 2 wks in women presenting with threatened preterm labor (PTL). Low CVF glutamate is associated with high vaginal pH and bacterial vaginosis, a risk factor of PTD. To determine whether glutamate, or other studied metabolites, enhanced the predictive ability of acetate for delivery within 2 wks of the assessment, we examined the combined discriminative capacity of CVF metabolites for delivery within 2 wks of an assessment in women presenting with symptoms of PTL.

METHODS: CVF obtained by high-vaginal swabs from 82 symptomatic women with singleton pregnancies (24-36 wks gestation), intact membranes and no evidence of genital infection, were analyzed by ^{1}H-Nuclear Magnetic Resonance (NMR) spectroscopy using a 400 MHz spectrometer. Acetate, glutamate and other metabolites implicated in vaginal host-microbial metabolic activities were identified in the ^{1}H-NMR spectrum, integrated for peak area and normalized to the total spectrum integral (excluding residual water). The ratio of acetate to glutamate normalized integrals (Ace/Glx) was then compared between the groups using Wilcoxon rank sum test and Receiver Operating Characteristics curve. Predictive endpoint was delivery within 2 wks of assessment.

RESULTS: Nine (~11%) women delivered within 2 wks of index assessment and showed a higher Ace/Glx (5.0±1.9 vs. 1.4±0.18, P=0.0002). The Ace/Glx (AUC=0.86, CI=0.76-0.95, +LR=3.0) was a better predictor of delivery within 2 wks of index assessment compared to either acetate (AUC=0.79, CI=0.66-0.92, +LR=2.4) or glutamate (AUC=0.68, CI=0.51-0.86, +LR=2.4) singly. Integrals for succinate, lactate, formate, glucose, alanine and branched chain amino acids did not differ significantly between the cohorts.

CONCLUSIONS: Decreased CVF glutamate appears to enhance the predictive ability of acetate for delivery within 2 wks of presentation with symptoms of PTL. Whether measuring CVF acetate/glutamate ratio could improve the triaging of symptomatic pregnant women at risk of imminent PTD, allowing patients to be discharged to outpatient care thereby providing maternal reassurance while appropriately allocating intensive care to those at highest risk, requires further larger prospective studies.

F-019

Placental Clearance Modulates Circulating Levels of Fetal Pro-Inflammatory but Not Anti-Inflammatory Cytokines During Term Parturition and May Contribute to Histological Chorioamnionitis. Imran N Mir, Lina F Chalak, Charles R Rosenfeld*. *University of Texas Southwestern, Dallas, TX, USA.*

INTRODUCTION: Pro-inflammatory cytokines contribute to the onset and progression of term parturition while anti-inflammatory cytokines, IL-10 in particular, are protective or inhibitory; however, their source and clearance in the fetal compartment are unclear.

METHODS: 40 term pregnancies were randomly selected for study: Group 1 included elective cesarean delivery without labor or pregnancy complications (n=20) and Group 2, vaginal delivery without pregnancy complications (n=20). Umbilical artery (UmA) and venous (UmV) blood were collected immediately after birth to measure arterial blood gases and serum IL-1β, IL-2, IL-6, IL-8,TNFα, and IL-10 by ELISA. Placental tissue was collected from both Groups (n=20) and 10 additional random vaginal deliveries (n=30) and fixed for histological analysis.

RESULTS: UmA gases were normal in both Groups. In Group 1, UmA and UmV levels were below sensitivity of the assay for all cytokines except IL-10, which did not differ (504±15 and 468±16 pg/ml, respectively; $P \geq 0.1$). In Group 2, UmA levels of IL-6 and IL-8 were detectable and increased >10-fold to 16.7±1.6 and 18.4±4.3 pg/ml, respectively ($P<0.001$). Notably, serum levels were decreased in the UmV to 0.29±0.2 and 0.74±0.3, respectively ($P<0.001$), demonstrating placental clearances of 98±0.6% and 97±1.3%, respectively, which were linear ($P<0.03$) and nonsaturable for both cytokines over the range of UmA concentrations. IL-10 levels also were similar in UmA and UmV in Group 2 ($P>0.05$); however, UmA levels were 34% greater in Group 2 vs. Group 1, 677±67 vs. 504±15 pg/ml, respectively ($P<0.02$). Placental histology demonstrated acute chorioamnionitis (HC) in 55% of Group 2 vs. 5% of Group 1 ($P<0.001$), occurring predominantly in males (13/16).

CONCLUSIONS: These are the first data demonstrating that term labor is characterized by >10-fold increases in *fetal synthesis* of IL-6 and IL-8 and that circulating levels are modulated by nonsaturable placental clearance. Although IL-10 synthesis increases ~34% during vaginal delivery, there is no placental clearance, demonstrating a mechanism for *maintaining cytokine balance* protective for the fetus. Notably, increases in fetal IL-6 and -8 during labor are paralleled by evidence of HC in >50% of vaginal deliveries, suggesting a placental response to fetal inflammatory cytokines.

F-020

A Role for IL-10 During Progesterone Mediated Prolongation of Gestation. Mark Phillippe*, Ingrid Liff†, Sharareh Adeli. *Massachusetts General Hospital, Boston, MA, USA.*

INTRODUCTION: Progesterone (P4) has long been known to play a key role during pregnancy and parturition. Although smooth muscle relaxation and/or poorly understood anti-inflammatory events have been proposed to be responsible for the effects of P4, a clearly defined physiologic mechanism in regard to uterine activity is yet to be described. Our laboratory has recently reported that: 1) P4-mediated prolongation of pregnancy is associated with elevated IL-10 levels and sustained IL-10 receptor expression in placental tissue, and 2) inhibition of the nuclear P4 receptor with RU486 leading to preterm delivery is associated with decreased expression of the IL-10 receptor β subunit (SMFM - 2017). The studies in this report sought to test the novel hypothesis that IL-10 signaling is a key intermediary in the physiologic effects of P4 during the maintenance of pregnancy and the onset of parturition.

METHODS: Pregnant homozygous IL-10 deficient mice (B10.129P2(B6)-IL10^{tm1Cgn}/J mice; Jackson Lab) and wild-type pregnant C57BL/6 mice were utilized for these studies. The pregnant mice underwent daily subcutaneous injections with P4 (1 mg per mouse) or vehicle (sesame oil) from gd 16 until gd 20 (i.e. 2 days beyond normal parturition). Subsequently the mice were assessed for delivery at term (on gd 18) vs. pregnancy extending beyond gd 19. IL-10 deficient mice that remained pregnant to day 20 were euthanized to check for signs of partial delivery; whereas, the wild-type B6 mice were electively euthanized on gd 20.

RESULTS: Eight pregnant IL-10 deficient mice and 7 wild-type B6 mice were utilized for these studies. After daily P4 injections, we observed that 5 out of 8 (63%) homozygous IL-10 deficient mice underwent spontaneous delivery on gd 19 – 20; whereas, 0 of 7 wild-type B6 mice spontaneously delivered before being electively euthanized on gd 20 (Fisher Exact test $p = 0.026$). Among the IL-10 deficient mice that delivered, 1 was partial and the other 4 were complete; and for the 3 undelivered IL-10 deficient mice, two were euthanized with intact pregnancies on gd 20 and the other was euthanized and found to have several dead fetuses in the uterus.

CONCLUSIONS: These preliminary studies when combined with our other studies demonstrating direct P4 modulation of IL-10 and its β receptor subunit provide evidence suggesting that IL-10 signaling in the placenta is a key component in P4-mediated prolongation of gestation. (Funded by the Burroughs Welcome Fund-Preterm Birth Initiative).

F-021

Amniotic Fluid Macrophage Activation Near Term Heralds the Initiation of Labor in Mice. Alina P Montalbano,[1] Carole R Mendelson*.[1,2] *[1]UT Southwestern, Dallas, TX, USA; [2]UT Southwestern Medical Center, Dallas, TX, USA.*

INTRODUCTION: Term and preterm labor are associated with increased inflammatory cytokines within amniotic fluid (AF) and infiltration of the myometrium by neutrophils and macrophages (Mφ). Whereas in preterm labor, infection likely provides the inciting inflammatory signal, we suggest that inflammatory signals for spontaneous labor at term arise, in part, from the fetus. We previously demonstrated that surfactant protein-A (SP-A), a developmentally regulated C-type lectin secreted by the fetal lung into AF near term, activates AF Mφ, inducing their migration to the uterus where they transmit inflammatory signals leading to labor. More recently, we reported that mice deficient in *SP-A,* doubly deficient in *SP-A* and *SP-D* (*SP-A/D*-dKO)*,* or deficient in Toll-like Receptor 2 (*TLR2*), a putative receptor for SP-A, manifest delayed labor. Moreover, F4/80$^+$ AF Mφ from TLR2$^{-/-}$ and *SP-A/D*-dKO mice express significantly lower levels of proinflammatory/M1 (*e.g.* IL-1β) and anti-inflammatory/M2 (*e.g.* ARG1) activation markers compared to WT controls. This suggests that disruption of the SP-A-AF Mφ signaling pathway results in delayed labor. The objective of this study was to characterize phenotypic changes in AF Mφ associated with developmental induction of *SP-A* and its secretion into AF near term.

METHODS: Flow cytometry, Illumina gene array, and RT-qPCR were used to characterize phenotypic changes in AF Mφ from WT ICR mice during late gestation.

RESULTS: F4/80$^+$ AF Mφ increased significantly between 15.5 and 18.5 days post-coitum (dpc) (19dpc=term). Analysis of 15.5 and 18.5 dpc AF Mφ revealed 15.5 dpc Mφ predominately expressed M2 markers, whereas 18.5 dpc Mφ expressed both M1 and M2 markers. Specifically, at 15.5 dpc, 82% of CD11b$^+$F4/80$^+$ AF Mφ were ARG1$^+$ and 0.5% were IL-1β$^+$. By 18.5 dpc 50% coexpressed ARG1 and IL-1β (ARG1$^+$IL-1β$^+$), while 15% were ARG1$^-$IL-1β$^+$ and 11% were ARG1$^+$IL-1β$^-$. Importantly, delayed labor in mice, induced by serial injection of progesterone (P_4) late in gestation, significantly decreased the proportion of Arg1$^+$IL-1β$^+$ AF Mφ at 18.5 dpc.

CONCLUSIONS: Near term, enhanced SP-A protein levels serve to activate AF Mφ inducing their expression of both anti- and proinflammatory markers. The effect of P_4 to delay labor and disrupt AF Mφ polarization near term serves to establish their causal link and sheds light on regulation of the fetal AF Mφ signal for the initiation of labor at term. March of Dimes #21-FY14-146.

F-022

Identification and Comparison of Bacteria in Brain Cortex and Placenta of Fetuses Exposed to Hypoxic Hypoxia. Miguel A Zarate†,[1] Michelle Rodriguez†,[2] Eileen I Chang†,[1] Thomas J Arndt†,[1] Maureen Keller-Wood,[3] Eric W Triplett,[2] Charles E Wood*.[1] *[1]University of Florida College of Medicine, Gainesville, FL, USA; [2]University of Florida Institute of Food and Agricultural Sciences, Gainesville, FL, USA; [3]University of Florida College of Pharmacy, Gainesville, FL, USA.*

INTRODUCTION: We have previously reported that transient hypoxic hypoxia (HH) produces a robust inflammatory response characterized by an upregulation of inflammatory markers, and an increase number of macrophages in different fetal brain regions and other peripheral organs. Based on these results, we hypothesize that bacterial invasion is the main cause for this inflammatory cascade and immune cells infiltration in the brain cortex of fetuses subjected to HH.

METHODS: We used a total of 16 brain cortex and placenta samples of fetuses exposed to HH or normoxia (n=8 per group). Paraffin embedded brain cortex tissues were sectioned (5 μm) and stained using the Gram technique for bacterial detection. Placenta and brain cortex snap-frozen samples were homogenized, cultured in brain heart infusion broth, and harvested for Gram staining and Sanger sequencing. We performed whole genome sequencing for *Staphylococcus simulans* strains isolated from placenta and brain.

RESULTS: We detected Gram (+) and Gram (-) populations on the fetal brain cortex in HH group, and their morphology was validated by a subsequent Gram staining of the harvested live bacterial colonies obtained from cultures. HH placental cultures also contained bacteria similar to those isolated from the HH fetal brains. Sanger sequencing revealed that the predominant bacteria found in brain and placenta of HH fetuses was *Staphylococcus simulans*, but also included other species of *Staphylococcus, Shigella, Enterobacter, Escherichia, and Pseudomona. S. simulans* strains found in brain and placenta were genomically identical. Tissues from normoxic animals contained very low levels of bacteria.

CONCLUSIONS: We conclude that HH induces bacterial invasion of the fetal cerebral cortex via placenta, predominantly by *Staphylococcus simulans*. This influx of bacteria into the brain might lead to the activation of inflammatory pathways, and immune cells (local and peripheral macrophages), previously observed in our work. The ultimate origin and complete route of the bacterial invasion remains unclear but is likely to originate in maternal tissues.

F-023

Treatment with Exendin-4 Reduces the Rate of Preterm Birth and Improves Adverse Neonatal Outcomes Induced by Systemic or Intra-Amniotic Inflammation. Valeria Garcia-Flores†,[1,2] Roberto Romero,[1] Marcia Arenas-Hernandez,[1,2] Chharitha Veerapaneni,[2] Tara N Mial,[1,2] George Schwenkel,[1,2] Sonia S Hassan,[1,2] Nardhy Gomez-Lopez.[1,2] *[1]NICHD, Detroit, MI, USA; [2]Wayne State University, Detroit, MI, USA.*

INTRODUCTION: Preterm birth (PTB) is the leading cause of neonatal morbidity and mortality worldwide and is commonly preceded by spontaneous preterm labor. Pathological inflammation is implicated

in the mechanisms that lead to spontaneous preterm labor. Therefore, it is essential to develop therapies to prevent inflammation-associated PTB. Herein, we aimed to determine whether treatment with an anti-inflammatory peptide, exendin-4, could prevent PTB and improve adverse neonatal outcomes caused by an intraperitoneal orintra-amniotic injection of an endotoxin.

METHODS: C57BL/6 mice were intraperitoneally (IP) injected with lipopolysaccharide (LPS, 10μg) on 16.5 days *post coitum* (dpc). Six hours after, mice were treated with exendin-4 (10μg/kg, n=10; 20μg/kg, n=8; and 30μg/kg, n=10) and pregnancy outcomes were video monitored. Control mice were injected with 1X phosphate-buffered saline (PBS; n=8), LPS (10μg, n=10) or exendin-4 [10μg/kg, n=10; 20μg/kg, n=5; and 30μg/kg, n=5) alone on 16.5 dpc. A second group of mice received an intra-amniotic (IA) injection of LPS (100ng per sac). Six hours after, dams were treated with exendin-4 (30μg/kg, n=8) and pregnancy outcomes were video monitored. Control mice received an IA injection of PBS (n=8) or LPS (100ng, n=8) alone.

RESULTS: An IP injection of LPS induced PTB [80±24.9% (8/10)] and caused pup mortality at birth [86.6%±9.09% (50/54)] and at 1 week of age [100%±0 (4/4)]. Treatment with exendin-4: 1) reduced the rate of IP-LPS-induced PTB by 10% at 10μg/kg or 30μg/kg; 2) reduced the rate of IP-LPS-induced pup mortality at birth by 5% at 10μg/kg; 3) decreased the rate IP-LPS-induced neonatal mortality by 12.5% at 10μg/kg and 85% at 30μg/kg.

An IA injection of LPS induced PTB [87.5±22.92% (7/8)] and caused pup mortality at birth [87.5±8.82% (47/54)] and at 1 week of age [100±0% (7/7)]. Treatment with 30μg/kg of exendin-4 reduced the rate of IA-LPS-induced PTB by 37.5% and the rate of pup mortality at birth by 26.27%. Administration of exendin-4 alone did not induce PTB or cause adverse neonatal outcomes.

CONCLUSIONS: Treatment with exendin-4 reduced the rate of preterm birth and improved adverse neonatal outcomes induced by systemic or intra-amniotic inflammation.

F-024

Cervical Length and Pregnancy Outcomes in Women with a History of Cervical Conization. Danielle M Panelli†,[1] Ann M Thomas,[3] Sarah Feldman,[2] Thomas F McElrath*.[3] *[1]Brigham and Women's Hospital, Boston, MA, USA; [2]Brigham and Women's Hospital, Boston, MA, USA; [3]Brigham and Women's Hospital, Boston, MA, USA.*

INTRODUCTION: Women with a history of cervical conization have an increased risk of preterm delivery during subsequent pregnancies. The average cervical length during pregnancies following a cold knife cone (CKC) is unknown, as is the best management approach. The purpose of this study is to establish an average cervical length in women during pregnancies that occur after CKC.

METHODS: Women who underwent at least one CKC and had prenatal care for a subsequent pregnancy at the same institution were included. Women with multiple pregnancies or incomplete prenatal records were excluded. The size of the specimen excised during the cone and the diagnosis were taken from pathology reports. Cervical lengths at 16-20 weeks were recorded.

RESULTS: A total of 17 women met inclusion criteria.

	Number (%)
Age > 35	5 (29%)
Ethnicity	
White	12 (71%)
Hispanic	4 (24%)
Other	2 (12%)
Number of prior deliveries	
0	13 (76%)
≥1	4 (24%)
BMI	
<25	2 (12%)
25-30	8 (47%)
>30	7 (41%)

Of these, 10 had one cervical procedure and 7 had two. All women had at least one CKC; women with more than 1 procedure had either a loop electrosurgical excision procedure (LEEP) or another CKC. The average depth of the CKC was 0.92cm. The most common diagnosis was adenocarcinoma in situ (ACIS). The mean cervical length at the 16-20 week fetal survey was 3.48cm. The average cervical length at the fetal survey at the same institution is known to be 3.0cm. Using a t-test to compare these populations, the mean cervical length among the cone patients was significantly longer (p=0.13). 3 women were managed with cervical cerclage, 2 with abdominal cerclage, and 1 with vaginal progesterone. 1 cervical cerclage was ultrasound-indicated for cervical length of 2.5cm, 1 was exam-indicated and 1 was prophylactic given two prior CKC. Only 1 of 17 delivered prematurely; she had preterm premature rupture of membranes at 35 weeks.

CONCLUSIONS: In comparison to the average cervical length in all women at our center, women with at least one prior CKC had a significantly longer cervical length at the 16-20 week fetal survey. This suggests that cervical length may not be the etiology of the increased risk of preterm delivery in women with a pregnancy following cervical cone biopsy.

F-025

Exam-Indicated Cerclage with or without Prior Amniocentesis. Laura G Rodriguez Riesco†,[1] Jeannie Zuk,[2] Zhaoxing Pan,[2] Henry Galan,[1,2] Michael Zaretsky*.[1,2] *[1]University of Colorado School of Medicine, Aurora, CO, USA; [2]Colorado Children's Hospital, Aurora, CO, USA.*

INTRODUCTION: Amniocentesis is utilized to determine the presence of an intrauterine infection prior to placement of an exam-indicated cerclage in midgestation. This is not a universally accepted practice, and many cerclages are placed without a prior amniocentesis. The objective of our study was to compare the outcomes of pregnancies treated with second trimester exam-indicated cerclage with and without prior amniocentesis.

METHODS: In this retrospective chart review from July 2008 through December 2015, 168 women underwent an exam-indicated cerclage. Of those, 65 patients had an amniocentesis prior to cerclage placement and 103 patients underwent a cerclage without a prior amniocentesis. Parametric 2-sample t-test was used to compare continuous variables, and Fisher's exact test was used to compare categorical variables.

RESULTS: Patients that had an amniocentesis before cerclage were found to have an earlier gestational age at time of procedure (20.30 ± 2.29 weeks vs 21.32 ± 1.81 weeks, p<0.001), a shorter cervical length on presentation (0.93 ± 0.61 cm vs 1.45 ± 0.66 cm, p<0.001), and delivered at an earlier gestational age (GA 34.6 [16.7 to 40.4] weeks vs 37.6 [19.9 to 40.7] weeks, p<0.001) with shorter latency periods from cerclage placement to delivery (Latency 13.9 [0.0 to 24.0] weeks vs 16.3 [0.3 to 23.2] weeks, p=0.010) . Three patients presented with clinical evidence suggestive of chorioamnionitis, had amniocentesis, and did not receive cerclages. Only one had evidence of infection by gram stain and culture and her labor was subsequently augmented. The other two spontaneously labored. In addition, two patients who met criteria for exam-indicated cerclage underwent amniocentesis with no evidence of infection but declined cerclage placement. They ultimately delivered at 28 weeks and 36 weeks.

CONCLUSIONS: There is no universally accepted indication for amniocentesis prior to exam-indicated cerclage placement and is likely based on physician's clinical assessment of severity upon presentation. In this cohort, results of amniocentesis rarely impacted clinical decision making. We found significant differences between those patients who underwent an amniocentesis before cerclage placement including earlier gestational age upon evaluation, shorter pre-operative cervical lengths, shorter latency period, and earlier gestational age at delivery.

F-026

Extracellular Vesicle Release of Matrix Metalloproteinases by Amniotic Cells. Bethany Hart,[1] Yasuko Yamamura,[1] Wei-Ting Hung,[2] Lane Christenson,[2] Jakub Tolar*.[3] *[1]U of MN, Minneapolis, MN, USA; [2]U of KS, Kansas City, KS, USA; [3]U of MN, Minneapolis, MN, USA.*

INTRODUCTION: Preterm rupture of membranes(PROM) is associated with matrix metalloproteinases(MMPs), IL-6, and extracellular matrix(ECM) degradation, however mechanisms underlying this process remain elusive. Recently, extracellular vesicles(EVs) containing MMPs were identified as a key component in ECM remodeling. We hypothesized that amniotic epithelial and mesenchymal cells release EVs containing MMPs, which will be altered by IL-6 exposure.

METHODS: EVs were collected from media of amniotic epithelial and mesenchymal cells(n=3). EV isolates underwent western blot, EM and nanoparticle tracking analysis. MMP activity was evaluated by zymography. The effects of IL-6 (500 ng/mL) was evaluated at 1, 2, 3, 5, 8, & 16hours. Vesicle concentration was compared for cell type, treatment and time by general linear regression with repeated measures.

RESULTS: EV isolation was confirmed by western blot (+ CD63, annexin V, B-actin, - calnexin),

**Figure(s) will be available online.*

EM, and nanoparticle tracking analysis. Pro-MMP-2, 9 and MMP-2 were identified by zymogram.

**Figure(s) will be available online.*

IL-6 exposure did not significantly alter the concentration of EVs compared to controls (p=.82) nor was there a temporal effect (p=0.44). A trend was observed in which IL-6 exposure increased EVs in epithelial cells and decreases in mesenchymal cells.

CONCLUSIONS: EVs containing Pro-MMP-2, 9 and MMP-2 were isolated from amniotic epithelial and mesenchymal cells. This is the first study identifying EVs released by amniotic cells. While no statistical difference was found in EV concentration following exposure to IL-6 compared to controls, the observed response difference of epithelial and mesenchymal cell may be representative of their differing roles in ECM remodeling in PROM which remained undetected in our underpowered study.

F-027

Characterization of Fetal Membrane Microfractures in and Their Potential Significance in Pregnancy and Parturition. L Richardson†,[1] G Vargas,[2] R Menon*.[1] *[1]UTMB, Galveston, TX, USA; [2]UTMB, Galveston, TX, USA.*

INTRODUCTION: Remodeling of human fetal membranes (FM) involves amnion epithelial shedding and formation of gaps in the intact epithelial layer identified as microfractures (MF). MFs, of FMs are characterized by: 1) altered amnion morphology, 2) deterioration of basement membrane, 3) tunnels due to collagen degradation, and 4) either shed or migratory cells in these tunnels. To further characterize these MFs, we quantified the amount, depth, and width of MFs in FMs. Additionally, we examined cellular and collagen changes around MFs.

METHODS: Biopsies of Mid zone FMs were collected from women undergoing cesarean sections (term not in labor –TNIL) or vaginal deliveries (term labor –TL). As TL is associated with oxidative stress (OS) associated changes, TNIL membranes in organ explant systems were treated with OS inducer cigarette smoke extract (CSE) for 48 hours. FMs were imaged using a combination of multiphoton autofluorescence and second harmonic generation microscopy as well as mosaic tiling. Deep tissue and subcellular imaging were carried out using a wavelength of 820 nm. From each explant an area around 1,255um x 817um was analyzed for quantity of MF with ImageJ and their depth and width were measured by IMARIS. Epithelial gaps and shedding's were quantified in ten images from each category.

RESULTS: High resolution microscopy techniques identified MFs in TNIL, TL, and in vitro in CSE treated explants. Epithelial shedding was identified to be 4 times higher in TL than CSE and 1.5 times higher than TNIL.The analyzed 1,255um x 817um area showed: 1) MF formation increasing with TL and CSE compared to media controls, 2) CSE MFs are significantly deeper then TNIL (p=0.001), while TL are almost significantly deeper then TNIL (p=0.06), 3) No significant difference was found between the top (p=0.17,p=0.17,p=0.48) and bottom width (p=0.17,p=0.10,p=0.68) of collagen tunnels in TNIL, TL, or CSE.

CONCLUSIONS: Amnion membranes contain MFs that are associated with FM remodeling. The higher number and depth of MFs in TL and its enhancement in response to OS in TNIL showed its physiologic and mechanical relevance in parturition. We hypothesis that MFs development and its resealing by collagenogenesis occur throughout gestation; however, at late gestation senescent amnion cells fail to reseal MFs that can enhance inflammation. Premature senescence of membranes can cause persistence of MFs in membranes leading to rupture.

F-028

Expression of Phospho-GSK3Beta Correlates with p38MAPK Activation in Human and Mouse Gestation. L Richardson†,[1] R Menon,[1] A Bonney*.[2,3] *[1]UTMB, Galveston, TX, USA; [2]UVM, Burlington, VT, USA; [3]UVM, Burlington, VT, USA.*

INTRODUCTION: Human parturition is known to be associated oxidative stress (OS) induced fetal cell senescence at term commonly activated by stress signaler p38 mitogen activated protein kinase (MAPK). This pathway has been shown in human and murine fetal tissues (placenta, uterus, fetal membranes) during parturition as well as recapitulated in vitro using amnion epithelial cells (AECs) exposed to cigarette smoke extract (CSE), an OS inducer. p38MAPK activation is often associated with phosphorylation and deactivation of Glycogen synthase kinase 3β(GSK3β) to promote cell survival. This study determined deactivation of GSK3β due to phosphorylation and its correlation with p38MAPK expression in mice (placenta, fetal membranes) and human (fetal membranes) parturition as a mechanism of cell survival property during gestation and labor.

METHODS: C57BL/6 Mice were sacrificed at days 9.5, 10, 12, 15, 17, 18 and fetal membranes and placentas were harvested. Primary AECs were isolated from normal term, not-in-labor human placental membranes and stimulated with OS inducer CSE for 48 hours to mimic conditions at term labor. Phosphorylated and total -GSK3β and p38MAPK expressions were determined in both mice (S389) and human (S9) samples using western blot.

RESULTS: P-GSK3β expression was seen in human and mice samples. Western blot analysis of mouse placenta showed P-GSK3β gradually increased from day 10 until day 18. While, mouse fetal membranes showed expression of P-GSK3β by day 15 that remained until day 18. P-p38MAPK expression correlated with this data in both tissues. Human AECs also showed the same trend of increasing P-GSK3β correlated with P-p38MAK in OS induced AECs.

CONCLUSIONS: Increased phosphorylation of p38MAK at term has been shown in humans and mice causing it to be known as one of the main activators of senescence in parturition. Here we show that P-GSK3β correlates with increased p38MAPK activation towards term in human (membranes) and mice (placenta and membranes) suggesting that a synergy between the two signals to provide a homeostatic balance to promote cell survival in wake of senescence activation.

Supported by the Dept. of OB/GYN UTMB Galveston, Dept. of OB., GYN. and Reproductive Sciences UVM Burlington and the Vermont Cent. for Immunology and Infectious Disease.

F-029

A Novel Three-Dimensional Cell Culture Model for Human Amnion Mesenchymal Cells. Kimberly Foca,[1] Eric S Collier,[1] Claire E Kendal-Wright*.[1,2] *[1]Chaminade University of Honolulu, Honolulu, HI, USA; [2]John A. Burns School of Medicine, University of Hawai'i, Honolulu, HI, USA.*

INTRODUCTION: Studying human amnion mesenchymal cells (AMC) is critically important to further our understanding of the mechanisms of fetal membrane rupture. However, typical two-dimensional culture is known to force cells to express an apical-basal polarity and alter cellular behavior by altering cell to cell and to matrix adhesions. Cells are able to change their behavior dependent on environmental cues, therefore research performed on AMC to understand their role in fetal membrane rupture may generate data that is not reflective of the *in vivo* behavior of these cells. Thus, the aim of this work was to develop a cell culture

system that enables AMC to maintain their in vivo morphology and behavior to improve our ability to understand the role of these cells in membrane rupture.
METHODS: Human AMC were isolated from normal, term, fetal membranes from repeat caesarean section at Kapi'olani Medical Center for Women and Children with IRB approval. The AMC were grown in regular 2D and 3D Alvetex™ polystyrene scaffold culture systems. Their survival behavior was validated based on cell density, proliferation, migration and changes in cellular morphology by histology, and cytochemistry, and their cytotoxicity level by LDH assay (n=6). The relative expression of cell adhesion genes between 2D and 3D culture was determined by RT² Profiler PCR Array (n=3), and subsequently confirmed by real-time PCR (n=3).
RESULTS: AMC were able to adhere to the Alvetex scaffold in a 3D fashion while proliferating and migrating throughout, with low levels of cytotoxicity. The most conspicuous change was that AMC morphology changed from a flattened hypertrophic appearance in traditional 2D culture to a thin spindle shape in 3D that was reminiscent of their morphology *in vivo*. Preliminary gene array data also showed that the 3D culture environment affected the behavior of the AMC as they had significant differential expression levels of cell adhesion genes, for example, collagen VIII and thrombospondin I.
CONCLUSIONS: This work demonstrates that AMC remain viable in the inert polystyrene scaffold, with clear morphological and behavioral differences compared to traditional 2D culture. The generation of a novel 3D system constitutes a leap forward in recreating an environment in which the vital role AMC in human fetal membrane weakening may be studied.

F-030

Progesterone Synergistically Augments Cytokine-Induced 11β-Hydroxysteroid Dehydrogenase-1 Expression in Cervical Stromal Fibroblasts. Douglas A Kniss*, Taryn L Summerfield, William E Ackerman IV. *The Ohio State University, Columbus, OH, USA.*
INTRODUCTION: Progesterone (P_4) is essential for the maintenance of pregnancy and exerts several anti-inflammatory functions in uterine tissues. In the current study, we tested the hypothesis that P_4 can stimulate local production of the anti-inflammatory steroid, cortisol. We also evaluated whether the steroid could reverse the effects of cytokine stimulation in cervical fibroblasts.
METHODS: Cervical stromal fibroblasts were cultured from specimens obtained following informed consent from premenopausal women undergoing hysterectomy for non-malignant indications. Cells were grown in DMEM+10% FBS then shifted to F12/DMEM+0.5% charcoal-stripped FBS in the presence or absence of 17β-estradiol (17β-E_2, 10^{-8} M) for 7-10 d. Cells were then incubated with progesterone (P_4, 10^{-7} M) for 1 d followed by a 24-h challenge with IL-1β (0.2 ng/ml). After treatments, media were collected for cortisol measurements and RNA was extracted for gene expression analysis by microarray and qRT-PCR. Cortisol production was measured by ELISA.
RESULTS: After 7-10 d of 17β-E_2 treatment, we detected both progesterone receptor isoforms (PR-A and PR-B) at nearly equal levels. Both P_4 and IL-1β stimulated a robust increase in 11β-HSD1 gene expression (P_4 > 5-fold; IL-1β>30-fold) using microarray analysis. When cells were co-incubated with both P_4 and IL-1β we detected a synergistic increase in 11β-HSD1 expression (>93-fold) using microarray analysis. When we confirmed the microarray data by qRT-PCR, we noted an even greater level of synergy, with both agents incubated together inducing a more than 500-fold increase in 11β-HSD1 mRNA expression. The enzyme was functionally active in that cells synthesized large amount of cortisol when incubated with cortisone. Cortisol production was inhibited by a 11β-HSD1-selective antagonist.
CONCLUSIONS: These data suggest that cervical stromal fibroblasts show P_4-inducible expression of the enzyme necessary for local cortisol biosynthesis as a means modulate tissue inflammation. We were surprised to also observe very robust stimulation of 11β-HSD1and cortisol production by IL-1β, indicating that stromal cells attempt to limit the extent of cytokine-driven inflammation. Supported by March of Dimes Prematurity Research Center Collaborative of Ohio.

F-031

A Dual Level of TLR4 Epigenetic Regulation Between Amnion and Choriodecidua at the Site of Rupture Prior to Labor. Corinne Belville,[1,2] Flora Ponelle-Chachuat,[1] Marion Rouzaire,[1] Gaël Clairefond,[1] Bruno Pereira,[3] Denis Gallot,[1,4] Vincent Sapin,[1,5] Loic Blanchon.[1] *[1]School of Medicine, Univ. Auvergne, Clermont-Fd, France; [2]UMR CNRS 6293-Clermont Université-INSERM U1103, Clermont-Fd, France; [3]CHU, Clermont-Fd, France; [4]CHU, Clermont-Fd, France; [5]CHU, Clermont-Fd, France.*
INTRODUCTION: Human fetal membranes (FM) protect the fetus against infections and regulate homeostasis of amniotic fluid. Before their rupture at term, FM develop a sterile inflammation associated with a global disorganization of the extracellular matrix between both layers: amnion and choriodecidua in a zone of altered morphology, abbreviated ZAM. This study analyze both methylomic and transcriptomic profiles of amnion and choriodecidua (from ZAM and a zone of intact morphology, ZIM) at term before labor.
METHODS: Amnion and choriodecidua explants of ZAM and ZIM were collected from 9 patients after caesarean births prior to labor. Samples were subjected to methylomic and transcriptomic screening. Bioinformatics analysis were conducted by comparing layers and zones on cytosine methylation and gene expression. A particular focus was done on TLR4 expression using RT-qPCR, Western-blot and miRNA targeting using 3'UTR-luciferase reporter experiments and transfection of pre-miRNA in primary amniocytes and established amniotic cell line AV3.
RESULTS: Analysis of methylomic results demonstrated no significant difference between ZIM and ZAM, whereas defense response looks like to be one of the most important biological process differentially regulated in ZAM between both layers at methylomic and trancriptomic level. Furthermore, in ZAM, as a center piece of such process, the expression of TLR4 (Toll Like Receptor-4) one actor of the sterile inflammation is regulated between both layers by a dual mechanism: 1) methylation of TLR4 and of miRNA promoters; and 2) new miRNA (let-7a-2 and miR-125b-1) targeting 3'-UTR of TLR4.
CONCLUSIONS: For the first time, we fully characterized at term without labor the complete methylomic and trancriptomic profile of ZIM and ZAM zones. Beyond all biological processes, sterile inflammation was confirmed to be of primary importance. These results, gain from physiological preparation of FM rupture, will permit to obtain a better knowledge of molecular dysregulations leading to premature rupture of fetal membranes.

F-032

Measuring *In Vivo* Uterine Contractile Activity of Pregnant Mice via a Transcervical Intrauterine Pressure Catheter (IUPC). Michael Robuck, Christine O'Brien, Jeff Reese, Jennifer Herington*. *Vanderbilt, Nashville, TN, USA.*
INTRODUCTION: In humans, uterine activity during labor is monitored externally by palpation or tocodynamometry, or internally utilizing a transcervical intrauterine pressure catheter (IUPC). While IUPC is the gold standard for measuring intrauterine pressure (IUP), its use is restricted to high-risk pregnancies. In mouse models used to study parturition, uterine contractions is measured by: *ex vivo* isometric tension, *in vivo* IUPC inserted transabdominally into the uterus or *in vivo* IUPC-radiotelemetry. The goal of this study was to develop a method for transcervical insertion of a MikroTip IUPC during mouse pregnancy to measure *in vivo* intrauterine contractile pressure, using similar clinical methods for humans.
METHODS: A speculum tube was used to visualize the cervical opening for IUPC placement into anesthetized (2.5mg/kg Avertin) pregnant CD1 mice (plug=day 1, delivery=day 19.5). IUP was measured on antepartum days 16, 18 and 19, and intrapartum. IUP was also examined in mice treated daily with progesterone (P_4, 2 mg/mouse) day 18-20, including the morning of IUPC or 24hr P_4-withdrawl prior to IUPC. IUP was measured in mmHg over time and analyzed for area under the contractile curve (AUCC). The ability to differentiate between AUCC obtained intrapartum versus from non-P_4 treated day 19 andP_4-treated (delayed labor) day 20 mice was determined by sensitivity, specificity and positive predictive value (PPV) calculations. N=2-5 mice for each timepoint and treatment.

RESULTS: IUP significantly ($p<0.05$, one-way ANOVA) increased from days 16-19 of pregnancy.

Day	**Non-P_4 tx** mean±s.d.	
16	0.51±0.13	
18	0.66±0.17	
19	1.84±0.55	
Intrapartum	3.57±0.84	
	P_4-tx (including day of IUPC) mean±s.d.	**P_4-tx (except 24hrs prior to IUPC)** mean±s.d.
19	1.02±0	
20	2.04±1.24	3.63±0
21	2.28±0.84	6.41±0.87

In P_4-treated mice, IUP remained significantly lower compared to time matched mice that had not received P_4 for at least 24hrs. The sensitivity, specificity and PPV were 100% for discriminating between active labor (intrapartum) and non-active labor when the AUCC threshold was set to 3.0mmHg. At a threshold of 2.5mmHg, the sensitivity remained at 100%, while the specificity and PPV decreased to 89% and 75%, respectively.
CONCLUSIONS: Transcervical IUPC is a sensitive method that can be utilized to assess *in vivo* contractile activity and labor progression in mouse models.

F-033

Expression Fingerprints of Human Primary Myometrial, hTERT and PHM Cells in Comparison to Term Myometrium for Myometrial Tissue Engineering. Minoo Heidari Kani†,[1,2] Jonathan W Paul,[1,2] Roger C Young,[1] Eng-Cheng Chan,[1,2] Roger Smith*.[1,2] *[1]University of Newcastle, Newcastle, NSW, Australia; [2]Hunter Medical Research Institute, Newcastle, NSW, Australia.*
INTRODUCTION: Dysregulated myometrial function can result in serious medical conditions, such as preterm labor and post-term pregnancy. The mechanisms that regulate uterine contractility during pregnancy are yet to be fully elucidated. Primary myometrial cells, human telomerase reverse transcriptase (hTERT) cells and Pregnant Human Myometrial (PHM) cells are used to study myometrial function. To identify the most appropriate cell model to mimic *in vivo* myometrium for tissue engineering, it is important to understand the gene expression and protein localization of key contraction-associated proteins (CAPs) between these cells compared to term-labouring myometrial tissue.
METHODS: Human myometrial tissue biopsies were obtained from term, non-labouring Caesarean sections. Isolated myocytes, hTERT cells and PHM cells were cultured under the same conditions. To characterize expression of key CAPs in Primary, hTERT and PHM cells, qPCR followed by Principal Component Analysis was performed to determine the expression levels of genes encoding α-actin, Caldesmon, Connexin-43, Myosin Light Chain, Oxytocin receptor and Vimentin. To assess protein localization, CAPs were visualised using immunocytochemistry coupled with confocal microscopy.
RESULTS: Principal Component Analysis revealed that Primary cells most closely resembled *in vivo* myometrium in terms of gene expression for CAPs, however, each cell type was similar to term non-labouring myometrium in different ways. Confocal analyses revealed that Primary cells and hTERT cells were consistent in their expression and localization of CAPs, whereas PHM cells exhibited different localization profiles.
**Figure(s) will be available online.*
CONCLUSIONS: These findings provide insight into the expression of key CAPs in cell lines that are commonly used to study myometrial function *in vitro*. Primary myocytes represent the best *in vitro* model, however limited life span may point to hTERT cells as an appropriate alternative in which to develop tissue engineering strategies.

F-034

Effects of Brief and Long Periods of Hypoxic Stress on Myometrial Contractility from Term Pregnant Women. Lele Wang†, Huiping Hu, Junjie Bao, Shao-Qing Shi, Robert E Garfield, Huishu Liu*. *Guangzhou Women and children's Medical Center, Guangzhou Medical University, Guangzhou, China.*
INTRODUCTION: Hypoxia is known to significantly reduce uterine contractile activity during labor. However, there are no studies of brief vs. long hypoxia periods on human uterine contractility. **Objectives:** The purposes of this study were to identify and analyze the effects of hypoxia on contractions of uterine myometrial strips from term pregnant women.
METHODS: Uterine strips were obtained from pregnant women at term undergoing elective cesarean section. Strips were equilibrated at 37 °C in normoxic solution (Kreb's, 95% O_2 and 5% CO_2). After steady spontaneous contractions were obtained, the effect of repeated episodes of transient hypoxia was investigated by replacing the oxygen in the chamber bath with 100% N_2 for 6 min, and then reoxygennation for 30 min. The activities of uterine strips were simultaneously recorded by Lab Chart software (ADInstruments). The contractions were analyzed to obtain mean frequency, amplitude, and duration of contractions.
RESULTS: 10 strips from 8 women were investigated. The mean age of patients was 31.40±2.73 years, and the gestational ages were 38.67±0.47 weeks. The mean amplitude of the uterine strips significantly increased ($P<0.001$) from baseline uterine activity (gm, 13.78±5.57) in the first cycle of hypoxia and reoxygenation (20.31±6.49). In the second and third cycles of hypoxia and reoxygenation, the values were significantly decreased ($P<0.001$,11.95±4.65 and 10.22±3.92). Significant differences were seen in the frequency of the strips during the brief hypoxia(no. contractions/10 minutes, baseline =Hz,1.42±0.63 vs. first hypoxia period = 1.25±0.39, 2nd hypoxia = 1.45±0.60, and 3rd hypoxia = 1.64±0.63, $P<0.001$). The duration of the contractions was increased ($P<0.001$) after the first cycle of hypoxia, but decreased significantly in the second and the third cycles (minutes, baseline = 1.86±0.96 vs. 1st hypoxia period = 2.58±1.34, 2nd hypoxia = 1.44±1.10, 3rd hypoxia = 1.31±0.99, $P<0.001$).
CONCLUSIONS: 1) Brief hypoxia periods increase in amplitude and duration but not frequency of myometrial contractions. 2) Perhaps the mechanism of increase in uterine contractions results in a more successful spontaneous birth. 3) Long periods of hypoxia decrease uterine contractility and results in delay in delivery. 4) Oxygen therapy is indicated in delays in delivery associated with hypoxia.

F-035

Circulating Markers of the Uterine Unfolded Protein Response Reflect Pregnancy Outcomes. Chandrashekara N Kyathanahalli†,[1] Offer Erez,[1,2] Piya Chaemsaithong,[2] Adi L Tarca,[2] Roberto Romero,[1,2] Sonia S Hassan,[1,2] Pancharatnam Jeyasuria,[1,2] Jennifer C Condon.[1,2] *[1]Wayne State University School of Medicine, Detroit, MI, USA; [2]NICHD, Detroit, MI, USA.*
INTRODUCTION: We have defined the functional relevance of the uterine unfolded protein response (UPR) in regulating gestational length. In the pregnant mouse model we observed an increase in the adaptive UPR (chaperone protein GRP78) promotes uterine quiescence to term, with a decline observed prior to the onset of labor(TL). In contrast the onset of preterm labor (PTL) was associated with a surge in uterine GRP78[1]. Moreover the gestational profile of uterine UPR in both TL and PTL was recapitulated in circulating PBMC's isolated from the serum of pregnant mice. This current study examines UPR markers in the serum of pregnant women and examine if their gestational profiles correlate with the onset of TL and PTL.
METHODS: Serum, PBMC's and uterine tissues were obtained from non-pregnant and pregnant CD1 mice (E1-E19) at TL and PTL (LPS, RU-486 and Tunicamycin). Protein lysates were evaluated for UPR markers by immunoblotting.
Serum samples from non-pregnant, pregnant, TL and PTL women were collected in a cross sectional manner. Intrauterine infection (IAI) is indicated by a positive amniotic fluid culture; and intrauterine inflammation (IF) by amniotic fluid IL-6 concentration ≥2.6ng/ml. PTL samples were obtained at the time of clinical presentation. ELISA was utilized to examine serum UPR profiles.

RESULTS: The uterine profile of GRP78 in the pregnant mouse undergoing TL and PTL was recapitulated in the circulating PBMC's ($p<0.01$). The median serum GRP78 levels in human samples,
(a) increased in pregnant women when compared to non pregnant ($p<0.01$)
(b) increased in TL women compared to term non laboring women ($p<0.001$)
(c) decreased in PT laboring women without IAI or IF compared to those with IAI and IF ($p<0.01$)
(d) decreased in PTL women without IAI and IF compared to those who delivered at term ($p<0.001$).
CONCLUSIONS: Our data demonstrates that circulating marker of the UPR are readily detectable in the pregnant mouse and human in a pregnancy dependent manner. Human TL is associated with increased GRP78, whereas PTL in the absence of IAI or IF is associated with decreased serum GRP78. We speculate that circulating markers of the UPR may reflect uterine refractoriness during pregnancy.
[1] Kyathanahalli CN et al., 2015, Proc Natl Acad Sci U S A.112(45):14090-5.

F-036

The Association Between Intrahepatic Cholestasis of Pregnancy and Gestational Diabetes. Eli Rimon*, Yael Raz, Michael Kupferminc, Yariv Yogev. *Tel Aviv Medical center, Tel Aviv University, Tel Aviv, Israel.*
INTRODUCTION: Intrahepatic cholestasis of pregnancy (ICP) is characterized by pruritus, elevated liver enzymes and elevated total bile acids (TBA)level. It is known to be associated with fetal complications but recently it was suggested to be associated maternal-fetal complications. The aim of this study was to investigate the association between ICP and gestational diabetes (GDM).
METHODS: The study group included 78 women (54 singletons and 24 twin pregnancies) who had been diagnosed with ICP based on clinical presentation, elevated liver enzymes, and elevated TBA (>10 mmol/L). Disease severity was based on TBA levels as being severe (>40 mmol/L), moderate (20-40 mmol/L), or mild (10-20 mmol/L). Screening for GDM was performed between 24 -28 weeks and 100 gr oral glucose test was used to confirm the diagnosis. The control groups were comprised of apparently healthy women with singleton (n= 200) and twin (n=100) pregnancies that were drawn randomly from a computerized registry.
RESULTS: The incidence of GDM was significantly higher for the patients with ICP who had singleton pregnancies compared with the control group (16.7% vs. 5.6%; $P < .05$, respectively). As for ICP severity, 4 women with GDM had severe ICP, 2 had moderate ICP and 3 had mild disease. No significant differences were found in the maternal age, gravity. parity, presentational body mass index (BMI), gestational age (GA) at the onset of ICP, GA at delivery, birth weight and neonatal outcome between women with or without GDM (table 1). In all cases of GDM the diagnosis was confirmed before the onset of ICP. The incidence of GDM in twin pregnancies with ICP was not significantly higher compared with the control group (8.3 % vs. 4.1 %; P =0.34, respectively).

	Singleton pregnancies with ICP		
(mean±SD)	GDM n=9	No GDM n=45	
Age (y)	33.4±6	33.3±5.5	NS
Gravity	1.7±1.1	2.2±1.3	NS
Parity	0.6±0.9	0.8±O.9	NS
Pregestational BMI (Kg/m²)	25±6.2	24.3±4	NS
GA at onset of ICP (wks)	32.4±2.4	33.4±2.7	NS
GA at deliveryh (wks)	36.7±2.2	37.2±1	NS
Birth weight (gr)	3070±680	2870±450	NS

CONCLUSIONS: The data suggest that there is an association between ICP and GDM. As there is an icreasing evidence that ICP is associated with glucose intolerance, there might be a common metabolic pathway that is altered in ICP and is also involved in glucose homeostasis and GDM.

F-037

Novel Use of an Intra-Aortic Balloon May Limit Morbidity in Patients with Placenta Percreta. Elizabeth Blumenthal†,[1] Rashmi Rao,[1] Aisling Murphy,[1] Jeffrey Gornbein,[2] Richard Hong,[3] John M Moriarty,[4] Daniel A Kahn,[1] Carla Janzen*.[1] *[1]UCLA, Los Angeles, CA, USA; [2]UCLA, Los Angeles, CA, USA; [3]UCLA, Los Angeles, CA, USA; [4]UCLA, Los Angeles, CA, USA.*
INTRODUCTION: The increasing incidence and significant morbidity of abnormal placentation have made novel procedures that assist in improving outcomes increasingly relevant. We study whether using an intra-aortic balloon (IAB) during cesarean hysterectomy decreases delivery morbidity in patients with suspected placenta percreta.
METHODS: Our IRB approved retrospective cohort study of deliveries complicated by suspected abnormal placentation between 2009-2016 compared maternal and neonatal outcomes with an IAB placed prior to cesarean hysterectomy versus no IAB. Primary outcomes included estimated blood loss (EBL), surgical complications, and surgical duration. P values for comparing binary variables were computed with Fisher's exact test. P values for comparing non normal continuous variables were computed with Wilcoxon rank sum test. EBL and surgical duration confounding was adjusted with multiple regression.
RESULTS: 35 cases were reviewed, 16 with IAB and 19 without. Controlling for 6 covariates (use of general anesthesia, multiple gestation, unscheduled cases, prior abdominal surgery), we found a decrease in the number of transfusions in the IAB group (median 1.5 vs 2, p =0.27) but we found no significant differences in median EBL (1351 cc vs 1397 cc; p=0.90), overall surgical complications (19% IAB, 21% no IAB, p=0.86), bladder complications (12% vs 21%; p=0.66), ICU admissions (12% vs 26%, p=0.41), or surgery duration (2.9 vs 2.8 hrs, p=0.83), after controlling for covariates. No significant differences in postoperative complications, length of hospital stay, NICU admissions or Apgar scores were detected. There was one groin hematoma at the balloon site that was managed conservatively. There were no complications involving thrombosis or limb ischemia in the IAB group.
CONCLUSIONS: Our study demonstrates a trend toward fewer bladder injuries, ICU admissions and blood transfusions with the use of an IAB for suspected placenta percreta that did not reach statistical significance due to sample size. Given the potential for extreme morbidity with abnormal placentation, this novel approach may assist in reducing blood loss and surgical complications and warrants larger studies powered to detect these differences.

F-038

Is the Effect of Hyperemesis Gravidarum on Gestational Weight Gain Risk Modified by Prepregnancy Body Mass Index? Michael J Fassett,[1] Darios Getahun,[2] Vicki Y Chiu,[2] Harpreet S Takhar,[2] Morgan R Peltier*.[3] *[1]Kaiser Permanente West Los Angeles Medical Center, Los Angeles, CA, USA; [2]Kaiser Permanente Southern California, Pasadena, CA, USA; [3]Winthrop University Hospital, Mineola, NY, USA.*
INTRODUCTION: Obesity among women of childbearing age is an important public health issue, as many serious adverse maternal and child outcomes are associated with it. Hyperemesis gravidarum (HG), a complication that can cause persistent nausea and vomiting leading to dehydration and malnutrition. The significance of maternal prepregnancy body-mass index (BMI) on the risk of and consequences of HG are unclear. Therefore, we examined if the effects of HG on gestational weight gain (GWG) as modified by maternal prepregnancy body-mass-index (BMI).
METHODS: We performed a retrospective cohort study using the 2007-2014 electronic medical records of 190,322 singleton pregnancies delivered at >22 weeks of gestation at the Kaiser Permanente Southern California hospitals. The Institute of Medicine (IOM) recommended GWG ranges of 28-40, 25-35, 15-25, and ≥15 pounds for women with BMI <18.5, 18.5-24.9, 25.0-29.9 and ≥30, respectively, were used in this study. The distribution of maternal characteristics by prepregnancy BMI categories were compared. The association between HG and GWG were compared based on pregnancy BMI category. Adjusted relative risks (RR) and their 95% confidence intervals (CI) were used to explain the magnitude of association.

RESULTS: The proportion of pregnant women at BMI <18.5, 18.5-24.9, 25-29.9, and ≥30 were 2.4%, 43.8%, 28.2%, and 25.6%, respectively. 45% of women with pre-pregnancy BMI <18.5, 39% of BMI 18.5-24.9, 28% of BMI 25-29.9, and 25% of women with BMI ≥30 gained IOM-recommended weight during their pregnancy. A total of 84,950 (45%) of pregnant women had weight gain over, and 43,738 (23%) under IOM-recommended weight gain ranges. Compared with women with IOM-recommended GWG, women with HG failed to achieve their target weight gain by 1.20 fold (95% CI: 0.92, 1.55), 1.30-fold (95% CI: 1.21, 1.40), 1.54-fold (95% CI: 1.37, 1.72), and 1.39-fold (95% CI: 1.25, 1.54) at prepregnancy BMI of <18.5, 18.5-24.9, 25-29.9, and ≥30, respectively.
CONCLUSIONS: Hyperemesis gravidarum is associated with an increased risk of not achieving IOM-recommended weight gain regardless of the woman's prepregnancy BMI.

F-039

Labor Induction Outcomes with Prostaglandin Vaginal Inserts in Obese Women. Mary N Zaki†,[1] Megan L Stephenson,[2] Kyle Raymond,[3] Olaf Rugarn,[3] Barbara Powers,[5] Deborah A Wing*.[1] *[1]University of California, Irvine, Orange, CA, USA; [2]Kaiser Permanente, Santa Clara, CA, USA; [3]Ferring Pharmaceuticals, Copenhagen, Denmark; [4]None, Phoenixville, PA, USA.*
INTRODUCTION: To evaluate the impact of obesity on women undergoing labor induction with prostaglandin vaginal inserts.
METHODS: This was a post-hoc analysis of data collected in Phase 2 and 3, multi-center, double-blind, randomized controlled trials of women undergoing induction of labor with dinoprostone (DVI) and misoprostol (MVI) vaginal inserts (Miso-Obs-004, 204, 303). Women were grouped according to baseline body mass index (BMI) with <30 kg/m^2 (non-obese) compared to 30 to <35 kg/m^2, 35 to <40 kg/m^2, and ≥40 kg/m^2 (obese). Outcomes included time to active labor, time to vaginal delivery, pre-delivery oxytocin use, and time to cesarean delivery (CD).
RESULTS: 1909 women were included in this analysis. Compared to women with a BMI <30 kg/m^2, the relative hazard rate of achieving active labor among women with BMI of 30 to <35, 35 to <40 and ≥40 kg/m^2 was reduced (0.85 [95% CI 0.76-0.97, p=0.01], 0.86 [95% CI 0.75-0.98, p=0.02] and 0.62 [95% CI 0.54-0.72, p<0.001], respectively). Increased BMI was also associated with a significant decrease in the cumulative incidence of vaginal delivery (Figure 1). Similarly, women with BMI of 35 to <40 and ≥40 kg/m^2 had significantly higher odds of receiving pre-delivery oxytocin than those with BMI <30 kg/m^2 (adjusted odds ratios (aOR) of 1.47 [95% CI 1.12-1.94, p=0.006] and 1.71 [95% CI 1.28-2.30, p<0.001], respectively). Obese women were also had an increased cumulative incidence of CD compared to women with a BMI <30kg/m^2 (adjusted sub-distributional hazard ratios of 1.39 [95% CI 1.08-1.80, p=0.012], 1.64 [95% CI 1.26-2.13, p<0.001], and 1.92 [95% CI 1.48-2.50, p<0.001] respectively).
**Figure(s) will be available online.*
CONCLUSIONS: Obese women in these studies took longer to achieve active labor and deliver and had an increased probability of pre-delivery oxytocin use and CD compared to the non-obese. These factors should be considered when counseling obese women regarding expectations for a successful labor induction.

F-040

Are the Genetics of Heme Oxygenase-1 Associated with Preeclampsia? Sarah Anderson†, Elena Lobashevsky, Keith Do†, Adrienne Wiggins†, Joseph Biggio*. *University of Alabama at Birmingham, Birmingham, AL, USA.*
INTRODUCTION: Heme oxygenase (HO-1) has many functions, including vascular tone, regulation of inflammation and apoptosis, angiogenesis, and antioxidant capabilities. HO-1 plays a key role in the production of CO, a vasodilator. HO-1 is important in spiral artery remodeling and placental development. HO-1 knockout mice are hypertensive and women who develop pre-eclampsia (PRE) have lower levels of HO-1. A SNP in the promoter of *HO-1* has been associated with lower levels of HO-1 production with the TT genotype. We investigated if women who developed PRE with severe features before 37 wks had a different genotype at this SNP.
METHODS: This is a case-control study of women with PRE with severe features (per ACOG definitions) delivered before 37 wks from 2011- 2016 at a single institution. Race-matched controls were women with full-term deliveries and no clinical diagnosis of PRE. All diagnoses were confirmed by chart review. Patients with chronic hypertension were excluded. DNA was extracted from stored blood samples, and Taqman PCR assay performed for genotyping of rs2071746 using a commercially available kit (Qiagen, Valencia, CA & Applied Biosystems, Foster City, CA). Differences were assessed at the allele and genotype levels, in dominant and recessive models, using chi-squared test and multivariable logistic regressions to evaluate for association with PRE. With a power of 90%, and prevalence of 29% for the TT genotype we calculated the sample size with a 1:2 match.
RESULTS: 113 patients with PRE with severe features and 223 controls were genotyped. The frequency of the T allele was similar between groups (62.4 % vs 58.3%, p=0.31). Genotype (Table 1) was not associated with development of PRE (p=0.38). Dominant and recessive genetic models were evaluated and found no association with PRE.
**Figure(s) will be available online.*
CONCLUSIONS: Although carriage of the T allele at rs2071746 in the promoter of HO-1 has been associated with lower levels of HO-1 mRNA and HO-1 concentrations, genotype at this SNP is not associated with early onset severe PRE. As HO-1 is an important candidate gene for PRE further genetic variants in this gene should be investigated.

F-041

Preterm Fetal Growth Restriction with Acidemia Is Associated with Changes in mRNA Expression in Maternal Blood: The FOX Study. Owen Stock,[1] Susan P Walker,[1] Lavinia Gordon,[1] Joanne Said,[1] Natalie Hannan,[1] Katie Groom,[2] Scott Peterson,[3] Sean Seeho,[4] Amanda Henry,[4] Stefan C Kane,[1] Clare L Whitehead,[1] Stephen Tong*.[1] *[1]University of Melbourne, Melbourne, VIC, Australia; [2]Univ of Auckland, Auckland, New Zealand; [3]Mater Hospital, Brisbane, QLD, Australia; [4]UNSW, Sydney, NSW, Australia.*
INTRODUCTION: Preterm, growth restricted fetuses with significant acidemia are at high risk of imminent stillbirth. We performed a large prospective study to develop a blood test to identify significant fetal acidemia in preterm fetal growth restriction (FGR).
METHODS: We performed a prospective study (The FOX study, Fetal Oxygenation Study) across six hospitals in Australia and New Zealand. We recruited 128 cases of FGR delivered by caesarean section <34 weeks due to clinical suspicion of fetal compromise. We obtained maternal blood within 2 hours of birth and measured umbilical cord pH at delivery (reflects fetal acidemic status during the final moments in utero). We also collected maternal blood from gestation matched controls (n=84, delivered at term). RNA in the maternal blood (collected in Paxgene tubes) was measured using RNA-seq (Illumina HiSeq 2500). To undertake bioinformatics, the statistical program R was used.
RESULTS: Sequencing yield was very consistent across the 212 samples (<10% variance), and the sequencing was of very high quality (median %>=Q30 of 96%). Gender, case status or sample location had no influence on sample profile.
When comparing mRNA expression in maternal blood among the FGR cohort (n=128) vs controls (n=84), there were global changes in gene expression (11,402 genes differentially expressed, adjusted p<0.05). Fold change threshold calculation identified 21 genes that were consistently expressed differentially among cases vs controls. Gene ontology analysis found genes involved in placental development were down-regulated in the FGR cohort and genes associated with hypoxia were significantly up-regulated in the FGR cohort.
We next dichotomised the FGR cohort according to whether the umbilical cord pH was ≤ 7.2 (low pH) or over and identified 11 genes that were differentially expressed. When we treated pH as a continuous variable, we identified 17 genes in maternal blood that were significantly correlated. These findings are currently being validated by RT-PCR and digital PCR.
CONCLUSIONS: The presence of acidemia in preterm FGR is associated with differential mRNA gene expression in maternal blood.

F-042

Induction of Labor with the Recommended Two Hourly Oral Misoprostol Regimen. Abdulrahim A Rouzi*, Nora Sahly, Nisma Mansouri, Nawal Alsenani, Rana Alamoudi, Rayyan Rozzah. *King Abdulaziz University, Jeddah, Makkah, Saudi Arabia.*

INTRODUCTION: Labor induction using oral misoprostol has been studied extensively, with a recommended dose and treatment interval published by FIGO and WHO; however, only one study has been reported that used the recommended regimen. The objective was assess the efficacy and safety of the recommended 2 hourly oral misoprostol regimen for labor induction.

METHODS: Between May and November 2013, the hospital records of 83 women who were induced for labor and met the eligibility criteria were retrospectively review. Eligibility criteria were singleton pregnancy of at least 34 weeks' gestation and a baseline Bishop score <6. Women with previous cesarean section or other uterine surgery, severe pregnancy-induced hypertension, and parity of 4 or more were excluded. Oral misoprostol was administered as 20 µg 2 hourly unless active labor. A maximum of 12 doses was allowed.

RESULTS: The age of the women was 27.9 ± 5.3 years (mean ± SD). Vaginal delivery within 24 hours occurred in 38 (45.8%) women. Cesarean delivery occurred in 17 (20.5%) women. Although more parous women achieved vaginal delivery within 24 hours (52.6%) compared with nulliparous women (40.0%), the difference was not significant (P=.35). Uterine tachysystole occurred in 12 (14.5%) women. No perinatal deaths or neonatal intensive care unit admission occurred in the study group.

CONCLUSIONS: Evidence supporting an optimal regimen is lacking and additional research is warranted to optimize the use of oral misoprostol for the induction of labor.

F-043

Risk Factors for Prolonged Interval from PROM to Delivery in Women with a Prior CS. Reem Elmikawy†,[1] Ruthy Beer-Weisel,[2] Eric Kachko†,[3] Shirley Greenbaum†,[2] Majdi Imterat†,[2] Tal Rafaeli-Yehudai†,[2] Neta Benshalom-Tirosh†,[2] Limor Besser†,[2] Offer Erez*.[2] *[1]Faculty of Health Sciences, Soroka University Medical Center, Ben Gurion University of the Negev, Beer Sheva, Israel; [2]Faculty of Health Sciences, Soroka University Medical Center, Ben Gurion University of the Negev, Beer Sheva, Israel; [3]Faculty of Health Sciences, Soroka University Medical Center, Ben Gurion University of the Negev, Beer Sheva, Israel.*

INTRODUCTION: The management of term pre labor rupture of membranes (PROM) in women with a prior cesarean section (CS) is under debate. The infectious morbidity associated with prolonged interval from admission to delivery, is countered by the risk for CS scar rupture during active management. Therefore, in these women, we aimed to study: 1) maternal risk factors for prolonged interval; and 2) the effect of prolonged interval on infectious and other obstetric complications.

METHODS: This population-based retrospective cohort study, included all women (n=819) who delivered in our medical center (1988-2013), with a prior CS and term PROM in the index pregnancy. Study population was divided into two groups; 1) those who delivered ≤24h from PROM (n=514) and 2) those who delivered >24h (n=305) from PROM. A negative binomial model was used for the identification of independent risk factors for prolonged interval.

RESULTS: The rate of smokers (p=0.03) and chronic hypertension (HTN) was higher among women with a prolonged interval (p=0.009). The indications for the prior CS varied between the study groups. Cord prolapse, non-reassuring fetal heart rate and placental abruption were more prevalent in the short interval group, while the rate of first stage arrest was higher in the prolonged interval group. The rate of chorioamnionitis and first and second stage arrest, blood transfusion and wound infection were all higher in the prolonged interval group. Gestational diabetes (GDM) and chronic HTN were both independent risk factor for prolonged interval. Additionally, prolonged interval and first stage arrest were both independent risk factors for infectious maternal morbidity.

CONCLUSIONS: Among women with a prior CS: 1) GDM and smoking increase the risk of prolonged interval from PROM to delivery; 2) previous CS due to dystocia is associated with prolonged interval and its related morbidities; 3) these findings warrant reconsideration of trial of labor in women with term PROM and a prior CS due to labor dystocia.

F-044

Ultrasound-Indicated and Rescue Cervical Cerclage and Immediate Pregnancy Outcomes: A Retrospective Observational Study. V Andrews†, M Meritahti, S Thomas, Angela Yulia, N Wales, V Terzidou*. *Chelsea & Westminster Hospital, London, United Kingdom.*

INTRODUCTION: Preterm birth (PTB) causes more than one million deaths every year. Cervical cerclage and progesterone are the only widely used clinical strategies to prevent PTB. Two million cerclages are performed annually and their use is recommended in high-risk women with short cervical length (CL). Its mechanism of action is uncertain and evidence behind rescue cerclage, remains controversial.

Aims

(1) To assess USS-indicated and rescue cervical cerclage and examine pregnancy and neonatal outcomes: (2) To identify factors predictive of good and poor outcomes.

METHODS: Retrospective study of USS-indicated (CL<25mm) and rescue cervical cerclage at UK Teaching Hospital between Jan 2011 and Dec 2015.

RESULTS: 74 USS-indicated and 16 rescue cerclages included in study. Of the USS-indicated group, 48 had Shirodkar and 23 Macdonald; 56 had monofilament and 14 polyfilament suture. 83% (n=57) of women delivered at term and 17% (n=12) delivered preterm. On average pregnancies were prolonged by 20 weeks. There were 66 livebirths, 2 stillbirths and 1 neonatal death. PPROM rate was 5.4% and NICU admission 14.1%.

In the rescue group, 14 had Macdonald and 2 Shirodkar. Twelve had monofilament and two polyfilament. 71%(n=10) delivered at term and 28% (n=4) preterm. The pregnancies were prolonged by 17 weeks on average. All fourteen were livebirths. PPROM rate was 18.7% and NICU admission 25%.

History of prior PTB or mid-trimester loss had a higher rate of PTB compared to history of cervical surgery (30.4% vs 12.1%) and a higher rate of PPROM (8.7% vs 3%).

Gestation at cerclage insertion did not affect PTB rates (<16/40 – 20%, 16-19/40 - 19%, 20-23/40 – 17.1%, >24/40 – 25%).

Early CL was shorter in those delivering at extreme prematurity compared to those delivering at term (<28/40 – 21.9% , 28-33/40 -20.1% , 34-36/40 – 27.4%, >37/40- 25.3%). CL change was greater in those delivering at term compared to those who delivered very prematurely (<28/40 – 5.3%, 28-33/40 - 1% , 34-36/40 – 7.7%, >37/40- 7%).

CONCLUSIONS: USS-indicated and rescue cerclage can, in careful selected high-risk patients, significantly prolong the pregnancy, with relatively low complication rates.Prior PTB confers high risk for poor outcome compared to previous cervical surgery. Timing of cerclage insertion does not appear predictive of outcome. Starting CL appears more predictive of a poor outcome compared to CL change.

F-045

Predictive Values of ROM Plus® and Amnisure® for Diagnosing Rupture of Membranes by Pre-Test Probabilities. Lauren Theilen†,[1,2] Sean Esplin,[1,2] Matthew Hoffman*.[3] *[1]University of Utah, Salt Lake City, UT, USA; [2]Intermountain Healthcare, Salt Lake City, UT, USA; [3]Christiana Healthcare, Newark, DE, USA.*

INTRODUCTION: We aim to determine the predictive values of ROM Plus® and Amnisure® by pre-test probability for SROM based on history.

METHODS: We performed a secondary analysis of a multicenter prospective observational study of pregnant women with possible SROM. Participants underwent a targeted history, sterile speculum exam, ROM Plus®, and Amnisure®. A final diagnosis of SROM or no SROM was made based on chart review. Women were considered to have had a high pre-test probability of SROM if they presented for leakage of fluid or oligohydramnios and complained of leaking clear watery fluid requiring a pad, intermediate pre-test probability if they presented for leakage of

clear mucous, and low pre-test probability if they presented for leakage of mucous not requiring a pad. Test characteristics for each immunoassay were calculated in the context of pre-test probabilities for SROM.
RESULTS: A total of 324 women were enrolled, of whom 121 (37.4%) had a final diagnosis of SROM. Within the high pre-test probability group (n=113), 64 women (56.6%) had a confirmed final diagnosis of SROM. Within the intermediate pre-test probability group (n=48), 21 women (44%) had a confirmed final diagnosis of SROM. Within the low pre-test probability group (n=43), 9 women (20.9%) had a confirmed final diagnosis of SROM. The test characteristics for each immunoassay in the setting of each pre-test probability category are provided in Table 1 and Table 2.
CONCLUSIONS: Although overall test characteristics for both immunoassays are favorable, a positive result in a woman with otherwise low clinical suspicion for SROM should be interpreted with caution.
**Figure(s) will be available online.*

F-046

Is Uterocervical Angle Associated with Gestational Latency After Physical Exam Indicated Cerclage? Kate Swanson†,[1] William A Grobman,[2] Emily S Miller*.[2] *[1]Northwestern University Feinberg School of Medicine, Chicago, IL, USA; [2]Northwestern University Feinberg School of Medicine, Chicago, IL, USA.*
INTRODUCTION: The ability to predict gestational latency after placement of physical exam indicated cerclage (PEIC) is limited. Uterocervical angle (UCA) has been shown to be associated with spontaneous preterm delivery in the general population. It is not known whether these findings could also be predictive tools in the setting of PEIC. Our objective was to examine whether UCA is associated with gestational latency in women with a PEIC.
METHODS: This retrospective cohort included women with a singleton gestation who had a PEIC placed due cervical dilation at a single tertiary care center between January 2010 and September 2015. Ultrasound images of the cervix obtained prior to placement of PEIC were reviewed and UCA was measured. A Spearman's correlation coefficient for the relationship between UCA and gestational latency was estimated. Based on previously identified cut-offs predictive of preterm birth, UCA was dichotomized at 95° and 105°. Survival analyses were performed and Cox proportional hazard ratios calculated for the outcome of gestational latency at each of these cut offs.
RESULTS: Of the 60 women who met inclusion criteria, the median gestational latency was 93 days (IQR 39-121 days). There was no significant correlation between UCA and gestational latency (Spearman's rho 0.08, p=0.54). There were 35 (58%) women with a UCA≥95° and 22 (37%) with a UCA≥105°. Survival analyses demonstrated no significant difference in gestational latency stratified by UCA≥95° (HR 1.19, 95% CI 0.70-2.04) or UCA≥105° (HR 0.95, 95% CI 0.56-1.63).
**Figure(s) will be available online.*
These findings persisted after adjusting for potential confounders (aHR 1.29, 95% CI 0.74-2.23 for UCA≥95° and aHR 1.04, 95% CI 0.60-1.82).
CONCLUSIONS: UCA is not associated with gestational latency in women with a PEIC.

F-047

Assoiciation of Urinary Flame Retardant Concentrations, Gestational Weight Gain and Gestational Diabetes. Rosemary J Froehlich†,[1] Phinnara Has,[1] Megan Romano,[2] Nicola Hawley,[3] Joseph Braun,[2] Erika F Werner*.[1] *[1]Brown University, Providence, RI, USA; [2]Brown University, Providence, RI, USA; [3]Yale University, New Haven, CT, USA.*
INTRODUCTION: Flame retardants (FR) are common environmental chemicals and may be endocrine disruptors. We examined urinary FR metabolite concentrations in pregnant women and their association with gestational weight gain (GWG) and gestational diabetes (GDM).
METHODS: Observational cohort of low-risk women with singleton gestations planning delivery at one hospital in 2014. Urine samples were collected at enrollment (12±2 weeks), GDM, and group B streptococcus screening visits. Pooled specimens were created for each subject with 1 mL from each specimen. Maternal histories and anthropometrics were recorded. GDM was based on Carpenter Coustan criteria. Spearman's rank correlation and Wilcoxon rank-sum tests used for comparisons where appropriate.
RESULTS: Of 62 women enrolled, three withdrew consent, 1 lost to follow-up, and 1 delivered at 22 weeks (n=57). Fifty-four gave two urine samples and 41 gave three. The majority were white (66.7%), non-Hispanic (83.3%) and completed at least some college (73.8%). At delivery, mean maternal age was 29.5 years and mean gestational age was 39.1 weeks. Over half the subjects were overweight or obese in early pregnancy (59.6%), but excessive GWG rare (1.8%). The GDM rate was 14%. Three FR metabolites were frequently detected (>70% of urine samples): BCEtP (84%), BDCPP (98%), and DPhP (96%). Their pooled urinary concentrations were not associated with GWG stratified by early pregnancy BMI or diabetes status
**Figure(s) will be available online.*
CONCLUSIONS: Three FR metabolites were found in the urine of most subjects. Though we did not identify an association with GWG or GDM, given the ubiquitous nature of these compounds, further investigation is warranted.

F-048

Placental Lipid Metabolism in Obese Women with Gestational Diabetes Mellitus and Fetal Macrosomia. Haijun Gao, Jia Chen, Chandra Yallampalli. *Baylor College of Medicine/Texas Childrens Hospital, Houston, TX, USA.*
INTRODUCTION: Gestational diabetes mellitus (GDM) in women is strongly associated with obesity. Newborns from GDM women are more likely to be macrosomic (FM,>4000gram at birth) and to develop cardiovascular and metabolic diseases later in life. GDM treatment with insulin and other medicines cannot prevent fetal macrosomia completely. Despite treatments for glycemic control, poor outcome persists in GDM, and the emerging evidence indicates this may be due to altered lipid metabolism during pregnancy. In this study we hypothesized that placental lipid transport and metabolism are altered in obese women with GDM and FM, enhancing lipid supply to promote fetal overgrowth.
METHODS: Placental tissues from obese subjects with A2 GDM either with or without FM (abbreviated as wFM and nFM, respectively), and without GDM and FM (CT) were obtained from our PeriBank repository. The prior to pregnancy BMI and gestational age were matched in these 3 groups (n= 10 placentas each group, associated with 5 female and 5 male fetuses). Total RNAs were extracted from 100 mg placental tissue and converted to cDNA. mRNA of genes related to fatty acid transport/uptake (*LIPG*, *LIPE*, *LPL*, *ATGL*, *ANGPTL3*, *4* and *8*, *CD36*, *GOT2*, *FABP4*), fatty acid oxidation (*CPT1B*, *PPKAA1*, *PPARA*), fatty acid accumulation/esterification (*ACC*, *FASN*, *MCAD*, *SCD*, *DGAT1*, *PLIN1*, *PLIN2*, *PPARG*, *SREBF1*) was measured by q-PCR and normalized to that of TBP. The effects of FM, gender and their interactions on gene expressions were analyzed by the general linear models procedures of the Statistical Analysis System.
RESULTS: Main findings include: 1) Expressions of most genes investigated in this study were not affected by GDM, FM and gender; 2) mRNA levels of *LPL* were 2.73- and 7.83-fold lower ($P < 0.05$) in wFM and nFM groups compared to CT group, respectively and this occurred in placentas with male fetuses; 3) mRNA levels of *FABP4* were 2.42-, and 1.67- fold higher ($P < 0.01$, < 0.05) in wFM group compared to nFM and CT, respectively, and this occurred in placentas with male fetuses; 4) mRNA levels of *ANGPTL3* were 1.72-fold higher ($P < 0.05$) in wFM group compared to nFM group.
CONCLUSIONS: Although the majority of genes involved in lipid transport, oxidation and accumulation were not altered, expressions of *LPL* and *FABP4* were enhanced in placentas from subjects with GDM and FM associated with male fetuses.

F-049

Maternal BMI and Gestational Weight Gain Are Significantly Correlated with Markers of Metabolic Endotoxemia in Both Maternal and Neonatal Serum. Maike K Kahr, Min Hu, Kathleen M Antony, Kjersti M Aagaard, Melissa A Suter*. *Baylor College of Medicine, Houston, TX, USA.*

INTRODUCTION: Obesity and inflammation have long been associated, but the cause of the inflammation is unknown. One hypothesis is that bacterial products, such as lipopolysaccharides (LPS) are translocated across the gut in association with a high-fat diet which drives inflammation, a condition termed metabolic endotoxemia (ME). Data have shown that an increase in serum LPS and reduced levels of endotoxin-core IgM (endoCAb IgM) antibodies are associated with both obesity and diabetes. In this study we sought to determine if changes in serum LPS and endoCAb IgM are associated with maternal obesity and if the fetus is exposed to these markers of ME. We also tested whether markers of inflammation (TNFα and IL-6) were increased with maternal obesity and are observed in the neonate.

METHODS: Commercially available ELISA assays were utilized to measure LPS and endoCAb IgM levels in matched maternal and neonatal (cord blood) serum samples (N=146). The Milliplex Human Cytokine Magnetic Bead Panel was used to measure TNFα and IL-6 in these same serum samples. Data was stratified based on maternal pre-pregnancy BMI (Normal weight (18.5-24.9), Overweight (25.0-29.9), Obese (≥ 30.0)) or by gestational weight gain. Spearman rank correlation coefficients and One-Way ANOVA analyses were performed using SPSS.

RESULTS: While we did not find any significant change in LPS levels in either maternal or neonatal samples, we found that maternal endoCAb IgM is significantly decreased in obese women compared to normal weight (102 vs. 96 MMU/mL, p=0.015). Levels of endoCAb are negatively correlated with gestational weight gain (-0.276, p=0.005). When stratifying the data based on prepregnancy BMI we find that both maternal and neonatal endoCAb levels correlate with BMI category (-0.277, p=0.001 and 0.204, p=0.042 respectively). We also found that maternal and neonatal TNFα are positively correlated (0.176, p=0.038) as is maternal and neonatal IL-6 (0.356, p<0.001).

CONCLUSIONS: The changes in maternal endoCAb IgM with maternal BMI and gestational weight gain are in line with reported findings of ME in non-pregnant women. Because IgM antibodies do not cross the placenta, the endoCAb IgM detected in neonatal serum is likely due to the fetal immune response to circulating LPS levels. The positive correlation of maternal and neonatal TNFα and IL-6 may similarly point to fetal exposure to markers of maternal ME during gestation.

F-050

Association Between Interval Change in Body Mass Index and Subsequent Pregnancy Outcomes Among Women with Gestational Diabetes. Ashley N Battarbee†,[1] Lynn M Yee*.[2] *[1]University of North Carolina at Chapel Hill, Chapel Hill, NC, USA; [2]Northwestern University Feinberg School of Medicine, Chicago, IL, USA.*

INTRODUCTION: Gestational diabetes (GDM) and obesity are associated with an increased risk of adverse maternal and neonatal outcomes. Our objective was to determine the association between the interval change in BMI and adverse maternal and neonatal outcomes in subsequent pregnancies following an index pregnancy complicated by GDM.

METHODS: Retrospective cohort study of all women with GDM who subsequently delivered at a single institution between 2008 and 2016. Prepregnancy BMI and BMI at delivery were assessed in the index and subsequent pregnancies. Women were stratified into 3 groups based on interval change in BMI at delivery: BMI increase of >1 kg/m2, BMI decrease of >1 kg/m2, and BMI stability (<1 kg/m2 increase or decrease). Bivariable and multivariable analyses were performed to determine the association between interval change in BMI and adverse outcomes.

RESULTS: Of 683 women with GDM in the index pregnancy, 140 (20.5%) had a subsequent delivery. Fifty-five women (39.3%) had a stable BMI between pregnancies while 60 (42.9%) had an increase in BMI and 25 (17.9%) had a decrease in BMI. There were no statistically significant differences among the groups in the amount of gestational weight gain during the index pregnancy or length of the interpregnancy interval. Women with interval increase or decrease in BMI were more likely to have recurrent GDM or T2DM in the subsequent pregnancy (Table), although this finding did not remain statistically significant in multivariable regression. In contrast, women with interval decrease in BMI were more likely to have preterm delivery (44.0% vs 16.4%, p=0.03) as well as a trend toward more frequent cesarean and lower birthweight neonates (Table). The association of interval decrease in BMI and preterm delivery remained significant on multivariable regression (aOR 3.5, 95% CI 1.1-11.2).

CONCLUSIONS: After a pregnancy complicated by gestational diabetes, interval decrease in BMI >1 kg/m2 is associated with 3.5 times increased odds of preterm delivery in subsequent pregnancy.

**Figure(s) will be available online.*

F-051

Association Between Serum Adipokine Levels and Insulin Resistance in Pregnant Women at High-Risk of Developing Gestational Diabetes Mellitus (GDM). Kym J Guelfi,[1] John P Newnham,[2] Shaofu Li,[2] Jeffrey A Keelan*.[2] *[1]University of Western Australia, Perth, WA, Australia; [2]University of Western Australia, Perth, WA, Australia.*

INTRODUCTION: Insulin resistance in pregnancy may be related to the production of adipokines by adipose & placental tissues. Several adipokines, including leptin, adiponectin & visfatin, have been implicated in the development of glucose intolerance and GDM. Others, such as TNF, IL-6, FABP4, chemerin and resistin, have been reported to play a role in glucose homeostasis, but their significance in insulin resistance in pregnancy is unclear. No studies have examined adipokines longitudinally in women at high risk of GDM recurrence. **Aims**: To describe the relationship between maternal adipokine levels, insulin resistance and GDM recurrence in women with previous GDM to assess prognostic utility.

METHODS: Women with a prior GDM pregnancy (n=172) were recruited at 14 and 28 wk of gestation for measurement of blood glucose and insulin (fasting or post OGTT); adipokines were measured in a subset (n=123). GDM was defined as a fasting venous blood glucose ≥5.5 mmol/L (99 mg/dl) and/or a 2-h OGTT glucose ≥8.0 mmol/L (144 mg/dl). Data were analysed using Chi-square for categorical variables, independent t-test or Mann-Whitney test for continuous variables. Variables were compared at 14 *vs*. 28 weeks by Kruskal-Wallis test.

RESULTS: Maternal plasma concentrations of visfatin and adiponectin decreased with advancing gestation (P<.01), while leptin and resistin increased (P<.005); TNF, IL-6, FABP4 and chemerin concentrations were unchanged. In women who developed GDM, levels of glucose and insulin at 14 wk were already significantly elevated (both fasting & post-OGTT) (P< .05); women who developed GDM later in pregnancy also had higher leptin and lower adiponectin levels. Adiponectin concentrations were inversely related to insulin resistance parameters at both 14 & 28 wk. In contrast, IL-6 and leptin levels were positively correlated with most indicators of insulin resistance at both time-points. At 28 wk, adiponectin levels remained lower in women with GDM, while TNF and visfatin levels were higher; other adipokines were not different.

CONCLUSIONS: Maternal circulating adipokine levels are altered early in pregnancy in women who subsequently develop GDM and are correlated with markers of insulin resistance; adipokine measurements in pregnancy may have prognostic utility in this high risk of GDM population.

F-052

Nobiletin as a Therapeutic for Gestational Diabetes Mellitus (GDM). Stella Liong†, Ratana Lim, Caitlyn Nguyen-Ngo, Stephanie Quak, Gillian Barker, Martha Lappas*. *University of Melbourne, Heidelberg, VIC, Australia.*

INTRODUCTION: Maternal insulin resistance, a central feature of GDM, contributes to increased nutrient supply to the fetus, predisposing the offspring to childhood obesity and later adult disease. Pro-inflammatory cytokines, secreted by placenta and adipose tissue, can

induce maternal peripheral resistance. There are no treatments that can prevent GDM and its adverse outcomes. Nobiletin, a citrus fruit flavonoid, is a promising therapeutic agent for type 2 diabetes; however, its effects on GDM are not unknown. The aims were to determine the effect of nobiletin on inflammation in human placenta and adipose tissue; and the insulin signalling pathway in human skeletal muscle *in vitro*. A genetic mouse model of GDM (heterozygous leptin receptor-deficient; db/+) was also used to determine if nobiletin can prevent the development of GDM and improve neonatal outcomes.

METHODS: Human placenta, adipose tissue and skeletal muscle explants were stimulated with bacterial (LPS) and viral (poly(I:C)) products, and pro-inflammatory cytokines (TNF-α, IL-1β) to generate a GDM-like model *in vitro*. The pro-inflammatory profile in placenta and adipose tissue was determined by qRT-PCR and ELISA. In skeletal muscle, expression of insulin signalling pathway intermediates was determined by Western blotting, and glucose uptake was assessed using a radiolabelled assay. *In vivo*, nobiletin was administered daily to pregnant GDM mice (day 1-17 of pregnancy), an oral glucose tolerance test was performed on d17 and tissues were collected at d18.

RESULTS: Nobiletin (i) decreased IL-6, IL-8 and MCP-1 mRNA expression and release from human placenta and adipose tissue, and (ii) restored the defects in insulin-mediated glucose uptake induced by inflammation or infection. Excitingly, in GDM mice, nobiletin (i) increased maternal glucose tolerance, (ii) decreased inflammation in placenta and adipose tissue; and (iii) improved offspring outcomes (littersize and fetal weights).

CONCLUSIONS: Nobiletin can reduce inflammation and improve insulin resistance in both *in vitro* and *in vivo* models of GDM. These findings have significant implications for nobiletin as a therapeutic for GDM, given a safe commercial preparation exists. The effects of nobiletin on the health of offspring of GDM mice up to 6 months of age are being assessed to determine if nobiletin can improve long-term adverse fetal outcomes.

F-053

Maternal Obesity Modulates Response to Omega-3 Fatty Acids Supplementation During Pregnancy. Carmen Monthé-Drèze†,[1] Annie Penfield-Cyr,[2] Marcela Smid,[3] Sarbattama Sen*.[2] [1]*Boston Children's Hospital, Boston, MA, USA;* [2]*Brigham & Women's Hospital, Boston, MA, USA;* [3]*University of Utah, Salt Lake City, UT, USA.*

INTRODUCTION: Pre-pregnancy obesity is associated with chronic inflammation and deficiency of key antioxidants, including n-3 polyunsaturated fatty acids (n-3 PUFA). We sought to examine whether pre-pregnancy Body Mass Index (BMI) modifies the response to n-3 PUFA supplementation during pregnancy. We hypothesized that maternal obesity is associated with higher baseline ratio of n-6 (pro-inflammatory): n-3 (anti-inflammatory) PUFAs and that n-3 PUFA supplementation leads to an attenuated change in systemic PUFAs in obese vs. lean women.

METHODS: Secondary analysis of MFMU trial of n-3 PUFA supplementation to prevent recurrent pre-term birth. Women had baseline plasma PUFA levels measured at 16-22 weeks, then were randomized to 2g of n-3 PUFA or placebo, with repeat levels drawn at 26-28 weeks. Plasma PUFA concentrations were measured by gas chromatography. Primary exposure was pre-pregnancy BMI, categorized as: lean (Ln) (≥ 18.5 to < 25 kg/m^2) or obese (Ob) (≥ 30 kg/m^2). Primary outcomes were change in n-3, n-6, and n-6:n-3 PUFA ratio with supplementation. We compared PUFA concentrations between Ln and Ob groups using linear regression, Kruskal-Wallis and Wilcoxon rank-sum tests.

RESULTS: We included 556 women in this analysis**;** 46% were Ln and 28% Ob. BMI correlated with n-6:n-3 PUFA ratio at baseline (r=0.15, p=0.002). In the n-3 supplementation group (n=278), Ln women had a significantly higher rise in n-3 PUFA concentrations vs. Ob women (Δ n-3 % molar (median (IQR)): Ln: 3.4 (-0.2, 6.6) vs. Ob: 0.4 (-0.8, 2.5); p=0.002). Rise in n-3 PUFA concentrations in Ob women after supplementation was 33% (*Beta*: -0.33; 95% CI -0.52, -0.14) lower than Ln women, in a fully adjusted model. Ln women also had a significant decrease in n-6 PUFA concentrations after supplementation, while Ob women did not (Δ n-6 % molar: Ln: -3.7 (-6.5, 1.6) vs. Ob: -0.5 (-4.2, 2.2); p=0.03). The attenuation in n-6:n-3 PUFA ratio was greater in Ln vs. Ob women after supplementation (Δ n-6:n-3 ratio: Ln: -1.6 (-2.2,-0.8) vs. Ob: -0.5 (-1.5, -0.1); p=0.001).

CONCLUSIONS: Ob women have an attenuated systemic response to n-3 PUFA supplementation during pregnancy compared to Ln women. Ob women may require higher dosing of supplementation, given that fetal supply is dependent on maternal levels.

F-054

Impact of an mHealth-Supported Behavioral Lifestyle Intervention on Behavioral Stage of Change and Physical Activity in Overweight and Obese Pregnancy: PEARs Randomized Controlled Trial. Kate M Ainscough†, Maria A Kennelly, Elizabeth J O'Sullivan, Karen L Lindsay, Fionnuala M McAuliffe*. *University College Dublin, Dublin, Leinster, Ireland.*

INTRODUCTION: Regular physical activity (PA) during pregnancy could help reduce the risk of poor obstetric outcomes associated with maternal overweight and obesity. However, overweight and obese women report barriers to improving PA behaviors. Mobile health (mHealth) technologies offer potential to assist antenatal lifestyle interventions; however a paucity of evidence on mHealth effectiveness during pregnancy exists. Our aim was to investigate the impact of an mHealth-supported lifestyle intervention on behavioral stage-of-change and PA among overweight and obese pregnant women.

METHODS: This is an RCT of n=565 pregnant women (body mass index ≥25 kg/m^2), randomized in early pregnancy to receive standard care (n=287) or a 'healthy lifestyle package' (n=278) involving nutrition and exercise advice supported by a smartphone app. In early (15 weeks) and late (28 weeks) pregnancy, behavioral stage-of-change score (1-5; where a higher score is favored) was measured using a validated questionnaire to assess 'readiness' to change PA behaviors. PA was measured through questionnaires derived from the IPAQ.

RESULTS: At baseline, there were no significant differences between intervention and control groups for demographics, stage-of-change score and PA. There was no difference in the proportion of women at stage 5 between intervention and control groups (32.4% *vs.* 33.3%; *P*=0.92). At 28 weeks, a higher proportion of the intervention group maintained or increased stage-of-change score for PA compared to controls (90.3% *vs.* 72.7%; *P*<0.001). A greater proportion of women in the intervention group were at stage 5 in late pregnancy compared with controls (56.0% *vs.* 32.9%; *P*<0.001). The intervention group had higher PA than controls at 28 weeks (662.9 ± 426.2 *vs.* 476.0 ± 323.8 METs per week; *P*<0.001) and a greater proportion of women meeting ACOG PA recommendations (27.1% *vs.* 15.5%; *P*=0.02).

CONCLUSIONS: An mHealth-supported intervention assisted women with maintaining or improving readiness to engage in PA and adherence to PA recommendations. These findings are significant for obstetric patients that may benefit from consistent, easily-accessible lifestyle advice to improve behaviors and pregnancy outcomes. This trial suggests the potential for mHealth to aid interventions helping women to overcome barriers to behavior change.

F-055

Isolated Oligohydramnios Near Term: Should We Be Looking at Umbilical Artery Doppler? Natalie Porat†, Zainab Al-Ibraheemi†, Dyese Taylor†, Meredith Kalberer†, Barak Rosenn*. *Mount Sinai West, New York, NY, USA.*

INTRODUCTION: This is a retrospective cohort study of all pregnant patients who delivered at our institution with oligohydramnios (AFI <5cm) between January 2013 and June 2016.

METHODS: Inclusion criteria were patients with an ultrasound finding of oligohydramnios at ≥36 weeks, EFW >10%, and umbilical artery Doppler indices performed within 2 weeks of delivery. Patients with growth restriction (IUGR), suspected rupture of membranes, fetal malformations, chromosome anomalies, and multiple gestations were excluded. Patients that met criteria (N=88) were reviewed and divided into two comparison groups. Those with umbilical artery Doppler S/D ratio ≥75 %ile (N=13) were compared to those <75 %ile (N=75), and patients

with S/D ratio ≥90 %ile (N=7) were compared to those <90%ile (N=81). Primary outcome was a composite of 1 of more of the following: operative delivery for nonreassuring fetal heart tracing (NRFHT), 5 minute Apgar score <7, arterial cord pH <7.2, NICU admission, or birthweight <10% (SGA). Secondary outcomes included each adverse event individually. Statistical significance was set at a p-value <0.05 using chi-square and pooled T-test as appropriate.

RESULTS: The composite outcome was not significantly different in the ≥75%ile group (77%) versus the < 75%ile (53%) group, (p=0.1129). There was also no difference between the ≥90%ile group (71%) versus the <90%ile (56%) group, (p=0.6940). The incidence of SGA was significantly higher in the group with Doppler ≥75%ile (62%) compared to <75%ile (24%), (p=0.017). Four of the seven patients in the ≥90%ile group were SGA but this finding was not significant, (p=0.1885).

	<75 %ile (N=75)	**≥75%ile (N=13)**	**p-value**
Composite adverse outcome (%)	53	77	0.1129
Operative delivery for NRFHT (%)	27	38	0.5058
5 minute Apgar score <7 (%)	0	0	
Arterial cord pH <7.2 (%)	27	50	0.2372
NICU admission (%)	8	4	0.4788
SGA (%)	24	62	*0.0170*
	<90%ile (N=81)	**≥90%ile (N=7)**	**p-value**
Composite adverse outcome (%)	56	71	0.6940
Operative delivery for NRFHT (%)	24	43	0.4003
5 minute Apgar score <7 (%)	0	0	
Arterial cord pH <7.2 (%)	28	60	0.3038
NICU admission (%)	5	0	1.0000
SGA (%)	27	57	0.1885

CONCLUSIONS: Doppler studies may be useful in patients with isolated oligohydramnios to predict those more likely to be SGA at birth despite normal EFW on ultrasound. Further studies are warranted to confirm these findings.

F-056

Maternal and Fetal Outcomes in Pregnancy Complicated with Eisenmenger Syndrome. Shinji Katsuragi,[1] Chizuko Kamiya,[2] Reiko Neki,[2] Takekazu Miyoshi,[2] Jun Yoshimatsu,[2] Koichiro Miwa,[3] Yaemi Takagi,[4] Takeshi Ogo,[4] Norifumi Nakanishi,[4] Tomoaki Ikeda.[5] *[1]Sakakibara Heart Institute, Fuchu, Tokyo, Japan; [2]National Cerebral and Cardiovascular Center, Suita, Osaka, Japan; [3]St. Luke's International Hospital, Tokyo, Japan; [4]National Cerebral and Cardiovascular Center, Suita, Osaka, Japan; [5]Mie University, Tsu, Mie, Japan.*

INTRODUCTION: Pregnancy complicated by Eisenmenger syndrome (ES) has a high mortality rate and pregnancy is regarded as contraindicated. The goal of the study was to examine risks for maternal and fetal outcomes complicated with ES during pregnancy.

METHODS: Data were examined retrospectively for 15 patients (15 pregnancies, 5 live births) with ES during pregnancy who were treated at our institution from 1985 to 2013. The background congenital heart disease in these patients were ASD (n=3), VSD (n=3), and PDA (n=9).

RESULTS: Ten women chose pregnancy termination before 12 weeks and 5 continued pregnancy. In the 10 termination cases, the median pulmonary arterial blood pressure (PABP) was 60 mmHg (range: 41-81); NYHA classifications were II (n=4), III (n=5) and IV (n=1); SpO_2 was 87.9 ± 2.6%; and PaO_2 was 55.5 ± 4.9 mmHg. In the 5 continuation cases, PaO_2 was 63 mmHg (54-68). Cesarean section was performed in 5 at a median week of 30.8 (28-33). Mean PABP did not change significantly before and during pregnancy (63 vs. 79 mmHg, p=0.09), and pulmonary vascular resistance did not change significantly before and during pregnancy (582, 885, 1476 to 592, 868, 1522 dyne×sec/cm^5). NYHA classifications before, during and after pregnancy were II, III and II-III, in 4 cases, and II, IV and II, in 1 case. Epoprostenol and tadalafil were used in 1 case during pregnancy and fetal growth was appropriate, whereas 3 other cases had small-for-gestational-age. Maternal and neonatal survival was 100%. In the five delivered cases shortness of breathes were worse at delivery and postpartum courses with slight body movement and are accompanied with HR elevation and decreased PaO_2 levels.

CONCLUSIONS: All pregnancies with ES are accompanied with decreased oxygenation, cardiac symptoms before 30 weeks and early termination of pregnancies are inevitable for minimizing maternal cardiac failure. Fetuses tend to be small for gestational age.

F-057

Intravenous Oxytocin Titration for Post-Dates Labor Induction Across Body Mass Index Groups. Angela B Maeder,[1] Susan C Vonderheid*,[1] Chang G Park,[2] Aleeca F Bell,[1] Barbara L McFarlin,[1] Catherine Vincent,[1] Sue Carter.[3] *[1]University of Illinois, Chicago, IL, USA; [2]University of Illinois, Chicago, IL, USA; [3]Indiana University, Bloomington, IN, USA.*

INTRODUCTION: Rates of obesity among childbearing women, and oxytocin use for labor induction or augmentation are increasing (Fisher, Kim, Sharma, Rochat, & Morrow, 2013; Martin, Hamilton, Osterman, Curtin, & Matthews, 2015). Women who are obese are more likely to experience induction of labor (IOL), longer length of labor (LOL), and cesarean delivery than women who are normal weight (Arrowsmith, Wray, & Quenby, 2011; Denison et al., 2008). Oxytocin, the medication most commonly used for IOL is high-alert (Institute for Safe Medication Practices, 2014). The aims of this study were to evaluate whether titration of oxytocin infusion for post-dates IOL differed among women who were normal weight, overweight, and obese, and to evaluate whether LOL and method of delivery for women who experienced post-dates IOL differed by oxytocin titration and body mass index (BMI).

METHODS: In this retrospective study, we extracted data on women receiving oxytocin for post-dates IOL between January 1, 2013 and June 30, 2013 from medical records. Oxytocin administration and labor outcomes were compared across BMI groups (normal weight: BMI < 25.0, overweight: BMI 25.0 to 29.9, obese: BMI ≥ 30.0 at labor admission) using ANOVA and multiple linear and logistic regression controlling for potential confounders.

RESULTS: Of 280 women, 21 (7.5%) were normal weight, 134 (47.9%) were overweight, and 125 (44.6%) were obese. Length of labor increased with BMI, with women who were normal weight, overweight, and obese having LOL of 14.64 hours, 17.45 hours, and 19.76 hours respectively (p = .008). Cesarean delivery rate increased with BMI group with women who were normal weight, overweight, and obese having a cesarean delivery rate of 4.8%, 33.6%, and 42.4% respectively (p = .003). Women who were obese received more total oxytocin (M = 7.50 units, SD = 6.46 units) than women who were overweight (M = 5.92 units, SD = 4.98 units, p = .031). No difference was found among groups for oxytocin units received divided by LOL.

CONCLUSIONS: Women who were obese experiencing post-dates IOL received more total oxytocin than women who were non-obese and had longer LOL and higher cesarean rates. Women who are obese may need more units oxytocin per hours of labor to achieve timely vaginal delivery.

F-058

Umbilical Artery Cord Oxygen and Neonatal Morbidity at Term. Nandini Raghuraman†, George A Macones, Alison G Cahill, Methodius G Tuuli*. *Washington University School of Medicine in St. Louis, St. Louis, MO, USA.*

INTRODUCTION: Umbilical cord blood gas analysis provides an objective measure of neonatal well-being at birth, with a large body of evidence linking lactate, pH and base excess to neonatal morbidity. However, there is a paucity of data on the value of umbilical cord PO_2 in predicting neonatal morbidity. We investigated the relationship between umbilical cord PO_2 and neonatal morbidity at term.

METHODS: This was a secondary analysis of a large prospective cohort study of term, singleton, cephalic pregnancies admitted for delivery

between 2010 and 2014. Paired umbilical cord gases were collected universally. The primary outcome was a composite neonatal morbidity including neonatal death, meconium aspiration syndrome, intubation, mechanical ventilation, hypoxic ischemic encephalopathy and need for hypothermia treatment. Median umbilical arterial PO_2 was compared between patients with and without the composite neonatal morbidity. The areas under the receiver operating characteristic (ROC) curve were used to assess the predictive ability of arterial PO_2.

RESULTS: Of 7789 patients with paired umbilical cord PO_2, 106 (1.4%) had the composite neonatal morbidity. Umbilical cord arterial PO_2 was significantly lower in patients with neonatal morbidity compared to those without (median [interquartile range]: 16 (12, 21) vs 19 (15, 24) mmHg, P<0.001). However, umbilical arterial PO_2 had limited predictive ability for the composite neonatal morbidity (ROC area: 0.61, 95% CI 0.5-0.7). **Figure(s) will be available online.*

CONCLUSIONS: While umbilical arterial PO_2 is significantly lower in patients with neonatal morbidity, PO_2 is a poor predictor of neonatal morbidity at term.

F-059

Hypertensive Disorders of Pregnancy and Postpartum Readmission in the United States: National Surveillance of the Revolving Door. Mulubrhan F Mogos,[1] Jason L Salemi,[2] Kiara K Spooner,[2] Barbara L McFarlin,[1] Hamisu H Salihu.[2] *[1]University of Illinois at Chicago, Chicago, IL, USA; [2]Baylor College of Medicine, Houston, TX, USA.*

INTRODUCTION: Although hypertensive disorders of pregnancy (HDP) collectively represent the most common cause of maternal-fetal morbidity and mortality, the prevalence and cost of postpartum readmission (PPR) among pregnancies complicated by HDP in the United States (US) remains unknown.

METHODS: We used the 2013 Nationwide Readmissions Database to generate national estimates of the prevalence and cost of PPR (hospitalization within 42 days of discharge following delivery) among delivery-related discharges to women 15–49 years of age. International Classification of Diseases, Ninth Revision, Clinical Modification codes were applied to define HDP and other clinical conditions. Rates of PPR were also stratified by HDP subtype (existing hypertension vs. hypertension diagnosed during pregnancy).Survey logistic regression was employed to generate adjusted odds ratios (AOR) that quantify the association between HDP and postpartum readmission.

RESULTS: In 2013, there were 3.4 million delivery-related hospitalizations, 360,214 (10.4%) of which were complicated by HDP. Among pregnancies complicated by HDP, the 42-day all-cause PPR rate ranged from 2.5% (gestational hypertension) to 6.5% (eclampsia). HDP-related postpartum readmission within 42-days of child birth alone was responsible for 38,748 hospital days and cost the U.S healthcare system $80.7 million in inpatient care. After adjusting for potential confounders, deliveries with preexisting hypertension and pregnancy-acquired hypertension were 2.1 times (95% CI: 2.0, 2.3) and 1.8 times (95% CI: 1.7, 1.8) as likely to be readmitted within 42-days of childbirth when compared to deliveries unaffected by hypertension.

CONCLUSIONS: HDP is associated with increased risk of PPR, high utilization of healthcare services, and substantial monetary costs. Efforts should be made to identify women at increased risk of PPR while they are in the hospital so that transition care intervention can be initiated to prevent PPR.

F-060

Risk Factors for Maternal and Fetal Outcome in Pregnancy Complicated with Arteriovenous Malformation. Shinii Katsuragi,[1] Tomoaki Ikeda,[2] Hiroaki Tanaka,[2] Kayo Tanaka,[2] Masafumi Nii,[2] Takekazu Miyoshi,[3] Reiko Neki,[3] Kazuko Minematsu,[4] Kazunori Toyoda,[4] Kazuyuki Nagatsuka,[5] Eika Hamamo,[6] Toru Sato,[&] Susumu Miyamoto,[6] Koji Iihara,[6] Jun Yoshimatsu.[3] *[1]Sakakibara Heart Institute, Fuchu, Tokyo, Japan; [2]Mie University, Tsu, Mie, Japan; [3]National Cerebral and Cardiovascular Center, Suita, Osaka, Japan; [4]National Cerebral and Cardiovascular Center, Suita, Osaka, Japan; [5]National Cerebral and Cardiovascular Center, Suita, Osaka, Japan; [6]National Cerebral and Cardiovascular Center, Suita, Osaka, Japan.*

INTRODUCTION: The goal of the study was to examine risks for maternal and fetal outcomes complicated with arteriovenous malformation (AVM) during pregnancy.

METHODS: Retrospective studies were done in 36 cases of intracranial AVM complicated pregnancies in 32 years (1981-2013) in one institution. Pregnancy and maternal neurological outcomes, and fetal prognosis were investigated.

RESULTS: 19 cases (16 patients) were diagnosed with hemorrhage (hemorrhage group) before and during the current pregnancy in 8, 11 cases, respectively. In the former 8, 7 had had intracranial operations before pregnancy. In the latter 11, 7 had intracranial operations (four during pregnancy, and three after delivery), and three had gamma knife surgery (GKS). Four needed terminations at the 2nd trimester for fear of re-bleeding. And another 17 cases (10 patients) were diagnosed incidentally (non hemorrhage group). In the non-hemorrhage group seven patients had been treated before pregnancy, three with GKS and four with operation. AVM related terminations below 37 weeks were 7/19 (36.8%) vs 0/17 (0%), p<0.01, in hemorrhage and non-hemorrhage group, respectively. The Glasgow Coma Scale during pregnancy were 11.2 vs 15, p<0.0005, respectively. The modified ranking Scale at enter of the hospital was 2.17 vs 0.28, p<0.05, respectively. Occurrence during pregnancy and disturbed consciousness during pregnancy (Glasgow Coma Scale ≤ 10) were significantly associated with maternal poor neurological outcome.

CONCLUSIONS: Neurological and pregnancy outcomes were poor in AVM complicated pregnancy especially hemorrhage occurs during pregnancy. In the non-hemorrhage group all patients except three delivered at full term without complications related to AVM.

F-061

Increased Obstetric Morbidity in a Hypertensive Haitian Population Compared to Hypertensive Non-Haitians. Conisha M Holloman†,[1] Neeraj Desai*,[1] Clifton Brock†,[3] Kesha Thomas†,[2] Priya Patel†,[2] Zoran Pavlovic†,[2] Kathryne Kostamo†.[2] *[1]Winnie Palmer Hospital/Orlando Health, Orlando, FL, USA; [2]University of Central Florida, Orlando, FL, USA; [3]Columbia University, New York, NY, USA.*

INTRODUCTION: Reducing health disparities among minority populations is a major public health initiative. The purpose of our study was to determine whether patients of Haitian descent with chronic hypertension have a higher frequency of adverse obstetric outcomes.

METHODS: This is a retrospective cohort study of patients diagnosed with chronic hypertension who delivered at Winnie Palmer Hospital between January 1, 2010 to September 1, 2014. Group 1 was comprised of women self-identified as Haitian (HN), n=59. Group 2 included all other ethnic groups with chronic hypertension (NHN), n= 1205. The primary outcome was a composite of perinatal morbidity (CPN), which included stillbirth, placental abruption, preeclampsia, eclampsia, and HELLP syndrome. Secondary outcomes included primary cesarean section rates, postpartum readmissions for a hypertensive complication (PPHTN), neonatal intensive care unit (NICU) admissions, and birth weight (BW). Student t-test, Fisher's exact and chi-square tests were used for statistical analysis in addition to multivariate regression analysis.

RESULTS: Results showed that the overall CPN was significantly higher in those of Haitian ethnicity (OR = 2.32; 95% CI, 1.1-4.7). HN were noted to have a higher parity (p=0.01), older age (p= <0.0001), increased chance of nephropathy (p=0.02), lower BW (p=0.014) and higher PPHTN (p=0.035). Also, HN were observed to have lower BMI (p=<0.001),

diabetic status (p=0.37), rate of induction of labor less than 37 weeks (p=0.08), cesarean section deliveries (p=0.07) and NICU admissions (p=0.42). Antihypertensives medications were equally utilized in all groups. When comparing CPN of blacks versus whites and Haitians versus whites, the OR was 1.2 (CI 0.76-1.90) and 1.46 (CI 0.82-2.6), respectively. This suggests that being of Haitian descent still had worse outcomes than blacks when compared to the majority population.

CONCLUSIONS: We observed significant differences in obstetrical outcomes between mothers of Haitian descent and other ethnic groups. Further study is warranted into what underlying factors may be contributing to these findings and whether clinical or public health interventions may lower health disparities in this population.

F-062

Maternal Low Vitamin D Status and Risk of Small for Gestational Age: A Systematic Review. Shu Qin Wei, Wei Guang Bi. *CHU Ste Justine, University of Montreal, Montreal, QC, Canada.*

INTRODUCTION: Small for gestational age (SGA), usually defined as birth weight below a certain cutoff, commonly less than the 10th percentile for gestational age, is a key determinant of mortality and morbidity in the neonatal period and an important factor in predicting health and development in childhood. Recently, several small epidemiological studies explored the association between vitamin D status during pregnancy and SGA and

LBW infants with contradictory results.

METHODS: This is a systematic review and meta-analysis. We followed the guidelines for meta-analysis of observational studies in epidemiology (MOOSE). We searched electronic databases of the human literature in PubMed, EMBASE and the Cochrane Library up to October, 2016 using the following keywords: 'vitamin D', 'pregnancy' and 'small for gestational age'.We included observational studies that reported the association between maternal vitamin D status during pregnancy and small for gestational age (SGA). Data on dichotomous outcomes were combined using the Mantel-Haenszel method, and measures of effect are presented as odds ratio (OR) with 95% confidence intervals (CIs). Odds ratio (OR) and 95% CIs were calculated using fixed or random effects models, as appropriate.

RESULTS: Nine studies assessed the association between maternal 25(OH)D status and SGA, including 11,791 subjects. Figure 1 presents the results for the association between maternal blood level of 25(OH)D <50 nmol/L and SGA. The summary crude OR (95%CI) was 1.60 (1.05-2.43). **Figure(s) will be available online.*

CONCLUSIONS: Low maternal vitamin D levels in pregnancy were associated with an increased risk of SGA.

F-063

Exposure to SSRI During Pregnancy and Postpartum Hemorrhage Risk. Silvia Corti†, Paola Pileri, Martina Mazzocco†, Ilenia di Bartolo†, Chiara Mandò, Irene Cetin*. *University of Milan, Milan, Italy.*

INTRODUCTION: Prevalence of depression during pregnancy has been reported to range between 12.7 - 18.4% worldwide and approaches 16% in Italy. SSRIs (Selective Serotonine Reuptake Inhibitors) are the drug of choice due to their reported safety and efficacy.

Recent studies have linked the use of SSRIs during pregnancy with a higher risk for postpartum hemorrhage (PPH) and consequent maternal anemia during puerperium, being serotonin involved in platelet function. Our aim was to evaluate the role of SSRI use during pregnancy in the risk of PPH.

METHODS: This is a prospective, observational and experimental case-control study. *Cases* (n. 43) were caucasian women with a diagnosis of depression and/or anxiety, in treatment with SSRIs during pregnancy. *Controls* (n. 86) were caucasian women without a psychiatric diagnosis and not exposed to SSRIs during pregnancy. Exclusion criteria for both groups were other psychotropic drugs, anti-epileptic drugs, drugs of abuse or alcohol addiction, maternal or fetal infectious diseases and fetal/neonatal chromosomal genetic abnormalities.

The two groups were compared for demographic, anthropometric and socio-economic variables, and were evaluated for pregnancy and delivery outcomes, with special attention to PPH risk.

RESULTS: The two groups were homogenous for demographic, anthropometric, socio-economic and obstetric variables except for smoking and mean haemoglobin values before delivery. The analysis of maternal outcomes did not show relevant differences in gestational age, pregnancy complications or type of delivery. However, SSRIs patients had twice the number of delivery complications than *controls*: *cases*=12/43 (28%) *vs controls*=13/86 (15%) (p>0.05). All complications in *cases* were PPH. Mean blood loss (*cases*=412.8 ml *vs controls*=306.2 ml, p=0.07), number of PPH (*cases* 12/43 *vs controls* 11/86, p=0.06) and severity (p=0.1) of PPH were higher in *cases* than in *controls*. These differences were not statistically significant but close to the relevance treshold. When stratifying the population according to type of delivery (vaginal vs caesarean sections) we found that *cases* had relevantly more PPH after vaginal delivery (27% vs 7%, p=0.04).

CONCLUSIONS: We found that women exposed to SSRIs during pregnancy are at increased risk of postpartum hemorrhage after vaginal delivery.

F-064

The Complex Relationship of Obesity and Spontaneous Preterm Birth. Abraham Tsur, Jonathan Mayo, Gary M Shaw, David K Stevenson, Jeffrey B Gould. *Stanford University, Stanford, CA, USA.*

INTRODUCTION: Previous studies have reported obesity as a risk factor for spontaneous preterm birth (sPTB). However, this association has been shown to be influenced by obesity related comorbidity. Our objective was to better understand the complex relationship of obesity and its comorbidity with sPTB.

METHODS: We conducted a retrospective cohort study utilizing records of approximately 2 million singleton California deliveries in 2007-2011. Women were categorized by body mass index (BMI) as defined by the World Health Organization. All BMI categories were subcategorized according to the existence of the comorbidities: pregestational and gestational diabetes, pregestational hypertension and pregnancy induced hypertension or preeclampsia. sPTB was defined as live birth <37 gestational weeks with diagnosis of premature labor or preterm premature rupture of membranes. Relative risks for sPTB were estimated using multivariable Poisson regression modeling.

RESULTS: Obese women had a higher relative risk for sPTB than their normal range BMI controls. Relative risks for sPTB increased with increasing BMI category (Table, P<0.05, for trend). When comparing only obese women without comorbidity to their normal BMI controls, the relative risk reversed direction, i.e., obese women had a lower relative risk of sPTB. This same reversal of risk direction was also observed among obese women with comorbidity. Thus, stratification of the study population on the basis of comorbidities revealed a seemingly paradoxical association.

	All sPTB	sPTB without comorbidity	sPTBs with comorbidity
Normal			
Overweight	0.98 (0.96,0.99)	0.91 (0.89,0.93)	0.91 (0.88,0.94)
Obese I	1.08 (1.06,1.10)	0.95 (0.92,0.97)	0.89 (0.86,0.93)
Obese II	1.13 (1.10,1.17)	0.94 (0.91,0.98)	0.87 (0.83,0.90)
Obese III	1.24 (1.20,1.29)	0.97 (0.93,1.02)	0.87 (0.83,0.91)

CONCLUSIONS: The overall population result of an increased relative risk between obesity and sPTB is reversed to a decreased risk upon stratification on the basis of presence or absence of obesity related comorbidities. This observed phenomenon is an example of what has been described as "Simpson's Paradox". This observation highlights the complexity of the underlying biologic association between increasing BMI, attendant comorbidities, and sPTB. These observations emphasize the need for further studies to elucidate these complex relationships.

F-065

Influence of SNPs in Immunoregulatory Genes in Morbidity of Preterm Newborns. Giovana F Bento†, Bruna A Ramos†, Hélio A Miot, Márcia G Silva*. *Botucatu Medical School, Botucatu, Sao Paulo, Brazil.*

INTRODUCTION: Prematurity is the main cause of perinatal and neonatal morbidity and mortality worldwide. Single nucleotide polymorphisms (SNPs) have been associated with the pathogenesis of morbidities in preterm neonates. We aimed to investigate the association between SNPs in regulatory genes of innate immune response *IL1B, IL6, IL6R, IL10, TIMP1, TIMP2, TNFA, TNFRII, TLR2* and *TLR4* and neonatal/infant morbidities in preterm infants.

METHODS: Oral swabs were collected from 299 newborns (118 preterm and 181 at term) seen at Botucatu Medical School, UNESP, between 2003 and 2014 and SNPs were identified using Taqman® Genotyping Assays. Medical records were examined to obtain data regarding neonatal/infant morbidity. Ordinal regression models were used to explain the morbidities, missing data was imputed using SAS software.

RESULTS: Neonatal morbidity was influenced by gestational age, fetal weight, apgar score 10, fetal alleles *IL6R1G*, *TNF238G* and maternal alleles *IL1B31T* and *IL1B511G*. Apgar score 10, fetal alleles *TIMP2G*, *TLR2A*, *TNF238G* and maternal alleles *IL6G* and *TIMP2G* were linked to infant morbidity. SNPs in the other genes did not influence neonatal/infant morbidities.

Table1.Ordinal Regression Models for Neonatal and Infant Morbidity

Neonatal Morbidity					
	Variable	**None**	**Minor**	**Major**	**OR(CI)**
Clinical data	Gestational age	39w2d (38w-40w4d)	39w (36w3d-40w)	32w6d (28w2d-35w4d)	0.98 (0.96-0.99)
	Newborn's weight	3130 (2828-3494)	3020 (2585-3010)	1983 (1099-2478)	0.99 (0.98-0.99)
	Apgar 10	10 (9-10)	10 (9-10)	9 (8-9)	0.66 (0.47-0.94)
Fetal SNP	*IL6R1 G*	0.91	0.87	0.84	0.15 (0.02-0.99)
Maternal SNP	*IL1B31 T*	0.55	0.49	0.50	0.29 (0.10-0.85)
	IL1B511 G	0.51	0.53	0.55	3.79 (1.30-11.03)
Infant Morbidity					
	Variable	**None**	**Minor**	**Major**	**OR(CI)**
Clinical data	Apgar 10	10 (9-10)	10 (9-10)	9 (9-10)	0.68 (0.49-0.94)
Fetal SNP	*TIMP2 G*	0.89	0.86	0.86	0.13 (0.02-0.92)
	TLR2 A	0.57	0.45	0.51	0.38 (0.20-0.71)
	TNF238 G	0.94	0.98	0.98	5.37 (1.58-18.24)
Maternal SNP	*IL6 G*	0.26	0.21	0.27	0.31 (0.12-0.83)
	TIMP2 G	0.89	0.85	0.90	12.39 (1.49-102.62)

Clinical data in median (P25-P75). SNPs presented in allele frequency, values of OR and CI for heterozygosis or homozygosis (TNF238).

CONCLUSIONS: The presence of SNPs that exacerbate the inflammatory response increases the susceptibility to neonatal and infant morbidity.

F-066

Longitudinal Pharmacokinetic and Psychiatric Analysis of Pregnant Women in Treatment with SSRI. Silvia Corti†, Paola Pileri, Carlo Personeri†, Anna Colombo, Caterina Viganò, Emilio Clementi, Irene Cetin*. *University of Milan, Milan, Italy.*

INTRODUCTION: Many pregnancies are complicated by depression with prevalences ranging between 12.7 and 18.4%. SSRIs (Selective Serotonin Reuptake Inhibitors) are considered the drugs of choice. Physiological changes of pregnancy can affect the pharmacokinetic of SSRIs and their dose requirements. However, data correlating maternal plasma drug concentration and psychiatric control are not available. Our aim was to evaluate the relationship between drug concentration in maternal plasma throughout pregnancy and psychiatric control.

METHODS: We recruited 43 pregnant women with diagnosis of depression in treatment with SSRIs and no other psychotropic drugs at their first obstetric evaluation and followed them longitudinally. The study design included 4 time points: 20 weeks, 30 weeks, delivery, 30 days postpartum. At each visit we collected maternal venous blood samples for pharmacokinetic analysis and administered objective and subjective psychiatric screening tests for depression and anxiety.

RESULTS: Drug plasma values were within therapeutic ranges throughout the whole pregnancy. SSRIs serum levels declined across pregnancy, reaching the lowest levels at delivery. Delivery was also associated to the lowest control of depression and the highest levels of anxiety.

**Figure(s) will be available online.*

CONCLUSIONS: This is the first report on the relationship between SSRIs pharmacokinetics during pregnancy and longitudinal psychiatric control. Delivery represents the time in pregnancy with the lowest maternal plasma drug concentrations and the worst depression control.

F-067

Trends and Severe Morbidity Associated with Postpartum Admissions for Hypertensive Diseases of Pregnancy. Joses A Jain†, Cande V Ananth, Zainab Siddiq, Jason D Wright, Mary E D'Alton, Alexander M Friedman*. *Columbia University Medical Center, New York, NY, USA.*

INTRODUCTION: Hypertensive diseases of pregnancy are a leading cause of maternal morbidity and mortality, and their sequelae often extend to the post-partum period. We aimed to evaluate and characterize the temporal trends and risk factors associated with post-partum readmissions for hypertensive diseases of pregnancy (HDP) and to determine risk for severe morbidity during these hospitalizations.

METHODS: We used a commercial hospitalization database, the Perspective (Premier) database, to identify a national cohort of women who were readmitted post-partum with hypertensive diseases of pregnancy (including eclampsia, preeclampsia and gestational hypertension of pregnancy) between 2006 and 2015. We evaluated temporal trends as well as demographic, hospital, and medical factors associated with readmission. Additionally, we analyzed risk for severe morbidity (defined as acute organ injury) during these readmissions.

RESULTS: Among 105,000 women who underwent a post-partum readmission in the study period, 23,210 (22.03%) had a HDP diagnosis. The proportion of women readmitted due HDP increased over the study period, from 18.03% in 2006 to 25.68% in 2015. Race was significantly associated with risk for readmission for HDP. The proportions of black, white, and Hispanic women readmitted for HDP were 34.5%, 19.20%, 12.60% respectively, compared to 65.47%, 80.80%, and 87.40% for non-HDP readmissions. Preeclampsia was associated with a disproportionate amount of severe morbidity (33.43% of overall severe morbidity) during postpartum readmissions. Severe morbidity significantly associated with post-partum preeclampsia included acute heart failure (n=2,015, 38.0% of all cases), acute renal failure (n=562, 33.2% of all cases), acute respiratory distress (n=933, 40.2%), and stroke (n=1,082, 46.5%) (all $p<0.001$).

CONCLUSIONS: Hypertensive diseases of pregnancy account for an increasing proportion of hospital readmissions. Women over the age of 35, and particularly black women, are at particularly high risk for readmission. Disproportionate risk for severe maternal morbidity is

associated with readmission for HDP. Improved hospital and discharge management of HDP may be necessary to reduce risk for readmission and severe morbidity from this cause.

F-068

Maternal BMI, Cytokine Profiles and Risk of Early Infection in Pregnancy. Marcela C Smid,[1] Carmen Monthe-Dreze†,[2] Kim Boggess,[4] Karen Gibbins,[1] Scott Commins,[5] Sarbattama Sen.[3] *[1]University of Utah, Salt Lake City, UT, USA; [2]Boston Children's Hospital, Boston, MA, USA; [3]Brigham and Women's Hospital, Boston, MA, USA; [4]University of North Carolina Chapel Hill, Chapel Hill, NC, USA; [5]University of North Carolina Chapel Hill, Chapel Hill, NC, USA.*

INTRODUCTION: Both pregnancy and maternal obesity alter cell-mediated immunity. Our objective was to assess the association between maternal BMI and early infection and to compare maternal cytokines after infection.

METHODS: Retrospective cohort study of the MFMU Omega-3 trial among women with ≥1 prior spontaneous preterm birth. Our primary exposure was pre-pregnancy BMI, categorized as lean (BMI < 25 kg/m^2), overweight (OW) (25-29.9 kg/m^2) and obese (OB) (≥ 30 kg/m^2). Our outcome was early (< 23 weeks gestation) infection (sexually transmitted infection (STI), urinary tract infection/pyelonephritis (UTI), bacterial vaginosis (BV), herpes and/or GBS). Modified Poisson regression estimated the relative risk of early infection by maternal BMI after adjustment for confounders. In a subgroup of women with serum samples taken after enrollment, we compared IL-10 (n=432) and TNF- α (n=466) levels in each BMI category stratified by early infection presence.

RESULTS: Of 839 women, 47% were lean, 24% OW and 29% OB. 199 (24%) had an early infection. Most common infections were UTI (13%), followed by BV (7%) and STI (5%). Infections were most frequent among OW women (34%) compared to lean and OB women (20 vs 24%, respectively) (p=0.007)

**Figure(s) will be available online.*

After adjustment for age, smoking, marital status, gestational age at enrollment and race, only OW women had an increased risk of early infection (aRR 1.54 (95% CI 1.17-2.03), particularly UTI (aRR 1.89, 95% CI 1.25-2.84), compared to lean women. Only OW women had a difference in IL-10 median levels with and without infection [10 pg/mL (IQR 5, 21) vs. 3 pg/mL (IQR 2,15), p=0.006]. There were no differences in TNF- α.

CONCLUSIONS: OW women have an increased early infection risk, specifically UTI, and increased post-infection systemic levels of IL-10, an anti-inflammatory mediator.

F-069

Acute Exposure to Lipopolysaccharide (LPS) Modifies Placental ABC Transporter Expression and Maternal Plasma Lipid Levels. Mila W Reginatto†,[1] Klaus N Fontes†,[1] Nathalia L Silva†,[1] Victoria RS Monteiro†,[1] Hannailly R Gomes†,[1] George Kluck†,[1] Flavia F Bloise†,[1] Guinever E Imperio†,[1] Atella Georgia,[1] Enrrico Bloise,[2] Stephen G Matthews,[3,4] Tania M Ortiga-Carvalho*.[1] *[1]Universidade Federal do Rio de Janeiro, Rio de Janeiro, RJ, Brazil; [2]Universidade Federal de Minas Gerais, Belo Horizonte, MG, Brazil; [3]University of Toronto, Toronto, OT, Canada; [4]Sinai Health System, Toronto, OT, Canada.*

INTRODUCTION: The ATP-Binding Cassette (ABC) transporters are transmembrane proteins that actively efflux substrates across the maternal-fetal interface. ABC transporters mediate the biodistribution of clinically relevant drugs and toxins in the placenta. The best characterized ABC transporters in the placenta, are the Abca1 and Abcg1 lipid transporters and the multidrug-resistance (MDR) transporters: P-glycoprotein (P-gp; encoded by *Abcb1a/b)*, Mdr-3 (*Abcb4)*, multidrug resistance protein 5 (Mrp-5; *Abcc5)* and the breast cancer related protein (BCRP; *Abcg2*). We hypothesized that pregnant dams exposed to lipopolysaccharide (LPS), a toll-like receptor (TLR)-4 agonist, exhibit a distinct pattern of placental ABC transporters expression and associated substrate levels.

METHODS: Pregnant female mice (C57BL/6, 8-10 weeks) exposed to LPS (150 μg/Kg-ip) or vehicle (PBS) at embryonic day 15.5 (E15.5 n=8/group) were sacrificed 4h after challenge and placentas and maternal plasma were collected. qPCR was used to analyze ABC transporter expression and maternal plasma lipid profiling was undertaken using HPLC.

RESULTS: LPS (4h) exposure resulted in 29% fetal loss. Placental expression of *Abcg1* and *Abcg2* mRNA was significantly increased (p<0.05), whereas no changes in *Abca1*, *Abcb1b*, *Abcb4* and *Abcc5* were observed. Since *Abcg1* and *Abcg2* are important lipid transporters, maternal plasma lipid levels were evaluated. Triacylglycerol content was increased (p<0.05), whereas monoacylglycerols and free fatty acids were reduced (p<0.05) in maternal blood after LPS; with no changes in cholesterol, lipid, esterified cholesterol and phospholipids classes.

CONCLUSIONS: LPS-induced fetal loss was associated with changes in placental *Abcg1* and *Abcg2* expression and with altered maternal blood lipid content, suggesting that LPS has the potential to alter the biodistribution of clinically relevant pharmacological and nutritional compounds in maternal-fetal interface, which may directly impact fetal survival and long-term health.

F-070

Early Pregnancy Infection as Risk Factor for PPROM < 37 weeks. Marcela C Smid,[1] Carmen Monthe-Dreze†,[2] Kim Boggess,[3] Alison Stuebe,[3] Karen Gibbins,[1] Sarbattama Sen*.[4] *[1]University of Utah, Salt Lake City, UT, USA; [2]Boston Children's Hospital, Boston, MA, USA; [3]University of North Carolina, Chapel Hill, NC, USA; [4]Brigham and Women's Hospital, Boston, MA, USA.*

INTRODUCTION: Mounting evidence suggests that infection likely triggers a pro-inflammatory cascade resulting in fetal membrane weakening. Although 50% of preterm premature rupture of membranes (PPROM) cases have infectious etiologies at time of delivery, little is known about the early pregnancy infections as risk factors for PPROM. We sought to examine the early pregnancy risk factors for PPROM in a high-risk cohort.

METHODS: This is a secondary data analysis of the MFMU Omega-3 trial of fatty acid supplementation among women with ≥1 prior spontaneous preterm delivery (PTD). Our primary exposure was early pregnancy infection (sexually transmitted infection (STI), urinary tract infection (UTI)/pyelonephritis, bacterial vaginosis (BV), herpes and/or GBS at baseline) prior to enrollment at 16-22.9 weeks gestation. Our primary outcome was PPROM < 37 weeks and secondary outcomes were chorioamnionitis and preterm delivery (PTD) < 37 weeks. We used modified Poisson models to estimate the relative risk of PPROM < 37 weeks, chorioamnionitis and PTD < 37 weeks by presence of early pregnancy infection after adjustment for maternal BMI, age, marital status, race and smoking.

RESULTS: This study included 839 women; 199 women (24%) had an early pregnancy infection. The most common early infection type was UTI/pyelonephiritis (13%), followed by BV (7%) and STI (5%). Of women who had an early infection, 13% had PPROM < 37 weeks compared to 7% who did not have an early infection (p=0.01 (adjusted risk ratio (aRR) 1.67 (95% confidence interval (CI) 1.05-2.66)). Other risk factors for PPROM < 37 weeks include maternal pre-pregnancy obesity (aRR 2.36, 95% CI 1.39-4.00) and smoking (aRR 1.83, 95% CI 1.09-3.07)). Women with early infections were also at increased risk for chorioamnionitis (aRR 3.87, 95% CI 1.12-13.3) but not PTD < 37 (aRR 1.18, 95% CI 0.98-1.42).

CONCLUSIONS: Early pregnancy infection is a risk factor for PPROM < 37 wks and chorioamnionitis, but not PTD<37 weeks, in a cohort at high risk for PTD.

F-071

The Relationship between Maternal Nutrition, Obesity and Diabetes During Pregnancy and Maternal and Offspring's Kidney Structure and Function: A Systematic Review. Yu Qi Lee†,[1] Kirsty Pringle,[1] Kym Rae,[2] Clare E Collins,[3] Adrienne Gordon.[4] *[1]University of Newcastle, Newcastle, NSW, Australia; [2]University of Newcastle, Newcastle, NSW, Australia; [3]University of Newcastle, Newcastle, NSW, Australia; [4]The University of Sydney, Sydney, NSW, Australia.*

INTRODUCTION: According to the Barker theory and the Developmental Origins of Health and Disease hypothesis, variation in the quality or quantity of nutrients consumed during pregnancy exerts permanent effects on the developing fetus. This study reports on a systematic review of the relationship between maternal nutrition, obesity, diabetes and maternal kidney structure/function during pregnancy and offspring's kidney structure/function in human.

METHODS: A search using protocol (PROSPERO registration: CRD42016047758) was conducted across databases (Medline/ Premedline (Medline In-Process), Cinahl, Embase, The Cochrane Library, Scopus) for experimental or observational studies published up to and including May 2016. Exposure variables were maternal nutrition, obesity and diabetes during pregnancy. Outcome measures were kidney structure, glomerular size and kidney function including hypertension, proteinuria, albumin: creatinine, microalbuminuria, albuminuria, glomerular filtration rate, renin-angiotensin system (plasma levels/activity, kidney levels/ activity), protein: creatinine, nephrin: creatinine and urinary sodium/ potassium excretion.

RESULTS: Of the 7465 abstracts identified, 249 studies met the inclusion criteria, of which there were 14 human studies and 235 animal studies. Only the human studies were included in this review. Generally, studies varied in population and study designs and results were inconsistent.

CONCLUSIONS: This systematic review demonstrates a limited number of studies focusing on humans. There is a lack of studies on maternal obesity and its influences on maternal and offspring kidney health. Results show some relationship between maternal nutrition, diabetes and maternal kidney structure/function during pregnancy and offspring kidney structure/ function. However, additional longitudinal prospective studies are required to confirm this relationship, especially in the Indigenous population, where the risk of renal disease is higher.

F-072

Development of Placenta-Specific Glut1 Knockdown Mouse Strains to Model the Influence of Varying Glucose Transporter Levels on Fetal Overgrowth and Offspring Health. Marlee Elston†,[1] Joel Marh,[2] Haide Razavy,[2] Kainalu Matthews†,[2] Vivien Klein†,[2] Johann Urschitz*.[2] *[1]University of Hawaii John A. Burns School of Medicine, Honolulu, HI, USA; [2]The Institute for Biogenesis Research, The University of Hawaii John A. Burn School of Medicine, Honolulu, HI, USA.*

INTRODUCTION: Maternal obesity has been associated with fetal overgrowth as well as adult disease risk in the offspring for a range of diseases, particularly metabolic and cardiovascular diseases. In order to gain a greater understanding of the impacts of glucose transporter levels and specifically the associated abnormally high levels of glucose transport to the fetus during pregnancy, a mouse model of placenta specific glucose modulation has been developed. By isolating the role of glucose transporter levels, we are able to examine the impact of varying glucose transporter levels on fetal health outcomes.

METHODS: The *piggyBac* transposase-enhanced pronuclear microinjection (PNI) technique was used to generate three lines of transgenic mice. The transgene cassette of each line contained one of three shRNAmirs against Glut1 under the control of the CYP19I.1 promoter for trophoblast specific expression. These different shRNAmir sequences were chosen to achieve different levels of Glut1 knockdown. We also engineered the knockdown to be a tetracycline inducible (Tet-on system) to allow for time point specific induction. Finally, two different reporter gene to allow for (1) visual validation of transgenesis (EGFP under the constitutive CMV promoter) and (2) confirmation shRNAmir expression after Tet-on activation (luciferase gene).

RESULTS: Transgenesis was assessed by visual inspection under UV light for the presence of EGFP fluorescence and then confirmed by PCR genotyping and sequencing of the inserted shRNAmir. We determined placenta specific knockdown of Glut1 expression in induced transgenic mice by qPCR and western blot.

CONCLUSIONS: Developing a better understanding of the causes of in-utero fetal programming is critical to adult health, including nutrient transport levels. The generation of three novel mouse strains that model Glut1 knockdown is a new tool allowing for further investigation into the effects of glucose transport levels on fetal overgrowth and fetal programming.

F-073

Chronic Fetal Hypoxia Results in Significant Renal Tubule Pathology in Adulthood. M R Sutherland†, KL Brain, KJ Botting, S Austin-Williams, EJ Camm, DA Giussani*. *University of Cambridge, Cambridge, Cambridgeshire, United Kingdom.*

INTRODUCTION: Chronic fetal hypoxia is a common outcome of pregnancy complications. Fetal responses to hypoxia include a redistribution of blood flow away from peripheral circulations (*J Physiol.* **594(5)**:1215, 2016). This encompasses a reduction in renal blood flow, which if sustained, may impair kidney development. We have reported that maternal antioxidant treatment in hypoxic pregnancy is protective against the programming of cardiovascular dysfunction (PLoS One **7(2)**:e31017, 2012). Here, we determined the effect of hypoxic pregnancy with and without maternal antioxidant treatment on renal morphology in adulthood.

METHODS: Ewes carrying singleton female fetuses were exposed to chronic hypoxia (10% O_2; H) or normoxia (21% O_2; N) from 105-138 days gestation (term=147 days). During this period, half of the ewes received 200 mg/kg/d of vitamin C. Lambs (n=6/group) were grown to 9 months of age. Stereology was used to determine kidney volume and nephron number. Fibrosis, glomerulosclerosis (capillary scarring), and renal tubule morphology were assessed histologically.

RESULTS: A markedly increased volume of the tubular portion of the renal cortex occurred in young adult lambs of hypoxic pregnancy (Fig. 1A); nephron number was not different between groups. Hypoxic pregnancy also resulted in severe proximal tubule injury (brush border loss), and increased fibrosis and glomerulosclerosis (Fig. 1B-D). Vitamin C treatment ameliorated medullary fibrosis in lambs of hypoxic pregancy.

CONCLUSIONS: Chronic fetal hypoxia resulted in significant renal tubule pathology in adulthood; vitamin C treatment, however, had little effect on kidney morphology. These findings have important implications for the long-term renal health of individuals born following complicated pregnancies.

The British Heart Foundation

**Figure(s) will be available online.*

Figure 1: Kidney volume (A), tubule wall diameter (B), fibrosis (C) and glomerulosclerosis (D) in fetal hypoxia-exposed and/or vitamin C treated lambs *versus* controls. Two-way ANOVA with factors hypoxia ($p_{Hypoxia}$), treatment (p_{VitC}) and their interaction (p_{HxVC}). Tukey's post-hoc *$p<0.05$ (for cortex in A), **$p<0.001$.

F-074

Postnatal Growth and Cardiovascular Phenotype Following Maternal Uterine Artery Adenoviral Vascular Endothelial Growth Factor-A_{165} Gene Therapy (Ad.VEGF) for Fetal Growth Restriction in Guinea Pigs. Owen R Vaughan†, Carlo A Rossi, Yuval Ginsberg, Tara I Krishnan, Hannah Barker, Anthony White, Anna L David*. *UCL Institute for Women's Health, London, England, United Kingdom.*

INTRODUCTION: Fetal growth restriction (FGR) increases perinatal mortality and lifelong cardiovascular disease risk. In experimental animals with FGR, uterine artery Ad.VEGF increases fetal growth velocity by improving uteroplacental perfusion. This study aimed to determine the longer term effects of mid-gestation Ad.VEGF on pregnancy outcome, postnatal growth and adult blood pressure in a guinea pig model of FGR.

METHODS: Under the Animals (Scientific Procedures) Act 1986, pregnant Dunkin Hartley guinea pigs were fed *ad libitum* (control, n=8) or 70% normal food intake to induce FGR. On day ~30 of pregnancy,

FGR dams received either Ad.VEGF ($1x10^{10}$ _viral particles, n=8) or vehicle (n=7), delivered to the external surface of the uterine arteries, via laparotomy. Controls were sham operated. Dams littered and pups were weighed at birth and weekly thereafter. Carotid arterial pressure and plasma cortisol response to adrenocorticotrophic hormone challenge were measured in adult pups at ~4 months of age. Mean±SEM results were compared by GLM.

RESULTS: There was no difference between control, FGR and FGR+Ad. VEGF groups in litter size, gestational age at delivery, prenatal or postnatal mortality. The effect of prenatal treatment on birth weight depended upon offspring sex, although both male and female FGR+Ad.VEGFpups (males 100±4g, females 96±3g) were heavier than untreated FGR pups (males 97±4g, females 95±3g; control males 107±4g, females 87±3g, P<0.05). Net postnatal weight gain was also greater in female, but not male, FGR+Ad.VEGFpups than untreated FGR animals from 12 weeks of age, although neither group differed from controls. When males and females were combined, carotid arterial pulse pressure was elevated in untreated FGR pups (3.2±0.4mmHg), but not FGR+Ad.VEGFpups (2.6±0.1mmHg), compared to controls (1.6±0.4mmHg, P<0.05). Neither systolic, diastolic nor mean arterial pressure, cardiac mass nor ventricular wall thickness differed between control, FGR and FGR+Ad.VEGF animals. Basal and post-challenge plasma cortisol concentrations were similar in all three groups.

CONCLUSIONS: Maternal uterine artery Ad.VEGF does not adversely affect perinatal mortality and may improve postnatal growth and ameliorate increased adult blood pressure associated with FGR.

F-075

Chronic Stress During Pregnancy Causes Sex-Specific Changes in Offspring Allergic Asthma Response by Influencing Fetal Immune Development. Arianna L Smith,[1] Elizabeth Witte,[1] Jack Harkema,[2] Daven Jackson-Humbles,[2] Karen Racicot*.[1] *[1]Michigan State University, East Lansing, MI, USA; [2]Michigan State University, East Lansing, MI, USA.*

INTRODUCTION: Maternal stress during pregnancy increases childhood risk of allergic asthma, although the mechanism is unknown. We hypothesize that maternal stress alters alveolar (lung) macrophage programming during fetal development, thus affecting offspring susceptibility to allergic asthma.

METHODS: Pregnant mice received the stress hormone, corticosterone (CORT), in drinking water from E12.5 until birth. After four weeks, offspring from CORT-treated and control dams were sensitized and challenged with house dust mite (HDM) and the allergic asthma response was characterized in the lung. Maternal programming of fetal alveolar macrophages (AM) was characterized by transferring AM of offspring from CORT-treated or control dams into the lungs of healthy offspring following endogenous AM depletion via clodronate liposomes administration into the lungs.

RESULTS: The allergic asthma phenotype of male and female offspring was differentially affected by maternal CORT. Females from CORT-treated dams had a heightened eosinophil response to HDM compared to females from control dams. Male offspring from CORT-treated dams showed no change in eosinophil accumulation but had a dramatic increase in neutrophil infiltration in response to HDM compared to males from control dams. In addition, asthma-associated cytokines IL-33, granulocyte-macrophage colony-stimulating factor, CD200 and thymic stromal lymphopoeitin were affected by maternal CORT in a sex-specific manner in the lung. Alveolar macrophages are long-lived resident cells that appear in the lung during fetal development, and are master regulators of lung immunity. Therefore, we postulated these cells were affected by maternal treatment and responsible for the changes in offspring asthma. To test this, AMs from offspring of control or CORT-treated dams were isolated and transferred into healthy recipient mice lacking AM following administration of clodronate liposomes into the lungs. Excitingly, control recipients that received AMs from CORT-offspring had an asthmatic response similar to those offspring from CORT-treated mothers.

CONCLUSIONS: Maternal stress during pregnancy affects programming of fetal AMs, which appear to mediate the allergic asthma response in offspring in a sex-specific manner.

F-076

Exposure to Excess Maternal Cortisol in Late-Gestation Prevents the Normal Metabolic Transition of the Heart at Birth. Jacquelyn Walejko†,[1] Andrew Antolic†,[1] Maureen Keller-Wood,[1] Arthur Edison*.[2] *[1]University of FL, Gainesville, FL, USA; [2]University of GA, Athens, GA, USA.*

INTRODUCTION: While cortisol is important for fetal heart maturation during late-gestation, little is known about the effects of maternal hypercortisolemia on the developing heart. Our laboratory has shown in an ovine model that maternal hypercortisolemia leads to increased fetal mortality during the peripartum period. In addition, transcriptomic analysis revealed alterations in fetal cardiac metabolism of fetuses in early labor. Therefore, I investigated the effects of chronic increases in maternal cortisol during late gestation on the global metabolic transition of the neonatal heart immediately following birth.

METHODS: Heart samples were collected from left and right ventricles and intraventricular septum in 9 untreated fetuses at gestational day 142, 13 untreated neonatal lambs immediately following birth, and 4 neonatal lambs exposed to maternal cortisol (1 mg/kg/day, gestational day 115-birth). High-resolution magic angle spinning (HR-MAS) proton nuclear magnetic resonance (^{1}H-NMR) spectroscopy was conducted on a 600 MHz NMR spectrometer to gain metabolic profiles of heart samples. Significance of metabolites was determined using a 1-way MANCOVA adjusted for ewe effects of the area under the metabolite peak(s) of probabilistic quotient normalized spectra.

RESULTS: Lactate, along with myo-inositol and poly-unsaturated lipids, are significantly increased ($p<0.05$) in fetal heart at gestational day 142; whereas glutamate and taurine were significantly increased ($p<0.05$) in neonatal tissue. In neonatal hearts from cortisol-exposed ewes, myo-inositol was significantly increased, whereas poly-unsaturated lipids, taurine and glutamate were decreased, as compared to control newborns ($p<0.05$).

CONCLUSIONS: Decreases in taurine and glutamate, along with elevations in myo-inositol, suggest altered TCA cycle flux and cardiac function at birth in excess-cortisol exposed neonates. Transcriptomic analysis revealed increases in peroxisome proliferator activated receptor, further supporting alterations in lipid metabolism. Our data suggests that fetal exposure to excess maternal cortisol prevents the fetal heart from undergoing normal metabolic transitions following birth, which may contribute to stillbirth during the peripartum period, or later life cardiomyopathies.

F-077

Effect of Maternal Antioxidant MitoQ Treatment on Offspring Vascular Function in a Rat Model of Intrauterine Growth Restriction (IUGR). Mais M Aljunaidy,[1] Jude S Morton,[1] Raven Kirschenman,[1] Patrick Case,[2] Christy-Lynn M Cooke,[1] Sandra T Davidge*.[1] *[1]University of Alberta, Edmonton, AB, Canada; [2]University of Bristol, Bristol, England, United Kingdom.*

INTRODUCTION: A suboptimal environment in fetal life is linked to cardiovascular disease in adult life. Maternal hypoxia can lead to placental oxidative stress, which is associated with abnormal cardiovascular function in the offspring. We hypothesize that maternal treatment with MitoQ, a mitochondrial antioxidant, may prevent the development of cardiovascular disease in adult offspring.

METHODS: Pregnant rats were injected with either MitoQ loaded nanoparticles (nMitoQ; 125 µM) or saline via tail vein on gestational day (GD) 15 (nanoparticles prevent MitoQ from crossing to the fetus). Rats then were subdivided into two groups exposed to either hypoxia (11% O_2) or normoxia (21% O_2) from GD 15-21 (term; 22 days). At 7 months of age vascular function (wire myography) was assessed in both male and female offspring. A 2-way ANOVA or Student's t-test was used for analyses.

RESULTS: The nitric oxide synthesis inhibitor (L-NAME) increased mesenteric artery sensitivity to phenylephrine (PE) in male offspring of normoxic ($P<0.05$) but not hypoxic ($P=0.22$) rats. nMitoQ treatment restored the nitric oxide effect on PE vasoconstriction in the hypoxic group (pEC_{50} PE: 5.50±0.05 vs. PE+L-NAME: 5.83±0.08, $P=0.008$). In

female offspring, sensitivity to PE was similarly increased by L-NAME in normoxic and hypoxic groups. However, in female offspring, nMitoQ diminished this increase in the prenatal hypoxia exposed group.
CONCLUSIONS: nMitoQ treatment in mid gestation restored nitric oxide modulation of vascular function in hypoxic male offspring. In female offspring, maternal treatment with nMitoQ led to a decreased nitric oxide involvement in hypoxic exposed animals. This study suggests that maternal/placental treatment can alter vascular function of offspring later in life.

F-078

Impaired Insulin Secretion in Pregnant Rats Fed a Low Protein Diet. Haijun Gao,[1] Eric Ho,[2] Meena Balakrishnan,[1] Chandra Yallampalli.[1] *[1]Baylor College of Medicine/Texas Childrens Hospital, Houston, TX, USA; [2]Rice University, Houston, TX, USA.*
INTRODUCTION: Glucose is the primary insulin secretagogue and in normal pregnancy the enhanced glucose stimulated insulin secretion (GSIS) in beta cells compensates for insulin resistance to maintain glucose homeostasis. Low protein diet during pregnancy leads to reduced plasma insulin levels in rodents, but the underlying mechanisms remain unclear. In this study we hypothesized that plasma insulin levels in pregnant rats fed a low protein diet is reduced due to the impaired GSIS of pancreatic islets.
METHODS: Pregnant SD rats were fed a diet with 20% (CT) or 6% casein (LP) from Day 1 of pregnancy until killed on Days 10, 14, 18, 19, 21 or 22 (n=6-10 rats/diet) and the plasma was collected for insulin ELISA. On Day 19, insulin and glucose tolerance tests were conducted in two different batches of pregnant dams (n=4-5 rats/diet). Also on Day 19, pancreatic islets were isolated and GSIS of pancreatic islets was measured in the presence of low and high concentration (2.8 and 16.7 mM) of glucose, and 3 plasma membrane depolarization reagents, KCl, glibenclamide and L-arginine. In addition, insulin gene expression and total insulin protein in pancreatic islets were measured by q-PCR and ELISA, respectively.
RESULTS: Main findings include: 1) Plasma insulin levels were unaltered on Day 10, but significantly reduced on Days 14-22 in pregnant rats fed LP diet compared to those of CT rats; 2) Insulin sensitivity was similar in both groups, while glucose intolerance was more severe in pregnant rats fed LP diet compared to CT rats, demonstrated by significantly smaller area under the curve (AUC) of insulin and larger AUC of glucose in LP rats; 3) GSIS in pancreatic islets was significantly lower in LP rats compared to CT rats in the presence of both high and low concentration of glucose, KCl and glibenclamide, while the response of pancreatic islets to L-arginine disappear in LP rats; 4) The total insulin content in pancreatic islets and also mRNA levels of *proinsulin 2* were reduced in LP rats compared to that of CT rats.
CONCLUSIONS: These studies demonstrate that impaired GSIS possibly together with reduced insulin content in beta cells of LP rats causes the reduced plasma insulin levels, which may result in placental and fetal growth restriction and program hypertension and metabolic diseases in offspring.

F-079

Breath Analysis Reveals Molecular Signatures of Developmental Programming. Andrew C Bishop,[1] Ahsan Choudary,[1] Mark Libardoni,[2] Biswapriya Misra,[1] Kenneth Lange,[2] John Bernal,[3] Mark J Nijland,[4] Cun Li,[5] Michael Olivier,[1] Peter W Nathanielsz*,[5] Laura A Cox.[1] *[1]Texas Biomedical Research Institute, San Antonio, TX, USA; [2]Southwest Research Institute, San Antonio, TX, USA; [3]Texas Biomedical Research Institute, San Antonio, TX, USA; [4]University of Texas Health Science Center San Antonio, San Antonio, TX, USA; [5]University of Wyoming, Laramie, WY, USA.*
INTRODUCTION: Maternal nutrient restriction (MNR) adversely affects development and can result in intrauterine growth restriction (IUGR), characterized by signature changes in the transcriptome, proteome and metabolome. By assessing metabolic changes in IUGR detailed molecular information on specific disease states may reveal molecular signatures of disease more sensitive than current clinical measures. We hypothesize that volatile organic compounds (VOCs) specific to IUGR will produce molecular signatures that translate to more sensitive and early markers of human disease.
METHODS: Breath samples were collected from 13 juvenile baboons: 3 CON and 3 IUGR males, 4 CON and 3 IUGR females. Animals were sedated with isoflurane (1.5%,v/v), breath air collected using Anasorb cartridges (SKC Inc. Eighty Four, PA) and analyzed with a thermal desorber (Perkin Elmer) in tandem with a 2D-GCxGC-ToF MS (LECO, St Joseph, MI). ChromaTOF software was used to identify and align VOCs by matching spectral data to the NIST 11 MS spectral library. Statistical analysis was performed using MetaboAnalyst.
RESULTS: We found breath metabolites that differed by sex and between CON and IUGR including differences in abundance between groups included ketones, alcohols, aldehydes, hydrocarbons, and esters.
CONCLUSIONS: To our knowledge, this is the first study of baboon breath to determine molecular disease signatures. VOCs specific to CON, IUGR, female and male groups were identified and categorized into breath signatures. We demonstrate feasibility of quantifying and identifying breath VOCs and show they differ by sex and metabolic status. Thus, these differences will give new insights into potential pathways of disease and uncover more sensitive clinical markers of metabolic diseases.

F-080

Nutrient Sensor and De Novo Lipogenesis Mechanism for Programmed Fatty Liver in Offspring of Obese Mothers. Mina Desai, Kavita Narwani, Niyati Joshi, Guang Han, Elaheh Mossayebi, Jocelyn McGill, Michael G Ross. *LABioMed at Harbor-UCLA, Torrance, CA, USA.*
INTRODUCTION: Non-alcoholic fatty liver (NAFLD) is associated with obesity and metabolic syndrome. One of the mechanism for NAFLD involves de novo lipogenesis which is regulated by a lipogenic transcription factor SREBP1 (sterol regulatory element-binding protein) and its downstream target SCD1 (stearoyl-coenzyme A desaturase). SIRT1 which is a nutrient sensor and a histone deacetylase regulates SREBP1 and SCD1. Activation of SIRT1 protects from NAFLD. We have shown that maternal obesity and high fat (HF) results in offspring obesity and lipid abnormalities. We hypothesized that SIRT1-mediated mechanism contributes to NAFLD in HF obese offspring. We determined the hepatic lipid content and expression of SIRT1, and its downstream targets SREBP1 and SCD1.
METHODS: Female mice were fed either a control (10% kcal) or high fat (HF; 45% kcal) diet to create maternal obesity prior to mating, and diets continued throughout pregnancy and lactation. At 21 days of age, offspring were weaned to a control diet. At 14 months of age, male offspring underwent DEXA scan and 48h later were sacrificed following an overnight fast. Liver protein was extracted for expression of SIRT1, SREBP1 and SCD1 and values shown as fold change. Liver sections were stained (H&E) and total number and size of lipid vacuoles were quantified.
RESULTS: HF newborn males were significantly heavier at birth and as adults (36.2±1.0 vs 29.2±0.6 g; $P<0.001$), and exhibited increased adiposity as compared to controls (29.5±1.3 vs 20.1±1.7 %; $P<0.01$). Further, HF males showed increased hepatic protein expression of SREBP1 (1.3-fold) and SCD1 (1.5-fold) with paradoxically upregulated SIRT1 (1.3-fold). The histological staining (Figure) and quantification showed increased lipid content (457±10 vs 207±8 lipid vacuoles) and increased size of vacuoles (208±7 vs 193±2 μm) in HF offspring.
**Figure(s) will be available online.*
CONCLUSIONS: In contrast to their nutrient status, HF males exhibited increased SIRT1 with paradoxically increased SREBP1 and SCD1. This suggests that dysregulated nutrient sensing occurs in HF offspring and this may contribute to increased lipogenesis, leading to NAFLD.

F-081

Folate Treatment Partially Reverses Gestational Low Protein Diet Induced Glucose Intolerance and the Magnitude of Reversal is Age and Sex Dependent. Chellakkan S Blesson, Amy Schutt, Pretty R Mathew, Daren Tanchico, Meena Balakrishnan, Uma Yallampalli, Chandra Yallampalli. *Baylor College of Medicine/Texas Childrens Hospital, Houston, TX, USA.*

INTRODUCTION: Gestational low protein (LP) programming causes glucose intolerance (GI) and insulin resistance (IR) in adult offspring. Folate supplementation has been shown to rescue the offspring from various programming effects. Our objective was to investigate if folate supplementation during pregnancy will reverse LP induced GI and IR.

METHODS: Pregnant rats were fed control (20% protein), isocaloric low protein (LP, 6%) or LPF (LP with 5mg/kg Folate) diet from gestational day 4 until delivery. Control diet was given during lactation and to pups after weaning. Glucose tolerance test (GTT) was done at 1, 2 and 3 months of age followed by euglycemic-hyperinsulinemic clamp at 4 months. Rats were sacrificed at 4 months and their gonadal, renal, inguinal, brown fat and pancreas were weighed and expressed relative to their body weight.

RESULTS: LP and LPF mothers showed similar weight loss during late pregnancy following decreased feed intake. Both LP and LPF pups were smaller at birth (Males: 6±0.1 in Controls, 5±0.1 in LP and 5±0.1 in LPF; Females: 6±0.1 in Controls, 4±0.1 in LP and 4±0.1 in LPF) but their weights caught up similar to that of controls by 3 months. Body fat contents at 4 months were similar but LPF showed an increasing tendency in both sexes. In males, folate supplementation reduced LP induced GI at 2 months (Glucose AUC: 1940 mmol/l*180min in LP vs 1629 mmol/l*180 min in LPF) but the effect diminished at 3 months. In females, folate reduced GI at 1 month (Glucose AUC: 1406 mmol/l*180min in LP vs 1264 mmol/l*180min in LPF) but had no effect at 2 and 3 months. Interestingly, LPF group had higher pancreatic weights than other groups suggesting that folate helps in pancreatic development enabling the LPF rats to secrete more insulin to maintain euglycemia. Euglycemic hyperinsulinemic clamp shows, both LP and LPF are insulin resistant when compared to controls by 4 months with LPF was more severe than LP in males. Interestingly, females were more insulin resistant than males.

CONCLUSIONS: Folate treatment partially reverses LP induced GI and the magnitude of reversal is age and sex dependent. Further, folate treatment does not reverse IR in both sexes but makes it worse in males at 4 months. Our study shows that folate treatment is not sufficient to rescue the LP programming effects.

F-082

Developmental Programming of Pulmonary Hypertension by Isolated Chronic Prenatal Hypoxia. AM Spiroski†, CJ Shaw, DA Giussani*. *University of Cambridge, Cambridge, United Kingdom.*

INTRODUCTION: Late gestation hypoxia-induced intrauterine growth restriction (IUGR) is associated with the early onset of ageing-associated cardiopulmonary dysfunction (Rueda-Clausen, *et al.,* Card Res, 81:713-22, 2009). However, the independent effects of prenatal hypoxia *vs.* IUGR on remodelling of the cardiopulmonary system remain unknown. Therefore, using an established rodent model of prenatal hypoxia that does not affect maternal food intake or decrease birth weight, the aim of this study was to determine whether prenatal hypoxia alone programmes *in vivo* indices of cardiopulmonary dysfunction in adult rat offspring.

METHODS: Pregnant Wistar dams were exposed to normoxia (N; 21% O_2) or (hypoxia (H; 13% O_2) from 6-20 days gestation (term ~22 days). Offspring were maintained in normoxia until 4 months of age. To control for sex and within-litter variation, one male per litter was selected for either echocardiography (under 10 $mg \cdot kg^{-1}$ xylazine and 100 $mg \cdot kg^{-1}$ ketamine; N: n=11, H: n=8), or conscious cardiovascular assessment. Femoral catheters were inserted under isoflurane anaesthesia and cardiovascular function was determined 4-5 days post-operatively (N: n=10, H: n=8).

RESULTS: Hypoxic pregnancy did not affect weight at postnatal day 2 (N: 7.4±0.3 *vs.* H: 6.9±0.3 g). Pulmonary valve velocity time integral (PV VTI) peak pressure (mmHg) and velocity ($mm \cdot s^{-1}$) were elevated, and tricuspid valve E/A ratio (TV E/A) was greater in adult offspring of hypoxic pregancy (Fig. 1 A-C). The ratio of diastolic right ventricle to left ventricle internal diameter (RVIDd/LVIDd) relative to bodyweight was also greater in offspring of hypoxic pregnancy (Fig. 1 D). M-Mode measurement of left ventricular ejection fraction and mitral E/A ratios were not different. Similarly, offspring of hypoxic pregnancy did not show alterations in conscious basal blood pressure or heart rate.

**Figure(s) will be available online.*

CONCLUSIONS: Chronic prenatal hypoxia independent of IUGR programmes echocardiographic indices of pulmonary hypertension prior to the development of significant left ventricular and systemic dysfunction. Supported by *The British Heart Foundation.*

F-083

Maternal Tobacco Smoke Exposure Alters Placental PPARγ Expression of Male and Female Rat Pups in a Sex-Divergent Manner. Claudia Weinheimer†,[1] Brent Locklear,[1] Haimei Wang,[1] Michelle Baack,[2] Lisa Joss-Moore*.[1] *[1]University of Utah, Salt Lake City, UT, USA; [2]Sanford Health Research Center, Sioux Falls, SD, USA.*

INTRODUCTION: Fetal exposure to maternal tobacco smoke (MTS) programs the development of long-term disease. Fetal programming mechanisms involve changes in placental function, structure and gene expression profiles, often in a sex-divergent manner. We previously demonstrated in a rat model, that in utero MTS exposure affects placental function, placental structure, placental lipid deposition, and placental expression of fatty acid transporter genes. Furthermore, all observed effects differed between male and female rat pups. Placental lipid metabolism and expression of placental fatty acid transporter genes is, in part, regulated by PPARγ. Specifically important for sex-divergent effects, PPARγ expression is also inversely related to estrogen signaling. However, the effects of MTS on placental PPARγ mRNA levels, as well as placental estradiol levels remain unknown. We hypothesize that, in the rat, MTS exposure alters placental PPARγ expression in association with inverse changes in placental estradiol levels.

METHODS: Pregnant rats were exposed to tobacco smoke (MTS) or room air (Control) from E11 to term (E21). Placentas from male and female MTS and control pups were collected at delivery. Real-time RT-PCR was used to measure mRNA transcript levels of PPARγ. Placental estradiol levels were measured by ELISA. Comparisons were male control to female control, and MTS to sex-matched control (n=6 placenta/group, *$p \leq 0.05$).

RESULTS: Basal levels of PPARγ mRNA are higher in male placenta compared to female placenta (128±31*). In contrast, basal levels of estradiol are lower in male placenta (80±8%*) than in female placenta. In male rat pups, MTS decreases placental PPARγ mRNA levels (78±13%*), with no change in placental estradiol levels. In female rat pups, MTS does not alter PPARγ mRNA levels or placental estradiol levels.

CONCLUSIONS: We conclude that in the rat, MTS exposure alters placental PPARγ expression in a sex-divergent manner. However, contrary to our hypothesis, MTS did not alter placental estradiol levels. Quantification of other components of estrogen signaling and of androgen signaling may be affected by MTS, and are the subject of ongoing investigations.

F-084

Leucine Potentiates Glucose Stimulated Insulin Secretion in Fetal Sheep. Brit H Boehmer†, Laura D Brown, Stephanie R Wesolowski, William W Hay, Paul J Rozance. *University of Colorado, Aurora, CO, USA.*

INTRODUCTION: Amino acids stimulate fetal insulin secretion. They also potentiate fetal glucose stimulated insulin secretion (GSIS). However, the ability of individual amino acids to potentiate fetal (GSIS) has not been tested. The objective of this study was to measure GSIS during an acute leucine (LEU) or saline (SAL) infusion in late gestation fetal sheep (n = 5).

METHODS: At 121 ± 1 dGA, catheters were surgically placed in the fetal abdominal aorta and femoral vein. A fetal square wave hyperglycemic clamp was used to measure GSIS following during an infusion of LEU (752 μmol/h) or SAL (0.3 mL/h), which were started 90 minutes prior to the hyperglycemic clamp. Multiple studies were conducted on each fetus with alternating treatment infusions every 2-3 days. Blood samples

were collected before and after treatment infusions and at -15, -10, 5 10, 15, 20, 30, 45, 60, 75, and 90 min during the hyperglycemic clamp (initiated at 0 min).

RESULTS: Prior to the hyperglycemic clamp, plasma glucose and insulin concentrations were similar after LEU and SAL infusions. During the hyperglycemic clamp, plasma concentrations of glucose were similar between LEU and SAL. Plasma concentrations of insulin increased to a greater extent 30 min after initiation of the hyperglycemic clamp in LEU compared with SAL infusions ($P = 0.05$).

CONCLUSIONS: These results indicate that leucine potentiates fetal GSIS and how multiple nutrients act in concert to increase fetal insulin concentrations.

F-085

Exposure to Maternal Nutrient Restriction in Development Increases Fructose Appetite in Juvenile Baboons. Laura A Cox,[1,3] Kenneth G Gerow,[2] Robert E Shade,[3] Kenneth Lange,[4] Shifra Birnbaum,[1] Natalia Kuhn,[3] Edward J Dick, Jr.,[3] John Bernal,[3] Anthony G Comuzzie,[1] Mark J Nijland,[5] Cun Li,[6] Peter W Nathanielsz.[3,6] *[1]Texas Biomedical Research Institute, San Antonio, TX, USA; [2]University of Wyoming, Laramie, WY, USA; [3]Texas Biomedical Research Institute, San Antonio, TX, USA; [4]Southwest Research Institute, San Antonio, TX, USA; [5]University of Texas Health Science Center San Antonio, San Antonio, TX, USA; [6]University of Wyoming, Laramie, WY, USA.*

INTRODUCTION: Compelling animal studies show poor fetal nutrition alters responses to later life nutritional challenges. We showed that 30% reduction of baboon maternal nutrient intake (MNR) leads to term offspring (F1) IUGR and upregulation of orexigenic and down regulation of anorexigenic arcuate nucleus peptides (1). We studied juvenile baboon response to a high-fat, high-carbohydrate, high-salt (HFCS) challenge and ad lib fructose drink intake to determine whether programming alters ingestive behavior.

METHODS: Pregnant baboons were fed *ad lib* (Control; CTR) or 30% global calorie reduction (MNR) from 0.16 gestation (G) through lactation. At weaning all F1 were fed chow diet. At~3.5 years n= 3 male and 3 female CTR F1 and 3 male and 3 female MNR F1 were fed a high energy diet with *ad lib* fructose drink challenge for 7 weeks. Male and female data did not differ and were pooled.

RESULTS: At the end of challenge, IUGR baboon weights, BMI and bone mineral density matched CTR. Heart rate and blood pressure did not differ between sex or groups. Measures of liver function and cholesterol, as well as glucose metabolism did not differ between CTR and IUGR. Potassium excretion was lower in IUGR than CTR at baseline and throughout the HFCS challenge. However fructose intake was increased by 64% in IUGR offspring (Fig 1).

**Figure(s) will be available online.*

Fructose consumption .* $p<0.05$.

CONCLUSIONS: IUGR F1 showed increased fructose intake in keeping with our published finding of increased orexigenic peptides in the hypothalamic arcuate nucleus of IUGR F1.

Ref: (1) Li et al. (2013) **J Endocrinol.** 217(3): 275-82.

F-086

Fetal Neuronal Exosome Morphine Receptor Levels and Maternal Opioid Use. Laura Goetzl*,[1] Laura Hart,[1] Nana Merabova,[2] Stephaniya Grebennikova,[2] Nune Darbinian.[2] *[1]Temple University Medical School, Philadelphia, PA, USA; [2]Shriners Hospitals for Children, Philadelphia, PA, USA.*

INTRODUCTION: Opioid use disorder in pregnancy is common, resulting in significant neonatal morbidity and health care costs. Compared to methadone, buprenorphine is associated with lower neonatal opioid requirements and shorter length of stay for neonatal abstinence syndrome (NAS). We hypothesized that methadone and buprenorphine would be associated with differences in fetal brain morphine receptor (MU) levels as measured non-invasively through fetal neuronal exosomes (FNEs) isolated from maternal blood.

METHODS: Maternal plasma samples were collected between 9 and 21 weeks gestation (GA). A detailed face to face questionnaire quantified maternal opioid exposure. FNEs were isolated as previously described. MU and CD81 protein levels were quantified using commercial ELISA kits and MU was normalized to CD81.

RESULTS: Samples were analyzed from 4 groups: control (n=19), methadone (n=10), buprenorphine (n=5) and buprenorphine/naloxone (n=6). MU was not different based on naloxone exposure; therefore the two buprenorphine groups were combined for analysis. Exposure to opioids increased MU levels in FNEs (Figure 1). Levels appeared to be higher with methadone compared to buprenorphine but the difference was not statistically significant ($p=0.25$). There was no correlation between morphine equivalent dose (MED) and MU ($r=0.21$, $p=0.36$).

CONCLUSIONS: Down regulation of MU is expected with prolonged exposure to opioids. The unexpected finding of increased MU in FNEs suggests that neurons may down regulate MU through disposal of MU as exosome cargo. The lack of a direct relationship between MU and MED suggests that the exposure of the fetal brain to opioids is also dependent on placental and maternal factors. Although not conclusive, our data suggest that buprenorphine has a lesser effect on fetal brain MU, concordant with known clinical outcomes. Finally, our data suggest that risk of NAS may be non-invasively predicted across the course of pregnancy through MU FNE levels as a measure of MU down regulation in the fetal brain.

**Figure(s) will be available online.*

F-087

A Single Course of Prenatal Glucocorticoid Programs the Stress Response and Pituitary Gene Expression Across Two Generations. Alexandros Mouratidis†,[1] Vasilis G Moisiadis†,[1] Alisa Kostaki,[1] Stephen G Matthews*.[1,2] *[1]University of Toronto, Toronto, ON, Canada; [2]University of Toronto, Toronto, ON, Canada.*

INTRODUCTION: Pregnant women at risk for pre-term delivery (roughly 10% of pregnancies) are treated with synthetic glucocorticoids (sGC) to mature the fetal lungs and reduce infant mortality. Single course treatment with prenatal sGC has been linked with increased hypothalamic-pituitary-adrenal (HPA) axis response to stress in children, and has been shown to result in altered HPA stress response in young second generation sheep offspring (F_2). In this study, we hypothesized that prenatal sGC would result in modified cortisol response to stress and altered anterior pituitary expression of HPA regulatory genes in F_1 and F_2 adult male guinea pigs.

METHODS: Pregnant guinea pigs (F_0) were treated with a single course of the sGC betamethasone (Beta; 1mg/kg) or saline (Veh; 1ml/kg) on gestational days 50 and 51. F_1 female offspring were mated with control males to produce F_2 offspring. Salivary cortisol response to open field stress was measured in adult F_1 and F_2 males (~day 80). Data were analyzed for net (AUC_N) and total area under the curve (AUC_T). *Avpr1b, Crhr1, Pomc, Nr3c1 (GR),* and *Nr3c2 (MR)* mRNA was analyzed in the anterior pituitary by qRT-PCR in F_1 and F_2 animals.

RESULTS: sGC exposure led to a reduced cortisol stress response in the F_1 animals (decreased AUC_{N-}; $P<0.05$), but there were no effects on pituitary gene expression. In the F_2 animals, Beta males exhibited an increased cortisol response to stress compared to Veh (AUC_T $P<0.05$). The expression of *Avpr1b* was reduced in F_2 Beta males ($P<0.05$), but there was no effect on the expression of the other genes.

CONCLUSIONS: This is the first study to demonstrate that prenatal treatment with a single course of sGC programs HPA function in adult F_2 offspring. The reduced HPA response to stress in F_1 does not appear to involve altered expression of HPA-related genes in the anterior pituitary and likely results from regulatory changes in other HPA regions. Altered HPA function in F_2 was associated with a reduction in pituitary sensitivity to vasopressin, though how this relates to increased HPA responsiveness to stress requires further investigation. Together, these data demonstrate that a single course of sGC results in long-term programming of the HPA axis. This is clinically important since alterations in HPA function can result in adverse cardiometabolic and neurobehavioural health outcomes.

F-088

Early Life Exposure to Environmental Estrogens Programs Uterine Signaling. Edwina P Kisanga†,[1] Shannon Whirledge,[1] Robert H Oakley,[2] John A Cidlowski*.[2] [1]*Yale School of Medicine, New Haven, CT, USA;* [2]*National Institute of Environmental Health Sciences, Research Triangle Park, NC, USA.*

INTRODUCTION: Endocrine disruptors with estrogenic activity can negatively impact development of the female reproductive tract. Early life exposure to the dietary phytoestrogen genistein alters gene expression and renders the uterus unable to support pregnancy. Glucocorticoid signaling has recently been shown to be important for endometrial receptivity in the female mouse uterus, and in immortalized human endometrial cells, genistein antagonizes glucocorticoid signaling. Our objective was to study the long-term effects of neonatal genistein exposure on glucocorticoid signaling in the mouse uterus as they relate to genistein-induced pathologies.

METHODS: C57Bl/6 pups were injected on postnatal day (PND) 1-5 with 50 mg/kg genistein or vehicle (corn oil). Ovariectomized and adrenalectomized mice were treated as adults on PND56 with either vehicle (saline) or 1 mg/kg of the synthetic glucocorticoid dexamethasone (Dex). Uteri were collected at 1.5 hr for chromatin immunoprecipitation (ChIP) and immunofluorescence, 4 hr for gene expression analysis, or 24 hr for cell proliferation studies. ChIP-sequencing was conducted to evaluate genome-wide changes in the glucocorticoid receptor (GR) cistrome following neonatal genistein exposure.

RESULTS: Neonatal exposure to genistein persistently altered the uterine transcriptome and impaired the transcriptional response to glucocorticoids. ChIP-seq analysis showed dysregulated recruitment of GR to regulatory sites in target genes. Genistein exposure also persistently dysregulated many genes involved in chromatin remodeling, suggesting that changes to chromatin architecture and accessibility may contribute to the disruption of glucocorticoid-induced gene expression following neonatal genistein exposure. Disturbances to GR signaling altered the biological activity of glucocorticoids in the uterus.

CONCLUSIONS: Our data show that neonatal genistein persistently disrupts glucocorticoid signaling in the female mouse uterus. These changes may directly contribute to infertility following exposure to environmental estrogens.

F-089

Trends in Mode of Delivery in Intrauterine Fetal Demise in the United States Between 2003 and 2013. Emily A Oliver†,[1] Kara M Rood,[1] Mark A Klebanoff,[2] Kathryn Berryman†,[1] Michael Cackovic,[1] Irina A Buhimschi,[2] Catalin S Buhimschi*.[1] [1]*The Ohio State University Wexner Medical Center, Columbus, OH, USA;* [2]*Nationwide Children's Hospital, Columbus, OH, USA.*

INTRODUCTION: Traditionally, cesarean sections were reserved for viable pregnancies even in the presence of a uterine scar. We sought to identify trends in mode of delivery in cases of intrauterine fetal demise, in which cesarean section represents an increased risk for maternal morbidity without fetal benefit.

METHODS: This is an observational study using fetal death certificate data from the United States National Vital Statistics System from deliveries between 2003 and 2013. We analyzed mode of delivery in intrauterine fetal demise in all gestations over 20 weeks. Data were analyzed by linear regression after confirming linear trend by testing of residuals.

RESULTS: During the study period, there were a total of 277,886 intrauterine fetal demises. Overall, the proportion of cesarean sections increased from 11.67% to 13.20% (P=0.012). The rate of cesarean section for intrauterine fetal demise peaked in 2009 (14.53%) with subsequent decrease in this practice.

CONCLUSIONS: In the U.S., cesarean section for intrauterine fetal demise increased between 2003 and 2013, although a recent decline was observed. Further investigation of the factors responsible for the remaining high rate of cesarean section for intrauterine fetal demise is warranted.

**Figure(s) will be available online.*

F-090

Congenital Malformation Risk in Obese Women of Advanced Maternal Age. Lauren Miller†, Stefanie Hollenbach†, Timothy Dye, Dongmei Li, Loralei Thornburg*. *University of Rochester, Rochester, NY, USA.*

INTRODUCTION: This study evaluates the odds of congenital malformations in advanced maternal age (AMA) women and assesses obesity as a modifying factor.

METHODS: The Upstate New York Perinatal Data System includes data from 2005-2014 on 724,802 pregnancies within Albany, Buffalo, Rochester, and Syracuse. The congenital malformations anencephaly, cleft lip/palate, diaphragmatic hernia, heart defect, hypospadias, omphalocele, limb anomaly, and spina bifida, were analyzed. Age and BMI cohorts were compared between 20-24 year olds (yo) and 35-39, 40-44, and ≥45yo for the following BMI classes: 19-24, 25-29, 30-34, 35-39, 40+. Chi-square and Fisher-exact tests were used for categorical variables, with significance set at $p<0.05$. Multivariate logistic regression was used to control for confounding variables (diabetes, fertility treatment, chronic hypertension, serious maternal illness, race, education, tobacco, alcohol and illicit drug use). Odds ratios (OR) with 95% confidence intervals (CI) demonstrate the magnitude of association.

RESULTS: AMA is associated with an increased OR of the aggregate outcome "Any Anomaly" in 35-39 and 40-44yo groups (OR1.3 CI[1.09-1.56] and 1.7 CI[1.31-2.3]). The OR of a fetus having an anomaly *and* a chromosomal abnormality was significantly higher across all AMA groups (35-39yo OR4.1 CI[1.87-8.74], 40-44yo OR12.3 CI[5.34-28.3], ≥45yo OR13.8 CI[2.7-72.5]). Congenital heart defect (CHD) is the only individual anomaly significantly increased across all AMA groups (35-39yo OR1.8 CI[1.34-2.48], 40-44yo OR2.8 CI[1.78-4.3], ≥45yo OR4.3 CI[1.73-11.24]), even after controlling for all chromosomal abnormalities. Stratifying by BMI, there is a greater percentage of CHD in all age groups compared to normal BMI (19-24) women. The OR for CHD is significantly increased in the BMI ≥40 groups (35-39yo OR4.15 CI[1.1-15.6] and 40-44yo OR8.01 CI[1.48-43.5]), though P>0.05 after controlling for Trisomy 21.

CONCLUSIONS: This regional population-based analysis reveals a significant increase in aggregate anomalies and CHD at birth for AMA women. Analysis by BMI class reveals a substantial increase in the odds of CHD in the offspring of women age 35-44 in the BMI class 40+. This significance persists after adjusting for non-Trisomy 21 chromosomal abnormalities and other confounders; however, this association is weakened after controlling for Trisomy 21. Careful screening for cardiac malformation in the obese AMA gravida may be warranted.

F-091

Anti-Müllerian Hormone Levels in Female Rheumatoid Arthritis Patients Trying to Conceive – The Role of Ovarian Function in Time to Pregnancy in a Nationwide Cohort Study. Jenny Brouwer†,[1,2] Radboud JEM Dolhain,[2] Johanna MW Hazes,[2] Jenny A Visser,[3] Joop SE Laven*.[1] [1]*Erasmus MC, University Medical Center, Rotterdam, Zuid-Holland, Netherlands;* [2]*Erasmus MC, Rotterdam, Zuid-Holland, Netherlands;* [3]*Erasmus MC, Rotterdam, Zuid-Holland, Netherlands.*

INTRODUCTION: Subfertility, a time to pregnancy (TTP) >12 months, is present in 40% of women with rheumatoid arthritis (RA) actively trying to conceive. Since RA patients appear to reach menopause at a younger age, the reduced fertility may be caused by a lower ovarian reserve (OR). Serum anti-Müllerian hormone (AMH) levels are currently the most reliable way to measure the OR. Our objective was to study preconception AMH levels and their association with TTP in women with RA.

METHODS: A post-hoc analysis was performed in patients of the Pregnancy-induced Amelioration of RA (PARA) cohort who were visited preconceptionally. Serum AMH levels were measured using the ultrasensitive and pico AMH ELISA assays, provided by Ansh Labs, and compared to converted AMH values from a cohort of 554 adult healthy controls (Lie Fong 2012).

RESULTS: Preconception serum was available in 209 women aged 32.1±3.9 years, of whom 45% were subfertile. The median AMH level was

2.5 ug/L (IQR 1.5–4.6). AMH levels were significantly lower compared to healthy controls (p=0.019), with 14.4% (95%CI 13.4-15.8%) of patients having levels below the age-specific 10th percentile.
**Figure(s) will be available online.*
Log-transformed AMH levels were negatively associated with age (-0.070 (95%CI -0.11;-0.031), p=0.001), and with the presence of anti-citrullinated protein antibodies (ACPA) (-0.38 (95%CI -0.71;-0.056), p=0.022), which represent a more severe disease. AMH levels showed no significant association with TTP (HR 1.09 (95%CI 0.94;1.27), p=0.26).
CONCLUSIONS: Women with RA have lower AMH levels than healthy controls. Reduced AMH levels were more pronounced in ACPA positive patients, suggesting that the OR may be compromised more strongly in patients with a more severe disease. However, since preconception AMH levels were not associated with TTP, the reduced levels do not explain the reduced fertility in women with RA.

F-092

Validation of Electronic Algorithms Based on Abstracted Clinical Data for the Diagnosis of Hypertensive Pregnancy Disorders. Elisabeth Codsi†,[1] Yvonne S Butler Tobah,[1] Wendy M White,[1] Andrea G Kattah,[2] Mie Saiki,[2] Lisa E Vaughan,[3] Amy L Weaver,[3] Layan Alrahmani†,[1] Pavan Parikh†,[1] Kristi S Borowski,[1] Norman P Davies,[1] Carl H Rose,[1] Michelle M Mielke,[3] Vesna D Garovic.[3] *[1]Mayo Clinic College of Medicine, Rochester, MN, USA; [2]Mayo Clinic College of Medicine, Rochester, MN, USA; [3]Mayo Clinic College of Medicine, Rochester, MN, USA.*
INTRODUCTION: Retrospective diagnoses of hypertensive pregnancy disorders (HPD) for research purposes are commonly based on diagnostic codes, maternal recall, or medical record review by an abstractor. However, there is a need for a standardized tool for use in large epidemiological studies that can confirm HPD years after affected pregnancies, to study long term pregnancy outcomes. The primary aim of this study was to develop a set of criteria for the retrospective diagnoses of HPD that would be amenable to the development of electronic algorithms.
METHODS: Using data available through the Rochester Epidemiology Project medical records linkage system (Rochester, MN, USA), we classified pregnancies into normotensive (NT), gestational hypertension (GHTN), and preeclampsia (PE) using an electronic algorithm applied to data abstracted from medical records. For validation, two physicians, in a blinded fashion, reviewed a random sample of clinical records from these pregnancies and assigned a specific diagnosis based on their clinical judgment. The algorithm classification was then compared to the physician diagnosis ("gold standard").
RESULTS: Sensitivities of the algorithm (with 95% confidence interval) for 25 NT pregnancies, 25 GHTN, and 25 PE were 100% (83-100%), 88% (67-97%) and 100% (83-100%), respectively. Specificities were 94% (82-98%), 100% (91-100%), and 100% (91 – 100%), respectively. The kappa was 0.94 (0.87-1.00) and the weighted kappa was 0.96 (0.91-1.00). Hospital discharge code sensitivities (with 95% confidence interval) were 96% (78-100%) for NT pregnancies, 32% (16-54%) for GHTN and 96% (78-100%) for PE. Specificities were 78% (64-88%), 96% (85-99%) and 88% (75-95%), respectively.
CONCLUSIONS: Our diagnostic algorithms were highly sensitive and specific in identifying HPD and distinguishing between types of HPD compared to the gold standard, physician diagnosis. The use of these validated algorithms for the diagnoses of HPD in large epidemiological datasets may help to standardize HPD exposure assessment for better comparisons across studies.

F-093

First Evidence of Intrinsic Fetal Heart Rate Variability Affected by Chronic Fetal Hypoxia. MG Frasch,[1] CL Herry,[1] Y Niu,[2] DA Giussani*.[2] *[1]U of Washington, Seattle, WA, USA; [2]OHRI, Ottawa, ON, Canada; [3]University of Cambridge, Cambridge, United Kingdom.*
INTRODUCTION: It is established that normal fetal HRV represents the integration of the autonomic nervous system, components due to fetal body and breathing movements, baroreflex and circadian processes (Jensen et al. *Am J Physiol* **297**: R998, 2009). There is also some evidence of possible intrinsic pacemaker rhythms of the SA node affecting HRV in adult disease (Papaioannou. *Curr Cardiol Rev* **9**: 82, 2013). However, whether intrinsic HRV (iHRV) exists in the fetal period and whether this is affected by chronic fetal hypoxia has never been tested. Here, we show iHRV in isolated hearts from fetal sheep in late gestation and significant effects on iHRV of pregnancy complicated by chronic fetal hypoxia.
METHODS: Chronically catheterized ewes carrying male singleton fetuses were exposed to normoxia (n=6) or hypoxia (10% inspired O2, n=9) for the last third of gestation (105-138 dG; term~145 dG) in bespoke isobaric chambers, as before (PMID: 26660546). At 138dG, isolated hearts were studied under a Langendorff preparation. CIMVA software was used to calculate basal iHRV matrix indices across five signal-analytical domains from the systolic peaks within 15 min segments in each heart, as before (PMID: 24829897). Data presented as Mean±SEM were compared by the Students *t* test for unpaired data.
RESULTS: This level of maternal H yields fetal PaO2 values of 11.5±0.6 relative to controls of 20.9±0.5 mmHg (PMID: 26926316). Hearts isolated from H pregnancy showed (Fig. 1) approximately 2-fold reductions in LF/HF ratio (*energetic* domain), coefficient of variation (*statistical* domain), Poincare SD2 (*geometric* domain), DFA alpha1 (Detrended fluctuation analysis: overall a), SDLEalpha (Scale dependent Lyapunov exponent slope; both from *invarant* domain). This was paralleled by significantly increased multiscale entropy, Shannon entropy and sgridTAU.
CONCLUSIONS: This is the first evidence that iHRV originates in fetal life and that chronic fetal hypoxia significantly alters it.
Supported by *The British Heart Foundation*
**Figure(s) will be available online.*

F-094

Utility of Screening Fetal Echocardiogram for IVF Pregnancies. Ann Lal, Nicole Sprawka. *Loyola University, Maywood, IL, USA.*
INTRODUCTION: The current recommendation by the American Institute of Ultrasound in Medicine (AIUM) is for a fetal echocardiogram for in vitro fertilization pregnancies. Fetal echocardiograms are performed at 22-24 weeks gestation, in addition to an anatomic survey at 18-20 weeks gestation. Pregnancies conceived from IVF have been reported to have an increased risk of birth defects, including cardiovascular defects. Because of this increased risk, increased surveillance is recommended. Despite this recommendation, in the AIUM Practice Guideline for the Performance of Fetal Echocardiography, they state, "most cases [of congenital heart disease] are not associated with known risk factors." The primary objective is to assess if any congenital heart abnormalities are detected with fetal echocardiogram, after a normal anatomic survey.
METHODS: This retrospective chart review is a descriptive study of all patients undergoing screening fetal echocardiogram due to IVF pregnancy. It was reviewed by the Institutional Review Board at Loyola University. The study participants, ages 18-45 with IVF pregnancy, were obtained through the obstetric ultrasound database. Patients had a documented anatomic survey and fetal echocardiogram. Exclusion criteria was a fetal echo performed for any indication besides screening due to IVF pregnancy. Baseline demographic data was obtained. At our institution, cardiac views in an anatomic survey include: 4 chamber heart, right ventricular outflow, left ventricular outflow, 3 vessel view and aortic arch. Any abnormalities in anatomic survey were documented. Routine screening fetal echocardiograms are performed by the maternal fetal medicine team at Loyola University. The fetal echocardiogram was reviewed for abnormalities.
RESULTS: 122 fetal echocardiograms were performed for the indication of IVF pregnancy during the study period. 51 of the screening fetal echocardiograms were performed on twin gestations. The mean age was 35.0 ± 5.3 and mean BMI was 28.0 ± 7.1. The average gestational age at the time of level II ultrasound was 19.75 +/- 1.56. In 81% of level II ultrasounds, all cardiac views were obtained. The average gestational age at the time of fetal echocardiogram was 24.0 ± 1.6 weeks gestation. All screening fetal echocardiograms were complete. No abnormalities were detected on fetal echocardiogram.

CONCLUSIONS: When a detailed level II ultrasound is performed at a tertiary care center and read by maternal fetal medicine physicians, no additional abnormalities were detected with screening fetal echocardiogram.

F-095

Echogenic Bowel in Pregnant Women Taking Spatone as Iron Supplement. Sharon Maslovitz, Avital Skornick-Rapaport. *Lis Maternity Hospital, Sourasky Medical Center Affiliated with Tel Aviv University, Tel Aviv, Israel.*

INTRODUCTION: Spatone is a naturally iron-rich mineral water with high iron bioavailability compared with oral tablets of iron supplements. While the absorption of iron from ferrous sulphate supplements ranges from 3 to 10%, the absorption is 28-34% with Spatone. The use of Spatone as an iron supplement during pregnancy gained popularity since the unpleasant side effects of iron therapy are largely avoided. Increased echogenicity of the fetal bowel is detected in 0.4-1% of second trimester scans and is considered a marker for fetal pathology (congenital viral infection, aneuploidy, intra-amniotic bleeding, or cystic fibrosis). Recently several cases of isolated fetal echogenic bowel were found among mothers consuming Spatone. We hereby describe a possible association between Spatone intake and isolated fetal echogenic bowel.

METHODS: This observational study was performed in a community maternity clinic between 2012 and 2015. Detection of echogenic bowel during a second or third trimester ultrasound led to thorough workup including detailed malformation screening, genetic counselling to rule out aneuploidy and Cystic Fibrosis, serologic testing for CMV and toxoplasmosis and prior significant bleeding. We compared the prevalence of isolated echogenic bowel with a negative work up between pregnant women taking daily ferrous sulphate tablets (one tablet of aktiferrin F containing DL-Serine 129 mg; Iron (Ferrous Sulfate) 34 mg; Folic Acid 0.5 mg) and those taking Spatone (one sachet daily).

RESULTS: During the study period, 358 women consumed daily iron sulphate tablet from 16 weeks' gestation and 2 of them (0.5%) had isolated fetal echogenic bowel with negative work up detected during the second trimester scan. On the other end, five of 116 (4%) women taking Spatone as their iron supplements had echogenic bowel, all with negative workup (RR=7.7, p=0.01). Four patients from the Spatone group who had echogenic bowel were rechecked 4 weeks after discontinuation of the supplement and were found to have normal appearing fetal bowel.

CONCLUSIONS: The prevalence of echogenic bowel with a negative workup may be higher in pregnant women taking Spatone. This observation may be explained by the high absorption of iron leading to coating of the bowel internal wall with iron, hence, to the appearance of echogenic bowel. In the light of the increasing popularity of Spatone, its possible effects on the sonographic appearance of the fetal bowel is highly important.

F-096

Fetal Hypothalamus-Pituitary-Adrenal Axis Alteration Through Late Gestational Low-Dose Dexamethasone Injection and Consequent Effects on ACTH and Cortisol Levels During Hypoglycemia in Pigs. Guadalupe L Rodríguez-González,[1] Martin Schmidt,[2] Florian Rakers,[3] Peter W Nathanielsz,[4] Sabine J Bischoff,[5] Marius Nistor,[3] René Schiffner*.[3] [1]*National Institute of Medical Science and Nutrition, Mexico City, Mexico;* [2]*Jena University Hospital, Jena, Germany;* [3]*Jena University Hospital, Jena, Germany;* [4]*University of Wyoming, Laramie, WY, USA;* [5]*Jena University Hospital, Jena, Germany.*

INTRODUCTION: Prenatal administration of glucocorticoids (GCs) alters the hypothalamic-pituitary-adrenocortical axis (HPAA) of the fetus, and correspondingly the adrenocorticotropic hormone (ACTH) and cortisol levels after birth. The exact dosages of GCs required to induce such effects are still subject to controversial discussions. We hypothesized that a low dosage of injected dexamethasone (DEX) in late pregnancy, alters ACTH and cortisol levels during hypoglycemia in pigs.

METHODS: 3 pregnant sows received a low-dose intramuscular injection of DEX (0,06 mg/kg body weight) on the 99th and 100th day of gestation. Three months after birth, 11 second-generation pigs underwent a 75-minute hypoglycemic trial (blood sugar levels below 3 mmol/l) under anesthesia . Furthermore, 6 pigs of a control group, without a prenatal dose of DEX, underwent the same procedure. Heart rate (HR), blood pressure (BP), ACTH and cortisol levels and body weight (at birth and 3 months after birth) were recorded. Mean ± SD, $p<0.05$.

RESULTS: DEX-treated animals exhibited significantly elevated ACTH (153.78 ± 45.32 pg/ml) and cortisol (458.42 ± 96.52 nmol/l) levels during an established hypoglycemia as compared to the control group (62.37 ± 17.68 pg/ml, respectively 215.47 ± 53.25 nmol/l). DEX-treated animals furthermore exhibited an elevated HR (200.64 ± 21.65 bpm) and BP (systolic: 126.73 ± 4.76, diastolic: 85.82 ± 3.03 mmHg) response under hypoglycemia as compared to the control group (157.5 ± 11.91 bpm;, respectively systolic: 117.33 ± 8.04, diastolic: 81.67 ± 3.62 mmHg).

CONCLUSIONS: To conclude, we were able to demonstrate that even a low-dose prenatal administration of DEX causes body weight restriction, elevated responses of ACTH and cortisol concentrations as well as an increased HR and BP during anesthesia and hypoglycemia.

F-097

Race and Gender-Based Overestimation of Fetal Weight May Lead to Missed Diagnoses of Fetal Growth Restriction. Yasaswi Paruchuri†*, Jacob Larkin. *Magee Women's Hospital at the University of Pittsburgh Medical Center, Pittsburgh, PA, USA.*

INTRODUCTION: Ultrasound-derived estimates of fetal weight (EFWs) depend on formulas, such as derived by Hadlock, et al., that convert two-dimensional biometric measurements into weight estimates. The EFW then determines which fetuses are diagnosed with growth restriction (FGR) and subject to heightened surveillance. Though EFW formulas are applied universally irrespective of race or sex, we hypothesized that race and/or gender-based differences in fetal biometry may contribute to systematic differences in the accuracy of fetal weight estimates. We sought to determine if accuracy of the Hadlock formula varied across racial or gender groups.

METHODS: We evaluated all liveborn neonates delivered beyond 24 weeks at Magee-Womens Hospital from 2003-2012 within 7 days of sonographic EFW. All EFWs were derived using the Hadlock formula based on AC, HC and FL (Radiology, 1984). We calculated the difference between EFW and birth weight, and compared percentage errors across racial and gender groups.

RESULTS: For the 3690 infants evaluated, the Hadlock formula overestimated weight by 3.9% on average. Overestimation was more pronounced for black infants than for whites (4.8%, 95% C.I. 4.0-5.6 for blacks vs. 3.6%, 95% C.I. 3.2-3.9 for whites, p=0.005 by t-test), and more pronounced for females than males (4.8%, 95% C.I. 4.3-5.2 for females vs. 3.0%, 95% C.I. 2.6-3.5 for males, $p<0.0001$). These differences contributed to racial and gender discrepancies in the likelihood of an SGA neonate being misdiagnosed as AGA on ultrasound (Table).

Proportion of SGA neonates misdiagnosed as AGA on ultrasound			
Race	Black	White	p-value (Chi-square)
	78/135 (57.8%)	192/404 (47.5%)	0.039
Sex	Female	Male	
	202/374 (54.0%)	107/237 (45.2%)	0.033

CONCLUSIONS: At our institution, the Hadlock formula tended to overestimate fetal weight. Systematic differences in the extent of overestimation may contribute to racial and gender-based outcome disparities stemming from failure to identify FGR antenatally.

F-098

β-Oxidation Compensates for Impaired Glucose Metabolism in Skeletal Muscle from Intrauterine Growth Restricted Sheep Fetuses. Amy Kelly†,[1] Hailey Davenport,[1] David Taska,[1] Leticia Camacho†,[1] Melissa Davis,[1] Christopher Bidwell,[2] Ronald Allen,[1] Sean Limesand*.[1] *[1]University of Arizona, Tucson, AZ, USA; [2]Purdue University, West Lafayette, IN, USA.*

INTRODUCTION: The intrauterine growth restricted (IUGR) fetus adapts to reduced nutrient supply through glucose-sparing metabolic rearrangements. Sheep models of IUGR reflect tissue-specific adaptations that include increased glucose utilization but decreased fractional glucose oxidation in skeletal muscle.

METHODS: IUGR sheep fetuses were collected at 0.9 of gestation following maternal hyperthermia-induced placental insufficiency. Differentially expressed genes were identified by high-throughput sequencing of semitendinosus (ST) mRNA (n=4/treatment). In a subsequent cohort (n=4 IUGR and 8 controls), soleus muscle was isolated, permeabilized with saponin, and placed in oxygen-sensing chambers to measure oxygen consumption rate (OCR) with glucose substrate (pyruvate+malate), fatty acid substrate (FA; palmitoyl-carnitine) or both substrates (maximum-coupled). Uncoupled respiration was measured with an ionophore.

RESULTS: IUGR fetuses were smaller ($P<0.05$) than controls in both cohorts. Of the 2,273 genes differentially expressed in IUGR ST muscle, glucose metabolism and mitochondria-related processes were significantly enriched in up-regulated genes. Specific genes included β-oxidation enzymes (ACADVL, EHHADH, HADHB) and enzymes that regulate pyruvate (PCK2, PDK4, PFKB3). These findings indicated altered substrate selection in IUGR mitochondria, which was then evaluated in permeabilized soleus fibers. Fiber OCR was not different in IUGR with FA-only substrate (996±47 versus 1000±169 nmolO_2/min/g). OCR with glucose substrates was reduced ($P<0.01$) in IUGR compared to controls (1033±71 vs. 1393±73 nmolO_2/min/g, respectively). However, there were no differences in glucose+FA substrate OCR or uncoupled OCR between IUGR and controls.

CONCLUSIONS: IUGR fetal skeletal muscle had increased expression of genes involved in β-oxidation and no defects in FA respiration. However, respiration with glucose substrates was impaired, down-stream of glycolysis, indicating defects in conversion of pyruvate to acetyl-CoA consistent with hypotheses of previous work using intact muscle. These data also indicate that β-oxidation may be preferred in IUGR skeletal muscle and is capable of compensating for impaired glucose oxidation.

F-099

Do Small for Gestational Age (SGA) Fetuses Also Exhibit Circadian Changes in Fetal Heart Rate Parameters as Do Appropriate for Gestational Age (AGA) Fetuses? Habiba Kapaya, Emma Dimelow, Dilly Anumba*. *University of Sheffield, Sheffield, S. Yorkshire, United Kingdom.*

INTRODUCTION: Small for gestational age (SGA) fetuses are at greater risk of complications compared to appropriate for gestational age (AGA) fetuses, and therefore they receive more regular monitoring to assess for fetal wellbeing. Previous studies have observed circadian changes in fetal heart rate (FHR) parameters in AGA fetuses. We hypothesised that similar circadian changes in FHR would be observed in SGA fetuses. The study was undertaken to investigate these changes in SGA fetuses using a portable fetal electrocardiogram recording device (Monica AN24), which does not restrict mobility, in pregnant women in their home environment.

METHODS: This was a prospective cohort study on 31 pregnant women with a singleton pregnancy of greater than 24 weeks gestation, no evidence of fetal malformation and an estimated fetal weight (EFW) measuring below the tenth centile on the ultrasound scan. FHR recordings were collected, at home, for up to 17h. FHR data collected over several 90min intervals were averaged and the day (7:00-23:00) and night (2:00-5:00) data from the same individual were compared. The data was also examined for evidence of differences due to gestational age.

RESULTS: During the night there was a significant reduction in basal FHR (129±6.6bpm) and decelerations (1.3±0.73) in comparison to the day time (137±8.9bpm and 2.1±0.81 respectively; $P<0.001$). Short-term-variation (STV), long-term variation (LTV) and the number of accelerations decreased during the night time. Basal FHR decreased significantly as gestational age increased ($P=0.013$), whereas other parameters remain unchanged. Circadian variation in FHR parameters were more pronounced in fetuses beyond 34weeks gestation.

CONCLUSIONS: Unlike AGA fetuses that exhibit circadian variation in basal FHR; accelerations; STV and LTV, SGA fetuses exhibited circadian variation only in basal heart-rate and deceleration. These changes became more pronounced with advancing gestation, implying a significant role of the fetal component in controlling the observed circadian pattern. Although STV and LTV decreased at night time, in SGA fetuses, it did not increase with gestational age, suggesting under-development of fetal autonomic nervous system. These differences between SGA and AGA fetuses need to be considered when interpreting FHR data in these two clinical settings.

F-100

A Compromised Maternal Vitamin D Status Is Associated with an Increased Risk of Congenital Heart Defects in Offspring. Linette van Duijn†,[1] Maria PH Koster,[1] Yvonne HM Krul-Poel,[3] Joop S Laven,[2] Willem A Helbing,[4] Suat Simsek,[2] Régine PM Steegers-Theunissen*.[4] *[1]Erasmus MC, University Medical Center, Rotterdam, Netherlands; [2]Medical Center Alkmaar, Alkmaar, Netherlands; [3]Erasmus MC, University Medical Center, Rotterdam, Netherlands; [4]Erasmus MC, University Medical Center, Rotterdam, Netherlands.*

INTRODUCTION: Interactions between genetic and environmental factors, including modifiable maternal lifestyle, play a significant role in the pathogenesis of congenital heart defects (CHD). Our aim was to study associations between maternal vitamin D status and the risk of congenital heart defects (CHDs) in offspring.

METHODS: We used data from a Dutch case-control family study performed between 2003-2005 that included 345 mothers of children with CHD (cases) and 432 mothers of children without CHD (controls). Approximately 15 months after pregnancy (i.e. 2 years after conception), these mothers filled out questionnaires and maternal blood was obtained to determine 25-hydroxyvitamin D (25(OH)D) and lipid levels. 25(OH)D concentration was stratified into a deficient (<50 nmol/l), moderate (50-75 nmol/l) and adequate (>75 nmol/l) status. This status was used as a proxy for the periconception period, since it is known that dietary habits are fairly stable over time. Logistic regression was performed to study associations between maternal vitamin D status and CHD adjusted for maternal age, BMI, ethnicity, smoking and total cholesterol concentrations.

RESULTS: The frequency of an adequate vitamin D status was significantly lower in cases than in controls (27% vs. 38%, $p=0.002$). The use of multivitamin supplements, ethnicity, season and BMI were associated with vitamin D concentrations. A moderate and deficient maternal vitamin D status were significantly associated with a higher CHD risk (adjusted OR 1.58, 95%CI 1.08-2.32 and OR 2.15, 95%CI 1.44-3.19, respectively). Post-hoc analyses in mothers with the same season and use of multivitamins during the periconception period and at study moment showed comparable associations.

CONCLUSIONS: We have demonstrated that a moderate to severely compromised maternal vitamin D status is associated with an increased risk of CHD in the offspring. Improvement of the periconception maternal vitamin D status is therefore strongly recommended. Future studies should focus on the beneficial and safety of strong adherence to a vitamin D rich diet or the use of a vitamin D supplement.

F-101

The Interaction Between the Maternal Systemic and Uteroplacental Circulations in Pregnancies Resulting in Small for Gestational Age Newborns. Asma Khalil, Helen Perry, Sophie Bowe, Basky Thilaganathan, Basky Thilaganathan. *St George's University of London, London, United Kingdom.*

INTRODUCTION: Pregnancies resulting in small for gestational age (SGA) newborns are associated with altered uteroplacental, maternal and fetal systemic circulations. However, data on the interaction between these cardiovascular changes are scarce. Whether these pregnancies result from placental insufficiency only, or combined with impaired

maternal cardiovascular adaptation, is yet to be established. The aim of this study was to ascertain the interaction between the maternal systemic and uteroplacental circulations in pregnancies resulting in SGA neonates.
METHODS: This was a prospective case-control study including pregnancies resulting in SGA neonates (n=142) and a group of pregnancies resulting in appropriate for gestational age (AGA) neonates (n=473), recruited after 20 weeks' gestation. Maternal cardiac output (CO), stroke volume (SV) and systemic vascular resistance (SVR) were recorded using the USCOM®, while the aortic augmentation index (AIx), heart rate and pulse wave velocity (PWV) were recorded using the Arteriograph®. The uterine artery (UtA) mean pulsatility index (PI) was assessed at the same visit using transabdominal ultrasound. The Mann-Whitney test was used to compare the two groups and logistic regression analysis was used to investigate and adjust for potential confounding variables.
RESULTS: Compared to controls, the SGA pregnancies had significantly lower CO (median 6.02L/min, IQR 5.22-6.98 vs 6.64L/min, IQR 5.68-7.73, p<0.001), SV (median 76.99ml, IQR 63.33-89.17 vs 80.02ml, IQR 68.26-93.66, p=0.035), but significantly higher SVR (median 1263 dynes-sec/cm^5, IQR 1030-1538 vs 1094 dynes-sec/cm^5, IQR 935.4-1337, p<0.001) and AIx (median 14.25%, IQR 2.89-28.82 vs 5.71%, IQR 0.49-15.26, p<0.001). UtA mean PI was significantly higher in the SGA pregnancies compared to controls (median 0.96, IQR 0.71-1.31 vs 0.71, IQR 0.58-0.88, p<0.001). Multivariable logistic regression analysis adjusting for both gestational age and the parameters of the uteroplacental and maternal circulations, demonstrated that both the CO and the UtA mean PI remained significantly associated with the risk of SGA [adjusted odds ratio (95% CI) 0.74; p=0.005 (0.63-0.87) and 6.40 (3.31-12.39); p<0.001, respectively).
CONCLUSIONS: Placental insufficiency and impaired maternal cardiovascular adaptation are independently associated with the risk of delivery of an SGA neonate.

F-102

Long-Term High Altitude Hypoxia During Gestation Represses Large Conductance Ca^{2+}-Activated K^+ Channel Expression *via* Upregulating DNA Methyltransferase in Ovine Uterine Arteries. Chiranjib Dasgupta, Xiang-Qun Hu, Man Chen, Daliao Xiao, Xiaohui Huang, Lubo Zhang*. *Loma Linda University School of Medicine, Loma Linda, CA, USA.*
INTRODUCTION: Pregnant sheep exposed to long-term high altitude hypoxia during gestation demonstrated a repression of large-conductance Ca^{2+}-activated K^+ (BK_{Ca}) channel expression and function, impeding uterine arterial adaptation to pregnancy. The present study tested the hypothesis that chronic hypoxia has a direct effect in upregulating DNA methyltransferase (DNMT) and epigenetically repressing BK_{Ca} channel β1 subunit (KCNMB1) expression in uterine arteries.
METHODS: Resistance-sized uterine arteries were isolated from near-term pregnant sheep maintained at ~300 m above sea level or animals acclimatized to high altitude (3,801 m) hypoxia for 110 days during gestation. For *ex vivo* hypoxic treatment, uterine arteries from normoxic animals were treated with 21.0% O_2 or 10.5% O_2 for 48 hours. The expression of DNMT and KCNMB1 was determined with RT-PCR and Western blot. DNMT activity was determined with EpiQuik DNMT activity assay kit. DNA methylation was measured with quantitative methylation-specific PCR and the binding of transcript factors was examined with chromatin immunoprecipitation (ChIP).
RESULTS: Long-term high altitude hypoxia significantly upregulated DNMT3b expression and enzyme activity in uterine arteries of pregnant sheep. In accordance, *ex vivo* hypoxic treatment increased DNMT3b expression and enzyme activity, which was blocked by a DNMT inhibitor 5-aza-2'-deoxycytidine. Of importance, 5-aza-2'-deoxycytidine inhibited hypoxia-induced hypermethylation of specificity protein (SP) 1 binding site at the KCNMB1 promoter and restored the transcription factor binding to the KCNMB1 promoter, resulting in the recovery of BK_{Ca} KCNMB1 gene expression in the uterine arteries.
CONCLUSIONS: Collectively, the results suggest that chronic hypoxia during gestation has a direct effect in upregulating DNMT expression and activity, resulting in hypermethylation and repression of KCNMB1 gene in the uterine artery of pregnant sheep.

F-103

Fetal Syndrome of Endocannabinoid Deficiency (FSECD) in an Experimental Model of Maternal High Fat Diet. Natalia Schlabritz-Loutsevitch*,[1] Cun Li,[2,5] Nadezhda German,[4] Eneko Larumbe,[3] James Maher,[1] Peter Nathanielsz,[2,5] Gary Ventolini.[1] *[1]TTUHSC-PB, Odessa, TX, USA; [2]UW, Laramie, WY, USA; [3]TTUHSC, Lubbock, TX, USA; [4]TTUHSC, Amarillo, TX, USA; [5]SNPRC, San Antonio, TX, USA.*
INTRODUCTION: Maternal obesity (MO) is associated with offspring (F1) inflammatory bowel syndrome, autism spectrum disorders, pancreatic dysfunction. These disorders have been termed Clinical Endocannabinoid Deficiency Syndrome (CECD) (Neuro Endocrinol Lett. 2004 25:31). Based on human population data, we hypothesized that Fetal Syndrome of Endocannabinoid deficiency (FSECD) is the mechanism by which CECD is programmed by MO (http://dx.doi.org/10.1016/j.mehy.2016.09.021). The precise role of MO and high fat diet remain unknown.
METHODS: Baboons ate 45% fat (HFD; n=11) or 12% fat (C; n=9) from at least 9 months prior to conception. Fetal and maternal serum collected at term Cesarean Section. Concentrations of eCB Anandamide (AEA) and 2-Arachidonoyl Glycerol (2-AG) were measured using LC-MS. P-values by Scheirer-Ray-Hare extension of Kruskal-Wallis test.
RESULTS: HFD Maternal 2AG increased and fetal concentrations decreased, independent of fetal sex. (Table 1)
CONCLUSIONS: MO decreased placental eCB synthesis and/or transfer to the fetus. We hypothesize that MO plus HFD play a role in FSECD.

Table 1. Anandamide (AEA) and 2-Arachidonoyl Glycerol (2-AG) levels (nM/L;data are mean ±SEM)

	C		HFD		Effect p-values		
	Female	**Male**	**Female**	**Male**	**Diet**	**Sex**	**Interaction**
Fetus	n=4	n=5	n=5	n=6			
AEA	0.71 (0.17)	1.10 (0.13)	0.89 (0.22)	0.65 (0.05)	0.21	0.53	0.06
2-AG	53.99 (12.82)	59.40 (26.38)	22.94 (3.22)	22.79 (3.66)	0.01	0.51	0.58
Mother	n=3	n=5	n=5	n=6			
AEA	1.82 (0.19)	1.46 (0.28)	1.81 (0.17)	1.83 (0.17)	0.60	0.44	0.40
2-AG	86.26 (11.86)	82.21 (11.76)	109.96 (29.08)	194.27 (30.61)	0.05	0.25	0.17
Maternal/ Fetal ratio							
AEA	3.58 (0.84)	1.39 (0.30)	2.37 (0.42)	2.91 (0.39)	0.49	0.16	0.03
2-AG	2.27 (0.73)	3.89 (2.30)	4.84 (1.00)	9.36 (1.64)	0.02	0.28	0.53

F-104

A Study of Three Risk Factors for Fetal Brain Injury Using a Mouse Model. Yupeng Dong,[1] Yoshitaka Kimura,[1] Nobuo Yaegashi.[2] *[1]Tohoku University, Sendai, Miyagi, Japan; [2]Tohoku University, Sendai, Miyagi, Japan.*
INTRODUCTION: Risk factors for fetal brain injury have been suggested, including infection, inflammation, and asphyxia. However, insufficient evidence is available for a systematic investigation of these multiple risk factors; moreover, it seems impossible to attain consensus by comparing several studies. In contrast, multiple risk factors exist in general clinical cases. It has become important to understand the mechanisms underlying fetal brain damage occurring in the presence of the multiple risk factors.
METHODS: We established a novel mouse model to expose pregnant mice to combinations of three risk factors: subclinical vaginal lipopolysaccharide (LPS) on gestational days 14 and 16 and lethal amniotic LPS and asphyxia-like ischemic reperfusion on gestational day 18. Using this method, molecular activation in fetal brain was investigated under 3 risk factors-induced 8 combinational conditions.
RESULTS: Fetal electrocardiography is sufficiently sensitive for the real-time diagnosis of asphyxia-like ischemic reperfusion but not for the LPS-

induced inflammation. Vaginal LPS protected against apoptosis induced by lethal amniotic LPS. In contrast, lethal amniotic LPS with continuous ischemic reperfusion caused a higher level of apoptotic cell death based on the whole-brain protein extraction. Consistent with these data, levels of phosphorylated cAMP response element-binding (CREB) protein were significantly increased in all conditions involving preconditioning with vaginal LPS,whereas ischemic reperfusion may have triggered IKK phosphorylation. Either CREB (r=0.7967; p = 0.0006)or IKK (r=-0.6608; p = 0.0101) phosphorylation correlated with all conditions.

CONCLUSIONS: We found that subclinical vaginal LPS did not induce preterm birth, but the fetal brain became sensitized to continuous stress. We suggest that molecular activation induced by risk factors can be used to understand the situation of fetal brain.

F-105

Cerebral Circulation in Fetal Growth Restriction. Shane Reeves,[1,2] Diane Gumina,[1] Mary Pinter,[1] Allison Gillan,[1] John Hobbins*.[1] *[1]University of Colorado School of Medicine, Aurora, CO, USA; [2]Colorado Fetal Care Center, Aurora, CO, USA.*

INTRODUCTION: In fetal growth restriction (FGR), the middle cerebral artery (MCA) identifies fetuses at risk for poor perinatal outcome. When used in conjunction with the umbilical artery (UmA), the cerebroplacental perfusion ratio (CPR) <1.08 has been shown to correlate with poor pregnancy outcome better than either vessel alone. One study suggests a front to back increase in cerebral blood flow with increasing severity of FGR. We hypothesize that intracranial vessels, other than the MCA, will provide useful information in the development of brain sparing associated with FGR.

METHODS: We evaluated waveforms from the anterior, middle, posterior cerebral arteries (ACA, MCA, PCA), and vertebral arteries (VA) in 49 FGR pregnancies (estimated fetal weight <10th percentile).The above Doppler waveforms were collected across 26-36 weeks gestational age and serially for each patient between 2-8 weeks. Based on existing normative data, pulsatility indices (PIs) were considered abnormal if the PI was <5th percentile. The cerebroplacental perfusion ratio (CPR) was determined by dividing the cerebral vessel PI by the UmA PI.

RESULTS: 1. We assessed the pattern of abnormal findings. The ACA became abnormal first in 5 cases (10%), the MCA in 17 cases (35%), and the PCA in 8 cases (16%). Other combinations included ACA and MCA together in 3 cases (6 %), ACA and PCA in 3 cases (6 %), and MCA and PCA in 3 cases (6%). All three were abnormal simultaneously in 3 cases (6 %).

2. The vertebral artery was never the first abnormal finding and only became abnormal when all three of the above were also abnormal (5 cases). When compared to normal VA, these five cases had earlier delivery (35.5 weeks vs 37.1 weeks) and lighter birthweights (1770 g vs 2250 g).

3. The MCA CPR has a strong correlation with the ACA CPR (r=0.79), the PCA CPR (r= 0.77) and the VA CPR (r= 0.78).

CONCLUSIONS: The MCA CPR correlates strongly with the CPR calculated from other intracranial vessels suggesting the other vessels are also reflective of fetal condition. The pattern of blood flow in the circle of Willis vessels is unpredictable with transient abnormal PI values. However, our data indicates that the vertebral artery is an indicator of the transition from dynamic brain sparing to global brain sparing and may represent a more compromised fetus.

F-106

Hormonal Therapy for Low Grade Endometrial Stromal Sarcoma. Rachel Passarelli†,[1] Uma Deshmukh†,[1] Jonathan Black†,[1] Amanda Rostkowski,[1] Javier Perez Irizarry,[2] Pei Hui,[1,3] Elena Ratner,[1] Dan-Arin Silasi,[1] Masoud Azodi,[1] Alessandro D Santin,[1] Thomas J Rutherford,[1] Peter E Schwartz*.[1] *[1]Yale University School of Medicine, New Haven, CT, USA; [2]Yale-New Haven Hospital, New Haven, CT, USA; [3]Yale University School of Medicine, New Haven, CT, USA.*

INTRODUCTION: We present a single institution's outcomes for patients treated with aromatase inhibitors (AI) or progestins as adjuvant therapy for low grade endometrial stromal sarcomas (LGESS).

METHODS: A single institution retrospective chart review was performed of all patients treated for LGESS from 1984-2016. Demographic data collected included age, cancer stage, preoperative diagnosis, initial surgery, hormone receptor status, and type of adjuvant hormonal therapy administered. Rates of disease recurrence and progression-free survival were assessed among patients who received AI, progestins, or no adjuvant therapy.

RESULTS: Thirty-four patients with LGESS were identified, including 19 who received progestins, 7 who received AI, and 8 who received no hormonal therapy. Median age at diagnosis was 47 years (range 19-76). Hysterectomy with bilateral salpingo-oophorectomy was the initial surgery performed in 21 (61.7%) patients. 85.3% of patients had stage I or II disease at the time of diagnosis. Three were diagnosed at stage III and one had stage IV disease. Among patients with stage I or II disease, recurrence rates were 0% (0/5) for those who received AI with a median progression-free survival (PFS) of 5.0 years (95% CI: 3.7 – 5.3); 24% (4/17) for those who received progestin, with a median PFS of 9.3 years (95% CI: 5.7 – 12.4); and 75% (6/8) for those who received no adjuvant therapy, with a median PFS of 5.9 years (95% CI: 3.8 – 8.8). Two stage IIIA patients receiving AI therapy were disease-free 2.7 and 5.1 years following diagnosis. One stage IIIB patient on progestins was disease-free at 12.6 years following initial diagnosis, while one stage IV patient on progestins recurred twice after 2.1 and 3.1 years. Median duration of treatment was 4.3 years for the progestin group (range 0-51) and 4.9 years for the AI group (range 0-11).

CONCLUSIONS: Hormonal therapy is effective adjuvant treatment for the initial management of LGESS, with lower rates of disease recurrence and favorable progression-free survival in the progestin group. However, given the rarity of this condition and the small sample sizes, further research is required.

F-107

The 17β-Hydroxysteroid Dehydrogenase Type 2 Expression Induced by the Androgen Signal in Endometrial Cancer. Chiaki Hashimoto*,[1] Yasuhiro Miki,[2] Sota Tanaka,[1] Kiyoshi Takagi,[3] Misaki Fue,[2] Zhulanqiqige Doe,[2] Bin Li,[1] Nobuo Yaegashi,[1] Takashi Suzuki,[3] Kiyoshi Ito.[1] *[1]Tohoku University Graduate School of Medicine, Sendai, Miyagi, Japan; [2]International Research Institute of Disaster Science (IRIDeS), Tohoku University, Sendai, Miyagi, Japan; [3]Tohoku University Graduate School of Medicine, Sendai, Miyagi, Japan.*

INTRODUCTION: Endometrial cancer, one of the most common female pelvic cancer, has been considered an androgen-related tumor. Several studies demonstrated the anti-cell proliferative effect of androgen on endometrial cancer cells. However, the mechanisms of anti-cancer effect of androgen are still largely unclear. 17β-hydroxysteroid dehydrogenase type 2 (17β-HSD2), which catalyzes the conversions of E2 to E1, is known to be up-regulated by androgen treatment in breast cancer cells. Therefore, in this study, we focused on the role of androgen on estrogen dependence of endometrial cancer.

METHODS: In nineteen endometrioid endometrial adenocarcinoma (EEA) tissues, intratumoral DHT concentration measured by liquid chromatography/electrospray tandem mass spectrometry was significantly correlated with 17b-HSD2 immunohistochemical status. We further examined the correlations between 17β-HSD2 immunoreactivity and clinicopathological parameters in 53 EEA tissues.

RESULTS: Dihydrotestosterone (DHT) could induce 17b-HSD2 mRNA and protein in endometrial cancer HEC-1B cells. DHT could also inhibit cell proliferation of HEC-1B induced by estradiol treatment. The 17β-HSD2 status was inversely associated with the histological grade, clinical stage, and cell proliferation marker, Ki-67 and positively correlated with the progesterone receptor expression. 17βHSD2 status tended to be positively associated with androgen receptor status. In 53 EEA cases, 17β-HSD2-positive group tended to have better prognosis than those negative group with respect to progression-free survival and endometrial cancer-specific survival.

CONCLUSIONS: These findings suggest that androgen suppresses the estrogen dependence of endometrial cancer through the induction of 17β-HSD2.

F-108

Neratinib Shows Efficacy in the Treatment of HER2/Neu Amplified Epithelial Ovarian Carcinoma In Vitro and In Vivo. Gulden Menderes,[1] Stefania Bellone,[1] Jonathan D Black,[1] Salvatore Lopez,[2] Elena Bonazzoli,[1] Francesca Pettinella,[1] Alice Masserdotti,[1] Luca Zammataro,[1] Dan-Arin Silasi,[1] Babak Litkouhi,[1] Elena Ratner,[1] Masoud Azodi,[1] Peter Schwartz,[1] Alessandro D Santin*.[1] *[1]Yale University School of Medicine, New Haven, CT, USA; [2]University Campus Bio-Medico of Roma, Rome, Italy.*

INTRODUCTION: Epithelial ovarian carcinoma is the most lethal gynecologic malignancy. There is a need to urgently develop novel therapeutic agents against chemotherapy-resistant disease. The objective of this study was to evaluate the preclinical efficacy of neratinib in the treatment of HER2 amplified ovarian cancer.

METHODS: The efficacy of neratinib in the treatment of HER2 amplified ovarian cancer was determined *in vitro* using six primary tumor cell lines with differential expression of HER2/neu. Data regarding IC_{50}, cell cycle distribution, and cell signaling changes were assessed by flow cytometry. The *in vivo* efficacy of neratinib was determined in treating mice harboring HER2 amplified epithelial ovarian carcinoma xenografts.

RESULTS: The cell lines with HER2/neu amplification were significantly more sensitive to neratinib than the non-HER2/neu amplified tumor cell lines (mean ± SEM IC_{50}:0.010 μM ± 0.0003 vs. 0.076 μM ± 0.005 $p < 0.0001$).

**Figure(s) will be available online.*

Neratinib significantly decreased the phosphorylation of the transcription factor S6 and lead to an arrest in G0/G1 phase of the cell cycle. Neratinib prolonged survival in mice harboring HER2 amplified epithelial ovarian carcinoma xenografts ($p = 0.003$).

**Figure(s) will be available online.*

CONCLUSIONS: Neratinib inhibits HER2 amplified epithelial ovarian carcinoma proliferation, signaling, cell cycle progression and tumor growth *in vitro*. Neratinib improves overall survival by inhibiting HER2/neu amplified ovarian cancer xenograft growth.

F-109

A Ten-Year Single Institution Experience Comparing Type 1 and Type 2 Endometrial Cancers. Jonathan Black†,[1] Rachel Passarelli†,[1] Margaret Whicker†,[1] Stefan Gysler†,[1] Benjamin Albright†,[2] Lingeng Lu†,[1] Gulden Menderes,[1] Gary Altwerger,[1] Babak Litkouhi,[1] Elena Ratner,[1] Dan-Arin Silasi,[1] Masoud Azodi,[1] Alessandro Santin,[1] Peter Schwartz*.[1] *[1]Yale School of Medicine, New Haven, CT, USA; [2]Hospital of the University of Pennsylvania, Philadelphia, PA, USA.*

INTRODUCTION: Type I endometrioid adenocarcinomas are estrogen dependent, slow growing tumors and Type II carcinomas (i.e. FIGO grade 3, serous or clear cell carcinoma) are non-estrogen dependent and more aggressive. The objective of this study was to complete a large, single institution evaluation of these two types of disease.

METHODS: A single institution retrospective review of 1100 consecutive endometrial cancer cases from January 2005 to December 2010. Over 30 variables were evaluated. Both univariate and multivariate analyses were completed using standard logistic regression models and Cox Regression models. Two sample t-test was used to compare means.

RESULTS: There were 619 cases of Type I disease and 256 cases of Type II disease. Type 2 disease was associated with older age (66.6yrs vs. 62.2yrs, $p<0.0001$), obesity, (BMI 31.1 vs. 34.3, $p=0.0003$) and higher gravidity (3 pregnancies vs. 2 pregnancies, $p<0.0001$) when compared to Type 1 disease. Patients with Type 2 disease were non-white ($p<0.0001$), menopausal ($p=0.0002$), with a history of another malignancy ($p=0.003$), and less likely to have had a dilation and curettage ($p=0.013$). Diabetes was slightly more common in Type 1 disease ($p=0.07$). There was no difference in oral contraceptive use, hormone replacement therapy, smoking or cardiovascular disease between groups. Factors associated with recurrence were Type 2 disease (HR=2.11, CI 1.32-3.36, $p=0.002$), advanced stage at presentation (HR=1.2, CI 1.13-2.26, $p<0.0001$), and age (HR=1.21, CI 1.04-1.55, $p=0.021$). Factors associated with death were Type 2 disease (HR=2.87, CI1.92-4.28, $p<0.0001$), advanced stage at presentation (HR=1.22, CI 1.16-1.28, $p<0.0001$), and age (HR=1.66, CI 1.42-1.94, $p<0.0001$).

CONCLUSIONS: Type 2 endometrial cancers are more aggressive than Type 1 cancers and associated with a higher risk of recurrence and death. They are more common in non-white, older and less obese patients with higher gravidity. Patients with a history of another malignancy are more likely to develop Type 2 cancers than their counterparts with Type 1 disease. These factors should be considered when approaching a patient with a suspected case of endometrial cancer.

F-110

The Effect of Copper on Endometrial Receptivity and Induction of Apoptosis on Decidualizated Endometrial Stromal Cells. JA Horcajadas*,[1] JP Carrascosa,[1] D Cotán,[1] P Sánchez-Martín,[2] JA Sánchez-Alcázar.[1] *[1]Pablo de Olavide University, Seville, Spain; [2]Clinic, Seville, Spain.*

INTRODUCTION: Copper IUD induces a local foreign body reaction, which makes the uterine environment hostile both to sperm and to implantation of an embryo, increasing its effectiveness with the liberation of copper ions. Copper IUD has also demonstrated to decrease the gene expression of several genes such as HOXA10, essential for embryo human implantation. The release of copper by IUD could affect the endometrial receptivity, being an additional contraceptive effect of this dispositive. However, the possible apoptotic effects on endometrial cells have not been described. During the execution phase of apoptosis the cells form the Apoptotic Microtubule Network (AMN) to maintain integrity of the plasma membrane and to avoid release of harmful molecules that provokes inflammation and some necrosis. The aim of this work was to analyze the induction of apoptosis by the copper using primary culture of human endometrial stromal cells, and how it compromises endometrial receptivity.

METHODS: Endometrial biopsies were obtained from 5 fertile women by Pipelle catheter under sterile conditions. Decidualization treatment started day 0 for 8 days. At day 6, copper (10.4 mg/L) was added to the treatment group, or camptothecin (CPT, 10 μM) as positive control, until day 8. Flow cytometer assays with annexin V and PI were done to evaluate apoptosis and necrosis levels. Immunofluorescence microscopy using anti αtubulin and phalloidin was done to visualize if decidualizated stromal cells form AMN. Gene expression was measured by quantitative RT-PCR using Fluidigm platform for 192 endometrial receptivity and immune response genes.

RESULTS: Decidualization process in vitro had a huge impact in apoptosis and necrosis levels in stromal cells, with a possible protective effect of copper and an increase of death cells with the CPT treatment. This is the first report where AMN has been described in decidualizated endometrial stromal cells, with or without treatment with CPT or copper. Copper effect on gene expression reveals 28 genes with a FC>2 or FC<-2 (21 up- and 7 down-regulated). The mainly over-represented biological processes were regulation of chemotaxis, taxis, regulation of cell proliferation, locomotory behavior, immune response and intracellular signaling cascade.

CONCLUSIONS: The liberation of copper ions has not apoptotic effect but compromises endometrial receptivity by changing the gene expression signature.

F-111

Surgical Outcomes of Minimally Invasive and Abdominal Hysterectomy for Benign Indications by Operative Time: An Analysis of the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP). Samantha L Margulies†,[1] Maria V Vargas,[2] Kathryn Denny†,[3] Richard Amdur,[4] Cherie Marfori*.[2] *[1]Yale-New Haven Hospital, New Haven, CT, USA; [2]George Washington University Medical Faculty Associates, Washington, DC, USA; [3]George Washington University, Washington, DC, USA; [4]George Washington University, Washington, DC, USA.*

INTRODUCTION: Minimally invasive surgical (MIS) approaches confer patient benefits but have longer operative times. Longer operative time (OT) (in both MIS approaches and laparotomy) has been associated with adverse outcomes. Our objective is to elucidate whether there is an OT at which outcomes for minimally invasive hysterectomy become inferior to a more expeditiously completed laparotomy.

METHODS: Using the database ACS NSQIP, we conducted a retrospective cohort studyof women undergoing hysterectomy for benign indications from 2005 to 2014 identified by CPT code. Hysterectomy cases and outcomes were stratified by approach and 90-minute intervals.
RESULTS: A total of 56,825 hysterectomies were identified, of which 31,583 (55.6%) were MIS and 25,242 (44.4%) were abdominal. Longer OT was associated with perioperative morbidity, regardless of approach. Older age, African American race, higher BMI, lower pre-operative hematocrit, specimen weight >250 grams, removal of the cervix, concomitant procedures and an MIS approach were associated with greater OT. Despite longer OT for MIS approach, complications were more common for abdominal procedures (13.5% vs 6.0%, p<.0001). In a multivariate logistic regression analysis, an MIS approach was protective against complications until cases reached ≥270 minutes (min), at which point the odds of complications increased compared to open cases <90 min (OR 1.55 (95% CI 1.20-2.02)). Of MIS hysterectomies, 97% were completed in <270 min.
CONCLUSIONS: OT was predictive of complications for both MIS and abdominal hysterectomy. After adjusting for confounders, MIS procedures had superior outcomes up to 4.5 hours. Only 3% of MIS hysterectomies were >4.5 hours in duration. An MIS approach should be offered to most patients undergoing benign hysterectomy, and preparation to increase surgical efficiency should be prioritized for any approach.

F-112

Possible Role of Double Strand Break Repair Impairment in the Pathogenesis of Endometriosis and Decreased Ovarian Reserve. Jung Ho Shin,[1] Jae Hoon Lee,[2] JiHyun Park,[2] JooHyun Park,[2] Bo Hyun Yun,[2] Seok Kyo Seo,[2] SiHyun Cho*,[2] Young Sik Choi,[2] Byung Seok Lee.[2] *[1]Korea University, Seoul, Republic of Korea; [2]Yonsei University College of Medicine, Seoul, Republic of Korea.*
INTRODUCTION: DNA double strand break (DSB) repair system is known to be an important mechanism for maintaining genetic stability during DNA damage in cellular process. The aim of this study to evaluate DNA DSB repair impairment in endometriosis and to elucidate whether extent of DNA DSB repair impairement correlate with decreased ovarian reserve in endometriosis.
METHODS: During laparoscopic surgery, endometrial and ovarian tissues in patients with endometriosis were obtained after informed consent. Benign ovarian cyst without endometriosis served as controls. After RNA extractions, expressions of genes associated with DNA DSB repair, BRCA1, BRCA2, Rad51, and ATM, were evaluated using qRT-PCR. Also, endometrial cells from the patients with endometriosis and Ishikawa cell lines were culture and treated with H2O2 and extent of DSB were evaluated using gamma-H2AX, which is known to be a DSB marker. Correlation between expressions of the genes associated with DNA DSB repair and serum AMH level were evaluated.
RESULTS: 38 patients with endometriosis and 31 patients without endometriosis were included in the study. Endometrial expressions of BRCA1, Rad51 and ovarian expressions of BRCA1 and BRCA2 were signifncatly lowere in patients with endometriosis. After H2O2 treatment in cultured endometrial and Ishikawa cells, significantly higher expressions of gamma-H2AX were found in Ishikawa cells and endometrial cells from patients with endometriosis in comparison to controls, indicating that these cells are more susceptible to H2O2 induced DNA DSB. Immunohistochemical staining also showed higher expressions of gamma-H2AX expressions in endometrial and ovarian tissue from the patients with endometriosis than controls. There showed a significant positive correlation between ovarian BRCA1 expressions and serum AMH levels with correlation coefficient of 0.541.
CONCLUSIONS: Expressions of several genes related to DNA DSB repair are significantly lower in endometriosis. Specifically, BRCA1 expressions were signficiantly lower in both endometrial and ovarian tissue of the patients with endometriosis and expression of this gene correlated with AMH levels, indicating that impairment of DSB repair may involved in the pathogenesis and decreased ovarian reserve in patients with endometriosis.

F-113

Predictive Model for Endometriosis Diagnosis Based in Uterine Aspirates. Júlia Vallvé-Juanico†,[1,4,5] Elena Suárez-Salvador,[2] Josep Castellví,[3] Hugh S Taylor,[6] Antonio Gil-Moreno,[2,4,5] Xavier Santamaria*.[1,4] *[1]IVI Barcelona S.L., Barcelona, Spain; [2]Vall d'Hebron Hospital, Barcelona, Spain; [3]Vall d'Hebron Hospital, Barcelona, Spain; [4]Vall d'Hebron Research Institute, Barcelona, Spain; [5]Universitat Autònoma de Barcelona, Bellaterra, Spain; [6]Yale University School of Medicine, New Haven, CT, USA.*
INTRODUCTION: Endometriosis affects approximately 15% of women at reproductive age and is usually diagnosed by surgery. Previous works demonstrated and abnormal presence of epithelial cells in the stroma of mice with experimental endometriosis. This process was also observed in women suffering from endometriosis. The abnormal migrating cells express the surface marker LGR5. We hypothesized that these changes would reflect molecular alterations in the Uterine Aspirate (UA) that could be used as a less-invasive diagnostic tool of endometriosis.
METHODS: We obtained 19 UAs by using a Cornier Pipelle from 5 oocyte donors as controls and subjects with deep endometriosis, adenomyosis as well as ovarian and pelvic endometriosis. We used FACS to sort LGR5+ cells, extracted RNA and performed RNA-High-Sequencing. We performed two *in silico* analysis to exclude the genes that vary with the menstrual cycle and in stimulated endometrium. As we did not find differences between LGR5+ cells from healthy women and patients, we analyzed the total RNA expression of UAs. We carried out statistical analysis and we developed a clustering test and a classifier using misclassification methods.
RESULTS: Significance testing for differentially expressed genes (DEG) were applied with EDGE testing. Statistical analysis revealed 1249 DEG (FC±2/FDR≤0.01) between healthy women and patients after excluding 6348 genes obtained from the *in silico* analysis. Variation between different types of endometriosis were also found. Clustering results showed two clusters that separated based on the aggressiveness of each type of endometriosis. In the classifier, we identified 213 candidate genes to predict endometriosis and observed a 100% of sensitivity and a 75% of specificity.
CONCLUSIONS: UA could serve as a less-invasive sample to diagnose endometriosis. We developed a classifier that can diagnose endometriosis and can also classify the aggressiveness of the disease. We are currently carrying out prospective validation.

F-114

RNA Binding Protein, HuR/TTP Axis in Endometriosis. Kasra Khalaj,[1] SooHyun Ahn†,[1] Mallikarjun Bidarimath†,[1] Yasmin Nasirzadeh†,[1] Steven L Young,[2] Bruce A Lessey,[3] Sukhbir S Singh,[4] Madhuri Koti,[1] Chandrakant Tayade*.[1] *[1]Queen's University, Kingston, ON, Canada; [2]University of North Carolina, Chapel Hill, NC, USA; [3]Greenville Health Systems, Greenville, SC, USA; [4]The Ottawa Hospital, University of Ottawa, Ottawa, ON, Canada.*
INTRODUCTION: Endometriosis is a reproductive pathology affecting 8-10% of reproductive aged women. It is chronic pro-inflammatory and is characterized by growth of endometrium-like tissues outside the uterus. The etiology of endometriosis is unknown. Previous studies have shown increased levels of proinflammatory cytokines in the peritoneal fluid of women with endometriosis. Tristetraprolin (TTP/*ZFP36*) is a TIS11 family member of RNA binding proteins that mediates stability of inflammatory and angiogenic cytokines. Another RNA binding protein, Human antigen R (HuR/*ELAVL1*) exerts the opposite effect of TIS11 family. Many cytokines can be mediated by the HuR/TTP axis. We hypothesized that this axis is involved in the dysregulation of inflammatory response in endometriosis.
METHODS: Normal endometrium from patients with no endometriosis as well as matched human endometrium and endometriotic lesions from women with endometriosis were obtained from multiple institutes. BALB/cByJ mice were used for *in vivo* mouse model of endometriosis. TTP, TIS11b, TIS11d, HuR mRNA and protein were quantified using real-time PCR & ELISAs/western blotting, respectively. TTP was inhibited *in vitro* in endometrial epithelial choriocarcinoma cells using siRNA.

RESULTS: Our patient results demonstrate lower *ZFP36* and *ELAVL1* in ectopic lesions compared to eutopic controls. Protein expression results reveal significantly lower amounts of HuR and TTP in ectopic lesions compared to eutopic controls. *In vitro* silencing experiments reveal significant downregulation of ZFP36/TTP family members and *ELAVL1* transcripts in TTP knock-down EECC cells. Mouse model findings demonstrate that the RNABP *ZFP36* is significantly upregulated in ectopic lesions when compared to matched eutopic controls and *ELAVL1* & *ZFP36L1* also are significantly upregulated in ectopic lesions compared to matched controls.
CONCLUSIONS: Our patient data points towards a role for HuR/TTP axis in dysregulation of inflammatory cytokines; further supported by our *in vivo* mouse model data and demonstrates an implication of HuR/TTP potentially contributing to the pathogenesis of endometriosis.

F-115

Tissue Specific Expression Analysis in Endometriosis by Laser Capture Microdissection (LCM). Lorenz Küssel,[1] Eva Simon,[2] Maik Obendorf,[2] Ralf Lesche,[2] Juliane Hundt,[2] Arndt Schmitz,[2] Agnes Jäger-Lansky,[1] Reinhard Obwegeser,[1] Thomas M Zollner,[2] Rene Wenzl*.[1] *[1]Medical University of Vienna, Vienna, Austria; [2]Bayer AG, Berlin, Germany.*
INTRODUCTION: Endometriosis is a chronic disease defined by the ectopic growth of endometrial like tissue outside the uterine cavity. Key symptoms are chronic pelvic pain, dysmenorrhea and subfertility, severely affecting women's quality of life. New therapeutic approaches beside hormonal treatment are highly anticipated, but are hampered by incomplete disease understanding. We aim to contribute to a better disease understanding by analyzing mRNA gene expression profiles of eutopic and ectopic patient samples across tissue sub-fractions and cycle phases.
METHODS: Samples from informed and consenting donors were collected at the Department of Gynecology and Obstetrics, University Hospital, Vienna, Austria. 21 controls and 29 patients were included. Epithelial and stromal fractions from endometrial tissue were separated by LCM on frozen tissue sections. mRNA expression profiles were generated by microarray analysis [Affymetrix Human Gene 2.1 ST array] and confirmed by TaqMan analyses.
RESULTS: Over 4000 genes were identified as significant ($q<10^{-6}$) differentiators between epithelial and stromal tissues and more than 2500 genes as significantly ($q<10^{-6}$) regulated between proliferative and secretory phase in eutopic tissue. Furthermore, 287 genes differentiated between endometriosis and control curettage samples after correction for tissue fraction and cycle phase. Finally, 762 genes differentiated between ectopic and eutopic samples after correction for tissue fraction and cycle phase. Pathway analysis revealed several pathways showing more pronounced activitiy in lesions compared to eutopic tissue, e.g. WNT pathway, nitric oxide signaling, as well as growth factor and inflammatory signaling pathways. Dissociation of epithelia and stroma allowed more detailed identification of deregulated expression, also suggesting paracrine interactions (e.g. wnt & frizzled).
CONCLUSIONS: By using LCM we generated high resolution expression profiles of eutopic and ectopic endometrial samples. Detailed tissue specific analyses of expression gave further insight into the pathology of endometriosis and may provide new hypotheses for possible treatment options.

F-116

IL-1β Disrupts Human Endometrial Stromal Cell Differentiation via Activation of the ERK 1/2 and p38 MAP Kinase Pathways: Potential Role in Endometriosis. Jie Yu, Sarah L Berga, Erika B Johnston-MacAnanny, Bansari Patel, Robert N Taylor. *Wake Forest School of Medicine, Winston-Salem, NC, USA.*
INTRODUCTION: Biomarkers of inflammation are prevalent in endometriosis-associated infertility. IL-1β, one of the quintessential cytokines produced in endometriosis, represses endometrial Cx43 gap junctions and their downstream differentiation markers, prolactin and VEGF. Using primary human endometrial stromal cell (ESC) cultures we showed that NF-κB signaling was briskly upregulated by recombinant IL-1β, however, inhibitors of this pathway failed to block IL-1β-induced repression of Cx43. The objective of this study was to evaluate the other four canonical pathways to determine which IL-1β signaling cascade(s) is responsible for regulating Cx43 and its critical role in endometrial receptivity.
METHODS: Human ESC prepared from eutopic proliferative phase biopsies and treated with 10 nM estradiol, 100 nM progesterone and 0.5 mM dibutyryl cAMP undergo decidualization. Dose- and time-effects of exogenous recombinant IL-1β were monitored by measuring Cx43 (Western blots of cell lysates), cell morphology (phase contrast microscopy) and secretion of prolactin and VEGF (ELISA in supernatants). Time and dose optima were determined for selective inhibitors of mTOR (Rapamycin), ERK 1/2 (PD98059), JNK (SP600125) and p38 MAPK (SB203580) and their effects on Cx43 expression were quantified.
RESULTS: IL-1β treatment showed a dose-dependent repression of Cx43 that could be neutralized with IL-1 receptor antagonist (IL-1RA). Quantitative RT-PCR showed the inhibitory effect is mediated in part at the level of transcription. Pharmacokinetics were similar for Cx43, prolactin and VEGF (IC_{50}=0.2 nM). PD98059 and SB203580 reversed the inhibitory effect of IL-1β on Cx43, whereas the other kinase blockers failed to overcome IL-1β-mediated inhibition.
CONCLUSIONS: IL-1β inhibits classical markers of ESC decidualization (eg, prolactin and morphological change) as well as emerging decidual biomarkers (Cx43 and VEGF). Inhibitor analyses revealed that the effect of IL-1β on Cx43 is primarily mediated via the ERK 1/2 and p38 MAP kinase pathways. While IL-1β can autoregulate its own production and also that of IL-1α, these cytokines are induced via mTOR, JNK and NF-κB mediated mechanisms. Elucidation of specific IL-1β pathways may allow selective targeting of proteins modulating inflammation-mediated implantation defects in endometriosis and other infertility conditions.

F-117

Large-Scale Integrated Genome-Wide RNA Sequencing, miRNA Array, and Genomic Analyses to Unravel the Functionality of Genome-Wide Association Results in Endometriosis. Nilufer Rahmioglu,[1] Helen Lockstone,[1] Teresa Ferreira,[1] Reedik Magi,[2] Martijn Van De Bunt,[1] Cecilia Lindgren,[1] Andrew Morris,[4] Christian Becker,[5] Krina Zondervan*.[5] *[1]Oxford University, Oxford, United Kingdom; [2]Tartu University, Tartu, Estonia; [3]Liverpool University, Liverpool, United Kingdom; [4]Oxford University, Oxford, United Kingdom.*
INTRODUCTION: Around 50% of endometriosis risk is due to genetic factors. Ten genome-wide significant loci have been associated with endometriosis, but most are located in intergenic regions of the genome. To understand how transcriptomic profiles are perturbed by genetic variants, we conducted a transcriptome-wide study of endometrium, fat and endometrial disease tissue from 190 endometriosis cases and 90 controls.
METHODS: Eutopic endometrium(N=221), and fat(N=180), from cases and controls and endometrial tissue(N=63) from cases were collected in the ENDOX study during laparoscopy. Surgical and patient data were collected using WERF EPHect standards. The tissues were profiled using RNA sequencing, Affymetrix-miRNA-4.1 array; DNA genotyped using Axiom UKBB array. Profiles were analysed in R using edgeR and limma.
RESULTS: MiRNA profiles did not significantly cluster by menstrual phase for any of the tissues, highlighting the tight control of these transcription regulators. Preliminary results show miRNA-148a, 88Kb downstream from one of the shared genome-wide significant loci for endometriosis and fat distribution, significantly differentially expressed in fat tissue of endometriosis cases vs. controls ($p=1.3x10^{-4}$). The RNA sequence profiles clustered by menstrual phase only in endometrium. We will present results of differential RNAseq and miRNA analyses comparing cases and controls, as well as expression quantitative loci (eQTL) analyses exploring the association between genetic variants and the transcriptome.
Further GWAS loci identified from ongoing meta-analyses, including the UKBiobank on >4,000 cases (full data release in Jan 2017) and EGCUT data. First results highlight the role of *FSHB* (rs11031006, $p=4.5x10^{-9}$, OR=0.80(0.74-0.86)).

Friday Posters

CONCLUSIONS: We have conducted the first, large-scale, integrated analysis of genome-wide RNA sequencing and miRNA profiles of three tissues relevant to endometriosis and genotyping of DNA variants. The results will shed light on understanding underlying genetic mechanisms of endometriosis.

F-118

Endometriosis Associated Risk of Ovarian Cancer Is Increased in Cases of Ovarian, but Not in Deep Infiltrating or Peritoneal Endometriosis. Liisu Saavalainen†,[1] Eero Pukkala,[2] Anna But†,[3] Mika Gissler,[4] Aila Tiitinen,[1] Päivi Härkki,[1] Oskari Heikinheimo*.[1] *[1]University of Helsinki, Helsinki, Finland; [2]Finnish Cancer Registry, Helsinki, Finland; [3]University of Helsinki, Helsinki, Finland; [4]National Institute for Health and Welfare, Helsinki, Finland.*

INTRODUCTION: Endometriosis is associated with increased risk of some cancers. We assessed the cancer risks in surgically verified endometriosis, stratified by the type of endometriosis.

METHODS: 55,430 women with endometriosis operated 1987-2012 using appropriate diagnostic codes combined with relevant concomitant surgical codes from the Finnish Hospital Discharge Registry and further classified into subgroups of ovarian (OE, n=21,836), deep infiltrating (DIE, n=10,138), peritoneal (PE, n=13,144) and other endometriosis (n=10,312). The cohort was linked to the Finnish Cancer Registry, and standardized incidence ratios (SIRs) calculated for various types of cancer.

RESULTS: Significantly altered SIRs (95% Confidence Interval) for various cancers and precancerous states are summarized in Table. Excluding the first 6 mo of follow-up the risk of ovarian cancer in OE persisted in age groups of 30-44 (2.44[1.45-3.85]) and 45-59 (1.38[1.00-1.84]) years.

Cancer site	ALL	OE	PE	DIE
Ovary	**1.22[1.05-1.39]**	**1.57[1.27-1.91]**	1.23[0.85-1.70]	1.00[0.69-1.39]
Ovary, borderline	**1.37[1.10-1.69]**	**1.58[1.11-2.16]**	**2.04[1.34-2.96]**	1.04[0.57-1.74]
Thyroid	**1.37[1.18-1.57]**	**1.33[1.04-1.67]**	1.36[0.98-1.84]	**1.49[1.09-1.99]**
Basal cell ca of the skin	**1.18[1.11-1.25]**	**1.11[1.00-1.21]**	**1.22[1.06-1.39]**	1.12[0.97-1.27]
Cervix uteri	**0.55[0.38-0.76]**	0.68[0.40-1.09]	0.53[0.23-1.05]	0.51[0.21-1.05]
Precancertos cervical lesions	**0.67[0.59-0.76]**	**0.62[0.49-0.77]**	0.83[0.66-1.02]	**0.62[0.45-0.82]**
Corpus uteri	**0.41[0.33-0.49]**	**0.48[0.35-0.63]**	**0.37[0.20-0.61]**	**0.50[0.32-0.74]**
Pancreas	**0.73[0.57-0.92]**	0.80[0.55-1.12]	0.81[0.43-1.39]	**0.54[0.27-0.96]**
All cancers	**0.95[0.92-0.97]**	0.92[0.92-1.00]	0.98[0.91-1.05]	**0.91[0.69-0.97]**

CONCLUSIONS: The endometriosis associated increased risk of ovarian cancer as was confined to only OE in younger ages. Decreased risk of uterine cancer occurred irrespective of the type of endometriosis and may be related to progestin treatment. Unexpectedly, the risk of thyroid cancer was increased in whole cohort, and in OE and DIE.

F-119

Inflammation and Fibrosis Mediate Distinct Phenotypic Progression in Endometriosis. Tiffanny L Jones†,[1] Chandra C Senoy,[1] Ye Zheng,[1] Abdulrahman M Saadalla,[2] Khashayarsha Khazaie,[2] Gaurang S Daftary*.[1] *[1]Mayo Clinic, Rochester, MN, USA; [2]Mayo Clinic, Rochester, MN, USA.*

INTRODUCTION: Endometriosis is characterized by ectopic implantation of endometrium, often accompanied by inflammation and fibrosis. Although inflammation is expected to precede fibrotic healing, we found these two pathogenic mechanisms operate exclusively, in Klf10-/- and Klf11-/- animal endometriosis models respectively. KLF10 and 11 are TGF-B driven transcription factors that are implicated in endometriosis. We followed inflammatory and fibrotic signaling mechanisms over a time course in wildtype (wt), Klf10-/- and Klf11-/- animals to determine establishment and progression of disease.

METHODS: Endometriosis was surgically induced by suturing autologous uterine segments (0.5 mm) to parietal peritoneum of Klf10 -/-, 11-/- or wt mice. Lesion phenotype, fibrotic progression, peritoneal, nodal and splenic inflammatory infiltrate was assessed at 1 or 2 weeks by FACS and immunofluorescence. Cytokine analysis was evaluated by Multiplex/ELISA. Gene expression was evaluated by PCR Array.

RESULTS: Klf10-/- animals demonstrate inflammatory disease progression and cystic lesion formation whereas Klf11-/- animals demonstrate fibrotic progression. Both phenotypes were minimally evident at 1 week and established by 2 weeks. Klf10-/- mice had robust peritoneal monocyte and granulocyte infiltration at 1 week. In contrast these responses were attenuated in Klf11-/- mice. Systemic splenic responses were significantly elevated only in Klf10-/- mice with T-reg cell proliferation; T-reg function was however deficient with decreased expression of CD25 and ROR-gamma-T. Cytokine expression matched cellular infiltrates. Despite prominent inflammatory responses, fibrosis in Klf10-/- mice was minimal compared to wt (17 +/- 2) and in contrast to Klf11-/- mice (17 and 34.45 at 1 and 2 weeks respectively; $p<0.05$). Gene expression showed distinct divergence in TGF-Beta signaling in Klf10-/- and Klf11-/- compared to wt.

CONCLUSIONS: Defective T-reg mediated systemic immune responses in Klf10-/- mice causes inflammation and prevents scarring. In contrast, suppressive systemic T-reg cells attenuate local immune response in Klf11-/- mice, which is associated with scarring. Differential progression is associated with distinct divergence in TGFB signaling. KLF10 and 11 also recruit epigenetic cofactors. Epigenetic and TGF signaling inhibitors offer novel, individualized therapies for endometriosis.

F-120

Novel High-Risk Damaging Mutations Discovered in Familial Endometriosis. Kenneth Ward, Rakesh Chettier, Hans Albertsen*. *Juneau, Salt Lake City, UT, USA.*

INTRODUCTION: Twin and family studies show that heritability of endometriosis is high, but causative mutations have not been elucidated. We studied women with familial endometriosis using whole exome sequencing (WES) study to identify high-risk gene variants contributing to the disease. Unrelated patients and population controls were used to confirm results.

METHODS: WES was performed on 489 women with surgically-proven familial endometriosis and 530 unrelated women (based on identity-by-descent test) with endometriosis and 370 population controls. WES was performed using Ion Proton Instrument and AmpliSeq Exome Capture Kit. All missense and truncating variants with genome-wide significance and a MAF<1% in ExAc database (Broad Institute) were considered for downstream analysis. Variant frequencies were compared with population frequency in ExAc database (n=33000) using Fisher's exact test to test significance. Seven software packages were used to predict whether missense mutations would damage the encoded protein.

RESULTS: Using familial endometriosis subjects, we identified 4 high-risk variants that pass genome-wide significance as shown in the Table below. Association was verified in the cohort of unrelated endometriosis patient

gene	mutation type	Amino acid change	Count in 489 related samples	P	OR	Count in 530 unrelated samples	ExAc Variant Frequency
LONP1	splicing		10	4.20E-19	Inf	3	Not seen
IGF2	stop-gain	p.Q33X	12	3.02E-10	15[8-27]	5	0.0009
BRD9	damaging	p.K39R	16	5.63E-09	10[5-21]	1	0.0017
SNAP91	damaging	p.T555A	24	1.09E-08	5[3-8]	11	0.0050

We identified genes that are associated with endometriosis. IGF2 (insulin-like growth factor 2) was previously implicated in endometriosis gene expression studies and an 820G>A IGF2 polymorphism was associated with the development of endometriosis in Korean women. We implicated SNAP91 in our prior association studies. BRD9 (Bromodomain-containing protein 9) and LONP1 (Lon protease) are known to be expressed in endometrium and endometrial cancer. 14 of the 16 carriers of the BRD9 mutation have the same haplotype (seen in 5% of population) and genealogy records show a common ancestor 16 generations ago (the "unrelated" BRP9 mutation carrier has the same haplotype as well).
CONCLUSIONS: Familial endometriosis subjects were studied to detect additional gene mutations likely to have major gene effects on the occurrence of endometriosis.

F-121

The Predictive Potential of Peripheral Blood Basophils in Endometriosis. Jun Guan†,[1,2] Karin Hellner,[1,2] Nilufer Rahmioglu,[3] Carol Hubbard,[1,2] Maryjane Dale,[1,2] Kevin Paddon,[4] Krina Zondervan,[1,2,3] Christian Becker*.[1,2] *[1]University of Oxford, Oxford, United Kingdom; [2]University of Oxford, Oxford, United Kingdom; [3]University of Oxford, Oxford, United Kingdom; [4]Oxford University Hospitals NHS Foundation Trust, Oxford, United Kingdom.*
INTRODUCTION: Endometriosis affects 5-10% of premenopausal women causing pelvic pain and impaired fertility. Diagnosis can only be established surgically, thus, less invasive means of diagnosis are urgently needed. Endometriosis has been suggested to induce local and systemic inflammation. Circulating leukocytes are used as markers of systemic inflammatory response in many conditions. However, their role in endometriosis is unclear. This study investigates the potential of leukocyte subpopulations in diagnosing endometriosis, using data from prospective ENDOX study.
METHODS: We analyzed preoperative full blood counts of 600 patients who underwent laparoscopy for symptoms suggestive of endometriosis. Medical and surgical data were collected according to WERF EPHect standards. Differences in leukocyte subgroups were evaluated using linear regression models including variables as the history of other inflammatory conditions and menstrual cycle phase. The predictive value was assessed using receiver operating characteristic curves.
RESULTS: Endometriosis was confirmed intra-operatively in 383 cases and excluded in 217 cases. In the endometriosis group 239 women had mild disease (ASRM stage I/II) and 144 women had moderate/severe endometriosis (ASRM stage III/IV). We found no difference in total white cell counts between groups. However, basophil counts were significantly increased in endometriosis patients (p=0.0012), in both mild (p=0.0455) and severe disease (p=0.0032). This yielded a sensitivity of 46.0% and specificity of 65.7% (AUC=0.577, p=0.0017) in diagnosing endometriosis. The increase of basophils in endometriosis patients was independent of other inflammatory conditions known to affect basophil counts including asthma, eczema and irritable bowel syndrome.
CONCLUSIONS: Investigating circulating leukocyte subpopulations revealed a significant increase of basophils in endometriosis patients. This was strongly correlated with disease severity and independent of prevalence of other inflammatory conditions. Implementation of basophil counts into clinical algorithms has the potential to transform non-invasive diagnosis of endometriosis.

F-122

Novel PTGES Inhibitor BAY 1202229 Showed Significant Effects Against Inflammatory Pain and Vaginal Hyperalgesia and Proliferation in a Rat Model of Endometriosis. Anne-Marie Coelho,[2] Marcus Koppitz,[1] Daryl Walter,[3] Nico Braeuer,[1] Andrea Rotgeri,[1] Susan Boyce,[2] Markus Koch,[1] Thomas M Zollner,[1] Andreas Steinmeyer,[1] Michaele Peters.[1] *[1]Bayer Pharma AG, Berlin, Germany; [2]Evotec AG, Hamburg, Germany; [3]Evotec (UK) Ltd, Abingdon, Oxfordshire, United Kingdom.*
INTRODUCTION: Endometriosis is a chronic, hormone-dependent, inflammatory disease, characterized by the presence of endometrial tissue outside the uterine cavity. It is associated with moderate to severe pelvic and abdominal pain symptoms and a marked reduction in health-related quality of life. In ectopic endometrium from patients the main PGE2 producing enzyme, prostaglandin E synthase (PTGES), is highly expressed and high PGE2 levels are found. Since PGE2 is involved in various mechanisms underlying endometriosis we hypothesized that PTGES inhibition has the potential to address multiple treatment paradigms associated with endometriosis such as pain and proliferation of ectopic endometrium.
METHODS: The novel PTGES inhibitor BAY 1202229 was identified as a highly potent and selective inhibitor of human and rodent PTGES. Efficacy on inflammatory pain was demonstrated in a mouse model of Complete Freund´s Adjuvant (CFA)-induced spontaneous pain behavior. To detect efficacy on endometriosis induced vaginal hyperalgesia we used a rat model of endometriosis. Endometriosis was induced by autologous transplantation of uterine tissues and detection of a visceromotor response to vaginal distension was used as a measure of vaginal sensitivity. Effects on endometrial proliferation were detected by markers of proliferation within endometriotic lesions.
RESULTS: BAY 1202229 demonstrated robust efficacy following p.o. administration to mice and rats. BAY 1202229 significantly reduced CFA-induced spontaneous pain behaviour and significantly reduced vaginal hyperalgesia in the rat model of endometriosis. The latter study revealed a sustained effect of treatment with efficacy still observable one week after cessation of treatment. In addition a significant reduction in markers of proliferation in endometriotic lesions was noted.
CONCLUSIONS: The effects induced by the novel PTGES inhibitor BAY 1202229 support the proposed prominent role of PTGES as a key driver of endometriosis disease progression and support the hypothesis that inhibition of PTGES with BAY 1202229 has the potential to provide an efficacious non-hormonal disease modifying therapy for human endometriosis.

F-123

The Effect of Operative Time on Outcomes in Minimally Invasive and Abdominal Myomectomy: An Analysis of the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP). Samantha L Margulies†,[1] Maria V Vargas,[2] Kathryn Denny†,[3] Richard Amdur,[4] Cherie Marfori*.[2] *[1]Yale-New Haven Hospital, New Haven, CT, USA; [2]George Washington University Medical Faculty Associates, Washington, DC, USA; [3]George Washington University, Washington, DC, USA; [4]George Washington University, Washington, DC, USA.*
INTRODUCTION: The goal of this study is to determine the effect of operative time (OT) on perioperative morbidity following minimally invasive and abdominal myomectomy and to elucidate if there is an OT at which a minimally invasive surgical (MIS) approach for myomectomy becomes inferior to laparotomy.
METHODS: Using the database ACS NSQIP, we conducted a retrospective cohort study of women undergoing myomectomy from 2005 to 2014 identified by CPT code. Myomectomy cases and outcomes were stratified by approach and 90-minute intervals.
RESULTS: A total of 6,417 myomectomies were identified, of which 2,644 (41.2%) were MIS approach, 3,747 (58.4%) were abdominal and 26 (0.4%) were conversions. The rates of pulmonary complications, venous thromboembolic events, sepsis, hemorrhage, reoperation and hospital stay > 3 days increased with OT. Longer OT was associated with African American race, higher BMI, lower preoperative hematocrit, hypertension, older age, large and/or numerous fibroids and an MIS approach. Women undergoing MIS were more likely to be Caucasian, older, have a lower BMI, higher hematocrit and were less likely to have hypertension or large and/or numerous fibroids. Overall morbidity was greater in abdominal cases (15% vs 6%), with the highest rates in converted cases (23%; p<.0001). After adjusting for confounders, mean OT in minutes (min) (95% CI) was 112.9 (110.25-115.62) for abdominal, 154.33 (150.25-158.51) for MIS and 156.10 (126.88-192.06) for conversions. An MIS approach was protective against complications until cases reached ≥ 270 min, at which point the odds of complications increased compared to abdominal cases < 90 min (OR 3.67 95% CI (2.38-5.64), p<.0001). Of MIS cases, 88% were completed in < 270 min.

CONCLUSIONS: OT was predictive of complications for both MIS and abdominal myomectomies. MIS procedures had superior outcomes up to 4.5 hours. Careful patient counseling and preparation to increase surgical efficiency should be prioritized for either approach.

F-124

Oxidative Stress: A Key Regulator of Leiomyoma Cell Survival. Nicole M Fletcher†,[1] Ira Memaj,[1] Mohammed S Abusamaan,[1] Ayman Al-Hendy,[2] Michael P Diamond,[2] Ghassan M Saed*.[1] [1]*Wayne State University, Detroit, MI, USA;* [2]*Augusta University, Augusta, GA, USA.*

INTRODUCTION: We have previously demonstrated that leiomyoma cells (DD) manifested an altered redox balance leading to overall enhanced oxidative stress as compared to normal myometrial cells (USMC). The objective of this study was to determine the effect of attenuating oxidative stress on the expression of key redox enzymes, myeloperoxidase (MPO) and inducible nitric oxide synthase (iNOS), as well as apoptosis.

METHODS: A matched pair of DD and USMC were treated with dichloroacetate (DCA, 20 µg/ml) that shifts anaerobic to aerobic metabolism thus modulating oxidative stress, with and without hypoxia (2% O_2, 24 hours). Nitric oxide (NO, an iNOS activity indicator), iNOS, MPO, and caspase-3 activity and levels were determined by real-time RT-PCR, Greiss Assay and ELISAs. Data were analyzed with SPSS by ANOVA with Tukey post hoc and independent t-tests, $p<0.05$.

RESULTS: MPO, iNOS and NO expression were higher, and further increased upon exposure to hypoxia, in DD as compared to USMC. Treatment with DCA decreased MPO, iNOS and NO levels and negated the effect of hypoxia, in both cell lines. Apoptosis, as indicated by caspase-3 activity, was lower in DD than USMC. Hypoxia further decreased apoptosis in USMC. Treatment with DCA resulted in increased apoptosis in both cell lines even in the presence of hypoxia.

Cell Line and Treatment	MPO mRNA (fg/µg RNA)	MPO Protein (ng/ml)	iNOS mRNA (fg/µg RNA)	Nitrate (µM)	Increase in Capsase-3 Activity (%)
Untreated USMC	0.028 ±0.003	4.4 ±0.5	0.57 ±0.09	3.5 ±0.9	
USMC +DCA	0.035 ±0.007	2.8 ±0.4*	0.54 ±0.09	2.3 ±0.2*	60.1 ±8.1*
USMC +Hypoxia	0.16 ±0.03*	6.2 ±0.2*	3.8 ±0.1*	4.5 ±0.5*	-29.9 ±12.7*
USMC +Hypoxia & DCA	0.066 ±0.01#	3.0 ±0.2#	1.4 ±0.3#	2.7 ±0.5#	53.4 ±6.0#
Untreated DD	0.045 ±0.006	5.3 ±0.2*	0.76 ±0.06	4.0 ±0.4*	-26.8 ±9.4*
DD +DCA	0.024 ±0.002**	2.7 ±0.2**	0.34 ±0.006**	2.5 ±0.1**	55.3 ±3.5**
DD +Hypoxia	0.085 ±0.003**	6.5 ±0.4**	0.85 ±0.05	5.0 ±0.9**	5.3 ±8.5
DD +Hypoxia & DCA	0.013 ±0.0009##	2.3 ±0.2##	2.3 ±0.2##	2.1 ±0.3##	25.2 ±6.5##
p<0.05 as compared to *USMC, #USMC+Hypoxia, **DD & ##DD+Hypoxia					

CONCLUSIONS: Oxidative stress and hypoxia play an important role in pathogenesis of fibroids. Modulation of oxidative stress may serve as a future therapeutic approach.

F-125

Ulipristal Directly Regulates Leiomyoma Fibrosis In Vivo and In Vitro. Minnie Malik,[1] Jeris Cox,[1,2,3] Joy Britten,[1] Lynnette Nieman,[4] William H Catherino*.[1,2] [1]*Uniformed Services University of the Health Sciences, Bethesda, MD, USA;* [2]*National Institute of Child Health and Human Development, NIH, Bethesda, MD, USA;* [3]*Fort Belvoir Army Medical Center, Fort Belvoir, VA, USA;* [4]*National Institutes of Health, Bethesda, MD, USA.*

INTRODUCTION: Ulipristal (UPA) decreased leiomyoma size and symptoms in multiple prospective, randomized trials. At the completion of one such study, hysterectomy was performed for tissue collection. We examined these tissues to assess the impact of UPA treatment on extracellular matrix (ECM) expression in leiomyomas compared to placebo treated patients. To characterize the critical concentrations of UPA to induce effect, we treated 3D leiomyoma and myometrial cultures with UPA to assess ECM. We hypothesized that UPA decreased both mRNA and protein expression of critical ECM components.

METHODS: Proteins related to ECM production were evaluated: fibronectin (FN), versican (VER), and collagen 1A1 (COL). For in vitro analysis, leiomyoma cells were grown in collagen gel and treated with different concentrations of UPA for 48hrs. RNA was extracted for qRTPCR analysis. Protein concentration and distribution was analyzed using immunohistochemistry (IHC) and Western Blot.

RESULTS: Assessment of fibronectin mRNA demonstrated elevated expression in human leiomyomas compared with patient-matched myometrium regardless of treatment with ulipristal or placebo. However, expression of mRNA decreased from 3.88 fold elevated in placebo-treated patients to 2.45 fold in UPA-treated women. A similar decrease in fibronectin protein was observed (2.48 fold to 1.07 fold), with UPA decreasing fibronectin to levels comparable to patient-matched myometrium. Collagen 1A1 demonstrated similar results (mRNA: 3.19 fold versus 1.81 fold; protein 2.27 fold versus 1.54 fold). While versican mRNA increased with ulipristal treatment (3.79 fold versus 6.39 fold), protein again decreased to levels comparable to patient-matched myometrium (2.32 fold versus 1.16 fold). Finally, IHC demonstrated spatial variation in protein expression in both surgical specimens and 3D cultures.

CONCLUSIONS: UPA directly regulates key ECM components involved in leiomyoma fibrotic bulk.

This research was supported by an independent investigator initiated grant by Allergan and by the Program in Reproductive and Adult Endocrinology, NICHD, NIH.

F-126

Screening the Antiproliferative Effect of Seven Vitamin D Analogs in Human Uterine Fibroid Cells. Mohamed A Ali, Heba ElHusseini, Sunil K Halder, Archana Laknaur, Ayman Al-Hendy*. *Augusta University, Augusta, GA, USA.*

INTRODUCTION: Uterine fibroids (UFs) are the most common gynecological benign tumors in reproductive age women. Our group and others have well characterized the role of 1, 25-dihydroxyvitamin D in UF management showing potent antiproliferative effect *in vitro* and *in vivo* animal model, while its deficiency is associated with UF risk. Vitamin D analogs are potential candidates as novel effective, safe and cheap strategy to cure UFs with advantage of reduced calcemic effect associated with vitamin D therapy. **Objective:**Screening the antiproliferative activity of seven Vitamin D analogs using human uterine leiomyoma (HuLM) cells.

METHODS: HuLM cells were treated with increasing concentrations (0.01-1000 nM) of Doxercalciferol and Elocalcitol (Axon Medchem) and 5 ZKs analogs (Bayer AG) ZK136607, ZK157202, ZK159222, ZK191784, ZK 203278 (Calcithiazol). The growth inhibitory effect was assessed by MTT assay after 24, 72, 120, and 168 h. Elected compounds were then used to treat HuLM cells for 48 h followed by Western blotting of whole cell lysate for proliferation associated markers such as PCNA and Cyclin D1 as well as extracellular matrix associated fibronectin, type 1 collagen, TGF-β3 receptor I and PAI-1 proteins as fibrosis indicators.

RESULTS: All analogs showed significant antiproliferative effect, as compared to untreated cells, after 120 and 168 h at concentration range of 100-1000 nM. Interestingly, ZK157202 showed significant inhibitory effect at all used concentrations after 120 and 168 h, and after 72 h starting from 0.1 nM, reaching 60% inhibition at 1000 nM after 168 h. Similarly, all used concentrations of Calcithiazol significantly inhibited growth after 120 and 168 h of treatment, and after 72 h at concentrations starting from 1 nM, reaching 55% inhibition at 1000 nM after 168 h ($P < 0.05$). The inhibitory effect of those two compounds was confirmed by western blotting, showing noticeable down regulation in expression levels of type 1 collagen, fibronectin, cyclin D1, PAI-1, TGF-β3 receptor I and PCNA proteins, particularly at (100-1000 nM) concentrations range.

CONCLUSIONS: Vitamin D analogs hold promising features as non-hormonal, non-invasive strategy for UF treatment, particularly compounds ZK157202 and Calcithiazol, paving the route for next endeavor of human clinical trial.Support: Bayer AG provided the ZK compounds, Augusta University startup package.

F-127

Differential Susceptibility of Chlamydial Infection in the Gastrointestinal Tract to Doxycycline Treatment. Courtney Failor†,[1] Luying Wang†,[2] Robert Schenken,[1] Guangming Zhong*.[2] *[1]UT Health Science Center, San Antonio, TX, USA; [2]UT Health Science Center, San Antonio, TX, USA.*

INTRODUCTION: Chlamydia colonization of the gastrointestinal (GI) tract has been detected in both humans and animals. The clinical significance of the GI tract infection is unknown, but may indirectly contribute to pathology in the upper genital tract by inducing profibrotic immune responses. Regardless of the mechanism, there is an urgent need to treat Chlamydia found in the GI tract, for which there is no standard treatment recommendation. In the current study, we set out to evaluate the efficacy of a 7-day doxycycline regimen in treating GI tract Chlamydia.

METHODS: Female mice developed both genital and GI tract infection following intravaginal inoculation with the murine strain *Chlamydia muridarum* (CM). The mice were treated with a 7-day course of doxycycline (Dox) via oral galvage at three different time points (3, 14, and 28 days postinoculation). CM live organisms were detected in vaginal and rectal swabs collected weekly. The live organisms were titrated in cell monolayers and inclusion-forming units (IFUs) were counted using an immunofluorescence assay.

RESULTS: Dox appeared to clear both the genital and GI tract CM infections during treatment. However, the GI tract CM reoccurred after the treatment was applied on days 3 or 14 but not 28 after inoculation. **Figure(s) will be available online.*

CM in the genital tract was readily susceptible to the same dose of Dox at all time points.

CONCLUSIONS: Prior human and animal studies have suggested varied efficacy in treating GI tract Chlamydia based on results from a single post-treatment time point. Here, by monitoring the treatment efficacy over time, we have shown that the efficacy of treatment of GI CM depends on timing. Unlike genital tract Chlamydia, for which early treatment is effective in eliminating infection and reducing pathology, a delayed application of Dox is required to completely eliminate the GI tract infection. The failed treatment in the early time course may correlate with the persistent status of CM in the GI tract, which can be refractory to treatment. Experiments to test this hypothesis are ongoing.

F-128

Gestational Diabetes Results in Increased Energy Expenditure in a Mouse Model. Kathleen Pennington, Nicola van der Walt. *Baylor College of Medicine/Texas Childrens Hospital, Houston, TX, USA.*

INTRODUCTION: Gestational diabetes mellitus (GDM) is defined as diabetes diagnosed during pregnancy and is one of the most common obstetrical complications, affecting 7-18% of all pregnancies. Pregnancy alone is a known stressor to maternal metabolism and physiology and the addition of GDM further stresses the maternal environment. The goal of this study was to evaluate the effect of GDM on whole body energy expenditure (EE) using a dietary mouse model. Previous studies show that exposure to a high fat, high sugar diet one week prior to and throughout pregnancy induces glucose intolerance in mice. We hypothesized that EE would be significantly increased in glucose intolerant dams compared to control dams.

METHODS: Female C57BL/6J mice were placed on either a 10% kcal/fat, 0% kcal/sucrose control diet (P-CD, n=5) or a 45% kcal/fat, 17% kcal/sucrose HFHS (P-HFHS, n=4) 1 week prior to and throughout pregnancy. Additional unmated females were subjected to the same diet regimen, either CD (NP-CD, n=3) or HFHS (NP-HFHS, n=4), for 4 wks to determine pregnancy-specific effects. Mice were placed into comprehensive lab animal monitoring system (CLAMS) from day 0.5 to 17.5 of pregnancy, during which time food consumption, activity, and EE were measured. Quantitative magnetic resonance (QMR) was performed on day 0, 7.5, 11.5, 14.5 and 17.5.

RESULTS: By day 12.5 of pregnancy, and after, EE was significantly increased ($p<0.05$) in P-HFHS dams compared to all other groups. NP-HFHS and P-CD animals had significantly increased ($p<0.05$) EE compared to NP-CD females beginning at day 12.5, and thereafter. Percent body fat, as measured by QMR, was not different between groups at day 0. At day 7.5 of pregnancy, percent body fat was significantly increased ($p<0.05$) in NP-HFHS and P-HFHS compared to NP-CD and P-CD groups. Percent body fat remained significantly higher in NP-HFHS compared to NP-CD on days 11.5, 14.5 and 17.5, although no differences were observed in P-HFHS compared to P-CD on these days. Food consumption and activity levels were not different between groups.

CONCLUSIONS: Glucose intolerance during pregnancy results in increased EE providing evidence for aberrant metabolic processing during GDM. Increases in EE may, in part, be related to increased fat metabolism as indicated by changes in body fat. Ongoing analysis is aimed at looking at alterations in fat metabolism due to GDM and how these alterations affect long term health of mother and fetus.

F-129

Optimal Non-Invasive Method of Measuring Cardiac Output During Pregnancy Reveals Marked Heterogeneity in the Magnitude of Responses Between Women. John W Petersen,[1] Jing Liu,[2] Yueh-Yun Chi,[2] Melissa D Lingis,[3] R Stan Williams,[4] Alice Rhoton-Vlasak,[4] Karen Hamilton,[1] Mark S Segal,[3,5] Kirk Conrad.[6] *[1]UF, Gainesville, FL, USA; [2]UF, Gainesville, FL, USA; [3]UF, Gainesville, FL, USA; [4]UF, Gainesville, FL, USA; [5]North Florida/South Georgia Veterans Health System, Gainesville, FL, USA; [6]UF, Gainesville, FL, USA.*

INTRODUCTION: Various non-invasive methods are available to measure cardiac output (CO) during pregnancy. We aimed to compare serial CO measures determined with various methods to determine which provided the least variability and should be used in future studies examining cardiovascular adaptations of pregnancy.

METHODS: Ten patients with spontaneous pregnancy had estimation of CO at baseline prior to becoming pregnant and at the end of the first and third trimesters. Echocardiographic data was used to estimate CO by Teichholz method (2D and M mode), the Simpson biplane method, and Doppler determined velocity time integral (VTI) method. In addition, a Bioz Dx device was used to estimate CO by impedance cardiography.

RESULTS: CO estimated with the VTI method had the lowest beat to beat variability. CO estimated with the VTI method was higher than CO estimated with the 2D-Teichholz method and Simpson's method, but comparable to M mode Teichholz method. The % change in CO during pregnancy was similar for all echo methods (VTI, Teichholz, and Simpson biplane). Baseline CO determined with impedance cardiography was higher than CO determined with the VTI method. However, change in CO during pregnancy was significantly lower when measured with impedance cardiography as compared to the VTI method. Change in heart rate had the strongest correlation with change in CO during pregnancy. There was marked heterogeneity in the degree of rise in CO during the first trimester ranging from little or no increase to as much as 60% above pre-pregnant (follicular phase) levels.

CONCLUSIONS: The Doppler determined VTI method of estimating CO provided the measure with the least beat to beat variability. We recommend use of Doppler determined VTI method for estimation of CO in pregnancy. The wide variation in the gestational rise in CO was unexpected, and at least in part secondary to variable increases in HR and decreases in systemic vascular resistance.

F-130

Pregnancy Upregulates Ten-Eleven Translocation (TET) Methylcytosine Dioxygenases and Increases Large Conductance Ca^{2+}-Activated K^+ Channel Expression in Ovine Uterine Arteries. Chiranjib Dasgupta, Xiang-Qun Hu, Man Chen, Xiaohui Huang, Lubo Zhang*. *Loma Linda University School of Medicine, Loma Linda, CA, USA.*

INTRODUCTION: The large conductance Ca^{2+}-activated K^+ (BK_{Ca}) channel plays a key role in regulating uterine vascular tone and blood flow during pregnancy. The expression of KCNMB1, which encodes BK_{Ca} channel β1 subunit, in uterine arteries is governed by methylation status at the KCNMB1 promoter. Pregnancy and estrogen induce demethylation of the promoter and increase the expression of KCNMB1 in ovine uterine arteries. However, it remains unknown how estrogen instigates the demethylation process.

METHODS: Resistance-sized uterine arteries were isolated from nonpregnant and near-term pregnant sheep. For *ex vivo* hormonal treatment, uterine arteries from nonpregnant animals were treated with 17β-estradiol (E2β, Sigma) (0.3 nM) and progesterone (P4, Sigma) (100.0 nM) for 48 hours in the absence or presence of a TET inhibitor fumarate. The expression of TETs and KCNMB1 was determined with RT-PCR and Western blot. The regulatory action of estrogen on the TET1 promotor activity in uterine arterial smooth muscle cells was determined with luciferase reporter gene assay.

RESULTS: Pregnancy upregulated expression of TET1 and TET2 at mRNA and protein levels in ovine uterine arteries. Estrogen in conjunction with progesterone mimicked this modulation by binding to the half-palindromic ERE at -1370 of the TET1 promoter and subsequently enhanced promoter activity. Accordingly, treatment of uterine arteries from nonpregnant animals with estrogen and progesterone enhanced expression of TET1 and TET2. The hormonal treatment also stimulated BK_{Ca} channel β1 subunit mRNA and protein expression. Of interest, the upregulation of BK_{Ca} channel expression by steroid hormones was ablated by fumarate.

CONCLUSIONS: Taken together, the results suggest that pregnancy stimulates KCNMB1 expression *via* estrogen-induced upregulation of TETs in uterine arteries.

F-131

Physiologic Adaptation of Endothelial Function to Pregnancy: A Systematic Review and Meta-Analysis. Tessa AG van Gansewinkel,[1] Veronica A Lopes van Balen†,[1] Sander de Haas,[1] Sander MJ van Kuijk,[2] Joris van Drongelen,[3] Chahinda Ghossein-Doha,[1] Marc EA Spaanderman*.[1] *[1]Maastricht University Medical Centre (MUMC+), Maastricht, Limburg, Netherlands; [2]Maastricht University Medical Centre (MUMC+), Maastricht, Limburg, Netherlands; [3]Radboud University Nijmegen Medical Centre, Nijmegen, Gelderland, Netherlands.*

INTRODUCTION: The purpose of this systematic review and meta-analysis is to establish reference values for flow mediated dilatation (FMD) and baseline brachial artery diameter in pregnancy (BBAD) and, to provide insight in the physiological and pathological course of endothelial adaptation throughout human singleton pregnancies.

METHODS: A meta-analysis was performed by a systematic review of current literature on FMD, as a derivative for endothelial function, throughout uncomplicated and complicated pregnancies. PubMed (NCBI) and Embase (Ovid) electronic databases were used for this literature search which was performed up until June 9th 2016. To allow judgment of changes as compared to a non-pregnant state, studies were required to report both a non-pregnant mean reference of FMD (matched control group, pre-pregnancy- or postpartum- measurement) and mean FMD during a predetermined and reported gestational age. Pooled mean differences between the reference and pregnant FMD values were calculated for predefined intervals of gestational age.

RESULTS: Fourteen studies which enrolled 1096 participants met the selection criteria. Publication dates ranged from 1999 to 2014. In uncomplicated pregnancies FMD was increased in the second and third trimester. BBAD increased progressively, by the second trimester in a steady matter, however not significantly in the first half of the second trimester. We could not discern differences in FMD and BBAD between complicated and uncomplicated pregnancies at 29 to 35 weeks gestation, reported in three studies that met our inclusion criteria. Despite the increase in FMD and BBAD throughout gestation both reference curves depict a large 95%CI.

CONCLUSIONS: During healthy pregnancy endothelial dependent vasodilatation and brachial artery diameter increase. Women with a complicated pregnancy fell within the lower range of FMD values when compared to uncomplicated pregnancies but, as a group, did not differ from each other.

F-132

Cardiac Remodeling During Physiologic and Complicated Pregnancies: A Systematic Review and Meta-Analysis. Chahinda Ghossein-Doha,[1] Sander de Haas,[1] Lauren Geerts,[1] Joris Drongelen,[2] Marc Spaanderman*.[1] *[1]Maastricht UMC, Maastricht, Limburg, Netherlands; [2]Radboud University, Nijmegen, Gelderland, Netherlands.*

INTRODUCTION: During human pregnancy the maternal cardiovascular system encounters major hemodynamic and cardio vascular alterations ensuring a normal course of pregnancy. The increase in circulating volume during pregnancy is thought to lead to an increase in cardiac left ventricular mass (LVM) and a proportional increase of ventricular dimensions with wall thickness. The aim of this systematic review and meta-analyses was to comprehensively describe the physiological pattern of cardiac remodeling during human singleton pregnancies and compare this to the cardiac remodeling in complicated pregnancies.

METHODS: We performed a meta-analysis of the current literature on cardiac remodelling during physiological and complicated pregnancies. Literature was retrieved from PubMed (NCBI) and Embase (Ovid) databases. Included studies needed to report a reference measurement (matched non-pregnant control group, pre-pregnancy, or post-partum) and measurements during a predetermined gestational interval. Mean differences between reference and pregnant measurements were calculated using random-effects model described by DerSimonian and Laird.

RESULTS: 47 studies were included for meta-analysis with publication dates ranging from 1977 to 2015. During normal pregnancy, left ventricular mass (LVM) increased by 24% (Fig. 1), and the relative wall thickness (RWT) increased with 11% compared to non-pregnant conditions. Cardiac remodeling in hypertensive pregnancies deviates from healthy pregnancy by a significantly larger increase in LVM (73%) and RWT (45%).

**Figure(s) will be available online.*

Fig. 1: LVM during pregnancy with the 5th,50th, and 95th percentile. Each point estimate is indicated as a value from a low quality (green), moderate quality (blue), or high quality (red) study as determined by the quality assessment.

CONCLUSIONS: During healthy pregnancies, there is a significant rise in LVM and RWT. During PE, an even larger rise of LVM and RWT occurs pointing towards concentric remodeling.

F-133

Intrinsic Circadian Rhythms of Reproductive Tissues Over Pregnancy. Carmel Martin-Fairey†,[1,2] Beakal Gezahegn,[1] Sarah Speck,[1] Xioafang Ma,[2] Ronald McCarthy,[2] Sarah England,[2] Erik Herzog.[1] *[1]Washington University, Saint Louis, MS, USA; [2]Washington University School of Medicine, Saint Louis, MS, USA.*

INTRODUCTION: Limited evidence implicates daily or circadian rhythms in the timing of birth in humans and other mammals. The hypothalamic suprachiasmatic nucleus (SCN) generates endogenous daily cycles in physiological processes and is believed to coordinate circadian oscillations in most tissues including the reproductive system. SCN-lesioned rodents deliver at random times of day although gestation length is unaffected, implicating the SCN in gating the time of day of parturition, but not gestation length. In mice, the uterus has been shown to have intrinsic daily regulation of core clock genes, such as Period2 (Per2). We therefore investigated the hypothesis that daily rhythms in reproductive tissues change during pregnancy to coordinate gestation length and the circadian gating of birth.

METHODS: Homozygous knock-in mPERIOD2::Luciferase (PER2::Luc) mice were maintained on a 12h:12h light dark cycle. Pregnant

dams were sacrificed at day 8.5, 9.5, 14.5, 15.5 or 18.5 of pregnancy. Explants of uterine, cervical and placental tissue from pregnant or non-pregnant females were cultured and placed under a photomultipier tube to monitor PER2::Luc bioluminescence for a minimum of 4 days of continuous recording. All bioluminescence traces were analyzed for circadian periodicity using custom software (Chronostar 1.0, A. Kramer and B. Maier).

RESULTS: We found that both the uterus and cervix were intrinsically circadian with similar periods in the non-pregnant state (uterus: 23.2 ± 0.2h, mean±SEM and cervix: 23.2 ± 1.8h). Similarly, uterine (23.4 ± 0.3h), cervical (24.2 ± 0.4h) and placental tissue (23.9 ± 0.3h) were circadian and had similar periods throughout pregnancy. We conclude that uterine, cervical and placental tissues contain an endogenous circadian clock throughout pregnancy.

CONCLUSIONS: Our data provide evidence that, regardless of reproductive state or stage of pregnancy, the uterus, cervix and placenta express intrinsic daily rhythms in PER2. These tissues may, therefore, act as peripheral circadian clocks in the timing of birth. Supported by the March of Dimes Prematurity Research Center.

F-134

Role of DNA Demethylation in Pregnancy-Mediated Increase in BK_{Ca} Channel-Mediated Relaxations and Decrease in Myogenic Tone of Ovine Uterine Arteries. Daliao Xiao, Xiaohui Huang, Xiang-Qun Hu, Lubo Zhang*. *Loma Linda University School of Medicine, Loma Linda, CA, USA.*

INTRODUCTION: The large conductance Ca^{2+}-activated K^+ (BK_{Ca}) channel plays a critical role in uterine hemodynamic adaptation during pregnancy. Our previous studies revealed that BK_{Ca} channel-mediated relaxations of uterine arteries in pregnant ewes were associated with a decrease in promoter methylation of BK_{Ca} channel β1 subunit (KCNMB1) and increase in KCNMB1 expression. However, it remains undetermined whether inhibition of DNA demethylation may reverse pregnancy-induced increase in BK_{Ca} channel-mediated relaxations of uterine arteries.

METHODS: Resistance-sized uterine arteries were isolated from nonpregnant and near-term pregnant sheep. For *ex vivo* hormonal treatment, uterine arteries from nonpregnant animals were treated with 17β-estradiol (E2β, Sigma) (0.3 nM) and progesterone (P4, Sigma) (100.0 nM) for 48 hours in the absence or presence of a ten-eleven translocation (TET) methylcytosine dioxygenases inhibitor fumarate.

RESULTS: Fumarate significantly inhibited BK_{Ca} channel-mediated relaxations and increased pressure-dependent myogenic tone in uterine arteries from pregnant sheep. Following *ex vivo* treatment with estrogen and progesterone, BK_{Ca} channel-mediated relaxations of uterine arteries from nonpregnant sheep were enhanced and myogenic tone was decreased. However, in the presence of fumarate the hormonal treatment failed to augment BK_{Ca} channel-mediated relaxations and was unable to lower uterine vascular tone.

CONCLUSIONS: Thus, our data suggest that TET plays an essential role in regulating BK_{Ca} channel-mediated functions in uterine arterial adaptation to pregnancy.

F-135

MicroRNA 210 Inhibits Large Conductance Ca^{2+}-Activated K^+ Channel Activity and Functions in Ovine Uterine Arteries. Xiang-Qun Hu, Daliao Xiao, Xiaohui Huang, Lubo Zhang*. *Loma Linda University School of Medicine, Loma Linda, CA, USA.*

INTRODUCTION: The large conductance Ca^{2+}-activated K^+ (BK_{Ca}) channel is a key element in the adaptation of uterine circulation to pregnancy. Gestational hypoxia has profound adverse effects on this adaptation in part by impairing BK_{Ca} channel function, leading to increased incidence of preeclampsia and fetal intrauterine growth restriction. MicroRNAs are small noncoding RNAs that regulate gene expression post-transcriptionally. Recent studies have established a link between a specific group of microRNAs and hypoxia, and microRNA 210 (miR-210) is one of the hypoxia-regulated miRs. Here we tested the hypothesis that miR-210 participates in regulating BK_{Ca} channel function in uterine arteries.

METHODS: Resistance-sized uterine arteries were isolated from nonpregnant and near-term pregnant sheep or animals acclimatized to high altitude (3,801 m) hypoxia for 110 days during gestation. Uterine arteries from pregnant sheep were treated with miR negative control or miR-210 mimic. For *ex vivo* hormonal treatment, uterine arteries from nonpregnant animals were treated with 17β-estradiol (E2β, Sigma) (0.3 nM) and progesterone (P4, Sigma) (100.0 nM) for 48 hours in the absence or presence of miR negative control or miR-210 mimic.

RESULTS: High altitude acclimatization resulted in a significant increase in miR-210 levels in uterine arteries of both nonpregnant and pregnant sheep. The miR-210 mimic significantly inhibited BK_{Ca} channel currents in uterine arteries of pregnant sheep and decreased BK_{Ca} channel-mediated uterine arterial relaxations. In addition, the miR-210 mimic also diminished steroid hormone-induced enhancement of BK_{Ca} channel activity and augmentation of BK_{Ca} channel-mediated relaxations of uterine arteries from nonpregnant sheep. Accordingly, the miR-210 mimic increased pressure-dependent myogenic tone in uterine arteries from pregnant sheep and ablated steroid hormone-induced attenuation of uterine arterial myogenic tone.

CONCLUSIONS: Collectively, we demonstrate that gestational hypoxia increased miR-210 that plays a role in the dysregulation of BK_{Ca} channel function in uterine arterial adaptation to pregnancy, which may contribute to the pathogenesis of pregnancy complications associated with gestational hypoxia.

F-136

Navigating New Motherhood: Evaluating the Role of Patient-Navigator Communication on Postpartum Follow-Up in a Low-Income Community. Angelina M Strohbach†, Fengling Hu†, Noelle G Martinez†, Nadia Hajjar, Melissa A Simon, Lynn M Yee*. *Northwestern University Feinberg School of Medicine, Chicago, IL, USA.*

INTRODUCTION: The Navigating New Motherhood (NNM) program aimed to increase postpartum follow-up among publically insured women by instituting a patient navigator to provide one-on-one support and logistical coordination. This study compares email/text communication between navigators and mothers who did (N=191) and did not (N=25) complete postpartum care.

METHODS: This is a mixed-methods secondary analysis of NNM email/text communication data. Data were analyzed by number of messages sent, received, and unanswered. Conversation (bidirectional message threads) themes were identified using constant comparative technique. T-tests, chi-squared tests, and qualitative analyses were conducted.

RESULTS: In this cohort of young (mean 28.9y), minority (49.5% black, 32.6% Hispanic) women, 98.2% of communication occurred by text message. Patients who completed postpartum follow-up sent and received more texts than patients who did not (7.8 vs 3.7, $p<0.001$ and 11.5 vs 8.0, $p=0.04$). This persisted on multivariable logistic regression, with exchange of ≥6 messages associated with greater odds of follow-up (aOR 2.89, 95% CI 1.13-7.41). Lack of patient response to navigator-initiated texts correlated with lack of patient follow-up ($p<0.001$). Four major content themes were identified: Relational (emotional support, family/personal life, introductions), Postpartum Care Support (appointment purpose/scheduling, transportation), Maternal Health and Transitions (contraception, primary care, insurance), and Motherhood (infant care, maternity leave, breastfeeding).

Theme	Frequency	Average # of Observations Per Thread (Per Patient)		
	N(%)	Completed follow-up (N = 191) Mean (SD)	Did not complete follow-up (N = 25) Mean (SD)	p-value
Relational	828 (44.3%)	3.99 (3.60)	2.64 (1.60)	.002
Postpartum Care Support	801 (42.9%)	3.74 (2.53)	3.48 (2.68)	.65
Maternal Health and Transitions	104 (5.6%)	.52 (1.39)	.20 (.41)	.016
Motherhood	74 (4.0%)	.36 (.80)	.20 (.50)	.17

Conversations with more Relational or Maternal Health and Transitions messages correlated with patient follow-up (p=0.002 and p=0.016).
CONCLUSIONS: In a patient navigation program designed to provide postpartum support, greater message frequency, as well as exchanges focused on maternal health and relationship-building were associated with increased postpartum follow-up.

F-137

Triclosan Exposure During Late Gestation Affects Placental Function in the Pregnant Ewe. Maria B Rabaglino†,[1] Maureen Keller-Wood,[2] Charlie E Wood.[3] *[1]CONICET, Córdoba, Argentina; [2]University of Florida, Gainesville, FL, USA; [3]University of Florida, Gainesville, FL, USA.*
INTRODUCTION: Placenta synthesizes fatty acids and cholesterol due the expression of fatty acid synthase (FASN). Also, placenta protects the fetus from chemicals to which the mother could be exposed. A xenobiotic compound utilized in cosmetics is Triclosan (TCS), which inhibits type I FASN at micromolar concentrations. We hypothesize that maternal exposition to low doses of TCS during a short period of time impairs the transcriptomics of genes related with lipid synthesis on placenta but this effect won't be evident if only the fetus is exposed to TCS. The objective was to determine the genomic effect of TCS exposure on ovine placenta during late gestation after maternal or fetal infusion.
METHODS: Chronically-catheterized ovine fetuses were intravenously infused with TCS (n=3) or DMS:water (n=3). To test maternal exposure, time-dated pregnant ewes were catheterized in jugular vein to infuse TCS (n=3) or DMSO vehicle (n=3). Samples from cotyledons were collected after 3 days of infusion for microarray analysis using the Agilent platform GPL14112. Differentially expressed genes (DEG) between maternal or fetal infused TCS data and control data were determined by moderated t-test. Functional analysis for the up or down-regulated DEG was performed with the DAVID database, using the functional annotation clustering tool.Selected DEG were validated by qRT-PCR.
RESULTS: The number of DEG after fetal TCS infusion was greater than after maternal TCS infusion (363 versus 189 DEG, respectively). The main clusters significantly enriched with the genes up-regulated in placenta after maternal TCS infusion were related with response to corticoid stimulus, intracellular signaling and hemopoiesis. For the down-regulated genes, and as hypothesized, the clusters were related with lipid, cholesterol and steroid biosynthesis. Fetal infusion of TCS induced different genomic responses: The up-regulated genes enriched for mitosis, cell cycle and DNA repair while the down-regulated genes enriched for clusters related with high density lipoprotein particle and regulation of lymphocyte proliferation.
CONCLUSIONS: Maternal TCS exposure to TCS during late gestation impairs important placental functions such as lipid/cholesterol biosynthesis and hemopoiesis. These effects could have potential consequences on fetal development and impact on its postnatal physiology.

F-138

Placental Gene Expression Is Affected by Male Fetal Sex and Maternal Genotype in Fetal Growth Restriction Model. Jessica F Hebert†,[1,2] Jess Millar,[2] Amie Romney,[2] Rahul Raghavan,[2] Jason Podrabsky,[2] Terry K Morgan.[1] *[1]Oregon Health and Science University, Portland, OR, USA; [2]Portland State University, Portland, OR, USA.*
INTRODUCTION: Our transgenic (TG) model has elevated maternal angiotensinogen expression (120% of WT controls), resulting in fetal growth restriction and abnormal uteroplacental angiogenesis that disproportionately affects male offspring. We hypothesized that placental pathways involved in angiogenic regulation may be negatively impacted by maternal genotype and fetal sex.
METHODS: Placental global gene expression was assessed by RNASeq (Illumina, CLC) using day 16.5 placentas from TG and WT dams (four litters each). Fetal sex was considered a potential covariate. Differentially expressed genes between maternal genotypes segregated by fetal sex were chosen based on significance (P<0.05, FDR-corrected). Gene ontology terms enriched among up/down-regulated genes were assigned using DAVID.
RESULTS: RNASeq analysis suggested males from TG dams upregulated more genes than female siblings and wild-type controls. Surprisingly, there was relatively increased, not decreased, expression of key genes within angiogenic and nutrient transporter pathways.
CONCLUSIONS: Our prior studies have demonstrated reduced uteroplacental angiogenesis in male growth restricted progeny. However, placental gene expression within angiogenic and nutrient transporter pathways appears to be upregulated in male progeny. Additional work is needed, but we suspect our observations are most consistent with a compensatory upregulation mechanism that is insufficient to rescue birthweight in our transgenic model.

F-139

Exosomal Profile of Enzymes Involved in the Biosynthesis of Eicosanoids Generated by Human Gestational Tissues. Hassendrini N Peiris†, Kanchan Vaswani, Sarah Reed, Murray D Mitchell. *University of Queensland, Brisbane, QLD, Australia.*
INTRODUCTION: Enzymes involved in the biosynthesis of clinically significant eicosanoids and their metabolites have been identified to be important in uteroplacental hemodynamics and other critical aspects of pregnancy. In fact, FAAH protein, mRNA expression and activity in peripheral lymphocytes, are reduced in women who miscarry spontaneously or fail to maintain pregnancy. Exosomes are stable nanovesicles acknowledged for their role in cell-to-cell communication through delivery of their protein, mRNA and miRNA cargo. The increased availability via exosome delivery of enzymes involved in eicosanoid biosynthesis may alter eicosanoid biosynthesis and in turn affect pregnancy outcomes. **Aim:** To investigate the exosomal cargo generated by early pregnancy and term placentae for mRNA transcripts of enzymes involved in eicosanoid biosynthesis.
METHODS: Exosomes isolated from the culture media of early pregnancy and term villous explants cultured for 24 hours under 3 oxygen conditions (8%, 3% and 1%). Total exosomal RNA was extracted by the Qiagen ™ RNeasy kit and quantified by Nanodrop™. Custom PCR arrays (Qiagen ™) were used to study the presence and relative expression of 18 enzymes involved in eicosanoid biosynthesis (KAT5, PLA2G2A, PLCB1, PLCB2, FAAH, PTGS1, PTGS2, HPGD, PTGES, PTGIS, TBXAS1, HPGDS, DAGLA, MGLL, PTGES2, PTGES3, NAT1, NAPEPLD) between the 3 oxygen conditions; 8%, 3% and 1%. Statistical analysis was by One-way ANOVA.
RESULTS: Several genes showed specific trends, with significant changes observed with oxygen concentration, whereby 16 of the 18 genes had decreased expression with decreasing oxygen. However two genesphospholipase A2, group IIA (PLA2G2A) which catalyses the conversion of phospholipids into arachidonic acid and prostaglandin E synthase 3 (PTGES3) which converts prostaglandin endoperoxide H_2 (PGH_2) to prostaglandin E_2 (PGE_2) increased at 3% compared to 8% and 1%. Low oxygen has been related to poor implantation, placental development and pregnancy complications.

CONCLUSIONS: Here we describe the detection of eicosanoid enzymes within exosomes generated by human placentae. These enzymes (e.g. PTGS2, PLA2G2A, PTGES3) have been shown to be critical in key areas of pregnancy and labor. Hence, exosomal content of these mRNA may have utility as specific biomarkers, and aid in the early detection of pregnancy complications and/or imminent preterm labor.

F-140

Exposure to CrVI During Early Pregnancy Increases Oxidative Stress and Disrupts the Expression of Antioxidant Proteins in Placental Compartments. Sakhila K Banu, Jone A Stanley, Kirthiram K Sivakumar, Joe A Arosh. *Texas A&M University, College Station, TX, USA.*

INTRODUCTION: Epidemiologic studies document relationships between chromium VI (CrVI) exposure and increased risk of spontaneous abortion, stillbirth, preterm birth, and neonatal death in pregnant women. Environmental contamination with CrVI is a growing problem both in the U.S and developing countries. CrVI is widely used in numerous industries. Once in contact with the cells or biological fluid, CrVI is rapidly converted to CrIII by endogenous antioxidants such as vitamin C, glutathione and N-acetyl cysteine. During this reduction process enormous amount of free radicals are released which increases oxidative stress. CrIII can bind with DNA and forms Cr-DNA adducts, causing mutations and/or DNA strand breaks.

METHODS: The current study was designed to understand the mechanism of CrVI toxicity on placental oxidative stress and antioxidant machinery. Pregnant mother rats were treated with or without CrVI (25 ppm $K_2Cr_2O_7$) through drinking water from gestational day (GD) 9.5 – 14.5, and placentas were analyzed on GD 18.5.

RESULTS: Results indicated that CrVI reduced the trophoblast cell population in the basal and labyrinth zones, and trophoblast invasion into metrial gland. CrVI increased reactive oxygen species (ROS) and decreased the expression of antioxidant proteins Gpx1, Sod1 Sod2, Prdx3 and Txn2 in a spatio-temporal manner. Interestingly, CrVI decreased cyp11a1, a trophoblast giant cell marker, and increased uterine natural killer cells in the labyrinth zone, which is an adverse indication of placental pathology. CrVI also disrupts the trophoblast proliferation of the placenta by decreasing cyclin D1.

CONCLUSIONS: The current study provides an insight into the critical role of CrVI and antioxidants in placental function.

F-141

Sex-Specific Differences in Placental Methylation That Are Associated with Transcript Abundance. MD Johnson†, S Gong†, U Sovio†, J Dopierala†, F Gaccioli†, M Constância, DS Charnock-Jones, GCS Smith*. *University of Cambridge, Cambridge, United Kingdom.*

INTRODUCTION: Fetal sex is associated with the risk of a number of specific pregnancy complications related to placental function. Previous studies have suggested sex-related differences in the placental transcriptome. However, the molecular basis of sex-specific differences in human placental gene expression remains unclear. Previous studies have demonstrated the role for DNA methylation in placental genomic imprinting, providing the possibility for DNA methylation regulating transcript abundance. However, the only study which has analysed the placental methylome using whole-genome bisulfite sequencing (*PNAS* 110:6037–6042,2013) could not address sex-specific patterns as only 1 placenta was analysed.

METHODS: Whole genome oxidative bisulfite sequencing (oxBS-seq) was carried out on 2 male and 2 female healthy term placentas from the Pregnancy Outcome Prediction study (*Lancet* 386:2089–2097,2015). Validation was carried out using an in-solution target capture methodology analysing two of the samples from oxBS-seq (technical replicates) and a further 6 samples (3 female and 3 male placentas, biological replicates). RNA-sequencing was carried out on 64 female and 67 male healthy term placentas with an average of 95 million mapped reads per sample.

RESULTS: oxBS-seq provided 14,960,649 CpG sites that were sequenced at a depth of >10x and shared among all four individuals. Sex-specific differential methylation analysis identified a locus with twenty 5000-base regions ranked amongst the top 100 differentially methylated regions (DMRs) (Fisher's Exact test,$P=5.6x10^{-40}$). These 20 regions were located within a 225kb locus in the CUB and Sushi Multiple Domains 1 (*CSMD1*) gene on chromosome 8. Females were consistently and significantly hypo-methylated compared to males (48% vs 72%, respectively). The pattern of differences were also observed in the technical and biological replicates (Fisher's Exact test,$P=3.5x10^{-22}$,$P=4.5x10^{-180}$, respectively). The transcript abundance of *CSMD1* was lower in females compared to males (Mann-Whitney test,$P=8.5\ x10^{-7}$). This sex-specific DMR is likely to be placental specific because it was not present in 8 female and 8 male somatic tissues from the RoadMap epigenetics consortium.

CONCLUSIONS: We show that a 225kb region of *CSMD1* is differentially methylated and differentially expressed in a sex-specific manner in the placenta. The consequences of this sex-specific DMR warrant further investigation.

F-142

Sex-Specific Differences in Human Placenta Transcriptome. Justyna Dopierala, Sung Gong, Ulla Sovio, Gordon CS Smith, D Stephen Charnock-Jones*. *University of Cambridge, Cambridge, Cambridgeshire, United Kingdom.*

INTRODUCTION: The transcriptome of the human placenta has been described but these studies are either not designed to capture sex-specific differences or are based on microarray, which has limited coverage of the transcriptome. Our aim was to characterize both protein-coding and long non-coding sex-specific transcripts in healthy human placenta using RNA-seq.

METHODS: We sequenced total RNA from 88 well phenotyped healthy placentas (40 female and 48 male) collected as part of the Pregnancy Outcome Prediction study in which the placental sample was obtained within 30 minutes of delivery (healthy individual=no hypertension during pregnancy, no diabetes mellitus, delivered a live baby with a birth percentile >=10). We performed quality assessment, trimming and mapping using FastQC, Trim Galore!, and TopHat respectively. Differential gene expression analysis was carried out using edgeR. We validated the significant transcripts in an independent set of 24 samples (12 male-female breech pairs, delivered at term by elective C-section and matched for maternal age, BMI and smoking status).

RESULTS: We obtained an average of 102 million reads per sample. We identified 243 differentially-regulated transcripts (DRTs) in the discovery set (FDR<0.05) and validated 84 of these (36 up- and 48 down-regulated in females). Interestingly, 26/84 (31%) DRTs were non-coding RNAs: 18/29 on the Y chr, 6/35 on the X chr and 2/20 on the autosomes. As expected, none of the Y chr transcripts were expressed in females. 28 X chr genes had higher levels of expression in females, indicating escape from X inactivation. But, surprisingly, we also identified 7 protein-coding X chr genes which demonstrated higher levels of expression in males (at least 3 located in the pseudoautosomal regions). 11 protein-coding Y chr genes were expressed in the placenta. All of these had an X chr paralog but only 6 of the X chr paralogs demonstrated escape from X inactivation.

CONCLUSIONS: (1) Male and female placenta show sex-specific transcript profile differences, and approximately one third are non-coding RNA. (2) Most (76%) DRTs in human placenta are X- or Y-linked. (3) 6/11 X chr genes with an expressed Y chr paralog demonstrated escape from X inactivation, but the remaining 5 did not. (4) Overall, our findings indicate multiple mechanisms leading to sex-specific variation in placental expression of protein coding genes, plus a large number of validated differences in non-protein coding DRTs.

F-143

Inter-Correlations Between Multiple Maternal Serum Placental Biomarkers in the First Trimester. Viola Seravalli, Dana Block-Abraham, Jena Miller, Ahmet Baschat. *Johns Hopkins Hospital, Baltimore, MD, USA.*

INTRODUCTION: Multiple first-trimester biomarkers of placental angiogenesis, placental mass and placental inflammation have been proposed for the prediction of placental dysfunction. While their association with pregnancy outcome, and their correlation with maternal factors have already been described, there is little information about

their inter-correlations in individual women. It was our aim to evaluate the relation of placental markers between each other in a U.S. patient population.

METHODS: Prospective observational study of women presenting for first-trimester screening at 11+0 to 13+6 weeks of gestation. Serum concentrations of Angiopoietin-2 (Ang-2), Placental growth factor (PlGF), Pregnancy associated protein-A (PAPP-A), placental protein-13 (PP-13) and Pentraxin-3 (PTX-3) were measured. Levels of markers were correlated to each other using correlation analysis.

RESULTS: Serum concentrations of biomarkers were measured in 111 patients. Median serum levels were 4.7 ng/mL (IQR 3.8, 6.3) for Ang-2, 48.6 pg/mL (IQR 29.3, 66.5) for PlGF, 67 pg/mL (IQR 42.2, 115.6) for PP-13, and 0.95 ng/mL (IQR 0.60, 1.73) for PTX-3. Median PAPP-A MoM was 1.07 (0.75, 1.51). Ang-2 had a moderate correlation with PlGF (Spearman's rho, r_s 0.46, p<0.001) and a weak correlation with PP-13 and PAPP-A MoM (r_s 0.31 and 0.20, p<0.05). PAPP-A MoM also weakly correlated with PlGF (r_s 0.35, p<0.001) and PP-13 (r_s 0.27, p=0.01). PTX-3 had no significant relationship with any other marker.

**Figure(s) will be available online.*

CONCLUSIONS: Biomarkers of placental angiogenesis and placental mass have weak inter-correlations in individual women at 11-14 weeks. It is possible that such biomarkers reflect placental development at different gestational windows, or that some markers perform better in selected populations with specific risk profiles.

F-144

Knockdown of GNA11 Decreases VEGFA- and FGF2-Stimulated Human Fetoplacental Endothelial Migration Under Physiological Chronic Normoxia. Qing-Yun Zou†,[1] Ying-Jie Zhao,[1,2] Hua Li,[1,3] Xiang-Zhen Wang,[1,4] Chi Zhou,[1] Jing Zheng*.[1] *[1]University of Wisconsin-Madison, Madison, WI, USA; [2]Qilu Hospital, Shandong University, Jinan, Shandong, China; [3]The Affiliated Hospital of Qingdao University, Qingdao, Shandong, China; [4]Nanshan District Maternal and Child Healthcare Hospital, Shenzhen, Guangdong, China.*

INTRODUCTION: During pregnancy, fetoplacental angiogenesis is dramatically increased in association with rapidly elevated blood flow. Any disruption of fetoplacental angiogenesis may cause pregnancy complications such as intrauterine growth restriction. Heterotrimeric guanine nucleotide binding proteins (G proteins) are known as key mediators of many endothelial functions. G protein α subunit 11 (GNA11), a member of Gαq subfamily, is actively involved in mediating vascular growth and basal blood pressure. However, little is known about its roles in mediating the VEGFA- and FGF2-stimulated fetoplacental endothelial functions.

METHODS: Human umbilical cord vein endothelial cells (HUVECs) were isolated from healthy pregnant women after term, and were constantly cultured under 3% O_2 (37°C, 5% CO_2, ~92% N_2, which is Physiological Chronic Normoxia) till passages 4-5. Human GNA11 siRNA was used for gene knockdown. Western blotting was used to determine knockdown efficiency. Cell migration and proliferation in response to VEGFA and FGF2 were assayed using a transwell system and crystal violet method, respectively.

RESULTS: GNA11 siRNA significantly decreased ($p < 0.05$) GNA11, but not GNA14 (another member of Gαq subfamily), protein levels by ~70% as compared with the scrambled siRNA control. GNA11 siRNA also dramatically inhibited ($p < 0.05$) the VEGFA- and FGF2-stimulated migration of HUVECs by ~50% and ~36%, respectively, as compared with the scrambled siRNA control. However, GNA11 siRNA did not alter either the VEGFA- and FGF2-stimulated cell proliferation, or the VEGFA- and FGF2-induced ERK1/2 and AKT1 phosphorylation.

CONCLUSIONS: Though its downstream signaling pathways remain elusive, GNA11 differentially regulates the VEGFA- and FGF2-stimulated migration and proliferation of HUVECs, suggesting its importance in fetoplacental angiogenesis under physiological chronic normoxia. NIH: HD38843 (JZ).

F-145

Autophagy Inhibition by Chloroquine Increased Invasion of HTR8/SVneo Trophoblast Cells. Juyoung Park†,[1] Ji-Hee Sung,[1] Minji Choi,[2] Jae Ryoung Hwang,[2] Suk-Joo Choi,[1] Soo-young Oh,[1] Jong-Hwa Kim,[1] Cheong-Rae Roh.[1] *[1]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; [2]Samsung Biomedical Research Institute, Samsung Medical Center, Seoul, Republic of Korea.*

INTRODUCTION: Trophoblast invasion is regulated by various cellular processes, including apoptosis, proliferation, and differentiation. Recent evidences have suggested that autophagy is involved in trophoblast invasion. In this study, we aimed to investigate the effect of chloroquine, which is a well-known drug for malaria and autoimmune disorders and also blocks autophagy by inhibiting lysosomal acidification, on trophoblast invasion using HTR8/SVneo cells.

METHODS: HTR8/SVneo cells (which was kindly given from Dr. Charles H. Graham) was treated with chloroquine and invasion assay was performed using Transwell inserts coated with Matrigel. Inhibition of autophagy by chloroquine was assessed by western blot for LC3 and p62 and also by autophagy flux assay with bafilomycin. Cell viability in the presence of different dose of chloroquine was measured by MTT assay.

RESULTS: Inhibition of autophagy by chloroquine in HTR8/SVneo cells was confirmed by western blot for LC3 and p62. We found that cell viability of HTR8/SVneo cells was not affected with 10 and 20μM of chloroquine. Notably, invasion of HTR8/SVneo cells treated with chloroquine (10 and 20μM) was significantly increased (approximately three-fold increase) compared with the control cells.

CONCLUSIONS: Autophagy inhibition by chloroquine increased trophoblast invasion in HTR8/SVneo cells. Autophagy modulators may be considered as one of therapeutic target to improve trophoblast invasion and to attenuate defective placentation.

Funding: This work was supported by National Research Foundation of Korea (NRF) funded by the Korea government (Ministry of Education, Science and Technology) [2011-0016004].

F-146

Variable Effect of Docosahexaenoic Acid (DHA), Depending on Their Concentration, in the Trophoblast Function In Vitro. Jorge A Carvajal, Ana M Delpiano, Gloria L Valdes. *Escuela de Medicina, Pontificia Universidad Católica de Chile, Santiago, RM, Chile.*

INTRODUCTION: Early reports suggested that DHA rich diet reduces the incidence of deep placentation disorders. We suggest prenatal administration of DHA improves migration of EVT contributing to normal deep placentation. However, the DHA doses to be used in clinical supplementation vary among studies. Here we evaluated the effect of different doses of DHA on EVT function in vitro.

METHODS: We measured trophoblast function (migration assay) and cytokine production, using immortalized extravillous trophoblast cell line (HTR-8/SVneo), under the chronic effect of different concentrations of DHA (0; 1; 10 and 50μM). HTR-8/SVneo cells were cultured until confluence in complete medium supplemented with DHA [0-50 μm]. **Migration assay (wound-healing):** a "wound" was generated by removing cells in the center of the well, and cell migration was measured after 10 h. The migration assay was performed 4 times in duplicate; three images were obtained along the wound and quantified using ImageJ v.1.34 software. The area of the wound was calculated and the "healing" of the wound was estimated as the area recovered by cells at the end of the experiment. We also measured cytokine production in the culture media of the migration assay by RT-qPCR: IL-1β; TNFα; IL-6; and IL-8.

RESULTS: After 10 h of experiment the wound was healed by 53% in the absence of DHA. At 1 μM DHA the trophoblast cell migration was significantly larger (58% of the wound was healed). Interestingly higher concentrations of DHA decrease EVT migration (51% and 43% at 10μM and 50μM DHA respectively). DHA, at 10 and 50 μM, but not at 1μm, significantly increased the levels of IL-1β. The levels of TNFα were not altered by DHA; however, IL-6 and IL-8 were significantly reduced by 10 and 50 μM DHA.

CONCLUSIONS: Chronic incubation with low concentration of DHA (1 μM) improves trophoblast function in vitro, without changes in cytokine

production. Higher concentrations of DHA (both 10 and 50 μM) reduced trophoblast migration. The reduced trophoblast migration induced by DHA can be explaining by increased levels of IL-1β. We postulate that DHA supplementation during pregnancy may exert a beneficial or detrimental effect on placentation, via different mechanisms and depending on dosage. This information should be considered when planning clinical trials of DHA supplementation during pregnancy. Financial Support: FONDECYT 1141207.

F-147

Chronic Hypoxia Disrupts Mitochondrial Function in the Guinea Pig Placenta. Hong Song,[1] Bhanu P Telugu,[2] Loren P Thompson*.[1] [1]*Univ. of MD, Baltimore, MD, USA;* [2]*Univ. of MD, College Park, MD, USA.*

INTRODUCTION: Oxygen plays an important role in trophoblast invasion and spiral artery remodeling in the placenta. We have previously shown that hypoxia (HPX) inhibits trophoblast invasion into spiral arteries of the guinea pig (GP) placenta. We propose that chronic HPX disrupts the cellular transformation of trophoblasts to an invasive phenotype by altering mitochondrial function. To test this, we investigated the effect of HPX on mitochondrial density, protein expression, and nitration of mitochondrial proteins of GP placentas.

METHODS: Pregnant GPs were exposed to either normoxia (NMX; N=6) or hypoxia (HPX; N=6; 10.5%O_2 at 25d gestation when TB invasion begins) until term (65d). GPs were anesthetized and maternal blood pressures (BP) measured from a cannulated brachial artery. Fetuses and placentas were excised and weighed and placental tissue was stored at -80C until the time of the assay. Mitochondria were isolated from placental tissue and density (mitoDNA/nuclear DNA ratio, qPCR), and protein expression (Western analysis) of nitrotyrosine and respiratory Complexes I-V were compared between NMX and HPX.

RESULTS: HPX decreased (P<0.05) mitochondrial density by 19% and increased nitrotyrosine expression of isolated mitochondria from GP placenta. Nitrated bands were detected at MWs corresponding to Complexes I and IV of the respiratory chain. HPX increased (P<0.01) nitrotyrosine expression (normalized to VDAC) by 2.7 (I: 0.18±0.08 vs 0.49±0.14 expression level) and 8.1 fold (IV: 0.10±0.02 vs 0.79±0.13; NMXvsHPX, respectively). HPX increased (P<0.03) normalized protein expression of Complex IV (0.037±0.003 vs 0.078±0.017) but had no effect on Complexes I-III,V. HPX increased BP (40.4±2.1mmHg vs 58.7±6.0mmHg), had no effect on placental wt but decreased (P<0.1) fetal body weight (94.2±4.3 vs 64.1±3.3g; NMX vs HPX, respectively), resulting in an increased placental wt/fetal wt ratio (0.051±0.002 vs 0.072±0.008) in HPX GPs.

CONCLUSIONS: Chronic HPX induces maternal hypertension, fetal growth restriction and placental insufficiency in the pregnant GP. Placental HPX may downregulate mitochondrial function by reducing its cellular density and increasing nitration of respiratory chain proteins. While this may limit oxygen consumption as an adaptive response, it may compromise normal processes of placental development such as trophoblast differentiation and spiral artery remodeling. (HL-126859-LPT).

F-148

How Well Does Ultrasound Identify Abnormal Placental Cord Insertion? Amelia S McLennan†, Victoria X Yu†, Cande V Ananth, Russell S Miller, Cynthia Gyamfi-Bannerman*. *Columbia University Medical Center, New York, NY, USA.*

INTRODUCTION: To evaluate the test characteristics of midtrimester ultrasound as a tool for identifying abnormal placental cord insertion (PCI).

METHODS: This was a retrospective cohort study involving singleton pregnancies from 2004-15 identified to have abnormal PCI at the time of anatomy ultrasound (16-24 weeks gestation). Abnormal PCI was classified as either marginal (placental mass visualized on only one side of cord insertion) or velamentous (no placental mass visualized on either side of cord insertion) upon image review by a single investigator (ASM). Cases were matched by date and gestational age at ultrasound with normal PCI controls. The decision to send a placenta to pathology was at the delivering provider's discretion according to departmental guidelines. Pathology evaluation was recommended for any suspicion of abnormal cord insertion. For placentas that were evaluated postnatally by a pathologist, ultrasound diagnosis and final pathology results were compared.

RESULTS: 464 cases of sonographically abnormal (marginal or velamentous) PCI were identified during the study period and matched with the same number of controls. 221 placentas (23.8% of overall cohort) had postnatal pathologic evaluation of PCI, including 126 (57%) with sonographically abnormal PCI and 95 (43%) with sonographically normal PCI. Upon placental evaluation, a normal PCI was identified in 43% of cases, marginal PCI in 26%, and velamentous PCI in 31%. There was a substantial proportion of crossover between the abnormal PCI groups, with 24 cases of sonographically marginal PCI found to be velamentous upon placental pathology, and 12 cases of sonographically velamentous PCI found to be marginal upon placental pathology. However, ultrasound correctly identified 93% of all abnormal cord insertions when marginal and velamentous PCI were considered together. Of the 69 cases of pathology-confirmed velamentous cord insertion, 100% were identified as abnormal prenatally (either marginal or velamentous), with a false positive rate of 3%.

CONCLUSIONS: Midtrimester ultrasound can accurately identify abnormal PCI.

Table 1: Accuracy of ultrasound to detect pathologically-confirmed abnormal cord insertion

	Sensitivity	Specificity	PPV	NPV
Marginal PCI (n=57)	63%	77%	49%	86%
Velamentous PCI (n=69)	65%	88%	70%	85%
Any abnormal PCI (n=126)	93%	79%	85%	89%

F-149

The Effectiveness of Tadalafil in Reversing Vasoconstriction in an *Ex Vivo* Human Placental Perfusion Model of Fetal Growth Restriction. Robert B Walton†,[1] Luckey C Reed†,[1] Sarah M Estrada†,[1] Peter G Napolitano,[1] Nicholas M Ieronimakis.[2] [1]*Madigan Army Medical Center, Tacoma, WA, USA;* [2]*Madigan Army Medical Center, Tacoma, WA, USA.*

INTRODUCTION: Fetal growth restriction (FGR) is a major cause of neonatal morbidity and mortality, and there are no treatments. Sildenafil citrate (SC), a phosphodiesterase 5 inhibitor (PDE5I), is a possible treatment to prolong pregnancies affected by FGR. Using a dual perfusion, dual cotyledon human placenta model we mimicked vasoconstriction-associated FGR. Previously, we found a 41.2% reduction in feto-arterial pressures with maternal infusion of SC. Tadalafil (TD), a more selective and potent PDE5I, has not been studied in FGR. We hypothesized TD is superior to SC in improving blood-flow in pregnancies with FGR. The primary objective was to determine if maternal infusion of TD would attenuate feto-arterial vasoconstriction in our model.

METHODS: Four of seventeen normal term placentas from scheduled C-sections were included. Two cotyledons from each placenta were isolated and infused with U46619, a thromboxane mimetic, into the maternal and fetal circuits to induce vasoconstriction. TD was then infused into the maternal circuit of the treatment cotyledon and normal buffer in the control for 30 minutes. Feto-arterial pressures were recorded. Results were reported as a ratio of maximum fetal arterial pressure divided by minimum pressure after TD or control. Statistical analysis was performed using a Student's *t* test.

RESULTS: Maternal infusion of TD did not significantly attenuate feto-arterial vasoconstriction in our FGR model, (10.0% vs. 14.0% reduction in pressures for treatment vs. control, p=0.50).

**Figure(s) will be available online.*

Direct administration of TD in the fetal artery did reduce feto-arterial pressures.

CONCLUSIONS: Maternal infusion of TD does not attenuate the vasoconstriction in our placenta model of FGR. However, direct administration of TD in the fetal circuit does attenuate the vasoconstriction. This suggests that TD may not cross the human placental barrier or is otherwise metabolized. Evaluation of the feto-venous effluents is underway to determine the transport of these PDE5s.

F-150

Novel Localization of Hepcidin at the Human Maternal-Fetal Interface. Elizabeth Taglauer†,[1] Danielle Wuebbolt,[2] Elizabeth Tully,[3] Fionnuala Breathnach,[3] Amir Khan,[4] Sarbattama Sen*.[5] *[1]Children's Hospital Boston, Boston, MA, USA; [2]Royal College of Surgeons Ireland, Dublin, Ireland; [3]Royal College of Surgeons Ireland, Dublin, Ireland; [4]Trinity College Dublin, Dublin, Ireland; [5]Brigham and Women's Hospital, Boston, MA, USA.*

INTRODUCTION: Hepcidin is a well-characterized peptide hormone involved in iron homeostasis. Recently, hepcidin has been implicated in alterations of iron transfer to the fetus during pregnancy. We have found that maternal serum hepcidin is upregulated by pro-inflammatory conditions such as maternal obesity, which may contribute to impaired maternal-fetal iron transport. Hepcidin also has significant antimicrobial properties, which may play a role in protection against transplacental infections. Hepcidin is primarily produced in the liver, but prior studies have also identified hepcidin mRNA and protein in first trimester placentas. However, a comprehensive localization analysis of this protein within the term placenta has not been performed to date. We hypothesized that hepcidin is expressed within key functional areas the term placenta.

METHODS: Using immunofluourence with confocal microscopy, we visualized hepcidin expression in healthy, term placental tissues (N=6). Our analysis included villous tissue, basal plate, decidua and fetal membranes.

RESULTS: We identified hepcidin in the outer syncitiotrophobst layer ubiquitously within the placental villous tissue. Additionally, we found consistent hepcidin expression in the endothelium of both large and small fetal blood vessels throughout placenta from all patients in our study.

CONCLUSIONS: Hepcidin is consistently expressed in the term fetal placenta, specifically within areas that are in direct contact with maternal blood. Given hepcidin's key role in iron homeostasis and its significant antimicrobial properties, our findings raise the possibility that hepcidin may be actively produced by the fetal placenta for a variety of functions during pregnancy. Further analysis of placental hepcidin could identify novel targets to improve fetal nutrient transfer and prevent transplacental infections.

F-151

Unexplained Antepartum Stillbirth Is Associated with Biochemical Evidence of Placental Aging. Kaushik Maiti,[1] Zakia Sultana,[1] John Aitken,[2] Roger Smith*.[1] *[1]University of Newcastle, Newcastle, NSW, Australia; [2]University of Newcastle, Newcastle, NSW, Australia.*

INTRODUCTION: Risks of unexplained stillbirth rise late in gestation consistent with aging. We hypothesized that placentas after 41 completed weeks of gestation would show biochemical changes consistent with ageing that would also occur in placentas from stillbirths.

METHODS: We collected placentas from women at 37-39 weeks gestation (term, n=35), at 41^{+} weeks (post-dates, n=29), and associated with unexplained still-birth (n=4). We compared the first two groups for: qPCR for telomere length and expression of aldehyde oxidase (AOX1), oxidized DNA (8-hydroxy-guanosine), oxidized lipid (4-hydroxynonenal, 4HNE), autophagosome formation (LC3B), lysosomal distribution (LAMP2) and mTOR pathways using immunohistochemistry (IHC) and western blot. We compared stillbirth placentas with term placentas for oxidative damage and distribution of autophagosomes and lysosomes. We tested whether aldehyde oxidase mediated the oxidative damage to lipids and the formation of autophagosomes using placental explant cultures.

RESULTS: Placentas at 41 weeks had shorter telomeres($p=0.0339$), higher oxidized DNA ($p<0.0001$) and 4HNE ($p<0.0001$), and larger autophagosomes ($p=0.012$). mRNA for AOX1, which generates 4HNE was increased ($p=0.0097$) andIHC demonstrated a change in the distribution of LAMP2, a lysosomal marker, to the basal side of the syncytiotrophoblast in post-dates placentas and Western blot showed increased mTORC1 activity (phos-P70S6 kinase, $p=0.0003$). All stillbirth placentas showed increased oxidative damage, increased AOX1, altered LAMP2 distribution and larger autophagosomes as seen in post-dates samples. Placental explant culture without serum significantly increased AOX1, 4HNE, and autophagosomes size at 24 hours. The production of 4HNE was inhibited by the rapamycin (mTOR inhibitor), raloxifene (AOX1 inhibitor), and G1, an agonist for the G-protein estrogen receptor 1.

CONCLUSIONS: Oxidative damage to DNA and lipids, accumulation of larger autophagosomes and altered lysosomal distribution are seen in placentas from both post-dates and unexplained antepartum stillbirth. 4HNE production in explant culture was inhibited by mTOR inhibition, AOX1 inhibition and estrogenic stimulation. These data suggest that placental aging involving oxidative damage to lipids and disruption of autophagy is mediated by AOX1, mTOR and inhibited by cell surface estrogen signaling, these are potential targets for therapeutics to reduce the risk of stillbirth.

F-152

High Maternal Omega-3 Fatty Acid Levels in Hawaiian Women Impair Placental Lipid Storage. Fernanda L Alvarado†,[1] Virtu Calabuig-Navarro†,[1] Pai-Jong S Tsai,[2] Perrie O'Tierney-Ginn.[1] *[1]Case Western Reserve University, Cleveland, OH, USA; [2]University at Buffalo, Buffalo, NY, USA.*

INTRODUCTION: Placentas of obese women have higher lipid content compared to lean women. We have previously shown that supplementation of overweight and obese women with omega-3 fatty acids, decreases placental esterification pathways and total lipid content, in a mid-western population (Ohio). We hypothesized that placental lipid esterification pathways and storage would be similar between lean and obese women living in a region of high omega-3 intake, such as Hawaii.

METHODS: 84 healthy, normal glucose tolerant women (pregravid BMI 16-53 kg/m^2) from Honolulu Hawaii, were recruited at scheduled term cesarean delivery. Maternal plasma DHA levels were analyzed by mass spectrophotometry. Expression of key genes involved in fatty acid esterification (*PPARg, DGAT1, FAS, and ACCa*) were measured in placental tissue using qPCR. Total lipids were extracted from placental tissue via the Folch method. One-way ANOVA was used to assess differences between groups. P value <0.05 was considered statistically significant.

RESULTS: As expected, maternal DHA levels were, on average, higher in this cohort (383 µmol/L) as compared to pregnant women with similar characteristics in Ohio (156 µmol/L, n=8). Furthermore, DHA levels were higher in lean Hawaiian women compared to overweight and obese women (P =0.01). Placental lipid content and expression of DGAT1, FAS, PPARg and ACCa were similar (P>0.05) between lean, overweight and obese women.

	Lean	Overweight	Obese	*P value*
n	29	24	31	
Pregravid BMI (kg/m^2)	21.1±2.2	27.6±1.3	37.2±7	**<0.0001**
Maternal DHA (µmol/L)	453±187	360±116	336±123	**0.01**
Gestational Age (wks)	38±0.6	38±0.4	39±0.3	0.207
Birth Weight (g)	3295±409	3459±538	3591±448	0.05
Placental weight (g)	472±88	523±99	562±98	**0.002**
Total lipid content (mg/g tissue)	18±6	15±7	17±4	0.28

CONCLUSIONS: Though overweight and obese Hawaiian women have lower DHA levels compared to their lean counterparts, these levels remain over twice as high as Ohio women. These relatively high plasma omega 3 levels in overweight and obese Hawaiian women may suppress the ability of the placenta to esterify and store lipids to the same levels of lean women. This curbed ability to store lipids may increase fetal growth.

F-153

Next-Generation miRNA Sequencing Reveals That Exosomes Present in Maternal Circulation of Gestational Diabetes Pregnancies Regulate Glucose Metabolism in Placental Cells. Stefanie Adam,[1] Dominic Guanzon,[1] Katherin Scholz-Romero,[1] Omar Elfeky,[1] Sherri Longo,[2] Andrew Lai,[1] Gregory Duncombe,[1] Gregory E Rice,[1,2] Martha Lappas,[3] Carlos Salomon.[1,2] *[1]The University of Queensland, Brisbane, QLD, Australia; [2]Ochsner Baptist Hospital, New Orleans, LA, USA; [3]University of Melbourne, Melbourne, VIC, Australia.*

INTRODUCTION: There has been explosive interest in the role of exosomes highlighting its ability in mediating cell-to-cell communication and delivering bioactive molecules during gestation. The aim of this study was to determine the exosomal miRNA profile in women with gestational diabetes mellitus (GDM).

METHODS: Samples were obtained from maternal plasma isolated from women with GDM, treated with diet (GDM-diet) or insulin (GDM-insulin), and normal (control) pregnancies at the time of delivery. Exosomes were isolated through differential and buoyant density centrifugation. Illumina TrueSeq Small RNA kit was used to construct a small RNA library. The resulting sequencing FASTQ file was analyzed using miRDeep2, a program specifically designed to identify both known and novel microRNA's. BeWo cells were incubated with exosomes under an atmosphere of 5% Co2 and 8% O_2. Glucose metabolism was assessed by RT2 Profiler PCR Array Human Glucose Metabolism kit for gene expression of 84 key genes involved in enzymatic pathways.

RESULTS: The total number of exosomes and placenta-derived exosomes present in maternal circulation was higher in GDM compared to control. Controls have different miRNA expression compared to GDM-diet and GDM-insulin. Gene target identification using CyTargetLinker of the top 40 miRNAs (sorted by increasing p-value) identified 968 gene targets. Gene ontology analysis shows that some of our candidate miRNAs regulate genes involved in insulin secretion in response to glucose stimulus, insulin receptor signalling, and glucose homeostasis. Functional analysis using BeWo cells showed that exosomes regulate several genes involved in glucose metabolism and modifying glucose uptake in the placenta in response to insulin.

CONCLUSIONS: These results suggest that exosomes present in maternal circulation, which are higher in number in GDM, may play an important role in glucose homeostasis in placental cells.

F-154

miR-210 Alters Mitochondrial Function in First Trimester Extravillous Trophoblast Cells. Lauren Anton,[1] Ann DeVine,[1] Amy G Brown,[1] Erzsebet Polyak,[2] Marni J Falk,[2] Michal A Elovtiz*.[1] *[1]Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA; [2]The Children's Hospital of Philadelphia, Philadelphia, PA, USA.*

INTRODUCTION: miR-210, a small non-coding RNA, is increased in the circulation and placenta of women with preeclampsia. As miRNAs target hundreds of gene networks with varying outcomes, the effects of elevated miR-210 levels on placental function remain unclear. The objectives of this study were to identify direct downstream targets of miR-210 in first trimester primary extravillous trophoblast cells and to investigate the functional biological pathways altered by elevated miR-210 in the placenta during early pregnancy.

METHODS: Primary extravillous trophoblast (EVTs) cells isolated from first trimester placentas (n=10) were transfected with miR-210 or miR-negative control (miR-neg) using Lipofectamine RNAiMAX. A custom TruSeq targeted RNA expression array (Illumina) was designed to include all known/predicted miR-210 targets based on the TargetScan (Version 6.2) database. The TruSeq array was run using miR-210 (n=10) and miR-neg (n=10) transfected EVTs. miR-210 altered gene targets were validated by QPCR. Mitochondrial function was assessed by high resolution respirometry (Oroboros Instruments) in transfected EVTs (n=5).

RESULTS: Of the 581 genes on the array, 494 genes were expressed in EVTs. Of those 494 genes, 49 genes had altered expression (adj $p<0.05$) in miR-210 vs miR-neg transfected EVTs with 27 genes being repressed and 22 increased. The top 7 genes with the most significant fold change (adj $p<2.72x10^{-7}$) were all decreased after miR-210 transfection. All 7 gene targets were validated by QPCR and were decreased similarly to the array ($p<0.05$). 3 of these genes regulate mitochondrial function including NDUFA4, SDHD and ISCU. miR-210 transfected EVTs had decreased maximal mitochondrial respiration ($p=0.0064$) with no change in basal or LEAK respiration.

CONCLUSIONS: This study suggests that miR-210 alters first trimester trophoblast function by regulating downstream gene targets with differing biological effects. Overexpression of placental miR-210 alters mitochondrial function of trophoblast cells in early pregnancy, a time of placental development when sensing oxygen tension is critical. Impairment of mitochondrial function may lead to increased production of reactive oxygen species, trophoblast cell damage and likely contributes to the development of preeclampsia. (R21-HD076271-02 and U54-HD086984).

F-155

***Inhibin Alpha Chain* Gene Is Differentially Regulated by GATA-2, GATA-6 and WT1 in Human Cytotrophoblasts.** Christophe L Depoix, Corinne Hubinont, Frédéric Debiève*. *Universite Catholique de Louvain, Brussels, Belgium.*

INTRODUCTION: During pregnancy, inhibin A is essentially produced and secreted by the placenta. In Down syndrome-associated pregnancies, maternal serum concentration of inhibin A is elevated, and GATA factors are upregulated while Wilm's tumor protein 1 (WT1) is downregulated compared to normal placentas. Two GATA sequences within the promoter of *inhibin alpha subunit* (*INHA*) gene have been identified in murine gonads. The role of GATA factors in regulating *INHA* gene expression has not been demonstrated in the human placenta yet. We decided to analyze the effect of oxygen tension on GATA factors expression in primary term cytotrophoblast cultures and to characterize their role in INHA expression.

METHODS: *INHA*, *GATA-2*, *GATA-4* and *GATA-6* mRNA expressions in primary term cytotrophoblasts and choriocarcinoma BeWo cell line were quantified by real-time PCR. The role of GATA factors in *INHA* gene expression was assessed by transient transfection experiments. A 3.9 kb-*INHA* promoter was cloned into a luciferase reporter plasmid and the GATA sites were mutated individually or together. The plasmids were transfected into BeWo cells and primary cytotrophoblasts. Dual-luciferase activity was measured 72 h after transfection.

RESULTS: There were more *INHA* transcripts in undifferentiated cytotrophoblasts than in BeWo cells while there were more *GATA-2* and *GATA-6* transcripts in BeWo cells than in cytotrophoblasts. *GATA-4* mRNA was detected only in placental explants. *GATA-2* and *GATA-6* mRNA expression increased in primary term cytotrophoblasts cultured for 96 h under 21% O_2. The increase was lower when the cells were cultured under 2.5% O_2. GATA-2 and GATA-6 overexpression in BeWo cells resulted in a decrease in *INHA* promoter-driven *Luciferase* activity. Mutation of the GATA sites revealed that WT1 also played a role in regulating *INHA* promoter, and that its transcriptional activities were dependent on GATA factors. WT1 seemed to be an activator in BeWo cells and an inhibitor in cytotrophoblasts when GATA factors were not allowed to bind to *INHA* promoter.

CONCLUSIONS: GATA factors regulate INHA expression by inhibiting its transcriptional activities mainly through the proximal GATA site. If GATA factors cannot interact with GATA sites, WT1 is able to activate *INHA* transcription in cytotrophoblasts or to inhibit it in BeWo cells.

F-156

Effect of Tetrabromo-Bisphenol A (TBBPA) on Expression of Biomarkers for Inflammation, Oxidative Stress and Neurodevelopment by the Placenta. Yuko Arita,[1] Michael Kirk,[1] Matthew Pressman,[1] Darios Getahun,[2] Ramkumar Menon,[3] Morgan R Peltier*.[1] *[1]Winthrop University Hospital, Mineola, NY, USA; [2]Kaiser-Permenante Southern California, Pasadena, CA, USA; [3]UTMB-Galveston, Galveston, TX, USA.*

INTRODUCTION: Maternal exposure to flame retardants is widspread and unavoidable due to their extensive use in consumer products for decades. In previous studies, we found that one class of flame retardants, polybrominated diphenyl ethers (PBDEs), increase the inflammatory response to bacteria by placental explant cultures. This may enhance the

risk of preterm birth and other adverse pregnancy outcomes. Whether or not other brominated flame retardants such as Tetrabromobisphenol A (TBBPA) have similar properties is unclear. Therefore, we evaluated the effects of TBBPA on the production of steroids, as well as biomarkers for inflammation, oxidative stress, and neurodevelopment by the placenta.
METHODS: Placental explant cultures were established from women undergoing elective Cesarean sections at term and treated with 5 to 50,000 nM TBBPA in the presence and absence of 10^7 CFU/ml heat-killed *E. coli*. Conditioned medium was harvested and concentrations of P_4, E_2, testosterone (T), IL-1β, TNF-α, IL-10, HO-1, IL-6, sgp130, F2-IsoP and BDNF were quantified using ELISA.
RESULTS: No effects of TBBPA were observed on viability of the cultures. In the absence of infection, high concentrations of TBBPA increased P_4 production, had limited effect on E_2 secretion, but significantly enhanced T production. Neither IL-1β, nor TNF-α was affected by TBBPA but IL-6 secretion was enhanced at most concentrations tested. TBBPA had little or no effect on IL-10, HO-1, sgp130, or BDNF production but enhanced F_2-IsoP production. For bacteria-treated cultures, TBBPA tended to inhibit P_4, E_2, T, IL-1β, sgp130, F_2-IsoP, and HO-1 production but enhanced TNF-α and IL-6 production with no detectable effects on BDNF secretion.
CONCLUSIONS: TBBPA has mixed effects on bacteria-stimulated production of inflammatory biomarkers, increasing TNF-α and IL-10 but reducing IL-1β production. TBBPA enhancement of IL-6 and reduction of sgp130 secretion by bacteria-stimulated cultures suggests that TBBPA may increase the levels of bioactive IL-6. IL-6 is necessary and sufficient to cause autism-like behaviors in animal models. Enhancement of its production by TBBPA may increase the risk of adverse neurodevelopmental outcomes.

F-157

Terminal Villi of the Human Placenta Have No Core Microbiome. Susanne Lager†,[1] Marcus de Goffau,[2] Sharon J Peacock,[2] Julian Parkhill,[2] D Stephen Charnock-Jones,[1] Gordon CS Smith*.[1] *[1]University of Cambridge, Cambridge, United Kingdom; [2]Genome Campus, Hinxton, United Kingdom.*
INTRODUCTION: Sequencing 16S rRNA has allowed characterization of bacterial populations. Using sequencing technologies, it has been reported the placenta harbors a unique microbiome. However in samples containing low microbiota biomass, bacterial DNA fragments that contaminate laboratory reagents will generate false positive results (called "kitome"). We sought (1) to determine the sensitivity of 16S rRNA gene sequencing to detect bacteria in placental biopsies, (2) to determine whether there is evidence of a placental microbiome.
METHODS: We studied human placentas from uncomplicated term pregnancies. Samples of terminal villi were taken after removal of maternal decidua, washed in PBS and flash frozen. DNA was extracted and PCR for 16S rRNA (region V1-V2) performed on samples with a wide range of collection times and modes of delivery and negative controls (n=60). In addition, placental biopsies were "spiked" before DNA isolation with known amounts of *Salmonella bongori* (1, 10, 100, 1000, or 10,000 bacteria in 25mg of placental tissue; n=3). Amplicons were sequenced (MiSeq, 250 base paired-end reads) and data analysis was performed with Muther and ARB software.
RESULTS: We found that "spiked in" *Salmonella bongori* could be reliably detected at <100 bacteria in 25mg of tissue (approximately equivalent to <1 microbe per 25,000 human cells). Strikingly, many other signals were also detected, yet the vast majority (~99%) were species typically found in soil or water (e.g. *Bulkholderia*, *Bradyrhizobium*, *Curvibacter* and *Mesorhizobium*) and all of these were also present in the negative controls. These were therefore not present in the original sample, but are processing contaminants. Only one sample had a clear non-kitome signal (~5% of reads); it had a weak vaginosis-like signature (*Leptotrichia amnionii, Gardnerella vaginalis* and *Lactobacillus iners*).
CONCLUSIONS: (1) Our spike-in experiments show that 16S rRNA gene amplification and sequencing is a sensitive method. However, when no bacteria are present in the original sample (low biomass samples) DNA from kit contaminants will still be amplified (resulting in a kitome signal). (2) Real bacterial signals are only rarely found in placentas from uncomplicated pregnancies. (3) Previous observations supporting a placental microbiome could have been caused by amplification of known sample processing contaminants.

F-158

State-by-State Trends in Labor and Delivery Costs: Association with Length of Stay and State-Specific Maternal Mortality Ratio. Mary C Tolcher†, Amirhossein Moaddab†, Catherine S Eppes, Alireza A Shamshirsaz, Gary A Dildy, Michael A Belfort, Steven L Clark*. *Baylor College of Medicine, Houston, TX, USA.*
INTRODUCTION: Pregnancy is the most common cause of hospitalization in the United States. The objective of this study was to examine national and state-by-state trends in labor and delivery charges and their association with length of stay (LOS) and state-specific maternal mortality ratio (MMR).
METHODS: Between 2004 and 2013, hospital charges for vaginal delivery (VD) and cesarean delivery (CD) with or without complications and LOS for these categories were identified using the Healthcare Cost and Utilization Project of the Agency for Healthcare Research & Quality (AHRQ). Cases were identified using DRG, CCS, and ICD-9 codes. State-specific MMRs were calculated using the CDC WONDER online databases. Jonckheere-Terpstra test was used to assess the statistical significance of changes in reported rates.
RESULTS: There were 38,412,277 deliveries in 37 participating states. LOS increased during this time period in cases of VD without complication (2.0 in 2004 to 2.2 in 2013, p=0.001) and decreased in cases of CD with (4.6 in 2004 to 4.2 in 2013, p=0.003) and without (3.4 in 2004 to 3.0 in 2013, p=0.001) complications. While CD with complication had the highest hospital charges ($26,505 in 2013, 70% increase from 2004), the cost of VD without complications also increased by 96% during these years reaching $12,250 in 2013). During the study period, only 6.5% of pregnancies were coded (ICD-9) as "normal pregnancy/delivery", ranging from 3.1% in Maryland to 10.0% in Arkansas. The mean state-specific delivery charges ranged widely from $3,367 in Wyoming to $20,691 in New Jersey but were not significantly associated with the state-specific MMR (p=0.06).
CONCLUSIONS: 1. To the degree that LOS reflects operative morbidity, our data suggest that CD may be becoming safer in the past decade. An alternative explanation involving economic pressure toward early discharge is not supported by the observation that LOS for VD increased during this same time frame. 2. A near doubling of hospital charges for both VD and CD does not reflect any proportional change in LOS or in complications, nor are individual state charges for delivery related to MMR. 3. In this series of over 30 million deliveries, only 6.5% were coded (ICD-9) as "normal pregnancy/delivery", suggesting that data derived from such coding has limited meaning.

F-159

How to Reduce Caesarean Section (CS) Rate: A Cultural and Organizational Issue. Denise E Rinaldo, Anna Zilioli, Claudio Crescini. *ASST Bergamo Ovest, Treviglio, BG, Italy.*
INTRODUCTION: Rising rates of cesarean delivery are an issue of international concern.In 2014 the overall rate of CS in our Unit was high (32,6%), in line with our national rate of 36%, therefore we decided to improve quality of care by implementing a serie of structured organizational and cultural changes.
METHODS: Before and after study comparing CS performed in 2014 and 2016 in our Obstetric Unit.
In 2015 we improved labour ward clinical organization introducing:
· Monthly monitoring of obstetric results
· Recruitment of a labour ward leader and of a midwife coordinator
· Improved teamwork
· Obstetrical morning round with daily discussion of every CS performed
· Fetal monitoring skills
· Obstetrical training on technical and non technical skills with simulators
· Revision of clinical protocols
· Introduction of VBAC and external cephalic version outpatient clinic

· Introduction of a new partogram allowing longer dilation curves and action times
· Different management of dystocia according to the so-called "comprehensive management" of labour
· Risk classification of women with midwife-led care for low risk women.
RESULTS: CS rate was 32,6% (412/1266 patients; 95% CI: 30.0 – 35.2 del) in before-group and 18,1% (172/948 patients; 95% CI: 15.7 – 20.8 del)(after- group) (Fisher's exact test: p< 0.0001) in after group.
Overall CS rate was reduced by 44,5%.
The reduction was statistically significant in Robson groups 1-5-10.
The incidence of children born with umbilical cord pH <7 and Apgar score <7 at 5'were the same over the years studied.
CONCLUSIONS: In the present study, we found a significant change in the pattern of CS rates that could be attributable to the implementation of the 11 items presented above.
Our study showed a significant reduction in CS rate in Robson groups 1, 5, 10, by a reduction of the more subjective indications to CS (non reassuring fetal status and arrest of dilation) especially in women belonging to group 1 and by the introduction of a dedicated VBAC outpatient clinic with careful selection of women admission to TOLAC.
With continuous care on cultural and organizational factors a labour ward leader can modify incongruous clinical behaviours reducing CS rate without increasing neonatal morbidity.

F-160

The Effect of Low Molecular Weight Heparin on Antithrombin III in Patients with Recurrent Spontaneous Abortion Caused by Antiphospholipid Syndrome. Hailan Wang, Danyang Kang, Chong Qiao*. *Department of Obstetrics and Gynecology, Shengjing Hospital, Shenyang, China.*
INTRODUCTION: Low molecular weight heparin(LMWH) is thought to improve the hypercoagulable state in patients with recurrent spontaneous abortion(RSA) by regulating the activity of antithrombin III(ATIII). However,we do not know if this effect is related to the dosage and using time of LMWH so it cannot make sure when we need to give the AT III test.**Objective**:To investigate the effect of LMWH on the activity of AT III in patients with RSA mainly caused by APS.
METHODS: The 82 patients in the first trimester who is met the standard above and admitted in Shengjing Hospital between January 2015 and June 2016 is included in the study.According to the daily dosage of LMWH(heparin sodium),the 82 pregnancies are divided into two groups,group A(two pieces per day) and group B(three pieces per day),and finally the decrease of ATIII activity after giving the treatment for two weeks is recorded and compared,respectively.
RESULTS: There is significant difference in the decrease of ATIII activity in group A and group B after treating by LMWH for two weeks.
CONCLUSIONS: The activity of ATIII decreases along with the increase of daily dosage of LMWH among the patients with RSA mainly caused by APS.

F-161

Effect of Altitude on Incidence of Hypertensive Complications of Pregnancy. Ibrahim Hammad†,[1,2] Jim VanDerslice,[3] Michael Varner*.[1,2] *[1]University of Utah Health Sciences Center, Salt Lake City, UT, USA; [2]School of Medicine, University of Utah, Salt Lake City, UT, USA; [3]Intermountain Health Care, Salt Lake City, UT, USA.*
INTRODUCTION: The purpose of our study is to determine the case incidence of gestational hypertension and preeclampsia at different altitudes in the Utah population.
METHODS: This is a retrospective cohort study including live birth (n=672,098) and stillbirth (n=3732) among Utah residents from 1989 to 2006. Maternal addresses, as recorded on birth certificates, were geocoded and linked to determine elevation of the mother's residence. Data pertaining to hypertensive complications of pregnancy were extracted from the birth certificate.
RESULTS: The incidence of hypertensive complications (HC) were 6.5% at >6,000 feet (ft.) and 5.3% at< 4,000-5,000 ft. When compared to different altitudes, women living at >6,000 ft. yielded a significant odds ratio for hypertensive disorder of pregnancy even after adjusting for maternal age, weight gain, body mass index, smoking, alcohol use, parity, socioeconomic status, the result was 1.29 (95% confidence interval 1.14-1.45).

	% HC	aOR	95%CI
Elevation at maternal residence			
<4,000	5.3	1	Reference
4,000-5,000	5.1	0.89	0.81-0.97
5,000-6,000	5.9	1.1	0.99-1.21
>6,000	6.5	1.29	1.14-1.45
Maternal age			
18-19	5.5	0.92	0.87-0.96
20-24	5.6	1.03	1.00-1.06
25-29	4.9	1.00	Reference
30-34	4.7	1.00	0.97-1.04
>34	5.8	1.24	1.19-1.30
Maternal race/ethnicity			
Black	4.7	0.79	0.68-0.92
Native American	7.2	1.14	1.03-1.25
White (non-Hispanic)	5.3	1	Reference
Hispanic	4.6	0.84	0.80-0.87
Other races	3.8	0.65	0.60-0.70
Pre-pregnancy BMI			
Lowest	2.5	0.73	0.68-0.78
Normal	3.8	1	Reference
Overweight	7.0	1.75	1.70-1.80
Obese	11.0	3.22	3.13-3.32
Multiple pregnancy			
Yes	11.5	2.48	2.3-2.61
No	5.0	1	Reference
Smoking during pregnancy			
Yes	4.1	0.81	0.77-0.85
No	5.3	1	Reference
Weight gain for BMI			
Recommended	3.8	1	Reference
Low gain	3.7	0.86	0.82-0.89
High gain	7.7	1.70	1.65-1.74
First pregnancy			
Yes	7.7	7.7	2.13-2.25
No	4.2	4.2	Reference

CONCLUSIONS: There is a small but significant association between high altitude and incidence of hypertensive complications of pregnancy. Our findings may be used for counselling and planning an interventional trial.

F-162

Prepregnancy Physiology Predicts Subsequent Preterm Preeclampsia. Ira Bernstein*,[1] Carole McBride,[1] Gary Badger.[2] *[1]Larner COM at UVM, Burlington, VT, USA; [2]Larner COM at UVM, Burlington, VT, USA.*
INTRODUCTION: In a prospective observational cohort we evaluated the contribution of prepregnancy cardiovascular physiology to the development of preterm preeclampsia (PP).
METHODS: We characterized cardiovascular physiology in 93 women with subsequent singleton pregnancies. 33 women had prior PP and 60 were nulliparous. We measured body composition, blood pressure (BP), uterine blood flow, cardiac output (CO), plasma volume, flow mediated vasodilation, pulse wave velocity (PWV), vascular adrenergic responsiveness, renal vascular resistance (RVRI) and CO, pulse and BP response to volume challenge. Pregnancy outcome was obtained through chart review. Statistical analysis was performed using SAS (version 9.4). Data are presented as mean ± sd.

RESULTS: Outcomes included 10 women with PP, 7 with term preeclampsia (NPP), 19 with gestational hypertension (NPP) and 57 with uncomplicated pregnancies (NPP). We found no difference in maternal age (p=0.87), study cycle day (p=0.24), height (p=0.32) or lean body mass (p=0.29) across groups. Women with subsequent PP had increased android fat content (PP: 3138 ± 1174, NPP: 1909 ± 1285 gs p=0.005), supine pulse (PP: 78 ± 8, NPP: 67 ± 10 bpm p=0.001), supine diastolic BP (PP: 82 ± 7, NPP: 69 ± 6 mmHg, p< 0.001), cardiac output (PP: 5.7 ± 1.1, NPP: 4.5 ± 1 L/min p<0.001), beta adrenergic responsiveness (PP: 32 ± 14, NPP: 22 ± 10 mmHg p=0.004), popliteal PWV (PP: 5.9 ± 0.9, NPP: 5.2 ± 0.7 m/sec p=0.002), and cumulative CO response to volume challenge (PP: 20 ± 9, NPP: 9 ± 12 L/min p=0.007). PP also had reduced RVRI (PP: 0.86 ± 0.08, NPP: 0.97 ± 0.12 p=0.008). ROC analyses based on logistic regression yielded an optimal sensitivity of 90%, specificity of 95%, and an AUC c=0.96 employing; supine diastolic blood pressure, pulse response to volume challenge and android fat. Neither a history of preterm preeclampsia nor evidence of placental under perfusion contributed independently to the risk of preterm preeclampsia.

CONCLUSIONS: Prepregnancy physiology linked to subsequent PP includes increased vessel stiffness, low compliance, high CO and reduced RVRI and increased android fat, consistent with elements of the metabolic syndrome and a perceived overfill state. While a validation cohort is necessary to confirm this experimental model we observed a significant contribution of prepregnancy cardiovascular physiology to subsequent PP in contrast to the prevailing view of PP as largely placentogenic.

F-163

Antenatal Blood Pressure Visit-to-Visit Variability and Risk of Pregnancy-Associated Hypertension. Christopher L Dixon†. *Maternal-Fetal Medicine Units Network, Bethesda, MD, USA.*

INTRODUCTION: In patients with hypertension, blood pressure (BP) visit-to-visit variability (VVV) is associated with cardiovascular disease morbidity and mortality. Our goal was to evaluate whether antenatal BP-VVV is associated with pregnancy-associated hypertension (PAH).

METHODS: Secondary analysis of a multicenter randomized trial of antioxidants to prevent preeclampsia (PE) in singleton nulliparous low risk women. VVV was defined as the total variability around mean BP (standard deviation). SBP-VVV and DBP-VVV between enrollment (9-15 weeks) and 27 weeks 6 days gestation, or the last visit before diagnosis of PAH were calculated. Women with fewer than four BP recorded and those with congenital anomalies were excluded. Our primary outcome was PAH, defined as new onset hypertension at ≥20 weeks gestation. Secondary outcomes included a composite outcome of severe PAH alone or PAH with adverse maternal or fetal/neonatal outcomes, and a three-category outcome of PE vs. gestational hypertension (GHTN) vs. normotensive. Quartiles for VVV were derived using BP from patients who remained normotensive until delivery. Logistic regression was performed adjusting for covariates; with lowest quartile as referent group.

RESULTS: 8514 (85% of the original study) women were included, of whom 2441 (28.7%), 503 (5.9%), 615 (7.2%), and 1829 (21.5%) developed PAH, the composite outcome, PE, and GHTN, respectively. All outcomes increased with increasing quartiles of SBP- and DBP-VVV **Figure(s) will be available online.*

Compared to the referent SBP-VVV group, those in the highest quartile had an adjusted odds ratio (aOR) and 95% CI of 1.4 [1.2-1.6] for PAH, 1.3 [1.0-1.7] for the composite outcome, 1.3 [1.1-1.7] for PE vs. 1.4 [1.2-1.6] for GHTN. The respective aOR [95% CI] for the highest to the lowest quartile DBP-VVV were 1.3 [1.1-1.5], 1.4 [1.1-1.9], and 1.4 [1.1-1.8] vs. 1.3 [1.1-1.5].

CONCLUSIONS: VVV of SBP and DBP before 28 weeks gestation is associated with PAH, serious maternal and fetal/neonatal outcomes, PE, and GHTN in low risk nulliparous women. Monitoring VVV during pregnancy may prove to be a marker of impending hypertensive complications.

F-164

Relaxin Reduces Vascular Sensitivity to Angiotensin II in Pregnant Relaxin-Deficient Mice and Prevents Onset of Vascular Dysfunction in Mouse and Human Arteries. Sarah A Marshall†,[1] Chen H Leo,[1] Kelly O'Sullivan,[1] Marianne Tare,[2,3] Natalie J Hannan,[4] Jane E Girling,[5] Laura J Parry*.[1] *[1]The University of Melbourne, Parkville, VIC, Australia; [2]Monash University, Clayton, VIC, Australia; [3]Monash University, Churchill, VIC, Australia; [4]The University of Melbourne, Heidelberg, VIC, Australia; [5]The University of Melbourne, Parkville, VIC, Australia.*

INTRODUCTION: Preeclampsia (PE) affects 3-8% of pregnancies worldwide and is a leading cause of maternal and fetal death. Characteristic of PE is widespread maternal systemic vascular dysfunction. The peptide relaxin (RLX) has gained considerable attention as a new vasoactive drug, largely through its therapeutic effects in cardiovascular disease. In this study, we tested the hypothesis that RLX treatment alleviates symptoms of PE by improving vascular function.

METHODS: We investigated vascular function and mechanisms of RLX action in both *in vivo* and *ex vivo* experimental models using wire myography and pharmacological agonists/antagonists. 1) Pregnant RLX-deficient (*Rln*-/-) mice, with enhanced vasoconstriction to angiotensin II (AngII), received 0.5µg/h RLX (Novartis Pharma AG) or placebo (n=7/treatment) subcutaneously via osmotic minipumps for 5 days from day 12.5 of gestation. 2) Wildtype non-pregnant mouse mesenteric and human omental arteries (elective Cesarean at term) were incubated *ex vivo* for either 24h at 37°C in trophoblast conditioned media (TCM) or 3h at 4°C in placental explant media (PEM) containing soluble Flt-1 (>20ng/ml) and sEng (~1ng/ml) in the presence or absence of 1-15 nM of RLX (n=5-7/treatment).

RESULTS: *In vivo* RLX treatment of pregnant *Rln*-/- mice normalized AngII-mediated contraction of mesenteric arteries. Denuding the arteries and preincubation with the sGC inhibitor ODQ had no effect in RLX-treated *Rln*-/- mice, demonstrating that RLX reduces AngII-induced vasoconstriction through endothelium-independent mechanisms and not involving the sGC-cGMP signaling pathway. TCM and PEM both induced endothelial dysfunction characterized by reduced acetylcholine- or bradykinin-mediated relaxation of mouse and human omental arteries, respectively. This endothelial dysfunction was prevented by co-incubation of arteries with 10 or 15 nM RLX.

CONCLUSIONS: RLX treatment ameliorates the enhanced sensitivity of mesenteric arteries to AngII and protects against endothelial dysfunction.

F-165

Women with Prior Preterm Preeclampsia Have Elevated Inflammation and Endothelial Dysfunction Compared to Nulliparous Women. Carole A McBride†, Erin A Morris, Ira M Bernstein*. *UVM, Burlington, VT, USA.*

INTRODUCTION: Markers of inflammation, endothelial dysfunction, and hemostatic dysregulation have been shown to be increased in the setting of preeclampsia. Apelin plays a role in fluid homeostasis, acts as an endothelium dependent vasodilator, and has been observed to be decreased in preeclampsia. We sought to determine whether women who have experienced prior preterm preeclampsia (pPE) have persistent differences in markers linked to these states when compared to nulliparous women in the non-pregnant state.

METHODS: Sixty-five nulliparous and 32 women with a history of pPE were evaluated for von Willebrand Factor (vWF), d-dimer, intercellular (ICAM) and vascular (VCAM) adhesion molecules, C-reactive protein (CRP), Interleukin-6 (IL-6), Tumor Necrosis Factor-α (TNF-α), and apelin. Women were studied on cycle day 9.3±3.5. Data are presented as mean ± SD.

RESULTS: All women were young (31±4 years), and healthy (MAP 82.8±9.1 mmHg). Prior pPE women were 2.0 ± 1.1 years postpartum and were larger than nulliparous women (BMI 28.4 ± 6.5 vs. 24.3 ± 5.4 mg/kg^2; p=.002) Women with a history of preterm preeclampsia had increased CRP (pPE=7.9.1±9.4 vs. 3.1± ug/mL; p<.001), increased IL-6 (pPE= 3.85±1.8 vs. 2.9±1.8 pg/mL; p=0.02), and increased apelin (pPE=

319±230 vs. 237±111 pg/mL; p=0.02) compared to nulliparous women. IL-6 levels corrected for BMI did not differ between pPE and nulliparous subjects, but apelin and CRP remained significantly elevated in pPE.
CONCLUSIONS: Levels of D-dimer, ICAM, VCAM, vWF, PLGF, and TNF-α were similar between groups. These findings, that women with a history of pPE have continued evidence of endothelial dysfunction, inflammation, and fluid imbalance, may play a role in their increased future risk of cardiovascular disease. Increased apelin levels in the pPE group are counter to those previously reported during disease, and may reflect a postpartum homeostatic response. It is unknown whether these findings predate or result from prior pPE.

F-166

Identification of Novel Genetic Variants from Whole Exome Sequencing in Preeclampsia. HS Gammill,[1,2] R Chettier,[3] A Brewer,[3,4] JM Roberts,[5] R Shree,[1] E Tsigas,[4] K Ward*.[3] *[1]Univ Washington, Seattle, WA, USA; [2]Fred Hutch, Seattle, WA, USA; [3]Affiliated Genetics, Salt Lake City, UT, USA; [4]Preeclampsia Foundation, Melbourne, FL, USA; [5]Univ Pittsburgh, Pittsburgh, PA, USA.*
INTRODUCTION: Epidemiologic data suggest genetic susceptibility to preeclampsia (PE), but the specific genetic contributors remain incompletely elucidated. We conducted genome-wide screening to identify novel genetic variants associated with PE.
METHODS: PE subjects derived from The Preeclampsia Registry and Biobank. After providing informed consent, subjects with prior PE completed a detailed questionnaire and provided medical records for diagnostic confirmation. Saliva samples were collected for DNA isolation. Whole exome sequencing (WES) was performed using Ion Proton Instrument with the AmpliSeq Exome Capture Kit. Rare variants were considered (minor allele frequency of <0.1%). Missense variants were deemed to be "damaging" if so classified by any of 7 prediction algorithms. Results were compared with data from 530 unrelated women with endometriosis who underwent WES by the same methods (EndoC) and 33,000 subjects in the Exome Aggregation Consortium (ExAC). PE was not excluded in these population controls.
RESULTS: Of 190 PE subjects (170 confirmed/20 probable/awaiting additional records), 87% were Caucasian. 72% had ≥1 preterm PE delivery <37 weeks. 8 PE-associated genes with rare damaging variants passed the genome-wide threshold (p<5E-08). Table 1 shows the variant associations, assuming all are equally pathogenic. 34 PE subjects (17.9%) carried ≥1 variant vs only 9 EndoC women (1.7%), p=1.19E-13.

Gene	Variant freq. (PE)	Variant freq. (ExAC)	Variant freq (EndoC)	p	OR	95% CI
KANK3	0.01842	0.00000	0.00000	1.91E-16	Inf	NaN
FAM71D	0.01316	0.00000	0.00189	5.99E-12	Inf	NaN
NDUFAF7	0.02368	0.00050	0.00000	3.08E-09	38	17-88
KCNJ12	0.02105	0.00100	0.00472	1.15E-08	22	10-45
TOE1	0.01316	0.00010	0.00094	1.62E-08	89	30-262
NHSL2	0.01579	0.00040	0.00094	2.83E-08	44	17-113
SRP72	0.01316	0.00020	0.00000	3.37E-08	74	26-211
KDF1	0.01053	0.00005	0.00000	3.97E-08	229	51-1028

CONCLUSIONS: We identified several novel, rare genetic variants strongly associated with PE. The implications of these findings include delineation of previously unconsidered biologic pathways contributing to PE as well as identification of genetic factors useful for risk stratification. Further study is needed.

F-167

Inhibition of the Auto-Inflammation Suppressor Protein ISG15 Blocks Proliferation and Induces Inflammatory Cytokine Expression in Trophoblasts: Implications for Preeclampsia. Sefa Arlier,[1] Ozlem Guzeloglu-Kayisli,[1] Nihan Semerci,[1] Kellie Larsen,[1] Selcuk Tabak,[2] Frederick Schatz,[1] Antony Odibo,[1] Charles Lockwood,[1] Umit Kayisli.[1] *[1]Univ. of South Florida, Morsani College of Medicine, Tampa, FL, USA; [2]Adiyaman Univ., Medical Faculty, Adiyaman, Turkey.*
INTRODUCTION: Interferon-induced ubiquitin-like modifier-15 protein (ISG15) induces stabilization/degradation of proteins by covalent binding, called ISGylation. Humans with homozygous mutations in the ISG15 gene display low interferon-γ (IFN-γ) production in lymphocytes and severe auto-inflammation due to hyper IFN-α/β mediated immune responses. Plasma and decidual interleukin-6 (IL-6) levels are increased in preeclampsia (PE). Our previous microarray and *in situ* analyses found that IL-6 significantly inhibits ISG15 levels in primary first trimester cytotrophoblast (CTB) cultures and that interstitial CTBs display significantly lower ISG15 immunostaining in PE *vs.* normal placentas. Thus, we investigated the role of ISG15 on CTB survival and inflammatory cytokine expression.
METHODS: Cell survival and pro-inflammatory cytokine IL-1β (10 ng/ml) responses were measured in normal and ISG15-siRNA silenced HTR8/SV cells (human first-trimester chorionic villi explant-derived immortalized cytotrophoblasts) using BrdU incorporation (proliferation), TUNEL (apoptosis) and qRT-PRC techniques. Statistical analyses used student's t-test.
RESULTS: Significantly reduced ISG15 mRNA and protein levels were confirmed in HRT8 cultures treated with ISG15 siRNA *vs.* control siRNA. Compared to control siRNA, ISG15 siRNA silencing in HRT8 cells significantly reduced BrdU incorporation levels (Mean±SEM 0.74±0.04 *vs.* 0.51±0.04 p=0.004; n=5) with no significant change in the apoptosis index in control siRNA *vs.* ISG15 siRNA (2.5±0.3 *vs.* 1.8±0.2, p=0.126; n=6). Moreover, recombinant IL-1β treatment of HTR-8 cells elevated mRNA levels of IL-6 (80.3±18 *vs.* 14.0±4.4), IL-1β (20.5±3.8 *vs.* 11.2±2.5), IL-8 (23.4±3 *vs.* 12.3±7.3) and MCP-1 (123.2±14.6 *vs.* 40.7±11.9) in ISG15 siRNA *vs.* control siRNA transfection (n=4, p<0.005).
CONCLUSIONS: These results indicate key roles for ISG15 in blocking pro-inflammatory cytokine expression and inducing proliferation/differentiation in trophoblasts. Low ISG15 levels in PE may contribute to local/systemic inflammation and impaired spiral artery transformation via reduced extravillous trophoblast proliferation. Conversely, compounds increasing ISG15 expression may exert therapeutic benefits in PE.
Supported by NICHD U01HD087213.

F-168

sFlt-1 Production Is Modulated Through the Activation of Angiotensin II Receptor Subtype 2 in Preeclampsia. Keiichi Matsubara, Yuko Matsubara, Yuka Uchikura, Takashi Sugiyama. *Ehime University SOM, Toon, Ehime, Japan.*
INTRODUCTION: Angiotensin II receptor subtype 1 (AT1) is involved in the pathogenesis and the subtype 2 (AT2) can antagonize the effect of AT1. Recently, AT2 agonist (compound21: C21) was discovered; however, there is no report of the effect of C21 during pregnancy. We evaluated the effect of AT2 agonist (C21) in the pathogenesis of PE.
METHODS: Blastocysts collected from pregnant ICR mice were incubated with adenovirus including CD40L gene and transferred into the uterine horns of pseudopregnant ICR mice to make PE model mice. Osmotic pumps were placed subcutaneously on the dorsal side with C21 or saline. On e17.5, peripheral blood was collected by cardiopuncture. Spleen cells were collected and the profile was evaluated using flowcytometry. Plasma concentration of Soluble fms-like tyrosine kinase 1 (sFlt-1) and soluble endoglin (sEng) was measured using ELISA.
RESULTS: On e15.5, blood pressure was significantly decreased (113 ± 2 mmHg vs. 126 ± 5 mmHg; p<0.05). The weight of neonates was increased by treatment with C21 (1.26 ± 0.03 g vs. 1.13 ± 0.03 g; p<0.05). The profile of T cell and B cell was not different. Plasma concentration

of sFlt-1 was significantly decreased by treatment with C21 (7497.1 ± 634.8 pg/ml vs. 9704 ± 508.5 pg/ml; $p<0.05$); however, the concentration of sEng was not different.
CONCLUSIONS: It is thought that AT2 can inhibit the pathogenesis of PE through the reduction of sFlt-1 production.

F-169

Telomere Homeostasis and Senescence Markers Are Differently Expressed in Placentas from Pregnancies with Early Versus Late Onset Preeclampsia. Sivan Farladansky-Gershnabel†,[1] Hilah Gal,[2] Dvora Kidron,[1] Valery Krizhanovsky,[2] Tal Biron-Shental*.[1] *[1]Tel Aviv University, Tel Aviv, Israel; [2]The Weizmann Institute of Science, Rehovot, Israel.*
INTRODUCTION: Early (prior to 34 weeks gestation) compared to late onset preeclampsia (PE) tends to have more severe features and morbidity for both the mother and the fetus. The pathophysiology and placental characteristics of different expressions of PE are not fully understood. Telomere homeostasis was shown to be disrupted in PE in addition to increased senescence markers. However, differences between early and late onset PE have not been studied.
METHODS: Placental biopsies from 24 early and late onset PE as well as healthy gestational age matched controls were examined. Clinical characteristics were compared between the groups. Telomere length and aggregate formation were assessed using Q-FISH and computerized electronic quantitative method. Senescence-associated heterochromatin foci (SAHF), β-galactosidase (SAβ-Gal) and P16 (a senescence marker) staining were evaluated.
RESULTS: The groups were similar in terms of the clinical characteristics. The percentage of trophoblasts with short telomeres was found to be significantly higher in placental samples from early onset (52.61±12.27%) compared to late onset PE (28.72±10.14%), both were higher relative to the control samples (7.53±5.14%, P=0.03). Also, aggregate formation was mostly enhanced in early (8.72±2.49%) compared to the late (4.54±1.45%) onset PE, both higher than the healthy control samples (2.72±1.08%, P=0.03).
Trophoblasts from early versus late onset PE were more likely to express SAHF, stain positive to SAβ-Gal and to P16, also compared to the control group ($P<0.001$).
**Figure(s) will be available online.*
CONCLUSIONS: Telomere impaired homeostasis and senescence markers are more prominent in early versus late onset PE. These findings may partially explain the clinical differences in the severity of those two expressions of PE.

F-170

Pregnancy-Associated Exosomes Changes in Pregnancies Complicated by Small-for-Gestational-Age (SGA) Neonates and Intrauterine Growth Restriction (IUGR). Jezid Miranda,[1] Cristina Paules,[1] Fatima Crispi,[1] Eduard Gratacos,[1] Vyjayanthi Kinhal,[2] Andrew Lai,[2] Carlos Palma,[2] Carlos Salomon*.[2,3] *[1]University of Barcelona, Barcelona, Spain; [2]The University of Queensland, Brisbane, QLD, Australia; [3]Ochsner Baptist Hospital, New Orleans, LA, USA.*
INTRODUCTION: Very little is known about exosomes in human pregnancy and in particular in fetal development. The aim of this study was to quantify the levels of circulating exosomes in maternal and fetal circulation in pregnancies complicated by SGA and IUGR.
METHODS: This cross-sectional study included patients in the following groups: (1) Appropriate for gestational age (AGA) (n=10); (2) SGA (n=30); (3) early IUGR (n=10); and (4) late IUGR (n=20). Exosomes were isolated from plasma (maternal and fetal) through differential and buoyant density centrifugation and characterized by morphology, enrichment of exosomal proteins, and size distribution by electron microscopy, western blot, and nanoparticle tracking analysis (NTA), respectively. The total number of exosomes and specific placenta-derived exosomes were determined by NTA (NanoSight™) using quantum dots coupled with CD63 or PLAP antibodies in fluorescence mode.
RESULTS: In Maternal plasma, the levels of total exosomes (vesicles/ml) were significantly higher in SGA (4.7×10^{11}) and early IUGR (4.8×10^{11}) compared to AGA (2.7×10^{11}) and late IUGR (2.5×10^{11}) ($p<0.05$). Interestingly, the number of placental exosomes in maternal plasma was significantly higher ~5-fold in SGA compared to AGA and early or late IUGR. Similarly, placental exosomes were higher ~5-fold in SGA compare to AGA in fetal plasma. Placental exosomes were significantly higher ~2.6-fold in late compare to early IUGR in fetal plasma. Finally, a positive association was found between the number of placental exosomes in maternal and fetal plasma for AGA and SGA.
CONCLUSIONS: We suggest the quantification of placental exosomes in maternal plasma may be a useful tool for monitoring fetal development and pregnancy outcomes.

F-171

A Tissue-Based Proteomic Study of VEGFR2 in Human Term Placentas Revealed Its Association with Pyruvate Dehydrogenase and MDMX. John C Tsibris,[1] Shannon Ho,[1] Dale Chaput,[2] Rachel Sinkey†,[1] Stanley Stevens,[2] Maja Okuka,[1] Angel Alsina,[3] Umit Kayisli.[1] *[1]University of South Florida, Tampa, FL, USA; [2]University of South Florida, Tampa, FL, USA; [3]Tampa General Hospital, Tampa, FL, USA.*
INTRODUCTION: VEGFR2 is the main regulator of placental angiogenesis. The pyruvate dehydrogenase (PD) complex is key to glucose metabolism; it's E2-component, DLAT/PDC-E2, is the "Achilles heel" of primary biliary cholangitis and may relate to severe intrahepatic cholestasis of pregnancy, a risk factor for preeclampsia (PE). MDMX and MDM2 are major negative regulators of p53 which controls apoptosis in the villous tree. Trophoblast MDM2 is depleted in PE.
METHODS: We studied 30 patients at term with a wide range of clinical presentations (BMI, diabetes, but no IUGR complications). Our limited tissue fractionation preserves protein-protein associations at the extracellular domain of VEGFR2 in endothelial cells (EC) of the fetal compartment. Membrane proteins were isolated and treated with detergent ASB-14 that extracted 97% VEGFR2, 86% DLAT and 64% TOMM20. Mass spectrometer QExactivePlus identified the proteins in 4 VEGFR2 or 4 DLAT immunoprecipitations (IP). An antibody to the C-terminus of VEGFR2 is used suggesting that proteins bound to the extracellular VEGFR2 domain are collected.
RESULTS: VEGFR2 IP pulled down 32 proteins (e.g., DLAT, PRDX2, annexins, heterogeneous nuclear ribonucleoproteins, plasma cell markers,titin). DLAT IP did not pull down VEGFR2. Probably, many of the VEGFR2-DLAT association occur in the EC nucleus where both proteins are known to translocate. IP seem to depend on deacetylation and ADP-ribosylation (data not shown). Ingenuity pathway analysis of VEGFR2-IP predicts an association (p-value of overlap $8X10^{-7}$) with tretinoin-mediated signaling. Only MDMX (not MDM2 or p53) was found in VEGFR2-IP and DLAT-IP. There is an apparent decrease of MDMX in PE than normotensive placental samples.
CONCLUSIONS: Our list of proteins associated with VEGFR2 and PD offers new signaling pathways to explore and to hypothesize that abnormal intracellular translocations may contribute to PE.

F-172

Preeclampsia Down-Regulates MicroRNAs in Fetal Endothelial Cells: Roles of miR-29a/c-3p in Endothelial Function. Chi Zhou†,[1] Qing-Yun Zou†,[1] Ai-Xia Liu,[1,2] Rui-Fang Wang,[1] Ronald R Magness,[1,3] Jing Zheng*.[1] *[1]Univ. of Wisconsin-Madison, Madison, WI, USA; [2]Zhejiang Univ., Hangzhou, Zhejiang, China; [3]Univ. of South Florida, Tampa, FL, USA.*
INTRODUCTION: Preeclampsia (PE) is a leading cause of fetal and maternal morbidity and mortality during pregnancy. PE-offspring are at increased risk of cardiovascular disorders in adulthood, implicating that PE programs fetal vasculature *in utero*. MicroRNAs (miRNAs) post-transcriptionally regulate many endothelial functions. We **hypothesize** that PE causes dysregulation of endothelial function-associated miRNAs in fetal endothelial cells, disturbing the VEGFA- & FGF2-induced endothelial function.
METHODS: Unpassaged (P0) human umbilical cord vein endothelial cells (HUVECs) were isolated immediately after C-section from normal term (NT) and PE pregnancies. Differentially expressed (DE) miRNAs between NT and PE P0-HUVECs were identified using a miRNome miRNA qPCR Array and confirmed using RT-qPCR with a separate set of

samples, followed by bioinformatics analysis to predict the key pathways that are involved. Selected DE-miRNAs of interest were knocked down in passage 4 NT HUVECs to investigate their roles in regulating the PI3K/AKT1 and MAPK/ERK1/2 pathways, as well as cell migration, proliferation, and monolayer integrity in response to VEGFA & FGF2.
RESULTS: 16 DE-miRNAs were identified and all of them were downregulated in PE vs. NT P0-HUVECs. Bioinformatics analysis predicted that the PI3K/AKT1 signaling pathway was dysregulated in PE vs. NT P0-HUVECs, which is linked with themiR-29a/c-3p downregulation. Knockdown of miR-29a/c-3p in NT HUVECs increased the total AKT1 protein level, and inhibited the VEGFA- & FGF2-induced AKT1 phosphorylation and cell migration; but did not affect the VEGFA- & FGF2-induced ERK1/2 phosphorylation and cell proliferation as well as the VEGFA-decreased & FGF2-increased endothelial monolayer integrity.
CONCLUSIONS: This is the first report of PE-induced DE-miRNAs in a single population of unpassaged fetal endothelial cells and miR-29a/c-3p downregulation in PE vs. NT P0-HUVECs. In addition, miR-29a/c-3p knockdown impaired the VEGFA- & FGF2-activated PI3K/AKT1 signaling pathway and inhibited endothelial cell migration, suggesting that miR-29a/c-3p are important to fetal endothelial function. These PE-induced DE-miRNAs may be potential biomarkers for fetal endothelial dysfunctions and increased risk of cardiovascular disorders in PE-offspring later in life.

F-173

Pro-Inflammatory Cytokines in Lean and Obese Women with Preeclampsia. HW Hunt†,[1] H Gammill,[1,2] E Schur,[1] S Chandrasekaran*.[1] *[1]University of Washington, Seattle, WA, USA; [2]Fred Hutchinson Research Institute, Seattle, WA, USA.*
INTRODUCTION: Preeclampsia (PE) is associated with inflammation, reflected by high circulating pro-inflammatory cytokines. Variations in phenotypes of PE pose challenges in developing predictive tests and optimal therapies. Outside of pregnancy, obesity is characterized as a pro-inflammatory state. We hypothesize that obese women with PE would have higher pro-inflammatory cytokines at the time of diagnosis compared with lean women. Identification of fundamental differences in PE among lean vs obese women would give insight into disease pathogenesis.
METHODS: We performed a cohort study of subjects with singleton pregnancies and PE at UW, including lean (n=25, BMI<25) and obese (n=37, BMI >30) women. Subjects were prospectively recruited and third trimester plasma samples collected prior to onset of labor and at the time of PE diagnosis. Medical record review was conducted to ascertain subject characteristics and obstetric outcomes. Preexisting hypertension, diabetes, autoimmune disease, or spontaneous preterm labor were exclusions. Cytokines were measured using Luminex-based assays. Appropriate statistical transformations for normality were applied to each marker and Student T tests were performed. Markers were compared according to the presence or absence of severe features of PE, as well as by lean vs obese status.
RESULTS: Results are summarized in Table 1. While, as expected, pro-inflammatory markers were elevated in PE with severe features vs without, profiles were similar between lean and obese subjects with PE.

Cytokine	Severe features			BMI		
	No	Yes	p	Lean (<25)	Obese (>30)	P
IFN-γ	10.3	25.7	<0.01	25.6	24.9	0.86
IL-6	3.0	7.1	<0.01	7.0	6.5	0.65
IL-1β	17.8	38.5	<0.01	42.5	38.8	0.26
IL-2	5.2	10.4	<0.01	10.2	10.9	0.45
*All data in pg/nL						

CONCLUSIONS: At the time of PE diagnosis, pro-inflammatory cytokines did not differ among lean vs obese women. Inflammation may be similar regardless of obesity, which may be explained in other manners. Any difference in inflammation according to obesity may be apparent only preceding clinical manifestations. Nonspecific markers of obesity like BMI may not best reflect the phenotypic variation of PE related to obesity. One possibility is that other markers, such as those related to fat distribution, may better align with differences in both pathophysiology and clinical manifestations.

F-174

Early Pregnancy Chemokine C-C Motif Ligand 2 (CCL2), Not Leptin, Is Associated with Increased Risk of Preeclampsia in Obese Parturients. Sarah A Wernimont†, Sabrina M Scroggins, Donna A Santillan, Mark K Santillan*. *University of Iowa, Iowa City, IA, USA.*
INTRODUCTION: Obesity in pregnancy is associated with complications including preeclampsia and gestational diabetes. It is unclear why some pregnancies affected by obesity are associated with poor perinatal outcomes while others remain largely unaffected. Adipose tissue containing adipocytes and inflammatory cells contribute to systemic inflammation, hypertension and diabetes outside of pregnancy. Chemokine C-C motif ligand 2 (CCL-2) produced by adipocytes and macrophages augment inflammation in multiple organ systems. Leptin, produced by adipocytes, is involved in metabolism and inflammation. Differential CCL-2 and Leptin levels may predate poor pregnancy outcomes before clinical signs are noted. The objective of this study is to determine if maternal plasma CCl2 and leptin early in pregnancy in control and obese women is predictive of poor pregnancy outcomes. We hypothesize that early plasma CCL2 will be predictive of poor pregnancy outcomes.
METHODS: In this case control study, banked maternal plasma samples at less than 20 weeks gestation and clinical data were obtained from the University of Iowa Maternal Fetal Tissue Bank (IRB# 200910784). Two cohorts are identified including those with a BMI<30 and those with a BMI>35. CCl2 and Leptin levels are determined by ELISA and normalized to total plasma protein measured by bicinchoninic acid assay.
RESULTS: The BMI>35 group expectedly had increased rates of Type 2 Diabetes, gestational hypertension, and cesarian delivery. The BMI>35 group also exhibited a significanty elevated CCL2 to protein ratio (0.341 vs. 0.230, p<0.001). After controlling for obesity, CCL2:protein were significantly associated with development of preeclampsia (aOR=89.6, p=0.02), but not gestational diabetes or Cesarean delivery. CCL2:protein ratio is moderately predictive of the development of preeclampsia (ROC AUC=0.70). The leptin to protein ratio was significantly elevated in those with a BMI>35 (0.42 vs 0.14, p<0.001). Yet, it was not associated with preeclampsia, gestational diabetes and C section after controlling for obesity.
CONCLUSIONS: Early pregnancy plasma CCL2:protein ratio is specifically associated with and predictive of the development of late pregnancy preeclampsia in the obese. These data suggest that early pregnancy changes in obesity associated inflammation, not simply the presence of adipose tissue contributes to development of preeclampsia.

F-175

Comparative Characteristics of Myometrial and Decidual Chemokines Responsible for the Infiltration of Peripheral Leukocytes into Term Uterine Tissues. Tali Farine†,[1,2] Oksana Shynlova,[2,3] Stephen J Lye*.[1,2,3] *[1]University of Toronto, Toronto, ON, Canada; [2]Lunenfeld Tanenbaum Res. Inst., Toronto, ON, Canada; [3]University of Toronto, Toronto, ON, Canada.*
INTRODUCTION: Infiltration of leukocytes into the uterine tissues is an important step in parturition. In this study we examined 1. chemokine profiles secreted by primary human myometrial and decidual cells, and 2. the effect of myometrial and decidual secreted factors on peripheral neutrophil transendothelial migration (TEM).
METHODS: Myometrial (N=16) and decidua samples (N=12) were collected from elective caesarean section (term not in labour, TNL) following informed consent. Tissues underwent collagenase digestion to obtain primary cells. To generate myometrial (MCM) and decidual conditioned media (DCM), cells were grown until confluence and incubated in serum-free media for 48 hours. Chemokine protein secretion was analyzed in DCM and MCM by 40-plex and 27-plex Luminex assays (Bio-Rad). For TEM assays, a monolayer of primary human uterine microvascular endothelial cells (UtMVEC) was formed in transwell inserts

(pore diameter 3μm) and primed with MCM, DCM or vehicle (serum-free media). Neutrophils were isolated from peripheral blood of 2nd trimester pregnant women via histopaque density gradient, fluorescently-labeled with calcein, added to the insert with the CM-primed endothelial monolayer and co-cultured for 1 hour. Fluorescence of the calcein-labeled immune cells which migrated through the endothelium was measured at 525nm with a plate reader.

RESULTS: Bio-Plex screening revealed 15 cytokines, such as IL-6, IL-8, CXCL1, MIF, whose levels were significantly ($p<0.05$) elevated in DCM compared to MCM. Luminex results were further confirmed by ELISA for the neutrophil chemoattractant IL-8, with significantly ($p<0.05$) higher levels in DCM compared to MCM. In TEM experiments (N=8), neutrophils showed significantly enhanced TEM through CM-primed endothelial cells compared to vehicle-primed endothelial cells (DCM $p<0.01$, MCM $p<0.05$), with DCM priming eliciting 6-times greater response compared to MCM.

CONCLUSIONS: Higher cytokine secretion was observed by decidual compared to myometrial cells as well as greater neutrophil TEM by DCM-primed endothelial cells, implicating a primary role of the decidua in peripheral leukocyte infiltration cells in the term human uterus in vivo. Further experiments will investigate the effects of labour on cytokine secretion, leukocyte activation, adhesion and migration.

F-176

Platelet Activation and Development of Preeclampsia. Heather Campbell. *Maternal-Fetal Medicine Units Network, Bethesda, MD, USA.*

INTRODUCTION: Platelet factor 4 (PF4) and RANTES are stored in platelet α-granules and released on activation. Aspirin inhibits platelet activation and has had modest success in prevention of preeclampsia for high-risk women. We examined plasma concentrations of PF4 and RANTES longitudinally in women who develop preeclampsia compared to control women. Our hypothesis was that platelet activation occurs early in the course of preeclampsia, and may explain the modest preventative effect of aspirin when initiated after 12 weeks.

METHODS: A frequency matched, case-control study was performed within a previous randomized, double-blind, placebo controlled clinical trial originally designed to evaluate the effectiveness of vitamin C and E supplementation for prevention of preeclampsia and identify markers predictive of the disease. Cases and controls were frequency matched by center, maternal age, and smoking status. Cases were women who developed preeclampsia as defined by the primary study after 33 weeks gestation. Controls included women who remained normotensive throughout pregnancy and had no diabetes, placental abruption, and who did not deliver a SGA infant (<10th centile). Plasma concentration of PF4 and RANTES was measured at 9-16 weeks, 23-25 weeks, 31-33 weeks, and postpartum. Adjusted logistic regression models were tested at each time point estimating the odds of preeclampsia.

RESULTS: The analysis included 50 cases of preeclampsia who had samples available at all time points and 100 controls. There were no significant differences in RANTES and PF4 concentrations between cases and controls at any time point. In a pre-specified subgroup analysis comparing cases with delivery > 37 weeks, cases with severe preeclampsia prompting delivery <35 weeks, and controls, there were again no differences identified.

CONCLUSIONS: Significant increases in platelet activation were not seen at any time in gestation for women who develop preeclampsia compared to normotensive control women. These findings may explain, in part, the limited success of aspirin in prevention of preeclampsia.

F-177

***Is One Elevated Blood Pressure Enough?* A Retrospective Analysis of Preeclampsia Labs Sent from the Emergency Room.** Martha B Kole†,[1] Phinnara Has,[1] Samantha P DeAndrade,[1] Sarah M Gaskell,[2] Valery A Danilack,[2] Erika F Werner*.[1] [1]*Alpert Medical School of Brown University, Providence, RI, USA;* [2]*Brown University School of Public Health, Providence, RI, USA.*

INTRODUCTION: Currently, there are no recommendations designating when laboratory evaluation for preeclampsia (PEC) should be initiated in the emergency department (ED). This study sought to compare the incidence of positive laboratory findings in women with isolated versus persistently elevated blood pressure (BPs) in the ED.

METHODS: This retrospective cohort included women ≥ 20 weeks gestation who presented to a tertiary care ED between January and July 2014 with an elevated BP (≥ 140 mmHg systolic or ≥ 90 mmHg diastolic). Exclusion criteria included chronic hypertension, diabetes mellitus, preexisting renal or liver disease, and gestational or immune thrombocytopenia. The primary outcome was abnormal laboratory values suggesting PEC (platelets, creatinine, liver enzymes, urine protein/creatinine ratio). The association between abnormal laboratory evaluation for PEC and one versus more than one elevated BPs in the ED was evaluated using Fisher's exact test. Secondary outcomes included a diagnosis of PEC at discharge from the ED and diagnosis of PEC at delivery.

RESULTS: 4,208 charts were screened, 351 met inclusion criteria and 271 had complete PEC labs sent. Of the 271 women with PEC labs sent, 122 had an isolated elevated BP and 149 had greater than one elevated BP. Women with multiple elevated BPs were more likely to have abnormal PEC labs than women with an isolated elevated BP, 34.2% vs 15.6% ($p<0.001$). Compared to women with isolated elevated BP, women with multiple elevated BPs were more likely to carry the diagnosis of PEC at the time of discharge from the ED (14.8% vs 5.3%, $p=0.003$), and at the time of delivery (17.9% vs 4.2%, $p<0.001$).

CONCLUSIONS: Women with multiple elevated BPs are at significantly higher risk for lab abnormalities consistent with PEC and at significantly greater risk for developing PEC by delivery. Delaying laboratory evaluation for PEC in patients presenting to the ED until two abnormal blood pressures are noted may be reasonable.

F-178

Comparison of the fullPIERS Model to Physician Clinical Risk Assessment of Patients with Preeclampsia. Emily E Hadley†, Luis Monsivais†, Guiseppe Chiossi, Sangeeta Jain, Tony Wen, Maged Costantine*. *University of Texas Medical Branch, Galveston, TX, USA.*

INTRODUCTION: The fullPIERS (Preeclampsia Integrated Estimate of RiSk) model was developed to identify women with preeclampsia (PE) at increased risk of adverse maternal outcomes (AMO). Our objective is to determine whether clinical medical judgment predicts the risk of AMO similar to the fullPIERS model.

METHODS: Ten clinical vignettes of patients with PE were developed and validated by independent senior maternal fetal medicine (MFM) faculty. Obstetric providers were asked to participate in a survey which included the vignettes, basic demographic and professional information, and a psychological screening questionnaire. Participants, blinded to the fullPIERS score, were asked to score the patient's risk of developing an AMO for each vignette as low (<10%), medium (10-30%) or high (>30%). Data analyzed using the Fisher exact test and a generalized linear model with logit link and binomial family with robust standard error.

**Figure(s) will be available online.*

RESULTS: Forty-two participants (16.7% MFM faculty, 11.9% OB/GYN faculty, 16.7% MFM fellows, and 52.4% OB/GYN residents) responded to the survey. There was 50% agreement between participants' and the fullPIERS score on risk estimation of AMO (median 47%, interquartile range 33%-60%). Participants who correctly predicted the fullPIERS risk category for the majority of vignettes scored lower on an anxiety questionnaire ($p=0.03$), while females were more likely to overestimate the risk category (93% vs. 60%, $p=0.04$). Older, male participants were more likely to agree with the fullPIERS estimate of a patient's risk

category (OR 1.46, 95% CI 1.05-2.04, p=0.02) and (OR 1.34, 95% CI 1.01-1.56, p=0.047) compared with participants < 30 years, and females respectively. The agreement with fullPIERS score was higher among fellows and faculty compared with residents (p<0.05).
CONCLUSIONS: Physician clinical assessment of patients with PE agreed with fullPIERS model risk stratification 50% of the time. Older physicians categorized risk more consistently with the fullPIERS model. Given these findings, the fullPIERS model may be useful for residents in their assessment of patients with PE.

F-179

Standardization of Sampling for Isolation of Exosomes from Peripheral Blood from Reproductive-Aged Women. Bruna Ribeiro de Andrade Ramos†,[1] Jéssica M Diehl,[1] Natália Prearo Moço,[1] Graziela G Romagnoli,[2] Márcia Guimarães da Silva.[1] [1]*Botucatu Medical School - UNESP, Botucatu, São Paulo, Brazil;* [2]*Biology Institute - UNESP, Botucatu, São Paulo, Brazil.*
INTRODUCTION: Exosomes are extracellular vesicles that act in cell communication and contain proteins and microRNAs. miRNAs are involved in several biologic processes and are associated with reproductive tract damage. While exosomes increase miRNAs stability, there is still a need for standardization of sampling and isolation of these microvesicles. We aimed to determine the best sampling method for isolation of exosomes from peripheral blood from reproductive-aged women.
METHODS: We included samples of plasma from our biobank collected in 2014 by venipuncture in heparin tubes and stored at -80ºC. We also included blood samples collected in heparin tubes and EDTA tubes and stored at -80ºC for one-two weeks prior processing. All blood samples were collected from the same nine reproductive-aged female volunteers and plasma was obtained by centrifugation at 1800g for 10 minutes. Exosomes were isolated from plasma by ultracentrifugation at 120,000g for 90 minutes at 4°C. Exosomes were indirectly quantified using Pierce BCA Protein Assay kit and transmission electron microscopy (TEM) was performed to visually confirm the isolation of exosomes. Paired T-test was used to compare the results (long vs. short-time storage and heparin vs. EDTA).
RESULTS: TEM confirmed the isolation of exosomes.
**Figure(s) will be available online.*
Protein concentration of short-time stored heparin samples was not statistically different from long-time stored heparin samples (1847.2±651.4 vs. 2363.2±1025.1, p=0.14) and there was no difference between heparin and EDTA plasma samples recently collected (2363.2±1025.1 vs. 2044.8±653.2, p=0.44).
CONCLUSIONS: Blood samples may be collected using heparin or EDTA for isolation of exosomes, though more investigation must be performed to evaluate downstream applications. While collection of fresh material may result in more fidelity in absolute quantification of exosomes, our results demonstrate that long-time stored plasma samples maintain exosomes integrity and may be used, especially in comparative studies.

F-180

Metabolic Hormonal Profiles of Follicular Fluid Are Abnormal in Obese Women Undergoing In-Vitro Fertilization. Laurice Bou Nemer†, Haolin Shi, R Ann Word, Bruce R Carr, Orhan Bukulmez. *UT Southwestern, Dallas, TX, USA.*
INTRODUCTION: Obese women experience diminished fecundity, even in the presence of regular menstrual cycles. It has been shown that a BMI>30 is associated with altered oocyte morphology, decreased fertilization, and lower embryo quality. Whereas the serum metabolic profile of obese women has been studied extensively, less is known regarding the metabolic profile of follicular fluid (FF). To test the hypothesis that obesity alters the metabolic profile of FF, we quantified levels of nine metabolic hormones in FF from normal weight, overweight, and obese women undergoing In-Vitro Fertilization (IVF).
METHODS: Ten women of normal weight, ten overweight, and five obese women undergoing IVF at our center were recruited for this study. Patients with medical illnesses, polycystic ovary syndrome, and endometriosis were excluded. All patients underwent the same stimulation protocol. FF was obtained during oocyte retrieval and analyzed through multiplex immunoassays. Bloody fluids were not analyzed.
RESULTS: Age, maximal serum levels of E2 and AMH were similar in all groups. Likewise, the metabolic hormonal profile of FF from normal weight and overweight patients was similar. Interestingly, however, levels of insulin, glucagon, Glucagon-like peptide 1 (GLP-1), C-peptide and leptin in FF from obese women were strikingly increased relative to non-obese patients. Specifically, glucagon, C-peptide, and GLP-1 were increased 1.7- to 2-fold. Concentrations of insulin and leptin were increased 3.5- to 4-fold, suggesting that obesity differentially alters the relative amounts of metabolic hormones in FF.

Hormone	BMI<30 (±SEM)	BMI≥30 (±SEM)	P value
Insulin (pg/mL)	96.4±17.5	398.0±150.2	0.0008
GIP (ng/dL)	25.3±2.6	32.9±6.3	NS
Glucagon (pg/mL)	36.0±3.1	62.1±6.4	0.0009
Ghrelin (ng/dL)	17.4±2.3	10.9±1.1	NS
GLP-1 (pg/mL)	31.4±1.2	43.3±4.8	0.0018
PAI-1 (ng/mL)	49.6±10.9	38.8±8.7	NS
Resistin (pg/mL)	53.8±18.7	38.3±11.7	NS
C-Peptide (ng/dL)	56.5±4.9	86.0±12.6	0.0181
Leptin (ng/mL)	3.6±0.8	12.8±1.4	0.0001

CONCLUSIONS: Overall, these data indicate that obesity significantly affects the metabolic hormonal profile of FF. Previous reports indicate that higher levels of insulin and leptin have a negative impact on IVF outcomes. Our results indicate that obesity is associated with complex abnormalities of metabolic hormone levels in FF, all of which may contribute to adverse outcomes in IVF.

F-181

Antimüllerian Hormone (AMH) Less Than 1 Is Associated with Increased Irregular Cell Cleavage in Women Less Than 35. I Okeigwe†, JC Robins, J Zhang, ME Pavone*. *Northwestern University, Chicago, IL, USA.*
INTRODUCTION: Time-lapse monitoring provides a non-invasive means to monitor early embryonic development. Recent data suggest that older women with low AMH levels are more likely to have abnormal morphokinetic cell cleavage patterns. It is unknown whether this observation holds true among younger women with AMH <1. The purpose of this study was to determine if AMH predicts early morphokinetic cell cleavage patterns in women less than 35.
METHODS: This was a retrospective analysis of women less than 35 years old undergoing fresh autologous IVF cycles. All embryos were cultured in the EmbryoScope®. The following cell cleavage patterns were analyzed: time to 2 cell (t2), 3 cell (t3), 4 cell (t4), 5 cell (t5), 6 cell (t6), 7 cell (t7), 8 cell (t8), and t4-t3 (s2) cleavage synchronicity. Data were analyzed by AMH grouping (<1 versus ≥1) using t-tests, chi squared and mixed model regression.
RESULTS: A total of 791 embryos from the AMH ≥1 group and 139 embryos from the AMH <1 group were analyzed. Baseline characteristics are shown below. Pregnancy rates were no different between both groups. This was true even after adjusting for baseline differences. Time to cell division (t2 through t8) did not differ by AMH group. However embryos from women with AMH <1 were more likely to undergo irregular cell cleavage, defined as a single blastomere dividing into two or more blastomeres (53% vs. 34% p=0.027). AMH <1 remained an independent predictor of irregular cell cleavage even after adjusting for baseline differences between both groups.

	AMH < 1	AMH ≥ 1	p-value
Age	33	32	.39
BMI	23	25	.2
Stimulation days	10	10	.4
Total gonadotropins used (IU)	6432	4384	<.001
Peak E2 (pg/mL)	1476	2165	<.001
Oocytes retrieved	8	14	<.001
Mature oocytes	6	10	<.001
2PN	5	9	<.001
Embryos transferred	1.83	1.58	.03
Positive pregnancy	48%	66%	.08
Clinical pregnancy	31%	50%	.06

CONCLUSIONS: Our data show that embryos from younger women with AMH <1 are more likely to undergo irregular cell cleavage, leading to fewer high quality embryos to transfer. Although we did not find a statistically significant difference in pregnancy rates, the 20% decreased clinical pregnancy rate in women with AMH <1 suggests that our study was underpowered to detect a true difference.

F-182

Differences in Serum and Ovarian Follicular Fluid Metabolites and Reproductive Outcomes of Obese Versus Non Obese Women. Mamie McLean†,[1] Wright Bates,[1] Emily Gordon,[2] Sara Cooper,[2] Lorie Harper*.[3] *[1]UAB, Birmingham, AL, USA; [2]HudsonAlpha, Huntsville, AL, USA; [3]UAB, Birmingham, AL, USA.*

INTRODUCTION: Maternal obesity is associated with poor reproductive outcomes such as infertility, miscarriage and stillbirth. We hypothesized that the mechanisms of these adverse outcomes is, in part, an altered follicular fluid (FF) and serum metabolite profile compared to non-obese women.

METHODS: We performed a prospective cohort study of women aged 21-39 undergoing transvaginal oocyte retrieval (TVOR). Exclusion criteria: endometriosis, BMI <20kg/m2. Serum and FF were obtained at time of TVOR. Samples were analyzed by GCxGC-TOFMS. Metabolites were included if measurable in >66% of samples, were normalized by sum and transformed to a Z-score. MetaboAnalyst was used to compare FF and serum between obese(BMI >=30 kg/m2) and non obese(BMI<25 kg/m2) women, as well as by demographics and reproductive outcome utilizing computational statistics. Demographics were compared using t-tests, Chi squared or ANOVA.

RESULTS: Serum and FF were analyzed from 21 obese and 23 non-obese women. Groups differed by BMI and live birth.

	Obese (n=21)	Non-obese (n=23)	P value
Age (years)	31.7 +/-3.5	31.3+/-3.9	0.70
BMI (kg/m2)	33.5+/-3.19	22.3+/-2.14	<0.001
Race			
Black	23%	4.4%	0.11
Caucasian	76%	82.6%	
Other	0%	13.1%	
Oocytes retrieved	17.2+/-10.5	17.6+/-6.9	0.90
Embryo transfer			
Yes	13 (61%)	11 (47%)	0.34
No	8 (38%)	12 (52%)	
Live birth			
No transfer	8 (38.1%)	12 (52.2%)	0.03
Yes	3 (14.3%)	8 (34.8%)	
No	10 (47.6%)	3 (13.0%)	

No differences were noted in serum or FF metabolites between groups. With age normalization, differences in metabolites were identified among obese women without live birth compared to those obese and non-obese women with live birth.

**Figure(s) will be available online.*

CONCLUSIONS: Differences exist in the FF and serum metabolites of obese women without live birth compared to obese and non obese women with live birth. Many of these metabolites are glucose derivatives. Further investigation into these differences is warranted, as well as validation in an independent cohort.

F-183

An Unconventional Choice of Embryo Transfer Day. Stephanie Baum†, Moti Gulersen†, Tomer Singer*. *Lenox Hill Hospital/Northwell Health, New York, NY, USA.*

INTRODUCTION: Successful implantation during in vitro fertilization (IVF) requires a synchronized dialogue between the endometrium and the embryo. The optimal time for transfer is usually determined by embryo quality on day 3, 5, or 6 following oocyte retrieval. Endometrial factors, the hormonal milieu or luteal phase supplementation may impact receptivity. Ovarian stimulation may also lead to a premature rise in serum progesterone, causing a dissynchronus endometrium. We present a case of a successful pregnancy following the transfer of two thawed euploid day-6 blastocysts 48 hours following retrieval.

METHODS: N/A

RESULTS: CASE: A 35-year-old, gravida 0, presented for evaluation following two years of infertility. Ovarian reserve testing was normal (AMH 2.0ng/mL; day 3 FSH 8.2IU/L). A saline sonohysterogram revealed endometrial polyps which were subsequently removed hysteroscopically. Semen analysis revealed male factor infertility (concentration, motility, morphology). The patient underwent a total of six IVF cycles. An initial IVF ICSI cycle resulted in a day-3 transfer of two embryos which failed to implant. We then proceeded with IVF ICSI preimplantation genetic screening (PGS) batching cycles yielding a total of four euploid embryos. The first frozen cycle was unsuccessful despite the transfer of two euploid blastocysts. During her 6th and final cycle, we decided to transfer two euploid embryos on a fresh endometrium. A premature rise in serum progesterone (1.7ng/mL on the day of the hCG trigger and 9ng/mL the following day) was noted and a decision was made to transfer the two frozen euploid day-6 blastocysts from two different prior IVF cycles, just two days following the retrieval (progesterone increased to 159.8ng/mL on the day of transfer). Endometrial thickness on the day of transfer measured 8mm. Serum hCG level twelve days later was 1504mIU/mL and a dichorionic/diamniotic twin pregnancy was confirmed by ultrasound at 6 weeks gestation. The patient was discharged to her obstetrician at 11 weeks gestation and progesterone supplementation was discontinued.

CONCLUSIONS: Recent significant trends in IVF include blastocyst embryo transfer, PGS and cryopreservation of embryos. We report here a novel concept of transferring a frozen euploid embryo on a fresh endometrium using serum progesterone levels to predict endometrial receptivity and determine the ideal transfer day. This approach may improve implantation rates by challenging the paradigm of blastocyst transfer on day-5 following egg retrieval.

F-184

Interleukin-1ß Regulates Thymic Stromal Lymphopoietin (TSLP) Expression in Cultured Human First Trimester Decidua Cells. Felice Arcuri,[1] Francesco Damiani,[1] Lucia Funghi,[1] Joseph Huang,[2,3] Felice Petraglia*.[1] *[1]University of Siena, Siena, Italy; [2]University of South Florida, Tampa, FL, USA; [3]E-Da Hospital, Kaohsiung, Taiwan.*

INTRODUCTION: Blastocyst implantation is a critical step in the establishment of pregnancy and is strictly regulated by a plethora of decidual molecules, including inflammatory cytokines. Implantation represents a challenge to the maternal immune system that needs to tolerate paternal antigens while maintaining normal immune competence. Among the mechanisms proposed to account for suppressing fetal rejection, the activity of dendritic cells, regulatory T cells (Tregs) and the establishment of a Th2 bias are considered crucial.

TSLP is an interleukin (IL)-7 like protein. Its functional receptor consists of IL-7 receptor α (IL-7Rα) chain and a TSLP-receptor (γc)-like chain (TSLPR). Trophoblast-TSLP targets decidual dendritic cells to induce Tregs differentiation and the acquisition of immunosuppressive features, and polarizes decidua T-cells toward a Th2 subtype. The present study

investigated the contribution of maternal decidua on TSLP synthesis at the fetal-maternal interface by assessing the expression and regulation of TSLP and its receptors in first trimester decidua and in cultured first trimester decidual cells (FTDCs).
METHODS: First trimester decidua was obtained from elective terminations of pregnancy (6-12 weeks). Purified FTDCs (n=5), were treated with control vehicle, 10^{-8} M E2, 10^{-7} M MPA or E2+MPA for 7 days. Cells were also treated with E2+MPA and 1 ng/ml of IL-1β, IFNγ or TNFα alone or in combination. RNA was extracted and relative levels of mRNA for TSLP and its receptors were assessed by quantitative RT-PCR.
RESULTS: The expression of TSLP, IL-7Rα and TSLPR was observed in all the first trimester decidual tissues examined. In cultured FTDCs, the addition of E2 and MPA, either alone or in combination, did not alter the expression of TSLP and its receptors. In contrast, the addition of IL-1β significantly up-regulated TSLP and IL-7Rα mRNA levels (4.3-fold and 69 fold respectively; $p<0.001$) while TNFα and IFNγ had no significant effect.
CONCLUSIONS: The present study indicates that FTDCs represent a novel source and target of TSLP. The observation that IL-1β augments TSLP and IL-7Rα mRNA levels suggests a link between implantation-related inflammation and the establishment of a tolerogenic immune response in early pregnancy.

F-185

Maternal Endometrial hsa-miR-30d Is Taken Up by the Human Blastocyst and Induces Transcriptional Modifications. Meera S Shah†,[1] Felipe Vilella,[1,2] Barry Behr,[1] Vikrant Reddy,[1] Wanxin Wang,[1] Roser Navarro,[3] Jorge Jimenez,[3] Steven Quake,[1] Carlos Simon*.[1,2,3] *[1]Stanford University, Palo Alto, CA, USA; [2]IVI/INCLIVA, Valencia, Spain; [3]Parc Cientific Valencia University, Valencia, Paterna, Spain.*
INTRODUCTION: The endometrial fluid (EF) is actively secreted by the endometrial epithelium containing microRNA (miRNA) which has been implicated in regulating the adhesion of the embryo to the endometrial epithelium (Development 2015). In this work, we aim to demonstrate the internalization of hsa-miR-30d into the *human* blastocyst and to analyze the transcriptomic modifications within the trophectoderm (TE) and inner cell mass (ICM) induced by miR-30d.
METHODS: Cryopreserved human blastocysts were thawed and exposed to culture media containing Alexa 488-labelled miRNA or culture media alone as a control. Embryos were incubated for 24 hours and confocal microscopy was used to localize miRNA within the human embryo. In a separate experiment, cryopreserved-thawed euploid human blastocysts were cultured in 3 conditions: embryo culture media (control #1), embryo culture media with a scramble sequence of miRNA (control #2), and embryo culture media with physiologic concentrations of hsa-miR30d (250nm). After 24 hours of incubation, embryos were washed and separated into trophectoderm and inner cell mass using laser dissection. All samples were sequenced using Next Generation Sequencing at the Stanford Genomics Center. ICM control (n=2), TE control (n=5), ICM scramble (n=1), TE scramble (n=2), mir-30d exposed TE (n=4) and mir-30d exposed ICM (n=4) were included in bioinformatics analysis.
RESULTS: Confocal microscopy results demonstrate that under physiological (250nm) concentration, mir-30d was internalized into the human blastocyst, specifically in a perinuclear distribution in the trophoectoderm. Transcriptomic analysis of ICM demonstrated up-regulation of 186 genes compared to controls, and down-regulation of 1,244 genes. The trophectoderm of mir-30d exposed embryos demonstrated up-regulation of 59 genes and down-regulation of 99 genes compared to controls. Bioinformatics analysis is currently underway to identify putative genes and functional pathways targeted by mir-30d in human embryonic ICM and TE.
CONCLUSIONS: Our results demonstrate that hsa-miR-30d is internalized within the human blastocyst and induces a significant impact on the gene expression profile of the pre-implantation blastocyst, particularly among the transcriptome of the ICM.

F-186

Different Expression Pattern of Transient Receptor Potential Channels in Endometrial Epithelial and Stromal Cells of Mouse and Human. De Clercq Katrien†, Hennes Aurélie†, Vriens Joris*. *KU Leuven, Leuven, Vlaams-Brabant, Belgium.*
INTRODUCTION: Embryo implantation is a complex process that requires a competent blastocyst, a receptive endometrium, and the intricate embryo-uterine crosstalk mediated by a myriad of factors. In order to achieve successful embryo implantation, an effective communication is required between the blastocyst, endometrial epithelial and stromal cells. However, the exact mechanism that allows communication between the epithelium and stroma upon embryo attachment and invasion remains to be elucidated. Possible candidates to govern these downstream events are calcium permeable ion channels that serve as important cellular sensors. Here, we investigate the functional expression of members of the Transient Receptor Potential (TRP) ion channel family in endometrial epithelial and stromal cells of mouse and human.
METHODS: Primary cultures of endometrial epithelial and stromal cells of mouse and human were studied for expression of TRP channels by quantitative RT-PCR and intracellular calcium imaging recordings.
RESULTS: Our results indicate a very distinct expression pattern in epithelial cells compared to stromal cells. Expression of TRPV4, TRPV6, and TRPM6 was significantly higher in epithelial cells whereas TRPV2, TRPC1/4, and TRPC6 were almost exclusively expressed in stromal cells. In addition, a significant positive correlation was observed between the expression pattern in mouse compared to human.
CONCLUSIONS: These data showed a very distinct expression pattern in epithelial and stromal cell populations, what could be linked to different functions during the implantation process. In addition, our data provide evidence that mouse endometrium is a valid representative for human endometrium to investigate the role of TRP channels in reproduction.

F-187

Reprogramming of the hCG Signaling Profile in Human Endometrial Stromal Cells from Recurrent Miscarriage Patients. Shirin Khanjani†,[1] Camilla West,[1] Jan J Brosens,[2] Stuart Lavery,[1] Phillip R Bennett,[1] Aylin C Hanyaloglu*.[1] *[1]Imperial College London, London, United Kingdom; [2]Warwick University, Warwick, Coventry, United Kingdom.*
INTRODUCTION: Cross-talk between an implanting embryo and the uterine endometrium is vital for successful implantation. Locally secreted factors within the uterine environment play a vital role in this feto-maternal communication. Human chorionic gonadotrophin (hCG), a glycoprotein hormone secreted by the embryo, plays key functions in the ovary and uterine endometrium via its cognate G protein-coupled receptor (LHCGR). The signal pathways activated by LHCGR within the endometrium are largely unknown. Perturbations in hCG action in endometrial stromal decidualization has been shown to be associated with recurrent miscarriage (RM), a key mechanism in perturbed embryo quality control at the feto-maternal interface in these patients. The goal of this study is to identify the LHCGR signalling pathways activated by hCG in the endometrial stroma, during deciudalization in control and RM patients. Regulation of LHCGR activity during decidualization may represent an important mechanism mediating hCG action in normal pregnancy and also to develop novel approaches in the prediction and management of RM.
METHODS: Human endometrial stromal cells (HESCs) from either control patients or RM patients were decidualised for 72 hours, or left undifferentiated. Expression of LHCGR was confirmed in both patient groups. Cells were then stimulated at 0, 5 and 30 minutes with hCG. The resulting protein lysates were used to probe phospho-MAPK array membranes that detect 26 different phospho-MAPKs. Fold change over basal for each target at the 5 and 30 minutes time points was calculated. Data was further validated using Western blotting.
RESULTS: Collectively, the array data strongly suggests that control and RM patients have opposing signalling pathways. In control, many pathways activated by hCG in undifferentiated cells are decreased in decidualised cells and only a subset of pathways are activated. In RM, the same pathways are either not activated or not deactivated following decidualisation.

CONCLUSIONS: Our data shows that decidualisation reprograms the signalling profile in control but not recurrent miscarriage HESCs. The failure of RM HESCs to reprogram their hCG signalling upon decidualisation could be an important defect which contributes to erroneous embryo selection at the time of implantation that can lead to pregnancy loss.

F-188

Extracellular Vesicles Secreted by the Human Endometrium Contain Specific DNA Sequences That Are Uptaken by Murine Embryos. David Bolumar†,[1,4] Inmaculada Moreno,[1,3,5] María Herrero,[3] Sergio Cabanillas,[2] Felipe Vilella,[3,5] Carlos Simon*.[1,2,3,4,5] *[1]Igenomix S.L., Paterna, VLC, Spain; [2]IVI Valencia, Valencia, VLC, Spain; [3]IVI/INCLIVA, Valencia, VLC, Spain; [4]Valencia University School of Medicine, Valencia, VLC, Spain; [5]Stanford University Medical School, Palo Alto, CA, USA.*

INTRODUCTION: Human endometrial fluid (EF) contains different extracellular vesicles (EVs) populations secreted by the endometrial epithelium as a convenient system for the delivery of molecules from the mother to the embryo protected from the extracellular environment. Here, we investigated the different EVs populations [apoptotic bodies (ABs), microvesicles (MVs) and exosomes (EXOs)] present in the human endometrial fluid as well as their cargo, focusing on their DNA content. We demonstrated that different human endometrial EVs contain specific DNA sequences that are internalized by murine embryos.

METHODS: EVs populations from the EF were isolated by ultracentrifugation/filtration, and analyzed by transmission electron microscopy, nanoparticle tracking analysis and western blot to check for EVs types, purity and yield. The DNA into the EVs was identified, purified and sequenced. In parallel, EVs were labeled with EdU and co-incubated with hatched murine embryos to study their uptake and DNA integration.

RESULTS: EVs characterization showed the existence of two ABs populations around 3.6 μm and 270 nm. MVs and EXOs presented smaller and overlapping size ranges (around 290 nm and 140 nm, respectively). The molecular signature of the different EVs was characterized by VDAC1, calreticulin, ARF6, CD63, CD9 and TSG101.

DNA cargo was quantified and sequenced, revealing that each EVs population was enriched in specific gene sequences (41, 143 and 193 unique sequences in ABs, MVs and EXOs, respectively), being EXOs the EVs fraction most abundant in DNA. Moreover, endometrial EVs DNA was uptaken by murine embryos and identified in their nuclei.

CONCLUSIONS: Here, we demonstrated for the first time the presence of three different types of EVs in the human EF with differential DNA cargo, and the uptake of this maternal DNA by the embryo. The functional relevance of this discovery is currently being assessed.

CS and FV contributed equally.

F-189

Plural Murine Follicles Can Ovulate Simultaneously In Vitro with Angiotensin II Receptor Analogue Treatment. Seung-Yup Ku,[1] Yoon Young Kim,[1] Yong Jin Kim,[2] Byeong-Cheol Kang,[3] Hung Ching Liu.[4] *[1]Seoul National University Hospital, Seoul, Korea; [2]Korea University Guro Hospital, Seoul, Korea; [3]Seoul National University Hospital, Seoul, Korea; [4]Weill Cornell Medical College, New York, NY, USA.*

INTRODUCTION: In vitro ovarian follicle culture is a valuable technique to get mature oocytes from preserved ovarian tissue of young cancer survivors. However, current in vitro follicle culture techniques require high burden of labor with low efficiency because only single follicle culture has been possible. We evaluated the feasibility of in vitro plural follicle culture using angiotensin II receptor analogues.

METHODS: Preantral follicles were isolated from 12-day-old C57BL6 mice and cultured with ATII-Rc treatment. The results of two-follicle culture was compared with those of single follicle culture.

RESULTS: When two-follicle clusters were cultured, up to two follicles ovulated in the ATII-Rc agonist group while none or one follicle ovulated in control group ($p < 0.01$). Significantly higher number of mature oocytes were obtained in the agonist group ($p < 0.01$). Fertilization efficiency did not differ between the two groups.

CONCLUSIONS: Conclusively, in vitro plural follicle culture can significantly improve the efficiency via ATII receptor modulation (HI14C2259).

F-190

FOXO3 Expression in the Human Ovary. Helen P Swenson,[1] Alice Rhoton*,[1] Dawn Beachy,[2] Harry Nick,[2] Demaratta Rush.[3] *[1]University of Florida, Gainesville, FL, USA; [2]University of Florida, Gainesville, FL, USA; [3]University of Florida, Gainesville, FL, USA.*

INTRODUCTION: The quality and quantity of primordial follicles is a primary indicator of ovarian reserve and thus female fertility. In a tightly regulated process, primordial follicles are maintained in a quiescent state until molecular recruitment signals lead to activation. An understanding of the molecular mechanisms of follicle recruitment may provide insights for potential interventions targeting fertility preservation. The transcription factor FOXO3 has been shown to be critical in folliculogenesis, acting specifically as a block to primordial follicle activation to primary follicles in rodent, cow and pig ovaries. The most definitive evidence is derived from mouse models, where $Foxo3^{-/-}$ mice become infertile by 15 weeks due to global follicle activation, whilst transgenic mice overexpressing Foxo3 specifically in the ovary are infertile due to a complete lack of follicle activation. To date, however, no definitive evidence documents the expression of FOXO3 protein or mRNA in the human ovary. We therefore have sought to evaluate FOXO3 protein expression by immunohistochemical (IHC) analysis in pre-menopausal and de-indentified human ovarian tissues.

METHODS: We evaluated mRNA expression in normal human ovary biopsies by real-time qPCR of genes associated with the FOXO3 pathway and folliculogenesis including: AKT, PTEN, PIK3CA, PIK3R1, INPP4B, FOXL2, KITLG, KIT, RSPO1, WNT4, and SGMS2.

We also evaluated FOXO3 protein expression by immunohistochemical (IHC) analysis in pre-menopausal and postmenopausal de-indentified human ovarian tissues.

RESULTS: Contrary to a single previous report, we observe FOXO3 protein and mRNA expression in human ovary in reproductive age women. The cellular pattern of protein expression, however, appears to be different than has been described in the mouse ovary. In addition, we have also evaluated and confirmed mRNA expression in normal human ovary biopsies by real-time qPCR of genes associated with the FOXO3 pathway and folliculogenesis including: AKT, PTEN, PIK3CA, PIK3R1, INPP4B, FOXL2, KITLG, KIT, RSPO1, WNT4, and SGMS2.

CONCLUSIONS: Our IHC and mRNA expression results provide the opportunity to address the relevance of the FOXO3 pathway and other factors potentially important to folliculogenesis and female fertility. We are currently now comparing these findings to postmenopausal ovarian tissue.

F-191

The lncRNA H19 Is Regulated by FSH and Estradiol, and H19 KD Results in Altered Follicular Dynamics and Enhanced Gonadotropin Response. Yanhong Fan,[1] Chunrong Qin,[1] Joshua Johnson,[2] Amanda Kallen*.[1] *[1]Yale School of Medicine, New Haven, CT, USA; [2]University of Colorado Anschutz Medical Campus, Aurora, CO, USA.*

INTRODUCTION: A successful response to fertility treatment requires proper steroid hormone production, ovarian follicle recruitment, and oocyte production. H19 is a long non-coding RNA with important roles in growth and development, which is expressed in increasing amounts in maturing ovarian follicles. H19 regulates the expression of steroidogenic acute regulatory protein (StAR), which is a key enzyme in ovarian steroidogenesis, and knockdown of H19 increases estradiol production *in vitro*. We therefore hypothesize that H19 may play a role in the regulation of ovarian follicle development and response to gonadotropin stimulation, and that H19, itself, may be regulated in response to gonadotropins or steroids.

METHODS: H19 KO mice (n=8, age 8-12 weeks, a gift from Dr. Stefan Muljo) were assessed to determine ovarian folliculogenesis and response to controlled ovarian stimulation with exogenous gonadotropins. KGN cells (a human granulosa cell line) were treated with FSH (100 IU/mL) or E2 (10^{-8}M), and RNA extraction and qRT-PCR performed to determine H19 expression.

RESULTS: H19 KO mice showed significantly higher number of secondary (4.6 follicles/slide for KO vs 1.9 follicles/slide for WT; p=0.05), pre-antral (4 vs 2.1; p<0.05) and antral follicles (2.1 vs 1.0), and produced significantly more oocytes in response to gonadotropin stimulation (21.9 for KO vs 14.6 for WT; p<0.05). We observed that treatment of KGN cells with FSH stimulates H19 expression by over 50% 4 hours after treatment (p<0.05). Additionally, E2 treatment increased H19 expression by 5x after 48 hours (p<0.05).
CONCLUSIONS: We find that in absence of H19, spontaneous development of secondary, preantral and antral follicles and ovarian response to gonadotropins are significantly increased, suggesting that H19 may act as a brake to achieve optimal follicle development under normal conditions and during ovarian stimulation. We also find that H19, in turn, is regulated by both FSH and E2, suggesting that increased E2 production during follicle development may upregulate H19 to prevent further follicle recruitment. Additional studies are required to further delineate H19's role in follicle development and whether it can be exploited for reproductive success in appropriate subjects.

F-192

Non-Invasive Imaging of Living Follicles in Human Ovarian Cortex with Reflectance Confocal Microscopy. Myra J Schleedoorn†,[1] Malou Peppelman,[2] Willianne LDM Nelen,[1] Kathrin Fleischer,[1] Ron Peek*.[1] *[1]Radboud University Medical Center, Nijmegen, Gelderland, Netherlands; [2]Radboud University Medical Center, Nijmegen, Gelderland, Netherlands.*
INTRODUCTION: Cryopreservation of ovarian tissue is a viable option for fertility preservation in girls and young women facing fertility threatening cancer treatments. Autotransplantation of cryopreserved/thawed ovarian tissue has resulted in restoration of ovarian function, and at present, more than 60 live births have been reported. The chance of getting pregnant is most likely related to the number of primordial follicles in the autograft. However, the follicular density in tissue fragments prepared from the same ovary may differ more than two orders of magnitude. To be able to select the tissue fragments with the highest number of primordial follicles we developed a non-invasive *ex-vivo* method to determine the number of follicles in living ovarian cortex tissue fragments.
METHODS: Cortex fragments of 8 bovine ovaries (ages 7-8 months) and 3 human ovaries (ages 5, 23 and 35 years) were imaged with reflectance confocal microscopy (RCM) by using the VivaScope® 1500. Afterwards, the tissue samples were fixed and embedded in paraffin for conventional histological analysis. The RCM images were then compared to the corresponding hematoxylin and eosin stained sections by two investigators. The distribution of follicles, the follicular density and other histological aspects of the ovarian tissue were assessed. The effect of RCM imaging on overall ovarian tissue viability was determined by a glucose uptake assay, while follicular viability was assessed using a neutral red viability stain.
RESULTS: RCM on ovarian cortical tissue provides microscopical images that correspondent to histochemical analysis to a maximum depth of 250 μm.
Primordial follicles could be detected from a depth of 50 μm to 200 μm, and were easily to distinguish from other ovarian tissue structures. The highest density of primordial follicles was seen between 75-175 μm. Remarkably, other stages of follicular development (e.g. antral follicles) were located at 150 μm and deeper. The viability of ovarian tissue and primordial follicles during the imaging process was found sufficient.
CONCLUSIONS: RCM is a promising, non-invasive imaging technique which can be used to detect *ex vivo* the total number of primordial follicles in living ovarian cortical tissue. In future, RCM could be used for selection of ovarian tissue fragments for autotransplantion.

F-193

Inflammatory Monocytes Regulate Endometrial Repair and Remodeling. Phoebe M Kirkwood,[1] Fiona L Cousins,[2] Philippa TK Saunders,[1] Douglas A Gibson*.[1] *[1]The University of Edinburgh, Edinburgh, Midlothian, United Kingdom; [2]Hudson Institute for Medical Research, Clayton, VIC, Australia.*
INTRODUCTION: The endometrium is a dynamic tissue that undergoes cyclical episodes of proliferation, degeneration, tissue repair and remodelling in response to the 'injury' inflicted on it during menstruation. Inflammatory cells play an essential role in tissue breakdown during menses but their role in repair and restoration of tissue homeostasis remains poorly understood. Defective post-menstrual repair and remodelling has been implicated in the aetiology of several gynaecological disorders including heavy menstrual bleeding and endometriosis. In the current study we utilised a mouse model of simulated 'menstruation' to investigate immune cell dynamics during endometrial repair and remodelling.
METHODS: Menstruation was simulated in MacGreen® mice, in which cells of the mononuclear phagocyte system express GFP. Uterine tissues were recovered prior to tissue breakdown and during endometrial repair and remodelling (0, 24, 48h after removal of progesterone pellet). Tissue distribution of immune cells (GFP^+; $F4/80^{+/-}$) and apoptosis was determined by immunohistochemistry. Flow Cytometry was used to quantify immune cell populations.
RESULTS: We found that 'menstruation' was associated with a striking transient influx of GFP^+ inflammatory monocytes (p<0.001). $GFP^+F4/80^+$ monocyte-derived macrophages were associated with discrete regions of tissue breakdown and repair. Influx of GFP^+ cells peaked 24 hours after withdrawal of progesterone. GFP^+ cells underwent apoptosis by 48 hours following restoration of tissue integrity and completion of endometrial repair. A stable, tissue-resident $F480^+$ macrophage population was detected that was unchanged throughout the time course and was not associated with regions of repair and remodelling.
CONCLUSIONS: These data provide the first compelling evidence to support a dynamic role for inflammatory monocytes in endometrial repair and provide the platform for future studies on the role of these cells in the regulation of endometrial function in health and disease.

F-194

First-Trimester Trophoblasts Promote Differentiation of IL-8 Expressing ILC3s. Kristina MT Hilz†, Damián O Muzzio†, Laura Núñez Castro†, Christine Lamb†, Marek Zygmunt*. *University of Greifswald, Greifswald, Germany.*
INTRODUCTION: One of the essential steps in the establishment of pregnancy is the highly regulated process of trophoblast invasion. Abnormal invasion can lead to severe pregnancy- associated pathologies such as preeclampsia, intrauterine growth-restriction and even loss of the embryo. The recent description of Innate Lymphoid Cells 3 (ILC3) in the uterus, which produce a number of trophoblast-related cytokines, suggests that they might play an important role in this sensitive phase. Here, we studied the influence of the first-trimester trophoblastic cell line HTR-8/SVneo on ILC3s ex vivo.
METHODS: PBMCs were isolated by density gradient from healthy non-pregnant fertile women. Cells were then cultivated for 48 h either with or in absence of supernatant from HTR-8/SVneo and the expression of intra- and extracellular markers of ILC3s (lin^-, $RORγT^+$), their cytokine production (IL-8, IL-17, IL-22, IFN-γ) and activation markers (CD69) were studied. Appropriate controls and blocking antibodies were used. Detection was performed by Flow Cytometry. Data was analyzed using FlowJo software. Statistical significance was assessed by t-test.
RESULTS: The expression of IL-8 producing ILC3s was more than doubled under the stimulation with supernatant from HTR-8/SVneo (p<0,05). Trophoblast supernatant decreased the level of activation of ILC3s as compared to controls (p<0,001). The percentage of IFN-γ producing ILC3s was elevated.
CONCLUSIONS: Our data suggests that trophoblasts may influence ILC3s expression and downregulate their activation in decidua. A possible role of this mechanism in the regulation of trophoblastic invasion and maternal immune response to pregnancy needs further investigation.

F-195

Elevation of Reactive Oxidative Species in Uterine Myeloid Cells During Early Pregnancy. Hui Zhao, Flora Kalish, Ronald J Wong, David K Stevenson. *Stanford University School of Medicine, Stanford, CA, USA.*

INTRODUCTION: In early pregnancy, leukocytes infiltrate the uteri to regulate vascular remodelling and development. At this time, uteri and placentas are exposed to hypoxia (2%–3% O_2), which is due to the presence of cytotrophoblast cell plugs in uterine spiral arteries. This is a normal physiological process, but its exact function is unknown. Here, we aimed to elucidate the role of hypoxia in the regulation of placental development during early pregnancy by measuring oxidative stress levels in infiltrating myeloid cells in uteri and subsequent alterations in their phenotype and function.

METHODS: Blood and uteri were collected and single cell suspensions prepared from timed mouse pregnancies at early- (E8.5–10.5) or mid-gestation (E12.5–14.5). Using flow cytometry, myeloid cells were identified and reactive oxidative species (ROS) levels in each individual cell population were quantitated. Myeloid cell surface markers and chemokine expression levels were also determined. In addition, total antioxidant capacity (TAC) in uteri and blood were measured using an antioxidant assay kit.

RESULTS: During early pregnancy, we found an elevation of ROS levels only in $CD45^+$, but not $CD45^-$ uterine cells. Flow cytometry revealed this elevation in infiltrating myeloid cells ($CD45^+CD11b^+$), such as macrophages, granulocytes, and dendritic cells, to be ~6–8 fold higher than blood, and also dependent upon gestational age, being highest in early pregnancy and decreasing gradually to blood levels by E14.5. Moreover, TAC in uterine tissues was significantly reduced compared with blood and liver. *In vitro* treatment of myeloid cells with heme or LPS significantly increased ROS levels, but were reduced by treatment with antioxidant vitamins E and C. These uterine myeloid cells also possess surface markers $Gr1^{hi/lo}CCR2^+CD11C^{lo}F4/80^-$, which is similar to myeloid-derived suppressor cells that are involved in immunosuppression at tumor sites. In addition, VEGFR-1 expression correlated with ROS levels. Finally, IL-10 expression was significantly reduced in uterine myeloid cells compared with blood, but pro-inflammatory cytokines displayed no significant differences.

CONCLUSIONS: We conclude that hypoxia during early pregnancy is necessary for normal placental development by inducing ROS levels in uterine myeloid cells, which, in turn, regulates cell function, such as immunosuppression, vascular formation, and inflammation, and may subsequently affect placental development.

F-196

Adherence to a "Healthy" Dietary Pattern Is Positively Associated with Semen Parameters Especially in Men with Poor Semen Quality. Eline C Oostingh†,[1] Régine PM Steegers - Theunissen,[3] Jeanne HM de Vries,[4] Joop SE Laven,[2] Maria PH Koster*.[1] *[1]Erasmus MC, University Medical Centre, Rotterdam, Netherlands; [2]Erasmus MC, University Medical Centre, Rotterdam, Netherlands; [3]Erasmus MC, University Medical Centre, Rotterdam, Netherlands; [4]Wageningen University, Wageningen, Netherlands.*

INTRODUCTION: Semen quality seems to decline worldwide. There is increasing evidence that besides intrinsic factors, semen quality can also be affected by modifiable behaviors, such as nutrition. Therefore, the objective of this study was to investigate the associations between dietary patterns and semen quality parameters.

METHODS: Men participating in the Rotterdam Periconceptional Cohort with an available semen analysis and completed Food Frequency Questionnaire were included. Food groups were determined using the Dutch food composition table. Principal Component Analysis was performed and identified a 'Healthy' and 'Unhealthy' dietary pattern. Linear regression analysis was performed to study associations between these dietary patterns and semen parameters, stratified for men with normospermia and low total motile sperm count (TMSC > or <10) and adjusted for total energy intake, body mass index, age, ethnicity and smoking.

RESULTS: Men included in our study (n=129) were on average 35±6 years and 84 (65%) of them had normospermia. Strong adherence to the 'Healthy' dietary pattern was positively associated with semen parameters, especially in men with low TMSC.

	TMSC		Concentration		Count		Volume		Progressive Motility	
	ß	p	ß	p	ß	p	ß	p	ß	p
Healthy										
TMSC <10	0.48	<0.01	0.47	<0.01	1.55	<0.01	-0.03	0.85	6.76	0.05
TMSC >10	0.07	0.28	0.05	0 44	0.48	0.35	-0.02	0 74	0.86	0.51
Unhealthy										
TMSC <10	0.04	0.78	0 06	0.70	0.04	0.92	0.27	0.01	-0.21	0.95
TMSC >10	-0.20	0.01	-0 03	0 72	-1.16	0.08	-0.12	0.09	-3.10	0.06

Although there was a trend towards a diminution in semen quality, we found no significant associations with strong adherence to the 'Unhealthy' dietary pattern.

CONCLUSIONS: The positive associations between strong adherence to a 'Healthy' dietary pattern and semen parameters support the importance of preconceptional tailored nutritional counseling and coaching of couples who are trying to conceive.

F-197

Genetic Variation Underlying the Clinical Heterogeneity of Endometriosis. Kenneth Ward*, Rakesh Chettier, Hans Albertsen. *Juneau Biosciences, Salt Lake City, UT, USA.*

INTRODUCTION: The clinical presentation of women with histology-proven endometriosis is quite variable. Some women are asymptomatic even with extensive lesions, some present with infertility only, and others have debilitating pain. We have generated an expanding list of gene variants associated with endometriosis. The purpose of this study is to ask whether any of these genetic markers have strong association with painful endometriosis versus endometriosis causing infertility without chronic pelvic pain or primary dysmenorrhea.

METHODS: 727endometriosis patients presentingwith pelvic pain and 138 presenting with infertility were genotyped on a custom designed microarray using the Affymetrix Axiom platform according to the manufacturer's instructions. All subjects were confirmed caucasian ethnicity using principal component analysis. Differences in allele frequencies between cohorts were tested for each SNP by a 1-degree-of-freedom Cochran-Armitrage Trend test.

RESULTS: Several genetic variants associated with endometriosis have significantly different allele frequencies in the pain cohort compared with the infertility cohort. Examples are shown in the table below.

Gene	ExAc Allele Frequency	Chronic Pain Allele Frequency	Infertility Allele Frequency	Odds Ratio Pain vs. Infertility	Odds Ratio Pain vs. Infertility
TBX18	0.5706	0.4805	0.5766		0.68
DFNB31	0.1636	0.1007	0.1606	0.0040	0.59
COL21A1	0.1274	0.0639	0.1159	0.0021	0.52
CRELD2	0.0313	0.0282	0.0616	0.0040	0.44
OR51Q1	0.0066	0.0089	0.0290	0.0259	0.30
LRP1B	0.0127	0.0000	0.0109	0.0001	0.00
SCLY	0.0006	0.0000	0.0073	0.0011	0.00
BIRC8	0.0004	0.0000	0.0072	0.0012	0.00
BMP3	0.0006	0.0000	0.0072	0.0012	0.00

CONCLUSIONS: It has been difficult to describe meaningful clinical sub-types of endometriosis based on histology or surgical staging. Our data suggest that a portion of the clinical heterogeneity may be explained

by the genetic risk factors underlying endometriosis. Of course, larger studies and further replication will be required to achieve the goal of classifying meaning phenotypes and individualizing patient care based on these insights.

F-198

Recombinant Luteinizing Hormone (rLH) Can Reduce FSH Requirements in Normal Responding IVF Patients without Endogenous LH Activity. Alice J Shapiro†,[1] Emily Holden†,[1,2] Peter McGovern*.[1,2] [1]*Rutgers New Jersey Medical School, Newark, NJ, USA;* [2]*University Reproductive Associates, Hasbrouck Heights, NJ, USA.*

INTRODUCTION: Previous studies have shown that addition of LH during controlled ovarian hyperstimulation (COH) increases ovarian response to FSH. It is thought that LH drives follicular maturation of the dominant follicle in ovulatory cycles as FSH levels decline in the late follicular phase. Our objective is to develop a new stimulation protocol that more closely mimics physiologic hormonal fluctuations in a natural menstrual cycle. We hypothesize that the addition of rLH (Luveris®, Ferring Pharmaceuticals, USA) in the mid-late follicular phase of COH while reducing then stopping the FSH will result in more mature follicles and improved birth rates.

METHODS: Women ages 18 to 38 were randomized to two groups: the standard stimulation protocol (Group A) or the experimental group (Group B). Women with hypothalamic amenorrhea, hyperprolactinemia or iatrogenic hypothalamic hypogonadism were included. Patients in Group A received a fixed dose of 75 international units (IU) of rLH daily with variable doses of FSH, as clinically indicated. In Group B, once an adequate ovarian response was observed (estradiol > 250 pg/mL), the patients' FSH dose was gradually reduced by 75 IU until zero while rLH was increased by 75 IU to a maximum dose of 225 IU. Pituitary suppression was achieved with either a GnRH agonist or antagonist. Ovulation was achieved with an hCG trigger. Total follicle number, amount of FSH used, oocytes retrieved and live birth rates were compared. Mann-Whitney tests were used to compare groups.

RESULTS: A total of 14 patients were included: 5 in Group A and 9 in Group B. Inadequate sample size occurred because of voluntary withdrawal of the medication from the US market. No statistically significant difference could be obtained in COH cycle outcomes. In the 8 normal responder patients who did not require increasing FSH doses beyond the starting dose, a significantly smaller amount of FSH was needed to obtain similar efficacy [mean units of FSH administered in Group A = 1668 IU vs 1162 IU in Group B ($P < 0.001$)].

CONCLUSIONS: Our analysis did not show any overall differences between groups. In the subset of normal responders, we found similar clinical outcomes using significantly lower amounts of FSH for stimulation in our Group B which replaced FSH with LH as ovarian stimulation progressed.

F-199

Racial and Ethnic Differences in Morphokinetic Cell Cleavage Patterns. I Okeigwe†, ME Pavone, J Zhang, JC Robins*. *Northwestern University, Chicago, IL, USA.*

INTRODUCTION: Time-lapse monitoring has allowed for a greater understanding of morphokinetic dynamics during embryonic development. However, it is unknown if cleavage times vary by race/ethnicity and thus if morphokinetic algorithms for embryo selection should vary by race/ethnicity. The purpose of this study was to determine if racial/ethnic differences exist in early morphokinetic cell cleavage patterns.

METHODS: This was a retrospective analysis of women undergoing fresh autologous IVF cycles. All embryos were cultured in the EmbryoScope®. Time to t2 through t8 cell division and cleavage synchronicity (s2) were analyzed. Data were analyzed by race/ethnic group: white (referent group), Hispanic, black, and Asian. Statistical analysis was performed using t-tests, chi squared, and mixed model regression.

RESULTS: A total of 1452 embryos were analyzed. Baseline characteristics are shown below. There were no differences in pregnancy rates for each minority group compared to white women even after adjusting for baseline differences. Morphokinetic parameters also did not differ between black and white women. However, Hispanic women had an earlier t2, while Asian women had an earlier t5 and t6. These parameters remained statistically significant even after adjusting for baseline differences.

	White (N=1019)	Hispanic (N=161)	Black (N=86)	Asian (N=186)
Age	35	37*	39*	34
BMI	25	27	28*	23
Stimulation days	10	9.8	9.9	10.3
Total gonadotropins (IU)	5101	4877	6088	4444
Peak E2 (pg/mL)	1811	1713	1701	2354*
Oocytes retrieved	11.6	9.6	13.3	13.6
Mature oocytes	8.5	6.6*	6.6	10.1
2PN	6.5	5.8	6.5	8.7*
Embryos transferred	1.9	1.9	2.5*	1.8
Positive pregnancy	54%	53%	53%	65%
Clinical pregnancy	36%	27%	33%	54%
*p<.05				

	White	Hispanic	Black	Asian
t2	26.8	25.2*	28.7	26.6
t3	36.2	34.6	35.8	35.9
t4	38.5	36.9	38.5	38.1
t5	48.1	45	49	42.6*
t6	52.9	50.6	51.8	47.7*
t7	56.4	52.8	54.3	55.5
t8	59.6	58	57.4	62.7
s2 (t4-t3)	2.5	2.3	1.7	3.0
*p<.05				

CONCLUSIONS: Hispanic and Asian women have earlier cell cleavage times during embryonic development. These racial differences may help explain inconsistencies within the morphokinetic literature. Our findings demonstrate that each IVF laboratory must develop morphokinetic algorithms specific to their diverse patient population.

F-200

Impact of Assisted Reproductive Technologies on Pregnancy Outcomes Among Patients of Extremely Advanced Maternal Age. Stefanie J Hollenbach†, Lauren A Miller†, Courtney Olson-Chen†, Dongmei Li, Timothy Dye, Loralei Thornberg*. *University of Rochester Medical Center, Rochester, NY, USA.*

INTRODUCTION: The proportion of women giving birth after the age of 45 following spontaneous conception (SC) and aided by assisted reproductive technologies (ART) has increased significantly over the last several decades. We set out to describe perinatal outcomes in a contemporary cohort of women of extremely advanced maternal age (≥45, EAMA) between those utilizing ART and those with SC.

METHODS: The NYS Perinatal Data System in Upstate New York contains information on 724,802 pregnancies from 2005-2014. Pregnancy outcomes were compared between women ≥45 at delivery with and without use of ART for all patients and for those with singleton pregnancies. Chi-square tests for categorical variable analysis with p-value <0.05 considered significant; odd ratios calculated for significant comparisons.

RESULTS: Of 1460 women of EAMA, 26% utilized ART technologies and 16% had multifetal pregnancies. Women with SC had higher rates of pre-pregnancy risk factors including obesity and diabetes as compared to women using ART. However, SC was associated with a decreased odds of cesarean delivery, preterm birth, low birth weight, pregnancy-associated HTN, and ICU admission as compared to ART conceptions. Pregnancy-associated hypertension OR 2.03 (CI 1.25-3.31), preterm birth OR 1.65 (CI 1.07-2.55), and cesarean delivery OR 1.5 (CI 1.12-2.03) remained significantly higher even in singleton pregnancies conceived through ART in the EAMA population.

CONCLUSIONS: There is an excess of maternal and fetal risk for women of EAMA with the use of ART. Although increases in the incidence of multi-fetal gestation contributes to this risk profile, it does not appear to comprehensively explain the difference in risk for these women. Appreciation of this risk profile may have implications for preconception counseling, antepartum care, and delivery planning.

F-201

How Should the Threshold Value for Determining Elevated Progesterone in ART Cycles Be Determined? Toral P Parikh†,[1] Mae Healy†,[1] Kate Devine,[2] Kevin Richter,[2] Alan DeCherney,[1] Micah Hill*.[1] *[1]NIH, Bethesda, MD, USA; [2]Shady Grove Fertility Center, Rockville, MD, USA.*

INTRODUCTION: Elevated progesterone (P) on the day of oocyte maturation trigger is associated with decreased live birth. The thresholds to define elevated P ranged from 0.8 to 2.5 ng/ml in the literature. The objective was to critically assess the threshold for P to predict live birth.

METHODS: A retrospective analysis of 5,344 ART fresh embryo transfer cycles were analyzed. Thresholds were validated in 889 ART cycles where P did not affect clinical decision-making. P thresholds were generated using 14 different methodologies: 95th percentile-donor cycles, 95th percentile-infertile cycles, ROC curve generated optimal threshold and 80%, 90%, 95% sensitivity or specificity, greater than efficiency curves with -5, -10, -15, -20% absolute reduction in birth, and lowest value with a statistical reduction in birth.

RESULTS: Calculated P thresholds varied from 0.4 to 3 ng/ml.

Study data set					
Method	**P Threshold (ng/ml)**	**Birth rate above value (%)**	**Birth rate below value (%)**	**Abnormal tests (%)**	**NNH**
ROC 80% sens	0.4	40	39.5	95	200
ROC 90% sens	0.5	40.5	39.5	90	100
ROC 95% sens	0.66	41	38.9	79	48
Significance threshold	0.7	42.2	38.7	76	29
ROC max sens/spec	1.04	41.9	36.3	46	18
absolute -5%	1.3	41	34.9	25	14
ROC 80% spec	1.33	40.9	34.2	23	15
ROC 90% spec	1.56	40.3	32.4	12	13
ROC 95% spec	1.75	40.1	29.5	7	10
absolute-10%	1.78	40.2	29.9	6	10
95% infertile	1.83	40	26.6	6	8
absolute-15%	1.87	40	25.6	4	7
absolute-20%	2	40	20.7	2	6
95% donors	3	40	20	0.2	5

Lowest thresholds were from ROC curves maximizing sensitivity. Highest thresholds were from greater than efficiency curves of donor cycles. Lower thresholds classified the majority of cycles as abnormal requiring large numbers needed to harm (NNH). Conversely, P thresholds (1.75 to 1.87 ng/ml) classified 6-7% of patients as abnormal with NNH between 6-9 cycles. Validation data confirmed the utility of P threshold above 1.75 ng/ml.

CONCLUSIONS: Analysis generated low P thresholds with large NNH at which the majority of ART cycles would be abnormal. Thresholds identified between 1.75-1.87 ng/ml appeared to maximize the screening utility of the test.

F-202

Neonatal Outcomes of Triplet Pregnancies Conceived via In-Vitro Fertilization. Danielle A Peress†,[1] Alan M Peaceman,[2] Lynn M Yee*.[2] *[1]University of Pennsylvania Perelman School of Medicine, Pennsylvania, PA, USA; [2]Northwestern University Feinberg School of Medicine, Chicago, IL, USA.*

INTRODUCTION: Although data suggest increased adverse perinatal outcomes for neonates conceived via in vitro fertilization (IVF) compared to those not conceived via IVF, it is unclear if these risks extend to triplet gestations. This study aimed to compare neonatal outcomes of triplet gestations conceived via IVF to those not conceived by IVF.

METHODS: Retrospective cohort study of all women who delivered a viable triplet gestation at a large academic center (2005-16). Women with unknown mode of conception were excluded. Women who conceived via IVF were compared to those conceiving spontaneously or through other infertility treatments. A composite neonatal morbidity (respiratory distress syndrome, necrotizing enterocolitis, intraventricular hemorrhage, retinopathy of prematurity or neonatal sepsis) was generated. Bivariable analyses and multivariable logistic regression were used.

RESULTS: Of 89 women with triplet gestations, 82 met inclusion criteria, of whom 51 (62.2%) conceived by IVF. Women who conceived by IVF were more likely to be older (35.2 vs. 30.7 years, p<0.001), non-Hispanic white (91.8% vs. 70%, p=0.008), and to have dichorionic-triamniotic placentation (37.2% vs. 16.3%, p=0.04). There were no differences in maternal adverse outcomes, including postpartum hemorrhage and blood transfusion. Triplets conceived via IVF delivered slightly earlier (32.9 (± 2.6) vs. 33.7 (± 3.0), p=0.02), although this difference did not persist on multivariable regression analysis. Triplets conceived by IVF were more likely to be <1000 grams (6% vs. 0%, p=0.015). There were no other differences in individual neonatal outcomes. There was no significant difference in the composite neonatal morbidity between triplets conceived by IVF and those not (34.7% vs. 28.0%, p=0.28).

CONCLUSIONS: Triplets conceived via IVF experience few significant differences in outcomes compared to those conceived without IVF.

F-203

ART Pregnancy Complications Are Significantly Associated with Endometriosis Severity Before Conception: A Retrospective Cohort Study. Tatsuya Fujii†, Osamu Wada-Hiraike*, Takeshi Nagamatsu, Miyuki Harada, Tetsuya Hirata, Kaori Koga, Tomoyuki Fujii, Yutaka Osuga. *The University of Tokyo, Tokyo, Japan.*

INTRODUCTION: Endometriosis has been shown to be associated with second- to third-trimester pregnancy complications such as preterm birth and placenta previa, but the evidence is inconsistent.

METHODS: The patients who achieved singleton pregnancy by assisted reproduction technology (ART) in our facility (N = 631) were included in this analysis. Among them, 92 women demonstrated surgically proven endometriosis, and 512 women were shown to not have endometriosis as a complication. Among the 92 cases of endometriosis, 10 were classified as revised American Society for Reproductive Medicine (rASRM) stage I and II, 31 cases were rASRM stage III, and 43 cases were rASRM stage IV; in 8 cases, the rASRM stage was unavailable. Logistic regression analysis was performed to calculate odds ratios (OR) and 95 % confidence interval (CI) for the rates of preterm birth, placenta previa, and small for gestational age. OR were adjusted by age, parity and the number of transferred embryos.

RESULTS: First we confirmed the frequency of preterm birth and placenta previa were significantly increased in women with endometriosis (preterm birth OR, 2.08; 95 % CI, 1.07-3.89, placenta previa OR, 15.1; 95 % CI, 4.40-61.7), while the frequency of small for gestational age was not. Moreover, we found the frequencies of preterm birth and placenta previa were significantly increased in women with rASRM stage IV endometriosis compared to other two groups: women with rASRM stage I-III endometriosis (preterm birth OR, 7.40; 95% CI, 1.83-50.3; placenta previa OR, 11.0; 95% CI, 1.75-216.5) and women without endometriosis (preterm birth adjusted OR, 4.11; 95% CI, 1.88-8.55; placenta previa adjusted OR, 39.8; 95% CI, 10.1-189.1).

	rASRM stage I-III	Odds ratio	rASRM stage IV	Odds ratio	Odds ratio
preterm birth	2(4.9%)	0.55 (0.09-1.90)	12 (27.9%)	4.11 (1.88-8.55)	7.40 (1.83-50.3)
placenta previa	1(2.4%)	3.61 (0.18-26.3)	7 (17.1%)	39.8 (10.1-189.1)	11.0 (1.75-216.5)
small for gestational age	4(10.3%)	0.99 (0.29-2.61)	7 (20.6%)	2.30 (0.88-5.37)	2.32 (0.63-9.70)

CONCLUSIONS: We found that the frequencies of preterm birth and placenta previa were significantly increased in women with endometriosis, and the severity of endometriosis might have an adverse impact on ART pregnancy.

F-204

ICSI Outcomes in Men Undergoing TESA for Azoospermia and Impact of Maternal Age. Silvina Bocca, Victor Brugh, Mahmood Morshedi, Laurel Stadtmauer, Sergio Oehninger. *EVMS-Jones Institute for Repeoductive Medicine, Norfolk, VA, USA.*

INTRODUCTION: Despite general success in fertilization with ICSI, review of the literature shows that cases of obstructive (OA) and non-obstructive (NOA) azoospermia yield different outcomes.

Whereas some have observed an increased incidence of major congenital malformations among children resulting from ICSI compared with children conceived naturally, others have not.

Objectives: (1) To compare clinical outcomes in men with OA and NOA azoospermia after ICSI following testicular sperm extraction (TESE); and (2) to examine the influence of maternal age.

METHODS: Embryo quality and fertilization, pregnancy, miscarriage, and live birth rates were evaluated in 73 consecutive patients (53 OA, 20 NOA) undergoing 122 IVF/ICSI/TESE cycles with 110 embryo transfers in an academic center.

RESULTS: Males with OA were significantly older (45±8.2 years [y]) and their female partners significantly younger (28.2±5.1 y) than in the NOA group (36.9±6.8 y, p= 0.0007 for males and 34.0±4.1 y for females, p=0.0001). The average number of recovered metaphase II oocytes per patient in each group was not significantly different (SD) (6.03 for OA vs 6.6 for NOA, p= 0.385).

Men with OA had significantly higher rates of diploid fertilization (63.1% vs 49.5%, p= 0.0010) but similar clinical pregnancy (40 vs 41, p=0.2567), miscarriage (3.6% vs 20 %, p= 0.1566) and live birth rates/transfer (36% vs 30%, p= 0.6439) than men with NOA. Neither the average number of embryos transferred/patient in each group (1.96 in OA vs 1.89 in NOA, p= 0.340) nor overall embryo quality were different. However, rates of fertilization, embryo quality, and clinical pregnancy in men with OA were significantly higher than NOA when their female partners were <35 y, but results were similar in both groups when female partners ≥35 y. No major congenital malformations were detected in either group.

CONCLUSIONS: Overall, both men with OA and NOA can achieve healthy babies. Although the OA group had better overall quality embryos than the NOA group when maternal age was <35 y, embryologists can select the morphologically better embryos for transfer, eliminating the effect of embryo quality differences present in these two groups. Understanding more about factors that affect TESE/ICSI outcomes will not only help us predict patients' outcomes but it can help us educate and better counsel our patients.

F-205

Melatonin Treatment Is Able to Restore Menstrual Cyclicity in PCOS Women: A Pilot Study. Anna Tropea, Valeria Tagliaferri, Valentina Immediata, Simona De Cicco, Daniela Romualdi, Christian Di Florio, Elisa Scarinci, Antonio Lanzone, Rosanna Apa. *Università Cattolica del Sacro Cuore, Rome, Italy.*

INTRODUCTION: Melatonin is an old and ubiquitous molecule in nature, controlling a variety of important central and peripheral mechanisms related to circadian rhythms and reproduction. A local production of this hormone by the ovary has been taken into account by several authors and it is conceivable that melatonin may directly affect ovarian function. Only few data have been published about the role of melatonin in women with PCOS. Serum melatonin concentrations were found to be higher in PCOS in respect to healthy controls. Nonetheless, lower levels of this hormone have been detected in the ovarian follicles of women affected by the syndrome and this finding has been related to the anovulation and to the putative poor oocyte quality that, according with some authors, characterize PCOS . Based on this rationale, we conducted the present study in the aim to investigate the effects of six months of melatonin administration on clinical, endocrine and metabolic features of women affected by PCOS.

METHODS: Forty normal-weight PCOS women were enrolled in an academic research environment. Ultrasonographic pelvic exams, hirsutism score evaluation, hormonal profile assays, oral glucose tolerance test (OGTT) and lipid profile at baseline and after 6 months of melatonin treatment were performed.

RESULTS: Melatonin treatment significantly decreased androgens levels (FAI $p<0.05$; T $p<0.01$; 17(OH)P $p<0.01$). FSH levels significantly raised ($p<0.01$) and AMH serum levels significantly dropped after six months of melatonin treatment ($p<0.01$). No significant changes occurred in gluco-insulinaemic and lipid parameters after treatment. Almost 95% of subjects experienced an amelioration of menstrual cycles. Data were further analyzed after dividing patients in partial and good responders on the basis of the increase in menstrual cycles. The group defined as good responders showed lower values of AMH and androstenedione.

CONCLUSIONS: This is the first study focused on the effects of the treatment with exogenous melatonin on the clinical, endocrine and metabolic characteristics of PCOS patients. After six months of treatment melatonin seems to improve menstrual irregularities and biochemical hyperandrogenism in PCOS women through a direct, insulin-independent effect on the ovary. Based on our results, melatonin could be considered a therapeutic agent for women affected by PCOS.

F-206

Elevated Testosterone Increases *Ins1* Transcription and Induces Pancreatic Beta Cell Proliferation and Glucose Intolerance in Female Rats. Jay Mishra†, Amar More†, Sathish Kumar. *University of Texas Medical Branch, Galveston, TX, USA.*

INTRODUCTION: Androgen excess is the central defect in polycystic ovary syndrome (PCOS). Insulin resistance is observed in 30-40% of women with PCOS and 5-10% women develop type 2 diabetes. The underlying role of androgens in regulating pancreatic beta cell function and glucose tolerance is not fully understood. This study evaluated the effect androgens and the mechanisms involved in dysregulation of pancreatic beta cell function and development of insulin resistance.

METHODS: Adult female Sprague-Dawley ratswere implanted with dihydrotestosterone (DHT; 7.5-mg, 90-d release) pellets or a matched placebo. After 10 weeks, glucose tolerance was measured using intraperitoneal glucose tolerance test (IPGTT). Pancreatic islet size, number, and proliferation and reactive oxygen species (ROS) production, mitochondrial copy numbers and *Ins1* and *Ins2* gene transcription in islets were determined. Insulin stimulated glucose uptake in islets and soleus muscle and gastrocnemius insulin receptor (IR) β protein levels were determined. Direct effects of androgens on *Ins1* and *Ins2* gene transcription were determined using an in vitro islet cell culture model.

RESULTS: DHT exposure increased plasma DHT levels by 2-fold and induced fasting hyperinsulinemia. In DHT females, plasma glucose and insulin responses were significantly elevated after IPGTT compared with controls. This exaggerated insulin response in DHT females was associated with unaltered islet numbers and size but with enhanced beta cell proliferation and increased *Ins1* and *Ins2* mRNA expression. The ROS production was increased and mitochondrial copy number was decreased in islets of DHT females. Insulin stimulated glucose uptake in soleus and islets was decreased by 60% and 50% respectively with associated decrease in IRβ expression in DHT females. In vitro exposure of DHT to cultured pancreatic islets dose dependently upregulated *Ins1* and *Ins2* mRNA transcription.

CONCLUSIONS: Elevated DHT levels, at clinically relevant concentrations, exhibit glucose intolerance with exaggerated insulin responses. The observed hyperinsulinemiain DHT females in spite of decreased mitochondrial numbers and increased ROS may be due to the enhanced β-cell proliferation and increased insulin gene transcription. Decreased IRβ expression in the skeletal muscles may contribute, in part, to glucose intolerance in this model.

F-207

Effects of Estrogen on Proliferative Activity of Murine Female Bone Marrow Stromal Cells. Seung-Yup Ku, Yoon Young Kim, Hoon Kim, Chang Suk Suh, Seok Hyun Kim, Young Min Choi. *Seoul National University Hospital, Seoul, Korea.*

INTRODUCTION: Estrogen (E_2), major female hormone, is well-known for its complicated metabolic roles throughout the life span of women. Bone marrow stromal cells (BMSCs) and other stem cells are known to show different responses to sex hormones in terms of gender difference or reproductive aging. In this study, we tried to demonstrate the effects of E_2 on the proliferation of BMSCs and its possible implication in menstrual cyclic fluctuation.

METHODS: Femurs of 8-week-old female C57BL/6 mice were harvested and the skin and muscle were removed using a mechanical procedure. Bone marrow stromal cells were isolated and cultured for further analyses. E_2 at 10^{-6}~10^{-8}M was treated for 24, 48, 72 hours and the characteristics and proliferative activity of samples were analyzed using FACS assay.

RESULTS: Isolated BMSCs were positive for CD90 and CD105 and negative for CD31 markers. Proliferative activity was increased after E_2 treatment and the highest response was observed at 48 hours. However, dose-dependent relationship was not observed. This proliferative effect was inhibited by the treatment of estrogen receptor blocker ICI-1640.

CONCLUSIONS: In conclusion, E_2 seems to have a role in the regulation of proliferation of murine BMSCs. Further investigations are necessary to elucidate the role of E_2regarding the fluctuation of BMSC population during menstrual cycle in women (HI14C2259).

F-208

Reproductive Aged Women Do Not View Employer Coverage of Egg Freezing as Coercive. Deborah E Ikhena†, Rafael Confino, Angela K Lawson, Susan Klock, MaryEllen G Pavone*. *Northwestern University, Feinberg School of Medicine, Chicago, IL, USA.*

INTRODUCTION: To understand young women's intentions and attitudes towards egg freezing, their views on employer coverage and what factors affect their decision to proceed with oocyte cryopreservation.

METHODS: An online survey was distributed to a cohort of medical students, law students, and lawyers. Participants were asked questions about their knowledge, attitudes, and intentions towards elective egg freezing. Demographics, data on fertility knowledge, whether they would consider elective egg freezing and their attitudes towards employer coverage were assessed via a self-reported multiple choice questionnaire.

RESULTS: A total of 167 surveys were completed; 99 (58.2%) were medical students, 36 (21.2%) were law students and 31 (18.2%) were lawyers. The average age of respondents was 27.5 ±6.5. Among respondents, 67.3% identified as potential freezers (PFs), 24.2% as doubtful freezers (DFs) and 8.5% would not consider elective egg freezing; never freezers (NFs). On age -adjusted analysis, neither lawyers, law students nor medical students were more likely to identify as PFs, DFs or NFs. 73.5% of respondents felt pressure to delay childbearing. Feeling pressure to delay childbearing was not predictive of whether a respondent identified as a PF.

Notably, 70.8% of respondents did not view employer coverage of egg freezing as coercive and 73.2% of women would not delay childbearing if their employer offered coverage. Interestingly, PFs were most likely to delay childbearing due to employer coverage (18.4%, p=0.042). Furthermore, 42% of PFs would change their decision to freeze their eggs when informed that the success rate per oocyte was 6-10%.

Lawyers, law students, and medical students were equally likely to report feeling pressure to delay childbearing and to not view employer coverage of egg freezing as coercive.

CONCLUSIONS: In this population of young women, most identified as potential egg freezers and most do not view employer coverage as coercive. Interestingly, 42% of women who identified as potential freezers would change their minds about egg freezing based on data regarding the success of the procedure. This underscores the importance of patient counseling in helping reproductive-aged woman navigate decision making around delaying childbearing. This information on young women's attitudes towards egg freezing is compelling in light of employers offering coverage for egg freezing to female employees.

F-209

The Potential Oligodendroglial Fate Specification Capacity of Exosomes Derived from Stem Cells of the Umbilical Cord Tissue. Marianne S Joerger-Messerli,[1,2] Marialuigia Spinelli,[1,2] Byron Oppliger,[1,2] Ivana Di Salvo,[1,2] Martin Mueller,[1,2,3] Daniel V Surbek,[1,2] Andreina Schoeberlein.[1,2] *[1]Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland; [2]University of Bern, Bern, Switzerland; [3]Yale University School of Medicine, New Haven, CT, USA.*

INTRODUCTION: The neuroregenerative effects of transplanted mesenchymal stem cells (MSC) in animal models of perinatal brain damage are presumed to rely on secreted factors including MSC-derived exosomes. Thus, the aim of this study is the evaluation of the oligodendroglial fate specification capacity of human Wharton's jelly-derived MSC (WJ-MSC) on neural progenitor cells (NPC).

METHODS: WJ-MSC-derived exosomes were isolated from culture supernatants by serial centrifugation, characterized by the expression of endosomal markers (membrane-based antibody array) and their size (electron microscopy). The exosomal microRNA (miRNA) content was assessed by real time PCR. The exosomes were stained with the red fluorescent celltracker dye CM-DIL to analyze the potential interaction with NPC. Exosomal RNA was further fluorescently labeled to investigate its potential release into NPC. After the culture with exosomes, NPC were evaluated for the expression of proliferation and oligodendroglial differentiation markers by real-time PCR.

RESULTS: WJ-MSC-derived exosomes were positive for endosomal markers, including TSG101 and ALIX, and had a mean diameter of 19 nm. The exosomes contained miRNAs that are involved in the differentiation of oligodendrocyte progenitor cells and in oligodendroglial fate determination (miR-338, miR-9, miR-19b, miR-138). Fluorescently labeled exosomal RNA was detected in NPC after co-culture. The gene expression of the transcription factor inhibitor of DNA binding protein (ID)2, which blocks oligodendrogenesis, was reduced in NPC post co-culture with exosomes. The transcription of ID4, which counteracts the function of ID2 was enhanced in NPC following incubation with exosomes.

CONCLUSIONS: We successfully isolated WJ-MSC-derived exosomes. The exosomes contain miRNAs having decisive roles in oligodendroglial fate specification and differentiation, ascribing a potential neuroregenerative role to WJ-MSC-derived exosomes.

Financial support by CryoSave Switzerland.

F-210

Mitochondria Inhibition at Normoxia Is Sufficient to Emulate Hypoxic-Stress Induced Potency Loss and TGC Differentiation in mTSC. Yu Yang, Jing Dai, Elizabeth E Puscheck, Daniel A Rappolee*. *Wayne State University, Detroit, MI, USA.*

INTRODUCTION: Stress induces differentiation of multiple types of stem cell despite the conditions that should normally maintain potency. Mouse trophoblast stem cells (mTSCs) are placental stem cells that are capable of differentiating into all placental cell lineages. Hypoxic stress (0.5% O2) induces differentiation of mTSCs despite the presence of mTSC potency maintaining growth factor FGF4. CDX2, ID2 and ERRB are 3 examples among the many potency factors that indicate the stem cell state of mTSC. Differentiated mTSCs lose the expression of potency factors. The link between hypoxic stress and loss of mTSC potency factors hasn't been established.

METHODS: Four mitochondria inhibitors (KCN, FCCP, NaN3 and Antimycin A) were added to normally cultured mTSC to investigate the

sufficiency of mitochondria inhibition in inducing mTSC potency loss and differentiation gain. Western blot was used to detect the relative levels of potency factors with/without mitochondria inhibitor. Immunofluorescence nuclear staining was used to monitor nucleus size after mitochondria inhibition. ATP measurement was done by firefly luciferase based luminescence measurement using plate reader. Micrographs of TSCs under hypoxic or mitochondrial inhibitor culture were measured for nuclear size (TGC are >4N). 8 protein kinases (AMPK, SAPK, MEK1/2, GSK3, AKT, p38MAPK, PERK, PI3K) were screened for their possible role in causing mTSC potency loss under hypoxia by adding individual kinase inhibitor to 0.5% O2 culture and measuring whether there was reversal of potency loss due the effect of certain kinase inhibitor by immunoblot.
RESULTS: NaN3 and Antimycin A caused mTSC potency loss just as 0.5% O2 did at the end of 2 days' culture and both of them induced trophoblast giant cell differentiation. Contrary to what was expected, ATP level at 0.5% O2 culture and with addition of mitochondria inhibitor (NaN3) was higher than normal mTSC culture control (20% O2). Inhibition of GSK3 produced around 50% reversal of ERRB or ID2, and inhibition of p38 MAPK produced around 25% reversal of ERRB. Inhibition of other protein kinases screened did not reverse 0.5% O2 induced TSC potency loss.
CONCLUSIONS: Mitochondria inhibition is sufficient to induce mTSC potency loss and increase in the TGC% at 20% O2, but it does not happen through depletion of ATP. GSK3 seems to be a good candidate for further testing of kinase-mediated mTSC potency loss under hypoxia.

F-211

Lens Tissue Development from Mouse Embryonic and Induced Pluripotent Stem Cells. Emma R McGuirk, Nicholas Ng, Parveen Parasar†, Samuel Hornstein, Raymond M Anchan*. *Brigham and Women's Hospital and Harvard Medical School, Boston, MA, USA.*
INTRODUCTION: Maternal gestational health significantly influences fetal outcomes. Congenital oculocerebrorenal anomalies and congenital cataracts are intrauterine developmental anomalies associated with maternal metabolic and genetic state. We previously showed that induction of paired box and homeobox genes (*Pax6/Six3*) in mouse and human embryonic stem cells (ESC) is sufficient to trigger lentoid development. Here, we optimize the differentiation of murine stem cell-derived lens tissue with defined differentiation conditions for greater generation of lens precursors and use fluorescence-activated cell sorting (FACS) to purify this precursor subpopulation.
METHODS: After induction of *Pax6* or *Six3* in mESCs or induced pluripotent stem cells (iPSC) using lentiviral vectors, we culture reprogrammed cells to differentiate into suspended or suspended-attached embryoid bodies (EBs) for 60 days. We then employed FACS for the surface antigens c-Met/HGFR and CD44, markers of presumptive early lens precursors, for the enrichment of differentiating populations of lens placode precursors. The identity of the sorted cells is verified by immunolabeling and RT/Qt-PCR using lens specific genes.
RESULTS: (1) Activation of *Pax6* in suspended cultured EBs generates greater c-Met/HGFR and CD44 immunoreactive cells than attached EBs (21.1% vs. 11.0%) or *Six3* (36.7% vs. 11.4%) induction. (2) EBs infected with *Pax6* and *Six3* demonstrate greater lens antigen differentiation relative to uninfected EBs (11.0%/11.4% vs. 9.1%). (3) The temporal differentiation of lens antigens mimics the *in vivo* pattern with early markers such as αA crystallin expression preceding that of γA crystallin, a terminal development marker for lens.
CONCLUSIONS: These results show that: (1) *Pax6/Six3* induction may initiate differentiation of stem cells into lens, (2) stem cell-derived lens placode precursors may be purified using FACS with the surface antigens c-Met/HGFR (3) ideal differentiation conditions include EB suspension culture and (4) *in vitro* differentiation patterns of antigen expression mimic *in vivo* development. Collectively, these data help establish a biologically relevant *in vitro* stem cell platform to better understand the pathophysiology of congenital oculocerebrorenal anomalies and develop novel therapies to improve reproductive outcomes.

F-212

The Role of TRF2 in Maintaining and Protecting Neural Cell Properties. Siti Aminah Muhammad Imran, Wei Cui*. *Imperial College London, London, United Kingdom.*
INTRODUCTION: Neural degeneration occur when the neurons have a loss of function that could be due to DNA damage or senescence where the DNA damage could occur naturally as part of ageing as the cells divide. Some DNA damage are repairable through a specific mechanism called the DNA damage response (DDR) that will lead the cell fate to either cell cycle arrest and DNA repair or apoptosis. Senescence is when the cells are no longer able to further divide due to shortening of the telomere. The telomere repeat binding factor 2 (TRF2) plays an important role in protecting the telomere from any unwanted recombination or DNA fusion and telomere shortening, where it can cause DNA instability and cell death. TRF2 also has a significant role in the DDR. Due to the high expression of TRF2 protein in the neural progenitor cells (NPCs), the NPCs were chosen as the model.
METHODS: Different types of cells (hESCs, BJ5A, HEK293T and NPCs) were cultured with 200μM H_2O_2 to induce oxidative stress. Loss of function experiment were done using the knock-down TRF2-sh1 NPCs cultured with and without the B27 supplement. The cells were counted after each treatment to get the cell number. The protein expression of TRF2, the proliferation marker (pH3) and apoptotic marker (cl-casp3) were determined using Western blotting.
RESULTS: The TRF2 protein expression in all the different types of cells dynamically changes through the time course of the treatment. There are no significant difference in terms of the cell number between the control and TRF2-knock down after the withdrawal of B27 supplement. The cl-casp3 protein expression increases as the medium changed from N2B27 to N2 for 1 hour in both cells. However, there is a massive decrease after the overnight culture. The pH3 protein expression is highly reduced in all the cells after the withdrawal of B27. No significant difference was observed between the control and knock-down.
CONCLUSIONS: The dynamic change in TRF2 protein expression in different types of cells treated in 200μM H_2O_2 shows that TRF2 is affected during oxidative stress. The increased TRF2 protein expression could either be helping cell survivability or inducing more cell death. The different cell number in TRF2 knock-down NPCs and the control shows the different phenotype in these cells, which will help to understand further the mechanism of TRF2 in DNA damage and stress conditions by looking at other proteins that are known to be associated with TRF2 such as ATM and ATR.

S-001

Impact of Hypoxia on PD-1/PD-L1 Interaction in the Immunosurveillance of Uterine Fibroid. Abdeljabar El Andaloussi,[1] Nahed Ismail,[2] Ayman Al-Hendy.[1] *[1]MCG, Augusta University, Augusta, GA, USA; [2]University of Pittsburgh, Pittsburgh, PA, USA; [3]MCG, Augusta University, Augusta, GA, USA.*
INTRODUCTION: Uterine fibroids (UF) are common reproductive benign tumors of the uterus. The common UF risk factors are African American race, obesity and unopposed estrogen exposure. The PD-1/PD-L1 interaction regulates peripheral tolerance and immune response. Several factors regulate PD-1/PD-L1 such as sex hormones, interferon gamma, and hypoxia. Tumor cells express high level of PD-L1 and PD-L2 as an immune evasion mechanism. However, there are no data regarding PD-1/PD-L1 expression in UF tissues or its involvement in the pathogenesis process.
METHODS: We assessed the expression of PD-1 and PD-L1 in human UF samples versus adjacent normal myometrium as a control, during the proliferative stage of the menstrual cycle. We used human immortalized cell line: HuLM/fibroid and UTSM/myometrium.
RESULTS: The screening of our cell lines UTSM and HuLM by real time PCR (RT-PCR) confirm the expression of PD-1 and PD-L1 at mRNA level. The PD-L1 expression level was significantly higher in HuLM versus UTSM ($p < 0.03$). At the protein level, we detected a significant expression of PD-1/PD-L1 on HuLM compared to UTSM cells using flow cytometry (UTSM: 33.1%; HuLM: 66.9%, $p< 0.01$ for PD-L1;

UTSM: 38.7%; HuLM: 62.6%, p < 0.02 for PD-1). Consistent with the *in vitro* data, analysis of fibroid tissues by immunohistochemistry and RT-PCR also demonstrated significant up-regulation of PD-L1 mRNA in 50 % of the patients when compared to adjacent normal myometrium. To understand the regulation of PD-L1 in UF, we examined the effect of hypoxia and INF-γ stimulation, as potential regulatory mechanisms of PD1/PDL1 expression in UTSM and HuLM. Our results show two folds increase in PDL-1 mRNA expression of HuLM (p < 0.04) under hypoxic conditions versus normoxic conditions, and three fold increase upon stimulation of cells with INF-γ (p< 0. 01) compared to UTSM. The effect of hypoxia on UF development was also evaluated and showed a significant upregulation of HIF-1a in HuLM (14.56 ± 1.95) compared to UTSM (1.27 ± 0.28) (p = 0.01).

CONCLUSIONS: Our study reveals, for the first time, a potential role for PD-1/PD-L1 interaction in the development of uterine fibroid and potential mechanisms involved in the expression of these molecules on fibroid cells. This investigation may facilitate a novel utility of anti-PD-1, anti-PD-L1 therapy for non-surgical treatment of UF.

S-002

Effect of OBE022, an Oral and Selective Non-Prostanoid PGF2α Receptor Antagonist in Combination with Nifedipine for Preterm Labor: A Study on RU486-Induced Pregnant Mice. Oliver Pohl,[1] Murielle Méen,[2] Philippe Lluel,[2] André Chollet,[1] Jean-Pierre Gotteland.[1] *[1]ObsEva SA, Plan-les-Ouates, Switzerland; [2]Urosphere SAS, Toulouse, France.*

INTRODUCTION: Management of preterm labor remains an unmet medical need. Pan-prostaglandin inhibition with non-steroidal anti-inflammatory drugs (NSAID) is an effective treatment for preterm labor, but is limited due to adverse effects on the fetus. PGF2α is a naturally occurring prostaglandin that acts to induce labor in pregnant women. Through specific antagonism of the PGF2α (FP) receptor, OBE022 is designed to control preterm labor by reducing inflammation, decreasing uterine contractions and preventing cervical changes and membrane ruptures while being safe for the fetus. The FP receptor antagonist OBE022 has shown not to have safety limitations of the NSAID indomethacin. The induction of labor by the antiprogestin RU486 activates endocrine pathways and a drop in progesterone level characterized by the up-regulation of labor-associated proteins as seen in the case of idiopathic preterm labor.

There is also evidence that FP antagonists when combined with tocoloytics acting through a different pathway may result in synergic effects on parturition as described for the beta-mimetic ritodrine, an agent acting through cyclic adenosine monophosphate elevation.

Currently, though not approved, one of the most recommended preterm labor treatments is the oral calcium channel blocker nifedipine. Therefore, targeting the FP receptor in combination with the nifedipine may be an optimized strategy for preventing or delaying preterm delivery.

METHODS: To demonstrate the effect of OBE022 alone or in combination with calcium channel blocker nifedipine on parturition in a RU486-induced pregnant mouse model.

Pregnant CD-1 mice were induced with RU486 on gestation day 17; time to delivery was measured.

RESULTS: Compared to the vehicle control, nifedipine (5mg/kg, p.o.) or OBE022 (100mg/kg, p.o.) alone significantly delayed RU486-induced preterm labor. Combination treatment of OBE022 and nifedipine demonstrated a clear synergic effect on the delay of delivery when compared to vehicle, nifedipine or OBE022 alone (p<0.001, p<0.001 and p<0.01, respectively).

CONCLUSIONS: This study confirms the effect of the FP antagonist OBE022 on parturition and establishes a rationale for the usage of combined FP and calcium channel antagonism in the prevention of preterm birth.

S-003

History of Retained Placenta Is an Independent Risk Factor for Major Complications in Subsequent Pregnancies: Evidence from a Large Retrospective Cohort Study. Shirley Greenbaum,[1] Tamar Wainstock,[2] Doron Dukler,[1] Elad Leron,[1] Offer Erez*.[1] *[1]Soroka University Medical Center, Beer Sheva, Israel; [2]Ben Gurion University of the Negev, Beer Sheva, Israel.*

INTRODUCTION: Placental hypoperfusion, invasive placentation, and inadequate contractility have been previously suggested as the underlying mechanisms of retained placenta (RP). The objective of this study is to test the hypothesis that the same pathway, leading to RP in one delivery, may manifest differently in subsequent pregnancies.

METHODS: A retrospective population-based cohort study included 176,419 deliveries of women with at least two deliveries in 1989-2014. Women with twins, fetal congenital malformations, or RP in the index pregnancy were excluded. Background characteristics, pregnancy complications, and perinatal outcomes of deliveries of women with history of RP, were compared with the remaining cohort. We designed generalized estimating equation (GEE) multivariable models, each aimed at exploring history of RP as a risk factor for a specific labor complication.

RESULTS: In the study population, 11,124 (6.3%) deliveries were of women with prior diagnosis of RP. Among these, the rates of numerous obstetric complications were significantly higher (Table 1). In the GEE multivariable analysis, history of RP was found to be an independent risk factor for PPH (aOR=20.41, 95%CI 15.38-27.03, p<0.001), PTD (aOR=1.33, 95%CI 1.22-1.44, p<0.001), and neonatal mortality (aOR=1.61, 95%CI 1.33-1.94, p<0.001) in the index pregnancy.

**Figure(s) will be available online.*

CONCLUSIONS: The major finding of this study is that history of RP is an independent risk factor for PPH, PTD, and neonatal mortality, possibly through similar underlying mechanisms. These findings suggest detailed monitoring of women with history of RP, which may facilitate earlier diagnoses of labor complications.

**Figure(s) will be available online.*

S-004

Exosomes Analysis and Characterization of Human Umbilical Cord Blood from Normal and Preterm Pregnancies. Christopher L Dixon,[1] Vyjayanthi Kinhal,[2] Carlos Palma,[2] Kechichian Talar,[1] Rheanna Urrabaz-Garza,[1] Carlos Salomon,[2] Ramkumar Menon.[1] *[1]The University of Texas Medical Branch, Galveston, TX, USA; [2]The University of Queensland, Brisbane, United Kingdom.*

INTRODUCTION: The human placenta serves as the primary interface between the maternal and fetal circulation that supply nutrients, blood and oxygen through the umbilical cord. The exosomes profile in fetal circulation under normal and pathological conditions remains to be elucidated. The aim of this study was to characterize the exosomes present in fetal blood obtained from preterm and term parturition.

METHODS: Umbilical cord blood (CB) samples (n=44) were collected from the umbilical vein immediately after delivery from group 1: term not-in labor (TNIL); group 2: term in labor (TL), group 3: preterm premature rupture of membranes (PROM); and group 4: preterm birth (PTB). Exosome were isolated by differential buoyant density centrifugation and characterised by morphology, enrich of exosomal proteins and size distribution by electron microscopy, western blot and nanoparticle tracking analysis, respectively. The exosomal protein profile was analysed by Liquid Chromatography (LC)/ Mass Spectrometry (MS) LC-MS/MS on a 5600 Triple TOF mass spectrometer.

RESULTS: Exosomes were identified as spherical vesicles, with a typical cup-shape and diameters around of 100 nm and positive for enrich exosomal proteins CD63 and TSG101. We did not find different in the physical properties of isolated exosomes between the groups. The total number of exosomes (exosomes/ ml plasma) present in CB was significantly higher in TL (1.8×10^{11}) and PTB (1.9×10^{11}) compared to TNIL (1.0×10^{11}), pPROM (5.8×10^{10}). The ratio PLAP/total exosomes was significantly higher ~5.7-fold in pPROM compared to TL, TNL or PTB. MS/MS analysis identified over 200 different exosomal proteins with 20 upregulated and downregulated proteins between the groups. Further

bioinformatics analysis (Ingenuity Pathway Analysis) indicated that these differentially expressed proteins correlate with enzyme regulator activity, binding and biological regulation suggestive of metabolic derangements.
CONCLUSIONS: We have identified total and placental exosomes specific changes in fetal circulation associated with preterm and term labor. Further characterization is expected to reveal underlying pathologic or physiologic changes in fetus associated with preterm and term parturition respectively.

S-005

Use of Mass Spectrometric Measurements to Determine Differential Expression of Prostaglandins and Prostamides in Amniotic Fluid of Women Delivering Preterm with and without Microbial Invasion of the Amniotic Cavity. Hassendrini N Peiris†,[1] Robert J Romero,[2,3] Kanchan Vaswani,[1] Sarah Reed,[1] Piya Chaemsaithong,[2] Sonia Hassan,[2] Eli Maymon,[2] Murray D Mitchell.[1] *[1]University of Queensland, Brisbane, QLD, Australia; [2]Wayne State University, Detroit, MI, USA; [3]National Institutes of Health, Detroit, MI, USA.*
INTRODUCTION: An increase in prostaglandin concentrations in amniotic fluid of women in labor at term and preterm with and without microbial invasion of the cavity (MIAC) is well established. Endocannabinoids can act as substrates for enzymes of the prostaglandin biosynthetic pathways and can be utilized to generate other related compounds such as prostamides. The related end products are indistinguishable by radioimmunoassay. The use of mass spectrometry allows accurate and relative measurements of prostaglandins and prostamides. **Aim:** To evaluate the use of mass spectrometry in identifying the relative concentrations of prostaglandins and prostamides in amniotic fluid of women with preterm labor who delivered preterm with (PTL-MIAC; n=15) and without (PTL-PTD; n=43) microbial invasion of the amniotic cavity (MIAC).
METHODS: Standards and samples were extracted in methanol/formic acid containing internal standards (PGE_2-d4, $PGF_{2\alpha}$-d4, PGFM-d4, PGE_2-EA-d4, $PGF_{2\alpha}$-EA-d4). These samples were measured by LC MS/MS. Following normality testing data were log transformed and Mann Whitney U test was used for analysis.
RESULTS: The concentrations (mean±SD)of PGE_2 (10.2±2.47), $PGF_{2\alpha}$ (10.1.±2.18), PGFM (11.1±2.25) in PTL-MIAC group were significantly higher than those ofthe PTL-PTD group: PGE_2; (6.09±1.2), $PGF_{2\alpha}$; (7.50±0.79), PGFM; (7.60±0.81), ($p<0.05$). The ratio of PGE_2 to PGE_2-EA was also higher in the PTL-MIAC (2.87±1) compared to PTL-PTD group (1.79±0.5) ($p<0.05$).
CONCLUSIONS: Using through mass spectrometric means of measurements we describe the differential expression of prostaglandins and prostamides in preterm deliveries with and without MIAC. We propose that separation of these products might reduce variability in current results and lead to potential utilization for the use of their measurement in the diagnosis of preterm labor.

S-006

Mid-Trimester Changes in Cervicovaginal Fluid Cytokine Profile of Asymptomatic Women as Early Indicators of Preterm Birth. David Chapman†, Emmanuel Amabebe†, Victoria Stern†, Dilly OC Anumba*. *The University of Sheffield, Sheffield, South Yorkshire, United Kingdom.*
INTRODUCTION: Ascending genital infection due to changes in the vaginal microbiota induces immune responses characterized by the release of inflammatory cytokines capable of initiating preterm labour (PTL) and preterm birth (PTB). Detecting early changes in cytokine levels during gestation could further elucidate the pathophysiology of PTB and provide useful diagnostic biomarkers. We investigated the changes in cervicovaginal fluid (CVF) cytokine profiles across the mid-trimester in asymptomatic women who delivered prematurely compared with those that delivered at term and determined their prognostic utility for PTB.
METHODS: A case-control study was performed using CVF (n=140), collected at mid gestation from a larger prospective cohort comprising of 93 asymptomatic high-risk pregnant women. Samples were obtained at two gestational time points (GTP); 20-22 weeks (GTP1, n=70: Preterm=35, Term=35) and 26-28 weeks (GTP2, n=70: Preterm=26, Term=44). A subset of women (n=48) were sampled at both GTP1 and GTP2. Cytokine concentrations were analyzed using a multiplexed bead-based immunoassay (BD™ Cytometric Bead Array). Also, the 16S ribosomal DNA of the vaginal bacterial species from 87 samples (GTP1=50, GTP2=37) were amplified by polymerase chain reaction. The GTP1/GTP2 ratios of CVF cytokines between preterm and term women were analyzed using receiver operating characteristics (ROC) curve to determine their predictive capacity for PTB.
RESULTS: There was a decrease in IL-1α (P=0.04) and RANTES (P=0.02) from GTP1–GTP2 in the term women, while the increase in IL-1α, IL-1β, IL-6 and IL-8 in the preterm women was not statistically significant (Mann-Whitney U-test). The ROC curve indicated GTP1/GTP2 ratios of RANTES (AUC=0.79, CI=0.63-0.91, OR=13.0) and IL-1β (AUC=0.71, CI=0.56-0.84, OR=7.1) to be the best predictors of PTB, followed by IL-8 (AUC=0.68, CI=0.53-0.81, OR=3.7) and IL-1α (AUC=0.67, CI=0.51-0.80, OR=6.5). This was corroborated by increased prevalence of anaerobic vaginal bacteria in the preterm women from GTPI-GTP2 i.e. Fusobacterium (16% vs. 41%), Bacteroides (16% vs. 71%) and Mobiluncus (0% vs. 29%) (P=0.007).
CONCLUSIONS: Mid-trimester increase in CVF cytokine levels particularly RANTES and IL-1β appear predictive of PTB in asymptomatic high-risk women. This could be preceded or accompanied by high prevalence of potentially pathogenic anaerobic vaginal bacteria.

S-007

Apoptosis in the Prepartum Cervix Increases at Term and Before Preterm Birth. Michael A Kirby,[2] Julia Tapelband†,[1] Anne C Heuerman†,[1] Steven M Yellon*.[1,2] *[1]Loma Linda University School of Medicine, Loma Linda, CA, USA; [2]Loma Linda University School of Medicine, Loma Linda, CA, USA.*
INTRODUCTION: Remodeling of the cervix stroma is characterized by an inflammatory process that includes extracellular matrix degradation, reduced density of cell nuclei, and increased presence of macrophages before birth at term. Evidence suggests that cell death may contribute to cervix remodeling at term in rats and women (PMIDs9579433,11239645). Activation of cleaved (c)-Caspase-3 is the critical step in apoptosis (PMID14713960), but whether this marker of cell death is increased in the cervix in associated with term or preterm birth is not known. The objective of this study was to determine if increased apoptosis accounts for reduced cell nuclei density in the cervix of prepartum mice at term and with progesterone receptor antagonist-induced preterm birth.
METHODS: On day 16 postbreeding, pregnant CD-1 mice were given vehicle or progesterone receptor (PR) antagonist (RU486, 6mg/kg/0.1ml i.p.). The cervix was obtained from controls on days 15, 16.5, 17, or 18 postbreeding, as before (PMID27233754) and from RU486-treated mice on day 16.5. Each cervix was processed and stained for cell nuclei (methyl green) and c-Caspase 3 (antibody #9661S, Cell Signaling).
RESULTS: Preterm birth occurred within 24h of the RU486 injection. In sections of cervix, the density of cell nuclei/area was the same among pregnant mice whether RU486- or vehicle-treated. By contrast, the density of c-Caspase-3 cells in the stroma increased to the same extent in prepartum mice given either RU486 or vehicle compared to vehicle-treated mice on day 16.5 postbreeding (day 16.5 or 18, respectively, vs day 16.5 controls; $p<0.05$).
CONCLUSIONS: During ripening before birth, increased apoptosis occurs in the cervix stroma to a similar extent by the day before term and within 12h of PR antagonist-induced preterm birth. However, increased apoptosis cannot account for remodeling during the shift from softening to ripening (days 15-17 postbreeding in controls). Whether preterm cervix remodeling, induced by loss of progesterone efficacy, accelerates a PR-mediated mechanism that promotes ripening at term remains to be determined.
Supported by NIH HD054931 and the Department of Pediatrics.

S-008

ATG16L1 and the Placental Response to Infection and Oxidative Stress via Exosomes. Bin Cao†,[1] Rheanna Urrabaz-Garza,[2] Helen Feltovich,[3] Ram Menon,[2] Indira Mysorekar*.[1] *[1]Washington University School of Medicine, St. Louis, MO, USA; [2]University of Texas Medical Branch, Galveston, TX, USA; [3]University of Utah School of Medicine, Salt Lake City, UT, USA.*

INTRODUCTION: During gestation, the fetus and associated placenta encounter oxidative stress (OS), a result of increased metabolic demands by the maturing fetus as well as inflammatory stress induced by infections. Both can lead to adverse pregnancy outcomes such as preterm birth (PTB). Here we investigate a cellular recycling mechanism, autophagy which we posit is at the heart of coordinating the maternal-fetal response to sterile or non-sterile stress and orchestrate pregnancy maintenance or delivery.A key autophagy protein, ATG16L1, has emerged a major regulator of this process. A polymorphism in *ATG16L1* is associated with rapid labour progression in pregnant women and is decreased in fetal membranes after spontaneous labour and delivery. We hypothesized that OS or infection-triggered modulation of ATG16L1 activity in the placenta can serve as a pivot point to trigger PTB and that small, membrane-bound vesicles called exosomes released by placental cells provide a snapshot of placental autophagy activity status and stress status.

METHODS: We used human placental biopsies, cultured human primary placental syncytial trophoblasts (STBs) and primary amnion epithelial cells (AECs) to test our hypothesis. First, we measured ATG16L1 expression in human preterm and term placentas as well as in STBS and AECs. Second, we inhibited autophagy in STBs using siRNAs specifically targeting ATG16L1. STBs were then stressed using by infecting with a pathogen (*E. coli*) and infectivity was measured. Finally, we induced OS in AECs with cigarette smoke extract, isolated exosomes, and measured effect on ATG16L1 expression.

RESULTS: We demonstrate that *first*, ATG16L1 expression is significantly lower in preterm placentas than in term placentas, *second*, STBs exhibit high basal levels of ATG16L1 activity and inhibition of ATG16L1 gene/protein expression impairs STB antibacterial defenses; *third*, exosomes isolated from AECs carry ATG16L1 as a cargo; and f*inally*, we demonstrate increased exosomal packaging of ATG16L1 in AECs upon induction of OS.

CONCLUSIONS: Our findings suggest that ATG16L1 likely governs the response to placental infection and oxidative stress via exosomes providing a new signaling mechanism that may triggers parturition in response to maternal-fetal stress.

S-009

Granulocyte Macrophage-Colony Stimulating Factor (GM-CSF) Expression Is Increased in a Mouse Model of Preterm Birth. Christopher Nold,[1,2,3] Julie Stone†,[2] Todd Jensen,[2] Anthony Vella*.[4] *[1]Hartford Hospital, Hartford, CT, USA; [2]University of Connecticut Health Center, Farmington, CT, USA; [3]Connecticut Children's Medical Center, Farmington, CT, USA; [4]University of Connecticut Health Center, Farmington, CT, USA.*

INTRODUCTION: Preterm birth is believed to be a final common pathway of a multitude of instigating factors, and it is clear inflammation plays a significant role in prematurity. However, the precise mechanisms of preterm parturition remain elusive. Previously, we have shown amniotic fluid cells and cervical epithelial cells will respond to lipopolysaccharide (LPS) increasing the expression and concentration of granulocyte macrophage colony-stimulating factor (GM-CSF). These studies assessed if the cervix, using an inflammatory mouse model of preterm birth, will produce GM-CSF.

METHODS: Using an animal model of preterm birth, CD-1 pregnant mice were treated with an intrauterine injection of 250 ug of LPS on embryonic day 17 (E17). Within six hours, mice were euthanized and the cervix was harvested. RNA was collected for quantitative real time PCR (qRT-PCR) for expression IL-6 and GM-CSF.

RESULTS: LPS administered intraperitoneally on day E17 significantly increased IL-6 ($p<0.05$) and GM-CSF ($p<0.005$) expression compared to control mice

**Figure(s) will be available online.*

CONCLUSIONS: These studies demonstrate LPS increases the expression of GM-CSF in the cervix using an inflammatory mouse model of preterm birth. This data is consistent with prior work from our lab, which has shown LPS will increase the expression of GM-CSF in human cervical epithelial cells as well as amniotic fluid cells. Further studies are needed to determine the mechanism of how GM-CSF and other pro-inflammatory pathways lead to preterm birth.

S-010

Inflammation on the Amniotic Membrane Induces Preterm Delivery in Mice with Chronic Dental *Porphyromonas gingivalis* Infection. Yuko Teraoka,[1] Hiroshi Miyoshi,[1] Haruhisa Konishi,[1] Satoshi Urabe,[1] Mutsumi Miyauchi,[2] Takashi Takata,[2] Yoshiki Kudo.[1] *[1]Hiroshima University, Hiroshima, Japan; [2]Hiroshima University, Hiroshima, Japan.*

INTRODUCTION: It is now widely accepted that inflammation induces preterm delivery. However, the mechanism is uncertain. We previously reported that mice with the dental *Porphyromonas gingivalis* (*P.g*) infection (*P.g* mice) could be used as an effective model of preterm delivery. In this model, inflammation on the amniotic membrane is thought to be the main cause of preterm delivery as cyclooxygenase 2 and interleukin (IL)-1β levels are highly upregulated in the amniotic membrane. Here, we aimed to investigate the mechanism through which inflammation was induced on the amniotic membrane in *P.g* mice.

METHODS: We observed *P.g* colonies in the placenta of *P.g* mice using immunohistochemistry. We measured TNF-α and IL-1β levels in the blood serum using ELISA and in the amniotic membrane, placenta, and myometrium using real-time polymerase chain reaction (PCR) at day 18 of gestation in control and *P.g* mice. We also evaluated toll-like receptor 2 (TLR2) and TLR4 levels in the amniotic membrane using real-time PCR. TLR2 plays an important role in the recognition of *P.g*-lipopolysaccharide (*P.g*-LPS) and the activation of inflammatory pathways. Western blot analysis was performed for detection of nuclear factor kappaB (NF-κB;phospho-p65), and mitogen-activated protein kinases (MAPKs;phospho-p38, and, phopho-JNK).

RESULTS: Immunohistochemistry revealed that the *P.g* colonies were expressed in the embryo side of the placenta and amniotic membrane. Serum TNF-α and IL-1β levels were 1.9 and 2.7 fold elevated in the *P.g* mice. IL-1β levels in the placenta and amniotic membrane were 2.3 and 5.7 fold increased but not in the myometrium. The TNF-α level increased 2.2 fold in the placenta but not in the amniotic membrane and myometrium. TLR2 levels in the amniotic membrane were increased 2.4 fold in *P.g* mice; however, TLR4 levels were not elevated. NF-κB and MAPK expression levels were enhanced on the amniotic membrane but not in the placenta and myometrium in *P.g* mice.

CONCLUSIONS: NF-κB and MAPK signaling pathways were activated via TLR2 leading to release cytokines. Inflammation on the amniotic membrane associated with *P.g* infection plays a role in promoting preterm delivery.

S-011

The Role of T Regulatory Cells in the Maternal-Fetal Rejection Phenotype of Preterm Birth. Jennifer B Gilner,[1] Abigail Fulp†,[1] Rex Bentley,[2] Joanne Kurtzberg,[3] Amy Murtha*.[1] *[1]Duke University Health System, Durham, NC, USA; [2]Duke University Health System, Durham, NC, USA; [3]Duke University Health System, Durham, NC, USA.*

INTRODUCTION: Immune activity in pregnancy must be tightly regulated to allow infection control yet prevent rejection of the semi-allogeneic fetus. Immunologic dysregulation in the form of maternal anti-fetal rejection has been linked to obstetric pathology including preterm delivery (PTD). T regulatory cells (Tregs) play a key role in maintaining immune tolerance, however mechanisms linking dysfunction of immune tolerance with PTD are incompletely understood. In addition, the extent of maternal anti-fetal rejection in PTD resulting from medical complications is not yet known. We investigated patterns of maternal adaptive immune responses in phenotypic subsets of PTD defined by molecular markers of maternal anti-fetal rejection.

METHODS: Patients delivering at 23 0/7 to 33 6/7 weeks were prospectively enrolled. Umbilical cord blood and placenta were collected at delivery and maternal blood was collected within 24h of delivery. Subjects were classified according to presence or absence of a maternal anti-fetal rejection phenotype, defined by placental histopathology, maternal anti-HLA serology, and fetal levels of the T cell chemokine CXCL10. Systemic inflammatory mediators were measured in maternal and fetal plasma delivery samples. Maternal cell-mediated immune tolerance was assessed by flow cytometry measurement of Tregs.
RESULTS: Blood samples were collected from 44 PTD (24 5/7 to 33 6/7 weeks), with comparable patient demographics between rejection phenotype positive (n=9) and rejection phenotype negative (n=35) PTD groups. No significant association was detected between maternal and fetal circulating levels of TNF-α or IL-6 proteins and rejection phenotype status. Percentage of immunosuppressive maternal Tregs did not differ between rejection positive (7.43%) and rejection negative (7.61%) PTD groups (p=0.98).
CONCLUSIONS: The maternal anti-fetal rejection phenotype, previously only described in spontaneous preterm deliveries, has now been identified in 24% of medically-indicated PTD. Maternal adaptive immune regulation, based on Treg numbers, did not differ significantly between PTD cohorts defined by molecular rejection phenotype. Further investigation of maternal Treg cell function (suppressive activity) in rejection-related PTD may provide a mechanistic link between dysfunction of immune tolerance and PTD.

S-012

Differential Expression of T Cell Receptor CXCR3 in Preterm Birth Placentas. Abigail Fulp†,[1] Tracy Truong,[2] Yi-Ju Li,[2] Rex Bentley,[3] Amy Murtha,[1] Jennifer Gilner*.[1] *[1]Duke University Health System, Durham, NC, USA; [2]Duke University Health System, Durham, NC, USA; [3]Duke University Health System, Durham, NC, USA.*
INTRODUCTION: Preterm birth is the leading cause of neonatal morbidity and mortality, but has been difficult to mitigate, as it is the common endpoint of multiple different biologic processes. One such etiology is inflammation stimulated by the allogeneic mismatch between mother and fetus, similar to transplant rejection. Lymphocytic infiltration of the placenta, called "chronic placental inflammation," includes maternal T cell infiltration of the fetal compartment. CXCR3 is a chemokine receptor expressed on Th1 T cells that has been shown to be the key leukocyte trafficking receptor in transplant rejection. Given biologic similarities between pregnancy and organ transplantation, we hypothesized that CXCR3 plays a critical role in mediating maternal T cell invasion in chronic placental inflammation in the pathologic setting of preterm birth.
METHODS: Patients delivering at 23 0/7 to 33 6/7 weeks were prospectively enrolled. Placentas from 56 singleton births were collected and histology sections were examined for chronic inflammatory lesions. Placental slides were stained for CXCR3 protein and staining was quantified as the ratio of CXCR3+ stained area to total tissue area. Wilcoxon rank sum and Fisher's exact test were used to analyze variables between each comparison group. Multiple linear regression modeling was used to test the effects on CXCR3 staining while controlling for preterm labor and acute chorioamnionitis.
RESULTS: CXCR3 protein expression was significantly lower in patients with evidence of chronic placental inflammation when compared to those without chronic placental inflammation after controlling for preterm labor and acute chorioamnionitis (-9.65; 95% CI = -18.03, -1.28; P = 0.03). There was no evidence of association between CXCR3 and indication for delivery after controlling for preterm labor and acute chorioamnionitis (-9.85; 95% CI = -21.81, 2.11; P = 0.11).
CONCLUSIONS: Our results demonstrate significant variation in CXCR3 protein expression on placental histology from preterm birth placentas. Differences in expression of CXCR3 suggests a functional role in the setting of chronic inflammation. The relationship of CXCR3 to chronic inflammation and the etiology of preterm birth requires more specific characterization.

S-013

A Comparison of Toll-Like Receptor 1-9 Induced Cytokine Responses in Whole Blood Collected in the First Trimester and at Term, and Matched Cord Blood. Denise CY Chan†, Yun S Lee, TG Teoh, Phillip R Bennett, David A MacIntyre, Lynne Sykes*. *Imperial College London, London, United Kingdom.*
INTRODUCTION: Preterm labour is characterised by an inflammatory response with increased cytokine production by immune cells both systemically and locally at the maternal-fetal interface. Toll-like receptors (TLR) play a key role in regulating innate immune activation of the inflammatory cascade at the maternal fetal interface in preterm labour. However, there are limited comparative studies on the responsiveness of systemic immune cells in pregnancy to bacterial and viral stimuli via the TLR receptors. We examined the immune response of whole blood to TLR 1-9 agonists during pregnancy and in matched cord blood.
METHODS: Whole blood was taken from women between 12 -15 weeks gestation and at term with matched cord blood at pre-labour caesarean section (n=3). Blood was cultured for 24 hours with either vehicle, medium alone, PMA/Ionomycin, or TLR agonists 1-9 for 24 hours. A dose response was performed for each TLR agonist, and cell culture supernatant was used to detect IL-6, IL-8 and TNF-α using the Multiplex Luminex Assay. Data were analysed using GraphPad Prism v7.02.
RESULTS: Dose-dependent upregulation of cytokine production was demonstrated with all TLR agonists except TLR3 in both maternal and cord blood (see Table 1 for agonist concentrations). The only cytokine to show significant differential effects between the first trimester and term was TNF-α, with lower cytokine production in the first trimester upon TLR4 (P<0.01) and 5 (P<0.01) stimulation. IL-6 and IL-8 production was dramatically greater in cord blood compared to term maternal blood in response to TLR 2,4,5,6,7,8 and TLR 1,2,4,5,6,8 agonists respectively.
CONCLUSIONS: We conclude that during pregnancy the systemic immune response has similar capacity to respond to both bacterial and viral ligands via the toll like receptors, although the neonate displays a dramatically heightened response.

Agonist (μg/ml, unless otherwise stated)	Low	Medium	High
TLR1 Pam3CSK4	0.01	0.1	1
TLR2 HKLM	10^6/ml	10^7/ml	10^8/ml
TLR3 PolyI:C	1	10	25
TLR4 E coli K12 LPS	0.01	0.1	1
TLR5 Flagellin	0.01	0.1	1
TLR6/2 FSL-1	0.01	0.1	1
TLR7 Imiquimod	0.1	1	10
TLR8 ssRNA40	0.1	1	10
TLR9 ODN2006 (μm)	0.01	0.1	1

S-014

Autophagy May Predispose to *Chlamydia Trachomatis* Infection and Bad Outcome in Pregnancy. Aswathi Jayaram†,[1] Tomi Kanninen†,[1] Steven R Inglis,[1] Ashwini Pandit,[1] Steven S Witkin*.[2] *[1]Jamaica Hospital Medical Center, Jamaica, NY, USA; [2]Weill Cornell Medical College, New York, NY, USA.*
INTRODUCTION: Factors influencing susceptibility to *C. trachomatis* (CT) infection, as well as the influence of a past or present infection on pregnancy outcome, remain incompletely elucidated. CT is an obligate intracellular pathogen and utilizes compounds in the host cytoplasm for proliferation. Autophagy is an intracellular process that maintains compounds in the cell to maintain physiological functions. We hypothesized that women with an increased autophagy may have increased susceptibility to CT infection that in turn affects pregnancy outcome.
METHODS: 216 pregnant women at Jamaica Hospital were tested for cervical CT by polymerase chain reaction (PCR) and for antichlamydial IgG in sera by ELISA. All subjects were also tested for *N. gonorrhoeae* (NG), *group B Streptococcus* (GBS) and *Human papillomavirus* (HPV) by standard assays. Peripheral blood mononuclear cells were isolated and intracellular level of p62 was measured by ELISA. The extent of

autophagy is inversely related to the p62 concentration. Buccal cells were collected from the subjects and the DNA tested for a polymorphism in the *ATG16L1* gene that codes for an autophagy-related protein. The presence of the G allele is associated with reduced autophagy activity.

RESULTS: Nine women (4.2%) were PCR positive while 28 (18.2%) were positive for anti-chlamydial IgG. The p62 concentration in PBMCs from women who were PCR (+) was lower than in PCR(-) women ($p = 0.0111$). Similarly, the p62 level was reduced in women with antichlamydial antibodies compared to antibody negative women ($p = 0.0194$). In contrast, there were no associations between p62 concentration and the presence or absence of NG, GBS and HPV. The G allele was present in 27.4% of the CT(-) women as opposed to 11.1% in the CT(+) group. Similarly, allele G was identified in 30.9% of the CT antibody (-) women vs. 20.4% of the CT antibody(+) group. The occurrence of a preterm birth was 25.0% in PCR(+) women, 13.6% in PCR(-) women, 19.0% in antibody(+) women and 11.4% in antibody (-) women.

CONCLUSIONS: An increased capacity for autophagy, related in some women to the absence of the ATG16L1 G allele, is associated with an increased occurrence of CT infection. Elevated autophagy may increase the level of compounds available for maintaining cell functions, allowing the cell to survive and predispose to chlamydial proliferation and infection.

S-015

Differential Effects of Five Lactobacilli Bacteria Strains on Infection-Induced Cytokine Production by Human Myometrial Cell. Bona Kim†,[1] Oksana Shynlova,[1,2] Alan Bocking,[1,2] Stephen Lye*.[1,2] *[1]Sinai Health System, Toronto, ON, Canada; [2]University of Toronto, Toronto, ON, Canada.*

INTRODUCTION: Preterm labour (PTL) is a leading cause of neonatal mortality and morbidity in developed countries. Recently, L.*rhamnosus GR-1* supernatant (SN) was shown to inhibit LPS-induced PTL in pregnant mice by suppressing pro-inflammatory cytokine expression in the myometrium, decidua, placenta, and amniotic fluid. We hypothesize that *GR-1*, unique from other Lactobacilli, can inhibit a pro-inflammatory response of the human myometrium to LPS stimulus and prevent PTL. We also suggest that *GR-1*SN acts by inhibiting toll like receptor (TLR) signalling.

METHODS: Immortalized human myometrial cells (hTERT-HM) were treated with five different strains of probiotics (L.*rhamnosus GR-1, GG,* L.*lactis*, L.*casei,* L.*reuteri* RC-14) prior to LPS stimulus (100ng/mL). Conditioned media (CM) was collected and analyzed by ELISA for pro-inflammatory cytokine secretion (MCP-1, IL-8, IL-6), cellular mRNA was extracted by TRIzol and examined for TLR1,2,3,4,6 expression by qPCR. Lactobacilli strains were cultured in MRS broth and collected at mid-exponential phase. Bacteria were washed, resuspended and cultured in PBS for 2h. PBS-based SNs were collected from five Lactobacilli strains and filtered to remove residual bacteria. ELISA of CM demonstrated that LPS stimulus significantly induced MCP-1, IL-8, IL-6 secretion by myometrial cells. Pretreatment of hTERT-HM with GR-1SN resulted in significant ($P<0.05$) decreases in MCP-1, IL-8 and IL-6 secretions (47.5%, 28.9%, and 47.6% respectively). Pretreatment with SNs from Lactobacilli *GG, lactis, casei, RC-14* did not result in suppression of pro-inflammatory cytokines.

RESULTS: RT-qPCR analysis of TLR gene expression demonstrated that LPS stimulus increased expression of TLR1 and TLR2 on hTERT-HM by 2.5 fold. Treatment of myometrial cells with five different PBS-based SNs alone at different dilutions (1:100, 1:50, 1:20) does not significantly alter TLR expression. When pretreatment with SNs was follow by LPS stimulus, TLR1 expression was decreased by GR-1, GG, and *casei*, while only *GR*-1SN was able to inhibit expression levels of TLR2 in a dose dependent manner.

CONCLUSIONS: Our research demonstrates that factors secreted by the probiotic *GR-1* uniquely suppress LPS-induced pro-inflammatory cytokine expression by human myometrial cells. Preliminary gene expression data suggest the involvement of TLR signalling in the anti-inflammatory effect of *GR-1*.

S-016

Anti-Inflammatory Activity of N,N-Diethylacetamide (DEA) and N,N-Dipropylacetamide (DPA) in *In Vitro* and *Ex Vivo* Models of Inflammation-Induced Preterm Birth. Samir Gorasiya,[1] Juliet Mushi,[2] Sabesan Yoganathan,[1] Sandra E Reznik.[1,2,3] *[1]St. John's University, Queens, NY, USA; [2]Montefiore Medical Center/Albert Einstein College of Medicine, Bronx, NY, USA; [3]Montefiore Medical Center/Albert Einstein College of Medicine, Bronx, NY, USA.*

INTRODUCTION: Preterm birth (PTB), defined as delivery before the completion of 37 weeks' gestation, occurs in 5 to 18% of all pregnancies worldwide. Intrauterine inflammation is the most common cause of spontaneous PTB. Thus, the development of pharmacotherapy to attenuate the exaggerated inflammatory response that leads to PTB is critical for improving neonatal health outcomes. Previous work in our lab has shown that N,N-dimethylacetamide (DMA) prevents preterm birth in a murine model and inhibits LPS-induced increases in placental pro-inflammatory cytokines. As part of a structure activity relationship study to identify DMA related compounds with maximal efficacy and minimal toxicity, we investigated the anti-inflammatory properties of two DMA analogs: N,N-diethylacetamide (DEA) and N,N-dipropylacetamide (DPA).

METHODS: To test whether DEA and DPA suppress the secretion of pro-inflammatory cytokines, HTR-8/SVneo human trophoblast cells and placental explants from normal term Cesarean deliveries were pre-treated with different concentrations of DEA and DPA (0.1, 1 and 10 mM) for 2 hr and then treated with E. coli LPS (1μg/ml) for 18 to 24 hr. Levels of cytokines secreted into cell and placental supernatants were determined using ELISA.

RESULTS: Similar to what we observed in our previous study with DMA, both analogs, DEA and DPA, inhibited the secretion of pro-inflammatory cytokines and chemokines in HTR-8/SVneo cell and placental explant supernatants. DMA analogs attenuated the secretion of Interleukin-6 (IL-6, $p<0.001$), IL-8 ($p<0.01$) and monocyte chemoattractant protein-1 (MCP-1, $p<0.01$) from LPS-stimulated HTR-8/SVneo cells and tumor necrosis factor α (TNFα, $p<0.01$), IL-6 ($p<0.001$), IL-8 ($p<0.01$), MCP-1 ($p<0.01$) and granulocyte macrophage-colony stimulating factor (GM-CSF, $p<0.01$) from LPS-stimulated placental explants.

CONCLUSIONS: For the first time, we show here that two DMA analogs, DEA and DPA, regulate the secretion of cytokines and chemokines from cultured human trophoblasts as well as from human placental explants. The mechanism underlying the anti-inflammatory activity of these DMA analogs requires further investigation.

S-017

Worse Outcomes in a Severe Sepsis Model in Pregnancy Were Not Associated with a TH1/Th2 Cytokine Bias or Immunosuppression. Julia Zöllner,[1] Noor Mohd Nasri,[1] James Leiper,[2] Mark Johnson*.[1] *[1]Imperial College London, London, England, United Kingdom; [2]Imperial College London, London, England, United Kingdom.*

INTRODUCTION: Sepsis is the leading cause of direct maternal mortality in the UK. The aim of this study was to investigate the impact of sepsis on cardiovascular function and the innate immune response under naive conditions and during pregnancy.

METHODS: Pressure transmitters were implanted into CD1 mice to non-invasively measure mean arterial pressure (MAP) and heart rate (HR). Temperature (Tp) was measured by subcutaneous (subc) probes. Non-pregnant (NP) and pregnant mice (day 16) then underwent CLP or a sham operation. In a separate study, tissue and serum were collected at 3 and 6 hours for flow cytometry and cytokine/chemokine multiplex assay. Peritoneal fluid for bacterial count was collected at 8 hours following CLP.

RESULTS: Polymicrobial sepsis resulted in a haemodynamic collapse. There was a 30% decrease in MAP and 50% decrease in HR as compared to the sham group in NP and pregnant mice (MAP: $p<0.01$ and $p<0.001$, respectively; HR: $p<0.01$ and $p<0.001$, respectively). A decrease of Tp below 32°Celsius determined a poor outcome in NP and pregnant mice ($p<0.001$). The innate immune response during pregnancy was exaggerated. There was a twofold increase of leukocyte trafficking into the lung during pregnancy ($p<0.001$). Cytokine and chemokine response, and bacterial count following CLP, was comparable in non-pregnant and pregnant mice.

CONCLUSIONS: The study demonstrated that there was a significant haemodynamic dysfunction following sepsis in pregnancy. The innate immune response to polymicrobial sepsis was altered during gestation. Approaches that provide cardiovascular support without impairing the pathogen-specific immune response may provide new prophylactic and therapeutic pathways during sepsis.

S-018

Antenatal Suppression of Interleukin-1 Protects Against Inflammation-Induced Fetal Injury and Improves Neonatal and Developmental Outcomes in Mice. Mathieu Nadeau-Vallée†,[1] Peck-Yin Chin,[2] Lydia Belarbi,[1] Marie-Ève Brien,[3] Sheetal Pundir,[1] Alexandra Beaudry-Richard,[1] David J Sharkey,[2] Xin Hou,[1] Christiane Quiniou,[1] Jean-Sébastien Joyal,[1] William D Lubell,[4] David M Olson,[5] Sarah A Robertson,[2] Sylvie Girard,[3] Sylvain Chemtob*.[1] *[1]CHU Sainte-Justine Research Center, Montreal, QC, Canada; [2]Adelaide Medical School and Robinson Research Institute, University of Adelaide, Adelaide, SA, Australia; [3]CHU Sainte-Justine Research Center, Montreal, QC, Canada; [4]Université de Montréal, Montréal, QC, Canada; [5]University of Alberta, Edmonton, AB, Canada.*
INTRODUCTION: Preterm birth (PTB) is commonly accompanied by in utero fetal inflammation, and existing tocolytic drugs do not target fetal inflammatory injury. Of the candidate proinflammatory mediators, interleukin-1 (IL-1) appears central and sufficient to trigger fetal loss.
METHODS: Therefore, we elucidated the effects of antenatal IL-1 exposure on post-natal development, and investigated two IL-1 receptor antagonists, the competitive inhibitor Kineret (anakinra) and a potent noncompetitive inhibitor 101.10, for efficacy in blocking IL-1 actions.
RESULTS: Antenatal exposure to IL-1β induced *Tnfa*, *Il6*, *Ccl2* and *Pghs2* expression in placenta and fetal membranes, and elevated amniotic fluid IL-1β, IL-6, IL-8 and PGF2α, resulting in PTB and marked neonatal mortality. Surviving neonates had increased *Il1b*, *Il6*, *Il8*, *Il10*, *Pghs2* and *Tnfa* expression in white blood cells with elevated plasma IL-1β, IL-6 and IL-8, increased IL-1β, IL-6 and IL-8 in fetal lung, intestine and brain, and morphological abnormalities including disrupted lung alveolarization, atrophy of intestinal villus and colon-resident lymphoid follicle, and brain microvascular degeneration and atrophy with visual evoked potential anomalies. Late gestation treatment with 101.10 abolished these adverse outcomes, whereas Kineret exerted only modest effects and no benefit for gestation length, neonatal mortality or placental inflammation. In an LPS-induced model of infection-associated PTB, 101.10 prevented PTB, neonatal mortality and fetal brain inflammation.
CONCLUSIONS: The results implicate IL-1 as an important driver of neonatal morbidity in PTB and identify 101.10 as an effective candidate therapeutic to counteract its harmful actions.

S-019

Prior Pregnancy History Influences the Level of Autophagy and Immune Activation in Peripheral Blood Mononuclear Cells from Pregnant Women. Aswathi Jayaram†,[1] Tomi Kanninen†,[1] Giovanni Sisti†,[2] Steven R Inglis,[1] Ashwini P Pandit,[1] Steven Witkin*.[2] *[1]Jamaica Hospital Medical Center, Jamaica, NY, USA; [2]Weill Cornell Medical College, New York, NY, USA.*
INTRODUCTION: Maternal immunity is altered during pregnancy. CD4+ T lymphocytes that recognize paternal and fetal antigens are induced and release cytokines to down-regulate immune responses. These lymphocytes persist in the circulation following parturition. They become reactivated and proliferate following a subsequent conception, resulting in enhanced immunity compared to primiparous women. We evaluated the influence of a prior gestation on autophagy activity in peripheral blood mononuclear cells (PBMCs) from pregnant women.
METHODS: PBMCs were isolated from 212 pregnant women and the extent of autophagy was determined by quantitation by ELISA of the concentration of p62 (sequestosome-1) in the cytoplasm. p62 binds to macromolecules that are targets for autophagy-directed degradation. Thus, the cytoplasmic p62 level is inversely related to the extent of autophagy. The cytoplasmic levels of the stress inducible 70 kDa heat shock protein (hsp70), tumor necrosis factor-alpha (TNF) and interleukin-10 (IL-10) were also measured in cell lysates by ELISA. All assays were performed by personnel blinded to all clinical data. Data were analyzed by the Spearman rank correlation or Mann-Whitney test, as appropriate.
RESULTS: The p62 concentration in PBMCs was positively correlated with the number of live births ($p=0.0235$), the number of preterm ($p=0.0056$) or term deliveries ($p=0.0461$) and the birthweight of the baby ($p=0.0247$). The PBMC p62 level was higher in the 137 women with a prior delivery than in the 46 women with a first conception ($p=0.0233$) and lower in the 29 women with a prior spontaneous abortion only as compared to women with a prior delivery ($p=0.0091$). The cytoplasmic concentrations of hsp70, TNF and IL-10 were all correlated with the p62 level ($p\leq0.0010$).
CONCLUSIONS: PBMCs from women with a prior delivery have an increased recognition of fetal antigens than do women with a first conception, resulting in enhanced immune activation and lower autophagy (higher p62). Conversely, PBMCs from women with only a prior spontaneous abortion have the highest level of autophagy, perhaps indicating a reduced capacity to recognize fetal antigens and possibly contributing to pregnancy failure.

S-020

D-Lactic Acid Inhibits Basal Inflammatory Pathways in Human Vaginal Epithelial Cells. Yun S Lee†, Maria Marianoglou, Fabienne Hanton, Richard G Brown, Phillip R Bennett, David A MacIntyre*. *Imperial College London, London, United Kingdom.*
INTRODUCTION: Microbial infections are associated with around 50% of preterm labour cases. Vaginal microbiota in healthy pregnancy are most frequently dominated by *Lactobacillus crispatus* or *L. iners*, which are thought to contribute to health status through vaginal acidification by lactic acid (LA) production and growth inhibition of bacterial vaginosis-associated taxa. However, we have recently shown that *L. iners* dominance of vaginal microbiota is a risk factor for preterm birth, whereas *L. crispatus* confers protection. A major functional difference between the two species is that *L. crispatus* preferentially excretes the D-LA isomer whereas *L. iners* primarily excretes L-LA. High L-LA levels are associated with increased vaginal expression of extracellular matrix metalloproteinase inducer, high cervicovaginal mucosal viscosity and poor trapping of viral particles. The impact of LA isomers on inflammatory pathway activation in vaginal epithelial cells is unknown. We therefore aimed to assess the effect of LA isomers on the activation of NF-κB and AP-1 as well as downstream inflammatory mediators in vaginal epithelial cells.
METHODS: Vaginal epithelial cells (VK2/E6E7) were treated with increasing concentrations of L- or D-LA (2.5-25mM) across a time course (30 min, 2 and 6h). Whole cell or cytosolic/nuclear protein was extracted and the levels of phosphorylated p65 (NF-κB) and p-c-Jun (AP-1) were examined using western blotting.Culture media was collected for examination of a total of 36 human cytokines and chemokines.
RESULTS: L-LA induced transient phosphorylation of p65 and nuclear translocation at 30 min post treatment ($P<0.05$, ANOVA). In contrast, D-LA did not alter basal p65 activation or nuclear translocation. Both L- and D-LA treatment inhibited basal phosphorylation of c-Jun and its nuclear translocation in a dose-dependent manner ($P<0.05$, ANOVA). Treatment of cells with L-LA (15mM) lead to increased production of IL-1R antagonist at 6h post treatment where as D-LA treatment was associated with decreased production of GROa/CXCL1, IL-6, IL-8, MIF, SerpinE1, RANTES and IL-1Ra.
CONCLUSIONS: Our data indicate that while L-LA has minimal impact upon basal inflammatory activity, D-LA is a potent inhibitor of basal inflammatory status in vaginal epithelial cells. This provides a potential mechanism explaining the observed protection conferred by *L. crispatus* dominated vaginal bacterial communities in the context of preterm birth risk.

S-021

The Role of Antenatal Inflammation, Specifically Interleukin-1β, in Retinal and Sub-Retinal Vasculopathy of Offspring. Alexandra Beaudry-Richard,[1] Mathieu Nadeau-Vallée,[2] Ankush Madaan,[2] Carlos Rivera,[1] Sheetal Pundir,[2] Xin Hou,[2] Christiane Quiniou,[2] Jean-Sébastien Joyal,[2] Sylvain Chemtob.[1,2] *[1]HMR Center of Research, Montreal, QC, Canada; [2]CHUSJ Research Center, Montreal, QC, Canada.*

INTRODUCTION: Each year, preterm birth (PTB; <37w of gestation) affects 15 million children worldwide, putting them at high risk of mortality and morbidity, often accompanied by permanent sequelae. Retinopathy of prematurity (ROP) affects 1 preterm child out of 5 and can lead to blindness. Inflammation and high oxygen concentration disrupt normal blood vessel proliferation in the retina, causing ischemia, chaotic neovascularisation and retinal detachment. Interleukin (IL)-1 is a pro-inflammatory cytokine that plays an important role in PTB and subsequent perinatal injuries. Hence, we hypothesize that administration of intra-uterine IL-1 can cause antenatal inflammation and its propagation in the eye, post-natal vascular development and retinal function anomalies. Two IL-1 receptor antagonists were administered to protect the retina: the competitive inhibitor Kineret (clinically approved) and the non-competitive inhibitor 101.10 (Rytlvela; recently developed by our lab).

METHODS: To induce PTB, IL-1β was injected to pregnant CD-1 mice *in utero* at gestational age (G) 16 and antagonists (Kineret or 101.10) were administered sub cutaneously (sc) from G 16 to 18. Antenatal inflammation was assessed in the foetal eye by qPCR. Propagation of inflammation and vascular development was observed by immunohistology (Iba-1 and lectin). Electroretinogram (ERG) was used to evaluate retinal function.

RESULTS: Presence of IL-1 *in utero* increased the expression of upstream pro-inflammatory genes (IL-6, CCL2, CXCL-16 and Caspase-1) in the eye before birth, indicating an inflammatory response independent of birth. Microglial infiltration was also observed before and after birth in the retina and the sub-retina. We also observed a decreased microvascular development and a thinner choroid. In the adult, retinal function was altered as shown by a decrease in b-wave amplitude of ERG. 101.10 prevented all of these phenotypes but Kineret was less efficient.

CONCLUSIONS: Presence of IL-1 *in utero* induces an inflammatory response in the foetus eye that can lead to deficits in vascular growth and retinal function later in life. Antenatal administration of 101.10 provides a promising approach to tackle detrimental inflammatory outcomes by acting upstream in the cascade of events leading to ROP.

S-022

Common Vaginal Bacterial Strains Regulate Cervical Epithelial Barrier Function Through Inflammation-Mediated Mechanisms. Lauren Anton, Ann DeVine, Amy G Brown, Luz-Jeannette Sierra, Michal A Elovitz*. *Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA.*

INTRODUCTION: Recent evidence suggests that preterm birth is associated with premature cervical remodeling initiated by cervical epithelial barrier breakdown. A cervicovaginal (CV) microbiota dominated by *Lactobacillus crispatus* (L. crisp) is associated with vaginal health while dominance by *Gardnerella vaginalis* (G. vag) is associated with bacterial vaginosis, an unhealthy vaginal state. The study objective was to determine if L. crisp and G. vag alter the cervical epithelial barrier through activation of inflammatory pathways.

METHODS: Human ectocervical cells (Ect1/E6E7) (Ecto) were treated with 10% v/v sterile filtered L. crisp or G. vag cell free supernatants (CFS) for 48 hrs with or without LPS (25 ug/ml) (n=6). The following treatment groups were studied 1) control, 2) LPS, 3) L. crisp, 4) L. crisp+ LPS, 5) G. vag and 6) G. vag+ LPS. Ecto cells were treated with anti-TLR2 or isotype control antibody (20 ug/ml) for 4 hrs prior to CFS exposure (n=3). Cell permeability assays and soluble E-Cad (sECAD) and IL-8 measurements (ELISA) were performed in all groups.

RESULTS: Ecto cell permeability was increased with LPS ($p<0.001$) and G. vag ($p<0.001$) but not with L. crisp. Ecto cells treated with G. vag+ LPS resulted in increased permeability ($p<0.01$) compared to LPS and increased sECAD ($p<0.05$) compared to G. vag+ LPS. L. crisp prevented the LPS-induced changes to the epithelial barrier ($p<0.001$) and sECAD ($p<0.001$). G. vag ($p<0.001$) and G. vag+ LPS ($p<0.001$) increased IL-8 compared to LPS alone. L. crisp increased IL-8 ($p<0.01$) compared to control and L. crisp+ LPS further increased IL-8 compared to L. crisp alone ($p<0.0001$). G. vag+ anti-TLR2 antibody reduced permeability ($p<0.01$), sECAD ($p<0.001$) and IL-8 ($p<0.001$) compared to G vag alone. The anti-TLR2 antibody had no effect on L. crisp-mediated alterations in permeability, sECAD and IL-8.

CONCLUSIONS: These data suggest that an unhealthy, G. vag-dominated CV space, especially in the presence of an additional inflammatory stimulus or bacterial by-product, is sufficient to compromise the cervical epithelial barrier. Important for future therapeutic strategies, this effect is mediated, in part, by TLR-2. A healthy, L. crisp-dominated CV space is able to protect cervical epithelial barrier integrity through a reduction in E-Cad cleavage despite an activated immune response. (MOD Prematurity Research Center at PENN).

S-023

An Objective Comparison of *In Vivo* Human Cervix Stiffness in Early and Late Pregnancy. Lindsey C Drehfal†,[1] Helen Feltovich*,[1,2] Ivan M Rosado-Mendez,[1] Mark L Palmeri,[3] Timothy J Hall.[1] *[1]University of Wisconsin, Madison, WI, USA; [2]Intermountain Healthcare, Provo, UT, USA; [3]Duke University, Durham, NC, USA.*

INTRODUCTION: The cervix must soften, shorten, and dilate to allow for vaginal delivery. Clinicians recognize the need for objective tools to monitor these changes. Shear wave elasticity imaging (SWEI) is a promising technique for quantifying the softness of tissues. As the cervix softens throughout pregnancy, the shear wave speed (SWS) should decrease. The hypothesis of this study is that shear wave speed (SWS) estimates can objectively detect changes in cervical softness between the 1st trimester and 3rd trimester of pregnancy.

METHODS: In a previous study, women (n = 18) scheduled for induction of labor at term were recruited. Similarly, women (n=12) in the 1st trimester (<14 weeks) were recruited. A Siemens S3000 ultrasound system with a prototype catheter transducer (128 elements, 14mm aperture, 3mm diameter) was used to scan from the outside of the cervix. The probe was secured to the clinician's hand, with the active aperture on her fingertip, and then placed into a sterile glove filled with gel for acoustic coupling. The clinician's finger was placed on top of the cervix and aligned parallel to the endocervical canal midway between the external os and the internal os. The cervix softness component of the Bishop score was also recorded in each case. The performance of SWS estimates for separating 1st from 3rd trimester cervix softness was assessed using Receiver Operating Characteristic (ROC) curves. Area under the curve (AUC), 95% confidence intervals were computed and compared via N = 1000 bootstrap replicates.

RESULTS: The SWS estimates were 4.42±1.32 m/s and 2.13±0.66 m/s in the 1st and 3rd trimesters, respectively, and this difference was significant ($p < 0.001$). AUC was 0.95 (95% CI: 0.82-0.99) for distinguishing between SWS in the 1st trimester and the 3rd trimester cervix. Although the softness of all 1st trimester cervices was rated 0 (firm, "rock hard"), and the differences in softness among 3rd trimester cervices correlated with differences in SWS, those rated 0 (firm) in the 1st trimester were much more firm (higher SWS) than those rated firm in 3rd trimester.

CONCLUSIONS: We have demonstrated that SWS can detect changes in cervical softening between early and late pregnancy**.** SWEI methods appear promising for objectively monitoring cervical stiffness.

S-024

Monitoring Collagen Remodeling in the Cervix with Quantitative Ultrasound. Quinton W Guerrero†,[1] Lindsey C Drehfal†,[1] Ivan M Rosado-Mendez,[1] Helen Feltovich,[1,2] Timothy J Hall*.[1] *[1]University of Wisconsin, Madison, WI, USA; [2]Intermountain Healthcare, Provo, UT, USA.*

INTRODUCTION: We have developed methods to detect the presence and magnitude of anisotropic ultrasound backscattering from tissues. Results obtained are consistent with known anisotropy, and subjective visual assessment, in skeletal muscle. In the cervix, this scattering anisotropy is theorized to arise from the organized and layered collagen

fibers that compose the cervix. This collagen structure, in animal models, transitions from being highly organized before pregnancy to nearly completely disorganized at term. Our hypothesis is that this measure of backscatter anisotropy is sensitive to the change in cervical collagen structure in the early pregnancy compared to the late pregnancy.

METHODS: Women in the first (n=9) and third trimester (n=20) were recruited for ultrasound scans of the cervix in the middle to mid-proximal region using a Siemens S3000 and a prototype transducer (128 element, 3 mm diameter, 14 mm aperture) operated in linear array mode with steered acoustic beams. Echo signal frames were collected at 18 different beam steering angles, from -28 degrees to +28 degrees in steps of 4 degrees. Reference phantom data was collected for the same angles and quantitative ultrasound parameters were calculated using the Reference Phantom Method. The magnitude of anisotropic scattering was measured using the mean backscattered power difference (mBSPD).

RESULTS: Average mBSPD estimates were 4.99 ± 2.03 dB and 2.83 ± 1.17 dB in the first and third trimesters, respectively, and the difference was significant ($p < 0.003$) indicating that the first trimester cervix is significantly more anisotropic (aligned and organized scattering sources) than the third trimester cervix.

CONCLUSIONS: The first trimester cervix has significantly higher backscattering anisotropy than the third trimester cervix. This is consistent with the breakdown in the cervical collagen structure from first to third trimester observed in animal models and with the hypothesis that we can monitor collagen structure changes using quantitative ultrasound.

S-025

Progesterone Modulates Cytokine-Induced Gene Expression in Human Cervical Stromal Fibroblasts. William E Ackerman IV, Taryn L Summerfield, Douglas A Kniss*. *The Ohio State University, Columbus, OH, USA.*

INTRODUCTION: Biomechanical integrity of the cervix (CX) is imperative for the success of pregnancy. Fibroblasts in the cervical stroma play a central role in maintaining the collagen-dense extracellular matrix (ECM), and progesterone (P_4) underpins many of the processes that retain a closed and rigid CX. The molecular mechanisms of P_4 function in the CX are poorly understood, but it appears that this hormone is crucial for pregnancy maintenance. We evaluated global gene expression programs elicited by P_4 and inflammatory cytokine challenge in cervical fibroblasts, and determined the extent to which P_4 modulates inflammation-associated gene expression.

METHODS: With IRB approval, human fibroblasts were isolated from premenopausal CX tissues. Cells were primed with 10^{-8} M 17β-estradiol for 7 d to induce progesterone receptors (PR), then stimulated with 10^{-7} M P_4 for 24 h, followed by incubation with or without IL-1β (0.2 ng/ml) for 4 h. RNA was extracted and subjected to transcriptional profiling by microarray on an Affymetrix platform. Expression patterns of select transcripts were validated using qRT-PCR in biological replicate samples.

RESULTS: Cells stimulated with IL-1β exhibited differential expression with significant up-regulation of 913 and down-regulation of 518 transcripts. The transcriptional response to P_4 was modest (changes in 51 genes; 33 of which were up-regulated). The transcriptional response to P_4+IL-1β vs vehicle was similar to that following IL-1β alone: 889 genes up-regulated; 504 down-regulated. We compared the IL-1β and P_4+IL-1β groups. Altered expression of 39 genes was noted in this context, including suppression of 16 IL-1β-induced genes. Using qRT-PCR, we validated the expression patterns of 8 transcripts ($p < 0.05$, Kruskal-Wallis/Dunn's). Of these, two (*HSD11B1* and *FKBP5*) showed synergistic responses to P_4+IL-1β compared to either treatment alone, three (*BDKRB1*, *BDKRB2*, and *IL8*) were induced by IL-1β but unaffected by P_4 in the absence or presence of IL-1β, and three (*IL6*, *PTGS2*, and *HAS2*) exhibited IL-1β-inducible expression that was attenuated by P_4.

CONCLUSIONS: Cervical stromal fibroblast transcriptional responses to IL-1β and P_4 differed markedly in scope and magnitude. Somewhat surprisingly, P_4 modestly altered the global expression of IL-1β-induced genes with both synergistic and inhibitory effects. Support: March of Dimes Prematurity Research Center Ohio Collaborative.

S-026

Interleukin 8 Expression by Human Cervical Stromal Cells is Mediated by Increased Intracellular cAMP. Shweta J Bhatt†, Emily C Holden†, Laura T Goldsmith*. *Rutgers NJMS, Newark, NJ, USA.*

INTRODUCTION: Understanding of the mechanisms responsible for the initiation of labor at term is limited. Term labor is associated with leukocyte infiltration in the cervix. The mechanisms involved in recruitment of inflammatory cells to the cervix are not well understood. The potent cytokine Interleukin 8 (IL-8) has been implicated as an important factor in cervical dilation during labor. However, cell type specific expression and regulation of IL-8 expression in the cervix are poorly understood. Prior studies of cervical IL-8 have largely been limited to cervical epithelial cells.

We have previously shown that regulation of IL-8 protein expression in endometrial stromal cells is mediated by increased intracellular cyclic adenosine monophosphate (cAMP). Whether this regulatory mechanism is cell type specific or more widespread is unknown. We therefore tested the hypothesis that cervical stromal fibroblasts express IL-8 and that cervical stromal expression of IL-8 is regulated by increased intracellular cAMP.

METHODS: A well characterized in vitro model of human term pregnancy cervix was used. Lower uterine segment stromal cells, isolated from a non-laboring uterus at the time of term cesarean section, were incubated as monolayer cultures. Replicate wells of cells were also incubated in the presence of 0.5 mM 8-br-cAMP to increase intracellular cAMP. The conditioned medium from each well was collected at 72 hours and cell counts were performed. Three experiments were performed with 4 replicates for each treatment group. Levels of IL-8 and, as a positive control, pro-matrix metalloproteinase 1 (pro-MMP1), were assessed using highly specific human ELISAs. Data were compared using Mann Whitney tests.

RESULTS: Mean IL-8 concentrations were 25.3±1.5 pg/10^5 cells (M±SE) in medium from the control cells. Levels of IL-8 significantly increased to mean levels of 86.5±18.6 pg/10^5 cells in response to increased intracellular cAMP ($p<0.0001$). As anticipated, medium levels of pro-MMP1 were abundant in control cells or those with increased intracellular cAMP (greater than mean concentrations of 777 pg/10^5 cells).

CONCLUSIONS: Human term pregnancy stromal cells express IL-8 and expression in this cell type is mediated by increased intracellular cAMP. Further studies regarding the cell type specific and temporal expression of cytokines in the female reproductive tract are likely to enhance our understanding of the mechanisms controlling the initiation of labor at term.

S-027

Biomechanical Simulations of Pregnancy: Fetal Membrane Properties Influence Cervical Tissue Stretch at the Internal Os. AR Westervelt†,[1] M Fernandez,[1] E Mazza,[2] A Ehret,[2] J Vink,[3] CL Nhan-Chang,[3] R Wapner,[3] M House,[4] K Myers*.[1] *[1]Columbia University, New York, NY, USA; [2]ETH Zurich, Zurich, Switzerland; [3]Columbia University Medical Center, New York, NY, USA; [4]Tufts Medical Center, Boston, MA, USA.*

INTRODUCTION: As a pregnancy grows, stretch occurs at the internal os of the cervix. We sought to construct 3D finite element (FE) computer simulation models of pregnancy to understand how mechanical factors of the fetal membrane influence cervical tissue stretch.

METHODS: We generated FE models (FeBio 2.4) using a custom computer script (Trelis Pro 15.1) based on input parameters from transabdominal and transperineal ultrasound (GE Voluson E8). For the baseline model (Fig. 1A), uterine diameter, uterine thickness, cervical length, cervical diameter, and cervical angle with anterior lower uterine segment (LUS) were measured for a 35 y/o normal P0 patient at 25 weeks (Fig. 1A&B). The uterus and cervix were modeled as collagenous composite materials, and the fetal membrane as a highly nonlinear hyperelastic material. Mechanical properties of the fetal membrane was defined based on the range of measured mechanical response in multiaxial mechanical experiments. Fetal membrane prestretch was investigated in three scenarios: no, slight, and large prestretch. Intrauterine pressure was then applied at both physiological and contraction magnitudes, and cervical stretch at the internal os was evaluated.

RESULTS: Cervical deformation significantly depends on fetal membrane properties. As fetal membrane prestretch is increased, fetal membrane load-bearing increases and cervical stretch at the internal os decreases (Fig. 1B-G). At the 25 week physiological intrauterine pressure (0.817 kPa), little stretch is seen at the internal os. At contraction-magnitude intrauterine pressure (8.67 kPa), internal os stretch dramatically increases. **Figure(s) will be available online.*

CONCLUSIONS: The mechanical properties and nonlinear behavior of the fetal membranes are critical to cervical tissue stretch at the internal os. Softer fetal membranes and larger intrauterine pressures increase cervical tissue stretch.

S-028

Transcriptomes of ER and PR Activation Reveal Unique Cross-Talk in Human Cervical Stromal Cells. Banupriya Mukundan†, Patrick Keller, Tulip Nandu, R Ann Word*. *Univ TX Southwestern Med Ctr, Dallas, TX, USA.*

INTRODUCTION: Preclinical trials in preterm guinea pigs indicate that estrogen receptor (ER) agonists and antiprogestins (RU486) alone are insufficient to induce cervical ripening and labor. The combination of RU486 + vaginal ERα agonist, however, readily induces cervical ripening and preterm birth. Here, we explored genomic mechanisms by which ERα and PR differentially transcriptomes of human cervical stromal cells.

METHODS: Human cervical stromal cells were treated with vehicle, ERα agonist (PPT, 3 nM), P4, PPT+P4, RU486, or RU486+PPT+P4 for 6 or 16 h. Total RNA isolated at 6 and 24 h was processed for whole-genome polyA+ RNA-sequencing. Data were filtered to include genes expressed ≥2 fragments/FKPM and significant ($P < 0.01$).

RESULTS: Quality control analysis showed duplicates were virtually identical with correlation coefficients >0.98. First, by far, the most pronounced differentially upregulated annotated gene in response to PPT was PR (*PGR*, 12.7-fold). Quantitative RT-PCR of multiple different cells preps confirmed E2- and PPT-induced upregulation of total PR (10-15-fold). Altered transcriptional profiles in the PPT, PPT+P4 and P4 reflect changes in pathways involved in cell proliferation (*GREB1 and IGF1)*, cell adhesion/matrix remodeling and antagonists of pro-fibrotic BMP/TGFβ (*WISP2, GREM1, SPARCL1* and *MMP11*). Unique transcription profiles of P4 and PPT mediated gene expression changes revealed a significant hallmark that P4 opposes estrogen-induced activation of these genes. Binding of PRs to RU486 relieved this inhibition thereby facilitating ER binding sites throughout the genome. P4 not only repressed many genes activated by ERα, but also brought about new changes in the transcriptome unique from either treatment alone. Further, P4 or RU486 induced unique transcriptomes suggest that antiprogestin-bound PR not only blocks PR binding to DNA but also activates its own set of unique genes.

CONCLUSIONS: Discovering that distinct gene sets and pathways are differentially regulated by ER and PR suggest that loss of cervical PR function results in increased ER activation and novel binding sites for ERα throughout the genome culminating in cervical ripening and dilation both at term and preterm. The work suggests a unique cross-talk between RU486-bound PR and ER activation in the cervical stroma.

S-029

Distinct Effects of Simvastatin, Rosuvastatin and Progesterone on p38MAPK Mediated Senescence and Sterile Inflammation in Human Fetal Membranes. Martina T Ayad,[1] Jayshil J Trivedi,[1] Rheanna Urrabaz-Garza,[1] Talar Kechichian,[1] George Saade,[1] Brandie Taylor,[2] Ramkumar Menon.[1] *[1]University of Texas Medical Branch, Galveston, TX, USA; [2]Texas A&M University, College Station, TX, USA.*

INTRODUCTION: OS induced p38 mitogen activated protein kinase (p38MAPK) mediated chorioamniotic senescence and sterile inflammation (senescence associated secretory phenotype [SASP]) are associated with human parturition. Premature senescence in response to OS inducing risk factors contributes to adverse pregnancy outcomes such as preterm premature rupture of the membranes (pPROM) and spontaneous preterm birth (PTB). Herein, we determined the effect of simvastatin, rosuvastatin and progesterone in down regulating p38MAPK mediated fetal membrane senescence and SASP.

METHODS: Normal term, not in labor, fetal membrane explants (n = 8) maintained in an organ explant system were exposed to cigarette smoke extract (OS inducer) alone or in combination with progesterone (10^{-6} mol/L), simvastatin (100 and 200 ng/ml) and rosuvastatin (100 and 200 ng/ml). Untreated tissues or simvastatin and rosuvastatin alone were also included. p38MAPK expression changes were studied by western blot followed by densitometric analysis, senescence was determined by senescence associated b-galactosidase (SA-b-Gal) staining and multiplex analysis determined changes associated with 4 SASP markers (IL-8, IL-10, TNF-a and GMCSF). Pairwise comparison between different groups was conducted by ANOVA.

RESULTS: As expected CSE induced p38MAPK mediated senescence and SASP compared to control. Co-treatment with simvastatin and rosuvastatin produced significant reduction in p38MAPK activation, senescence (decrease in SA-b-Gal stained cells) and SASP markers, GM-CSF, TNF while increasing antiinflammatory IL-10 in a dose dependent manner. IL-8 was not changed. Higher dose of rosuvastatin was more effective than simvastatin and rosuvastatin alone increased anti-inflammatory IL-10. Conversely, co-treatment with progesterone had no effect on reducing p38MAPK activation, senescence or SASP.

CONCLUSIONS: Both simvastatin and rosuvastatin down regulated CSE-induced p38MAPK activation, senescence and sterile inflammation with rosuvastatin showing very pronounced effect. Progesterone was ineffective in reducing OS induced fetal membrane senescence and SASP. OS induced premature senescence and sterile inflammation of fetal tissues associated with PTB and pPROM may be reduced by treatment with simvastatin or rosuvastatin.

S-030

Effects of Tension on cAMP-Driven Control of Contractility in Human Myometrial Tissue. Pei F Lai†,[1] Rachel M Tribe,[2] Mark R Johnson*.[1] *[1]Imperial College London, London, England, United Kingdom; [2]Kings College London, London, England, United Kingdom.*

INTRODUCTION: Acute pro-relaxation effects of cAMP elevating agents in the myometrium are well-known. Expression profiles of myometrial tissue from non-labouring and labouring women suggest that this aspect of cAMP signalling is reduced during labour. Our current study aims to test the hypothesis that an increase in myometrial tension causes a decrease in cAMP signalling activity to promote a contractile phenotype.

METHODS: Myometrial biopsies obtained from non-labouring women undergoing caesarean section at term pregnancy (n=23) were dissected into either explants (~2x2x2 mm size) or strips (~9x3x1 mm size); strips were attached to 0, 0.6-0.7, or 2.2-2.4 g weights to maintain no, low or high tension, respectively. All tissues were treated with adenylate cyclase agonist, forskolin (0.1 mM), or DMSO vehicle for 6 h in serum-free DMEM before flash freezing in liquid nitrogen and extraction for measurements of cAMP content and PKA activity, as well as HSP20 (Ser16-phosphorylated and total), OTR, COX-2 and PKARIIα protein levels. Data expressed as mean ± SEM and analysed using Student's t-test, Wilcoxon test or 1-way ANOVA (significance taken as $P<0.05$).

RESULTS: Comparison of explants and low tension-maintained (LT) strips showed forskolin exposure for 6 h was associated with increased PKA activity and HSP20 Ser16-phosphorylation to a similar extent ($P>0.05$). PKARIIα protein levels was reduced in explants (0.3 ± 0.1 mean fold change; n=8) but not in LT strips. COX-2 and OTR protein expression in the presence of forskolin and vehicle treatments were similar for both explants and LT strips. Biopsy-matched strips maintained under no, low and high tension showed similar levels of increase in cAMP content after 6 h forskolin treatment; [cAMP] increased by 5.1 ± 0.9, 6.0 ± 0.9 and 6.5 ± 1.0 mean fold change, respectively (n=8).

CONCLUSIONS: Comparison of explants and LT strips suggests that stretch of myometrial tissue has minor effects on cAMP signalling and cAMP activity enhancement for 6 h has no effect on labour-associated protein expression. Tension does not influence forskolin-driven cAMP accumulation. Future experiments will further explore the effects of varying myometrial tension at the tissue level by examining other key components of the cAMP pathway, direct assessment of contractile output and adjustment of both forskolin concentrations and exposure times using the tissue strips experimental model.

S-031

Both OTR Antagonists, Atosiban and Nolasiban, Inhibits PGE_2/$PGF_{2\alpha}$-Induced Contractions of Human Pregnant Myometrium *In Vitro*. Sung Hye Kim†,[1] Hauwa Ahmed†,[1] Lucia Riaposova†,[1] Oliver Pohl,[2] Andre Chollet,[2] Aylin Hanyaloglu,[1] Phillip R Bennett,[1] Vasso Terzidou*.[1] [1]*Imperial College, London, United Kingdom;* [2]*ObsEva SA, Geneva, Switzerland.*

INTRODUCTION: Currently the only drug licensed in Europe for inhibition of preterm contractions is the intravenous oxytocin (OT)/arginine vasopressin receptor antagonist Atosiban. Nolasiban is a more selective OT receptor antagonist (OTR-As) than Atosiban and may be administered orally. Prostaglandins (PG) also play key roles in cervical ripening and myometrial contractility and inhibition of PG synthesis or action has been used to delay preterm birth. Targeting the PG receptors or in combination with PG receptor antagonists and OTR-A may therefore be a more effective strategy for preventing or delaying preterm delivery. Previously we have shown that Nolasiban is more effective than Atosiban and that it inhibits spontaneous as well as OT-stimulated contractions. Here we examined the effects of Atosiban and Nolasiban on PGE_2/$PGF_{2\alpha}$-induced contractions of human pregnant myometrium.

METHODS: Experiments were performed using a DMT Myograph 800MS in oxygenated Kreb's solution, with ADI Powerlab software.Once regular contractions had been established for 20 min baseline measurement of contraction frequency, contraction peak, contraction duration, work per contraction and total work were made. The inhibitor compound was then added (6, 60 or 600nM), its effects upon spontaneous contractility measured in the next 10 min. The effect of the inhibitor upon agonist (PGE_2/$PGF_{2\alpha}$) was then measured by adding increasing concentrations of PGE_2/$PGF_{2\alpha}$ (1, 10, and 100nM) at 10 min intervals.

RESULTS: Atosiban antagonized the effects of $PGF_{2\alpha}$ upon the rate of contractions and contraction duration in a dose-dependent manner. Nolasiban inhibited $PGF_{2\alpha}$-induced contractions affecting rate, peak tension, and contraction duration therefore having an overall effect upon total work done. Nolasiban suppressed the effect of $PGF_{2\alpha}$ in a dose-dependent manner, reaching statistical significance at 600nM. Both Atosiban and Nolasiban reduced the effect of PGE_2 to similar extent.

CONCLUSIONS: In conclusion, our findings provide first evidence for receptor crosstalk between OTR and PG receptors which introduces a potential combinational therapeutic target for the management of term and preterm labour via the manipulation of the differential GPCR interactions/crosstalk.

S-032

HSPA1A Is Abundantly Expressed in the Myometrium During Late Pregnancy and Labour and Regulated by Uterine Distension. Mckenzie F Russell†,[1] Ewa I Miskiewicz,[2] Daniel J MacPhee*.[2] [1]*University of Saskatchewan, Saskatoon, SK, Canada;* [2]*University of Saskatchewan, Western College of Veterinary Medicine, Saskatoon, SK, Canada.*

INTRODUCTION: The myometrium goes through phases of differentiation during pregnancy to become a powerful contractile tissue at term. The initiation and progression of labour within the myometrium also appears to require an inflammatory response as it is infiltrated by immune cells and it produces pro-inflammatory mediators. Inducible Heat Shock Protein 70 (HSPA1A) is a molecular chaperone that functions in proteostasis, but it is also a marker of extracellular vesicles termed exosomes and is functionally linked to regulation of inflammatory processes. Thus, it was hypothesized that HSPA1A would be highly expressed in the myometrium just prior to and during labour.

METHODS: Rat uterine tissue samples (n=4 per timepoint) were collected from non-pregnant rats, from day (D) 6 to D23 (active labour) of pregnancy, as well as from 1-day post-partum (PP). Samples of gravid and non-gravid horns were also collected from unilaterally pregnant rats on D19 and D23 (n=3 and n=4, respectively). The spatiotemporal expression of HSPA1A in myometrium was then examined in these models using immunoblot and immunofluorescence analysis.

RESULTS: HSPA1A protein expression in pregnant rat myometrium was significantly increased on D21, D22, D23, and PP (ANOVA, Neuman-Keuls, $p<0.05$). HSPA1A was also detected in the cytoplasm of rat myometrial cells and in extracellular vesicle-like structures during late pregnancy and labour. In unilaterally pregnant rats, HSPA1A protein expression was unchanged between non-gravid and gravid horns at D19, but significantly elevated at D23 in gravid uterine horns compared to non-gravid horns (t-test, $p<0.05$).

CONCLUSIONS: HSPA1A is highly expressed in myometrium during late pregnancy and labour and expression appears to be regulated, in part, by uterine distension at labour. HSPA1A may play a role in mediating the inflammatory pathway(s) needed for immune activation in the myometrium during labour. Funded by the Natural Sciences and Engineering Research Council of Canada.

S-033

Investigation of Human Myometrial Transcriptome and Progesterone Receptor Cistrome. San-Pin Wu,[1] Matthew L Anderson,[2] Tianyuan Wang,[3] Xilong Li,[4] Francesco J DeMayo*.[1] [1]*National Institute of Environmental Health Sciences, Research Triangle Park, NC, USA;* [2]*Baylor College of Medicine, Houston, TX, USA;* [3]*National Institute of Environmental Health Sciences, Research Triangle Park, NC, USA;* [4]*Baylor College of Medicine, Houston, TX, USA.*

INTRODUCTION: Myometrium maintains the uterine integrity and provides contractile force in response to hormone regulation. During pregnancy, myometrium undergoes extensive remodeling for structural alterations of uteri prior to parturition. We hypothesize that a change of myometrial molecular profile underlays the structural remodeling and is associated with PGR signaling.

METHODS: Transcriptomes of human myometrial tissues from non-pregnant (NP, n=3) and full-term pregnant (TP, n=3) groups were examined by RNA-seq. RNA profiles of myometrium from virgin (n=5) and pregnant (18.5 days postcoitus, n=5) mice were identified by re-analyzing published dataset GSE17021. PGR occupancy patterns were examined by ChIP-seq in human and mouse myometrial tissues.

RESULTS: NP and TP samples have 2862 genes expressed in different levels, in which 1004 and 1858 genes express in higher levels in NP and TP groups, respectively. Gene ontology analyses further show enrichment of transcription regulation and histone modification genes in the NP group and that of immune responses and carbohydrate metabolism genes in the TP samples. Pathway analyses predict SRF, TGFβ, PDGF and PGR as potential regulators that mediate the change of myometrial molecular profiles in human. Interspecies conservation of these regulatory mechanisms finds support from a similar prediction that these pathways are also potential regulators for remodeling of mouse myometrium. Meanwhile, the PGR cistrome in non-pregnant myometrial samples exhibits enriched SRF-binding motif in the PGR occupying sites, suggesting a potential interaction between PGR and SRF in regulation of this hormone-responsive smooth muscle tissue. Moreover, PGR occupancy is found in the SRF locus of both human and mouse myometrial tissues, which implicates a conserved PGR-SRF regulatory axis.

CONCLUSIONS: Myometrial remodeling is associated with PGR, SRF, TGFβ and PDGF signaling. An association between SRF and PGR, master regulators for smooth muscle homeostasis and hormonal responses, is also found in the myometrial PGR cistrome.

S-034

Inhibition of GSNOR in the Management of Preterm Labor. Scott D Barnett†, Iain LO Buxton*. *University of Nevada Reno School of Medicine, Reno, NV, USA.*

INTRODUCTION: Preterm labor is defined as labor prior to 37 weeks of gestation and the costs to families and society are incalculable. Uterine smooth muscle is unique in that it relaxes in a cGMP-independent manner in the presence of nitric oxide (NO). S-nitrosation of cysteines via NO carried as S-nitroso glutathione (GSNO) acts as an important mediator in numerous disease states. S-nitrosation of cysteines via NO acts as an important mediator of disease states. Our analysis of the myometrial S-nitrosoproteome has revealed that several smooth muscle contractile proteins are differentially S-nitrosated based upon the state of labor in women. An important regulator of protein S-nitrosation is the availability

of S-nitrosoglutathione (GSNO), an endogenously expressed NO donor. The enzyme GSNO Reductase (GSNOR) regulates GSNO availability in smooth muscle levels. We performed experiments to test the hypotheses that GSNOR activity is increased myometrium from women in preterm labor and that inhibition of GSNOR attenuates myometrial contraction.
METHODS: GSNOR expression was measured by Western blot and WES analysis normalized to GAPDH expression. GSNOR activity was measured by the decrease in absorbance at 340nm via conversion of NADH to NAD+ by GSNOR in the presence of GSNO. Eight nM N6022, a potent and specific inhibitor of GSNOR, was used to verify GSNOR specific activity. Freshly isolated human myometrial tissue from women in labor at term and preterm was dissected, and muscle strips were mounted in tissue baths and tested for the ability to contract. The GSNOR-specific inhibitor N6022 was added to contracting tissue and changes in the contraction profile were recorded.
RESULTS: GSNOR expression is increased in myometrial tissue from women in spontaneous preterm labor compared to term laboring controls ($p<0.05$, n=5). GSNOR enzymatic activity was also higher in protein lysates from myometrial tissue from patients undergoing spontaneous preterm labor than those in labor at term. A potent and selective inhibitor of GSNOR (N6022) decreases the peak force of contraction in guinea pig myometrium.
CONCLUSIONS: GSNOR is more highly expressed in preterm laboring myometrium. This information, when coupled with the facts that laboring myometrium exhibits a blunted response to nitric oxide and that the GSNOR inhibitor N6022 reduces peak contraction, suggests an increase in GSNOR may contribute to a preterm contractile phenotype through the enzymatic degradation of endogenous GSNO.

S-035

Predictors of Neonatal Sepsis and Death Among Deliveries at <32 Weeks of Gestation. Anna Palatnik†,[1] Lilly Y Liu,[2] Andy Lee,[2] William A Grobman,[2] Lynn M Yee*.[2] *[1]Medical College of Wisconsin, Milwaukee, WI, USA; [2]Northwestern University, Feinberg School of Medicine, Chicago, IL, USA.*
INTRODUCTION: The objective of this study was to develop a predictive model for neonatal sepsis and death among infants born at <32 weeks.
METHODS: Case-control study of all deliveries <32 weeks between 2011- 2015 in a single tertiary center. Cases were defined as neonates diagnosed with sepsis based on a blood or cerebrospinal fluid culture or neonates who expired prior to discharge. Controls consisted of neonates without these outcomes. Variables previously identified to be associated with neonatal sepsis or death were abstracted from the medical record. Bivariable analyses and multivariable logistic regression were used to determine independent risk factors for neonatal sepsis or death. An ROC curve was created and AUC calculated to estimate the predictive capacity of these associations.
RESULTS: Of 779 eligible neonates, neonatal sepsis or death occurred in 73 (9.4%). In bivariable analyses, mothers whose neonates were diagnosed with sepsis or death were more likely to be obese, have an intrapartum fever and have meconium, and were less likely to have received betamethasone or antepartum/intrapartum antibiotics. Gestational age at delivery and birthweight were significantly lower among neonates diagnosed with neonatal sepsis or death. In multivariable analysis, factors remaining independently associated with neonatal sepsis or death were gestational age at the time of delivery, intrapartum fever, presence of meconium and birthweight.

	aOR	95% CI	P-value
Gestational age at delivery	0.75	0.63 – 0.90	0.002
Intrapartum fever >38.1	2.58	1.06 – 6.30	0.036
Meconium	2.80	1.01 – 7.75	0.047
Birthweight	0.29	0.09 – 0.99	0.048

The AUC for this regression was 0.81 (95% CI 0.77 – 0.83).
**Figure(s) will be available online.*
CONCLUSIONS: Lower gestational age at the time of delivery, intrapartum fever, meconium and lower birthweight are independently associated with neonatal sepsis or death among deliveries occurring at <32 weeks of gestation; these factors can be used to create a model with fair predictive capability.

S-036

Implementation of Delayed Cord Clamping in Premature Neonates. Phoebe L Bacon*,[1] Clark T Johnson,[2] Karen Frank,[3] Johana Diaz,[4] Janine E Bullard,[5] Angie C Jelin.[2] *[1]Johns Hopkins University, Baltimore, MD, USA; [2]Johns Hopkins School of Medicine, Baltimore, MD, USA; [3]Johns Hopkins School of Nursing, Baltimore, MD, USA; [4]Johns Hopkins School of Medicine, Baltimore, MD, USA; [5]Johns Hopkins School of Medicine, Baltimore, MD, USA.*
INTRODUCTION: Delayed cord clamping (DCC) is associated with increased hematocrit (Hct) and decreased risk of intraventricular hemorrhage in premature neonates. After implementation of institutional DCC guidelines, we evaluated neonatal Hct among those who did or did not receive DCC based on inclusion/exclusion criteria.
METHODS: This is a retrospective cohort study of all preterm singleton births delivered between 24 and 37 weeks gestation at a tertiary care center between July 2014 and December 2015. Our primary outcome was initial Hct, drawn within 48 hours of delivery. We compared neonates who did and did not receive DCC, as well as those who should or should not have received DCC based on protocol.
RESULTS: 481 cases were included. 306 (63.6%) did not receive DCC, 131 of whom had no documented reason for exclusion. 15 received DCC despite meeting exclusion criteria.
**Figure(s) will be available online.*
Mean Hct for neonates who received DCC was 49.9 (95% CI 48.8-50.9), significantly higher than those who did not (47.5, 95% CI 46.6-48.3) ($p<0.01$). Hct (49.9, 95% CI 48.8-51.0) among neonates who were eligible for and received DCC was not significantly higher than Hct (48.4, 95% CI 47.3-49.5) in those with no documented reason for exclusion ($p=.07$). When DCC was not indicated, those who received DCC (n=15) had an increased but not significantly different Hct (48.9, 44.7-53.1) than those who did not (46.4, 45.2-47.6).
CONCLUSIONS: This supports other studies that demonstrate DCC is associated with higher Hct in the postpartum period. Following implementation of a DCC protocol, not all preterm neonates will receive DCC. Neonates who received DCC despite relative contraindications had higher Hct without polycythemia. Further investigation is needed to evaluate the risk of DCC to certain cohorts of premature neonates and to refine exclusion criteria.

S-037

Acute Fatty Liver of Pregnancy and Risk of Preterm Birth. Megan E Foeller†,[1] Jonathon Mayo,[2] Amanda Yeaton-Massey,[1] Anna Girsen,[1] Samantha Do,[1] Amen Ness,[1] Gary Shaw,[2] Yasser El-Sayed,[1] Maurice Druzin*.[1] *[1]Stanford University Medical Center, Stanford, CA, USA; [2]Stanford University Medical Center, Stanford, CA, USA.*
INTRODUCTION: Acute fatty liver of pregnancy (AFLP) is a rare and potentially fatal obstetric complication most often arising in the third trimester or the early postpartum period. This severe obstetric syndrome is also associated with significant neonatal morbidity, including an increased risk of preterm birth (PTB). The objective of this study was to better characterize the population-based risk of PTB in women diagnosed with AFLP.
METHODS: A case-referent analysis was performed on 2007-2011 California singleton birth certificates which were linked with maternal hospital discharge information. Cases were defined as pregnancies with simultaneous diagnoses of (1) AFLP (ICD-9-CM codes 571.8 or 646.7) and disseminated intravascular coagulopathy (286.6) or (2) AFLP and ICU admission (birth certificate complication of labor/delivery code 43). Analyses were performed for PTB 24-27 weeks, 28-31 weeks, and 32-36 weeks. Logistic regression was used to calculate odds of PTB.
RESULTS: In this cohort of 2,499,824 births, 68 fulfilled our case definition of AFLP (2.72 per 100,000). The majority of births to mothers with AFLP were delivered via cesarean section (N=61, 90%). Maternal mortality was also high (N=4, 6%) among AFLP cases. Of all births

complicated by AFLP, 39 (57%) were delivered preterm (< 37 weeks), with 26 occurring between 32-36 weeks, 9 at 28-31 weeks, 3 at 24-27 weeks, and 1 at 20-23 weeks. AFLP was associated with up to a 49-fold increase in PTB.

**Figure(s) will be available online.*

CONCLUSIONS: In addition to a high maternal mortality rate, we also demonstrate a significant risk of prematurity for neonates with over half delivered preterm. Additionally, the risk of extreme prematurity with delivery at < 32 weeks was significantly higher in pregnancies complicated by AFLP.

S-038

Improving Safety on Labor and Delivery Through Team Huddles and Teamwork Training. Elizabeth A Blumenthal†,[1] Myung Shin Sim,[3] Leslie Carranza*.[2] [1]*University of California, Los Angeles, Los Angeles, CA, USA;* [2]*Olive View- UCLA Medical Center, Sylmar, CA, USA;* [3]*University of California, Los Angeles, Los Angeles, CA, USA.*

INTRODUCTION: Leading health care organizations recommend that Labor and Delivery (L&D) Units establish patient safety and teamwork training programs, however how these programs should be constructed and measured is less clear. This study aimed to assess baseline and follow up safety culture data as well as outcome metrics after the initiation of a patient safety program.

METHODS: The Safety Attitudes Questionnaire (SAQ) has been widely validated in healthcare to assess safety culture. All professionals who work on the Unit completed the survey at the start of the intervention and 15 months (mths) after. Changes in SAQ categories were assessed with the student t test. Clinical outcome measures were reviewed 12 mths before initiation of the program and 15 mths after using the chi-squared test. Twice-daily interdisciplinary safety huddles were initiated to discuss patients in active labor, high acuity antepartum, and postpartum patients. Four nursing centered team trainings reviewed TeamSTEPPS principles, medication safety, and simulation of emergency scenarios. This study was approved as IRB exempt.

RESULTS: 144 surveys were completed, 68 before and 76 after the intervention. Safety (p=0.02), error management (p=0.04), and safety practices (p=0.03) demonstrated the most improvement overall. OB faculty reported improvement in interactions with nursing (p=0.02) and safety practices (p=0.02). In response to the question: "I would feel safe being treated here as a patient" scores overall improved (p=0.04). L&D RN and OB faculty job satisfaction (p=0.06 and 0.08), teamwork culture (p=0.06), and overall interactions with nursing (p=0.06) also improved. No L&D outcome measures collected over the 26 mth period demonstrated significant change.

CONCLUSIONS: This study demonstrates a sample patient safety program that was able to improve overall safety culture particularly in areas of error management and safety practices, but even extending to staff perceptions of job satisfaction and working conditions. Given that we are a low volume center and adverse events are rare, we did not expect to see significant differences in adverse outcome measures, however this provides an example of a program that could used by other Units and a metric that may be relevant beyond clinical outcomes.

S-039

Low and Slow: Duration of Antenatal Steroid Exposure Determines Functional Maturation of the Preterm Ovine Lung. Matthew Kemp*,[1] Haruo Usuda†,[1] Peter Eddershaw,[3] Alan Jobe.[4] [1]*UWA, Perth, WA, Australia;* [2]*GSK, Stevenage, Herts, United Kingdom;* [3]*CCHMC, Cincinnati, OH, USA.*

INTRODUCTION: Antenatal steroids (ANS) to improve outcomes for preterm infants remain largely un-optimized. Concerns remain regarding ANS-induced changes to fetal development and adverse outcomes in low income countries. We aimed to study the effects of altering the magnitude and duration of fetal steroid exposure on lung maturation in a sheep model of pregnancy.

METHODS: Ewes with single fetuses (120d gestation) received one 12h betamethasone phosphate (BP) infusion to give fetal plasma betamethasone levels of either: i) 10ng/mL; ii) 2ng/mL (n=9/group); or iii) two intramuscular injections of 0.25mg/kg Celestone Chronodose (CC) separated by 24h (n=10/group). Saline-treated animals served as controls (n=19). At 122d gestation, fetuses were delivered, ventilated to assess gas exchange, and euthanised. Lung tissue was collected for transcriptome analysis. Serial samples from additional, identically-dosed catheterised fetuses (n=4/group) were collected to confirm betamethasone levels by LCMS. Group differences were tested with ANOVA.

RESULTS: LCMS analysis confirmed BP infusions achieved fetal plasma targets of approximately 10ng/mL and 2ng/mL betamethasone for 12h. Fetal betamethasone concentrations in the 2ng/mL BP and 0.25mg/kg CC groups were similar, and 2-3 times lower than the 10ng/mL BP group. The duration of fetal betamethasone exposure in the 0.25mg/kg CC group was approximately twice that of the 10ng/mL and 2ng/mL BP infusion groups. After 30 minutes of ventilation, arterial cord blood pH (7.1±0.2; p=0.04), paCO2 (75.0±36.0mmHg; p<0.01), tidal volume (7.1±1.9mL/kg; p<0.01) and compliance (0.4±0.2mL/cmH_2O; p<0.01) in the 10ng/mL BP group and paCO2 alone (89.0±23.7mmHg; p=0.02) in the 2ng/mL BP group were improved vs. control. Arterial cord blood pH (7.2±0.1), paO2 (237.2±125.4mmHg), paCO2 (62.4±11.1mmHg), tidal volume (8.0±1.1mL/kg), compliance (0.6±0.2mL/cmH_2O), peak inspiratory pressure (32.3±3.6cmH_2O) and lung gas volume (16.6±2.4mL/kg) in the 0.25mg/kg CC group were all significantly improved (p<0.01) vs. control.

CONCLUSIONS: In preterm lambs, extended low-magnitude ANS exposure more effectively induced lung maturation than shorter, high dose regimens. These data suggest that lung maturation can be induced at levels of fetal steroid exposure substantially lower than those achieved with current clinical dosing.

S-040

Attitudes of Pregnant Women Towards Intrapartum Acupuncture Provision in a UK Maternity Unit. Melissa Rowe†,[1] David J Carr†*.[1,2] [1]*UCLH, London, United Kingdom;* [2]*NYU School of Medicine, New York, NY, USA.*

INTRODUCTION: Acupuncture is increasingly accepted as a method of pain relief and is recommended by the UK National Institute of Health and Care Excellence (NICE) for management of tension-type headache, migraine and low back pain. A recent individual patient data meta-analysis demonstrated efficacy over sham for chronic pain (Vickers et al. *Arch Intern Med* 2013; 172(19):1444-1453). Acupuncture for pain relief in labour is supported by a Cochrane review demonstrating a large effect size (Cohen's d=1.0) relative to untreated controls and significant reduction in the use of pharmacological analgesia vs. sham (Smith et al. *Cochrane Database Syst Rev* 2011; 6(7):CD009232). Intrapartum acupuncture (provided by trained midwives) is widely available in countries such as Sweden (uptake ~25%) but not currently the UK (Carr & Lythgoe. *Pract Midwife* 2014; 17(5):10-14). We aimed to measure potential patient interest to support its introduction into routine care in a London maternity unit.

METHODS: A paper-based survey was distributed to pregnant women attending low/high-risk antenatal clinics, fetal medicine and day assessment units. Patients were asked about their previous experience of acupuncture (positive/negative) and current plans for intrapartum pain relief.

RESULTS: Responses were received from 405 women (243 nullips, 162 multips) aged 33±0.3 yrs at a median gestation of 28 weeks [IQR 18–34]. Most (75.3%) reported no medical problems. Previous acupuncture experience was disclosed by 144 patients (35.6%), of which 28 (19.4%) reported ≥1 minor side-effects including pain (n=14, 9.7%) drowsiness (n=13, 9.0%) and bleeding/bruising (n=9, 6.3%). In total, 173 women (42.7%) said they would consider acupuncture during labour. Interest was greater among those who had previously received acupuncture compared with those who had not (54.9% vs. 36.0%, p<0.001) and tended to be greater in nullips vs. multips (46.5% vs. 37.0%, p=0.065). Unsurprisingly, women planning to have epidurals (n=134) were less likely to accept acupuncture than epidural-averse/indifferent women (38.1% vs. 45.0%, p=0.045). Among those reporting indifference to intrapartum acupuncture (n=102), 37.5% would consider receiving it prenatally.

CONCLUSIONS: Disclosed levels of interest in intrapartum acupuncture were higher than anticipated and influenced by previous experience of labour/acupuncture and plans for regional analgesia. Prenatal acupuncture provision may increase uptake during labour.

S-041

Maternal and Neonatal Outcomes in Triplet Gestations by Trial of Labor Versus Planned Cesarean Delivery. Danielle A Peress†,[1] Alan M Peaceman,[2] Lynn M Yee*.[2] [1]*University of Pennsylvania Perelman School of Medicine, Philadelphia, PA, USA;* [2]*Northwestern University Feinberg School of Medicine, Chicago, IL, USA.*

INTRODUCTION: Recent data suggest <20% of women with triplet gestations who undergo trial of labor (TOL) achieve vaginal delivery (VD), and associate TOL with maternal and neonatal morbidity. Yet, data with detailed records to confirm intent for labor are lacking. We aimed to determine likelihood of VD among women with triplet gestations, and to examine outcomes of TOL versus planned cesarean delivery (CD).

METHODS: Retrospective cohort study of all women who delivered a viable triplet gestation at an academic center (2005-16). Women who underwent TOL included all who attempted VD (spontaneous and induced labor); this group was compared to women who underwent CD (spontaneous labor and pre-labor). The primary outcome was rate of VD. Secondary outcomes were maternal and neonatal complications and factors associated with achieving VD. Bivariable analyses and multivariable regression were used.

RESULTS: Of 83 eligible women, 21 (25.3%) underwent TOL. A majority (57.1%) achieved VD. Four (19%) had both VD and CD. We identified no differences in maternal, neonatal or labor characteristics between those who had VD and those who did not. Gestational age at delivery did not differ (TOL: 34.6, IQR 30.3-35.5 v. planned CD: 34.0, IQR 31.4-35.2 weeks). Women who underwent TOL were more likely to be multiparous (52.4% v. 25.8%; aOR 4.3, 95% CI 2.0-9.1) or to have spontaneous labor (85.7% v. 53.2%; aOR 8.3, 95% CI 3.2-21.6). There were no differences in maternal outcomes or neonatal outcomes.

Table 1. Neonatal outcomes

	Trial of Labor n= 63	Planned cesarean delivery n= 186	P-value
Arterial cord blood gas <7	2 (3.2)	3 (1.6)	0.37
Apgar <7	3 (4.8)	4 (2.2)	0.25
Respiratory distress syndrome	17 (27)	45 (24.2)	0.39
Necrotizing enterocolitis	4 (6.4)	10 (5.4)	0.81
Intraventricular hemorrhage	1 (1.6)	0	0.18
Retinopathy of prematurity	4 (6.4)	11 (6)	0.57
NICU admission	45 (71.4)	137 (76.1)	0.46
Data displayed as N(%) or mean(SD)			

CONCLUSIONS: The rate of VD among women with triplet gestations is higher in this institution than in reported literature, and TOL was not associated with increased morbidity.

S-042

Umbilical Cord Arterial pH and Birth Order in Twins: A Comparison Between Monochorionic and Dichorionic Pregnancies. Amelia S McLennan†, Audrey A Merriam†, Clifton O Brock†, Russell S Miller, Cynthia Gyamfi-Bannerman*. *Columbia University Medical Center, New York, NY, USA.*

INTRODUCTION: It is unknown whether the shared placental physiology in monochorionic (MC) twin gestations has an effect on the risk of acidemia in either twin at birth. The purpose of this study was to assess whether MC twins are at greater risk for low cord arterial blood pH when compared to dichorionic (DC) twins.

METHODS: Secondary analysis of a randomized controlled trial of 17-alpha hydroxyprogesterone caproate for prevention of twin preterm delivery. Neonates were included if they resulted from live-born twin deliveries at 24 weeks gestation or greater, with ultrasound-assessed chorionicity and arterial umbilical cord blood pH results available. Arterial pH was both assessed as a continuous and a dichotomous variable (low: <7.1, normal: ≥7.1). The primary analysis was to evaluate the difference in low pH between MC and DC twins, using a log-linear regression model adjusting for factors related to low pH. We also evaluated the differences in median pH by chorionicity, as well as the inter-twin difference in pH by birth order and chorionicity.

RESULTS: Of included 525 neonates, 101 (19%) were MC twin pregnancies and 424 (81%) were DC. Women delivering DC twins were more likely to be overweight/obese, were delivered at a later gestational age, and were more likely to be born by cesarean than MC twins. After adjusting for maternal and delivery characteristics, MC twins were 60% less likely to have abnormal pH (Table), but the findings did not reach statistical significance (aRR 0.40, 95% CI 0.07-2.22). In a linear regression with pH as a continuous variable, birth order (twin B) and gestational age at delivery, but not chorionicity, were associated with a significant decrease in median pH. Of 212 twin-pairs with matched delivery data, twins A and B had similar pH in MC twins, but twin A had a significantly higher pH in the DC twins (+0.011 +/-0.07, p=0.03).

CONCLUSIONS: There are no clinically significant differences in arterial cord pH by chorionicity or by birth order.

**Figure(s) will be available online.*

S-043

Assisted Reproductive Technology and Preterm Delivery in Twin Gestations. Clifton O Brock†, Cynthia Gyamfi-Bannerman*. *Columbia University Medical Center, New York, NY, USA.*

INTRODUCTION: Assisted reproductive technology (ART) is associated with preterm delivery in singleton pregnancies, but studies in twin gestations are conflicting. We seek to determine whether ART is associated with spontaneous (SPTD) or indicated preterm delivery (IPTD) in twins.

METHODS: This is a secondary analysis of a multicenter, randomized controlled trial designed to assess preterm birth in twins. Women were excluded from the parent study if they had monoamniotic placentation, fetal anomaly, fetal death, twin to twin transfusion syndrome, discordance > 3 weeks, uterine anomaly, need for anticoagulation, or major chronic medical disease. We further excluded women less < 18, or > 45 years of age. The primary outcome was SPTD before 35 weeks by exposure to ART. Secondary outcomes included SPTD before 32 weeks, IPTD before 32 and 35 weeks, and a neonatal outcome composite including death, respiratory distress, intraventricular hemorrhage, necrotizing enterocolitis, periventricular leukomalacia, bronchopulmonary dysplasia, retinopathy of prematurity, sepsis, and pneumonia. We fit logistic regression models to compare outcomes between ART patients and those that conceived spontaneously. Models were adjusted for maternal age, race, BMI, parity, chorionicity, drug use, chronic hypertension, and history of preterm birth.

RESULTS: Patients that conceived spontaneously had greater rates of preterm delivery. However, adjusting for confounders, ART is associated greater risk of SPTD before 35 weeks (aOR 2.10 95% CI 1.15-3.81). ART is associated with a trend towards increased risk of all preterm delivery before 35 weeks, but the result is not statistically significant (aOR 1.44 95% CI 0.85-2.46). ART is not associated with SPTD or IPTD before 32 weeks, IPTD before 35 weeks, or the neonatal morbidity outcome composite.

Outcome	**OR**	**95% CI**	**aOR**	**95% CI**
Delivery < 35 wk				
Spontaneous	0.7	0.5-1.1	2.1	1.2-3.8
Indicated	1.4	0.8-2.4	0.6	0.3-1.4
All	0.9	0.6-1.3	1.4	0.9-2.5
Delivery < 32 wk				
Spontaneous	0.4	0.2-0.7	1.2	0.5-3.1
Indicated	0.9	0.4-2.1	0.5	0.2-1.6
All	0.5	0.3-0.8	0.8	0.4-1.7
Neonatal composite	0.5	0.3-0.8	0.9	0.5-1.6

CONCLUSIONS: ART doubled the risk of late SPTD in twin gestations. ART does not appear to be associated with early SPTD, IPTD, or severe neonatal morbidity associated with SPTD. This information may be useful in counseling and reassuring ART patients about pregnancy outcomes.

S-044

Delivery Outcomes and Prostaglandin Use for Induction of Labor in Growth Restricted Fetuses Based on Umbilical Artery Velocimetry.
Drew D Benac†, Rebecca Pollack*, Matthew Finneran, William Anderson.
Carolinas Medical Center, Charlotte, NC, USA.
INTRODUCTION: Retrospective study designed to evaluate fetal outcomes and cesarean section frequency at the time of labor induction by prostaglandin agents compared to other induction methods in a cohort of pregnancies complicated by fetal growth restriction with and without abnormal umbilical artery Doppler studies.
METHODS: This data represents secondary analysis of a larger retrospective review of neonatal and delivery outcome for 297 pregnant women with intrauterine growth restriction (IUGR), divided into two groups based on normal or abnormal umbilical artery (UA) Doppler velocimetry (absent or reversed flow). Primary outcome was cesarean section (CS) frequency for patients undergoing induction of labor with prostaglandin (PG).
RESULTS: Two hundred and thirteen (72%) patients from the original study had normal umbilical artery Doppler studies prior to delivery, and 130 (61%) were induced. 63 of these patients (48%), were induced with prostaglandins while the remaining 52% were induced by other methods. The remaining 84 patients had abnormal UA Doppler flow and of those, 20 (24%) were induced. Nine (45%) were induced using prostaglandins, and the remaining 55% (n=11) were not.
Of all patients who were induced, CS rate was statistically different between the normal and abnormal Doppler groups, 23.9% for normal UA vs. 65% for abnormal UA [p=0.0002].
Of patients with normal UA Doppler studies who were induced with PG, 25.4% delivered by CS compared to 22.4% CS rate when other induction methods were used [p = 0.69]. Among those with abnormal Doppler testing who underwent PG induction, 77.8% delivered by CS compared to a 54.6% CS rate in the other induction methods group [p = 0.37].
CONCLUSIONS: Among patients who underwent induction by all methods, CS rate was higher in IUGR pregnancies complicated by abnormal vs. normal UA velocimetry. PG induction was not associated with increased CS rate in IUGR pregnancies when UA velocimetry was normal. PG induction did show a trend towards higher CS rate by a 23% difference when abnormal UA Doppler studies were present. This trend failed to achieve statistical significance due to sample size. Further study is needed to evaluate this clinical question. PG should be judiciously used in the setting of growth restriction with abnormal UA flow but appears to be a safe and viable induction agent for pregnancies complicated by fetal growth restriction and reassuring UA Doppler flow.

S-045

A Human Clinically-Relevant Dose of Betamethasone Compared with Dexamethasone Has More Potent Direct Adverse Side-Effects on the Structure and Function of the Fetal Heart.
KL Skeffington†,[1] FG Conlon†,[1] Y Niu†,[1] NEWD Teulings†,[1] SG Ford,[1] KJ Botting†,[1] JB Derks,[2] DA Giussani*.[1] *[1]Cambridge University, Cambridge, Cambridgeshire, United Kingdom; [2]Utrecht Medical Center, The Netherlands.*
INTRODUCTION: Antenatal glucocorticoid therapy (AGT) to accelerate fetal lung maturation is used worldwide in pregnancies threatened with preterm labour. Despite being stereoisomers, human studies (Ballard & Ballard. *Am J Obstet Gynecol* **173**:254, 1995) suggest more potent maturational effects on the fetus of betamethasone (Beta) over dexamethasone (Dex). Since human studies also suggest that AGT promotes adverse effects on the cardiovascular system (Kelly et al. *Pediatrics* **129**:e1282, 2012), we wondered whether Beta and Dex would have differential adverse effects on the developing heart. To isolate the direct effects of both stereoisomers on fetal cardiac function at its purest level, without confounding effects of treatment on the maternal or placental physiology, this study determined the effects of the same human clinically-relevant dose of Dex or Beta on fetal cardiac structure and function in the chick embryo.
METHODS: On day 14 of incubation (0.7 of gestation equivalent, term = 21 days), embryonated chicken eggs were treated (by dropping the drug onto the chorioallantoic membrane) with Dex or Beta at a dose (both 0.1mg/kg) which is lower of equivalent to the concentration the human fetus receives after the glucocorticoid has crossed the placenta. Control eggs were administered with an equivalent volume of vehicle (water). At day 19, following biometry, cardiac function was determined via a Langendorff preparation. A separate cohort of animals underwent perfusion fixation (at 2.66kPa) and their hearts used for stereology.
RESULTS: The same dose of Beta compared to Dex led to more pronounced asymmetric fetal growth restriction, greater systolic and diastolic dysfunction and more significant dilated cardiomyopathy in the chick embryo by the end of incubation (Fig.1).
CONCLUSIONS: Here, we show that the same human clinically-relevant dose of Beta compared with Dexa has more potent direct adverse side-effects on the structure and function of the fetal heart.
Supported by *TheBritish Heart Foundation* and *The Lister Institute*
**Figure(s) will be available online.*

S-046

Obesity and Periodontal Diseases In Pregnancy: miRNome in Saliva.
C Mandò,[1] S Abati,[2] GM Anelli,[1] L Dioni,[3] C Novielli,[1] C Favero,[3] L Cantone,[3] M Cardellicchio,[1] I Cetin,[1] V Bollati.[3] *[1]Univ Milan, Milan, MI, Italy; [2]Univ Vita Salute San Raffaele, Milan, MI, Italy; [3]Univ Milan, Milan, MI, Italy.*
INTRODUCTION: Both obesity and periodontal diseases (PD: gingivitis, periodontitis) represent a source of low-grade systemic inflammation with higher gestational risks. We showed increased inflammation and oxidant levels in saliva (S) of obese (OB) vs normalweight (NW) pregnant women, heightened by PD. Here we quantified 758 microRNAs (miRNA) in S of these women.
METHODS: 29 singleton pregnancies (14 NW, BMI 18-24.9; 15 OB, BMI≥30) with no obstetric complications were studied at 3rd trimester. Periodontal status was assessed by oral clinical examination. Unstimulated saliva was collected and 758 miRNA from microvescicle fractions were quantified by QuantStudio OpenArray.
Fold change (FC) of each miRNA was calculated as the ratio between the relative quantity in OBvsNW or in PD vs oral-healthy (OH) women. Raw p-values, from univariate and multivariate linear regression models, were adjusted for multiple testing by controlling the false discovery rate (FDR). Informatics investigation was performed by FireFly (AbCam) and TargetScan Database.
RESULTS: 11/15 OB and 8/14 NW had PD, confirming higher PD rate in OB.
Prepregnancy BMI was inversely correlated to placental efficiency (PlE, fetal/placental weight) that among PD was significantly decreased in OBvsNW (p 0.047).
334/754 miRNA were expressed in at least 1 subject. 103 were differentially expressed (FC≤0.5 or ≥2) in OBvsNW and 91 in PDvsOH. miR483-5p was significantly lower in PDvsOH in univariate analysis and adjusted for BMI (FDR p 0.028 and 0.043). Only in NW miR330 was significantly lower in PDvsOH (FDR p 0.114), while in OB it maintained low levels both in PD and OH.
CONCLUSIONS: We found different S miRNA expression profiles in both OB and PD that might reflect molecular systemic changes in these previously described high-risk pregnancies.
Moreover, miR483-5p was significantly decreased in PDvsOH. This miRNA regulates genes involved in fat metabolism and cell growth/differentiation i.e. *IGF2* and *TGFβ1*.
miR330, regulating genes involved in placentation and fetal growth i.e. *AKT*, also had different expression in PDvsOH, but only in NW. This suggests a role of the obese environment in its regulation with a synergistic action of OB and PD to miR330 downregulation, possibly leading to higher risk pregnancies, as suggested by lower PlE in women presenting both PD and OB.

S-047

Placental Lipid Metabolism in Obese Women with Fetal Macrosomia. Haijun Gao, Jia Chen, Chandra Yallampalli. *Baylor College of Medicine/ Texas Childrens Hospital, Houston, TX, USA.*

INTRODUCTION: Maternal obesity is one of the major contributors to fetal macrosomia (FM, >4000gram at birth), which predisposes the development of cardiovascular and metabolic disease later in life. Emerging evidence indicates that FM is associated with an altered lipid metabolism in utero during pregnancy. To date, few studies have investigated in placental lipid metabolism in obese women with fetal macrosomia. In this study we hypothesized that placental lipid transport and metabolism are altered in obese women with fetal macrosomia, enhancing lipid supply to promote fetal overgrowth.

METHODS: Placental tissues of obese subjects with or without FM (CT) but not complicated by other pregnancy disorders from our PeriBank repository (n= 10 placentas each group, associated with 5 female and 5 male fetuses). The prior to pregnancy BMI and gestational age were matched in these two groups. Total RNAs were extracted from 100 mg placental tissue and converted to cDNA. mRNA of genes related to fatty acid transport/uptake (*LIPG*, *LIPE*, *LPL*, *ATGL*, *ANGPTL3*, *4* and *8*, *CD36*, *GOT2*, *FABP4*), fatty acid oxidation (*CPT1B*, *PPKAA1*, *PPARA*), fatty acid accumulation/esterification (*ACC*, *FASN*, *MCAD*, *SCD*, *DGAT1*, *PLIN1*, *PLIN2*, *PPARG*, *SREBF1*) was measured by q-PCR and normalized to that of TBP. The effects of FM, fetal gender and their interaction on gene expressions were analyzed by two-way ANOVA.

RESULTS: Main findings include: 1) Expressions of most genes were not affected by FM and gender; 2) mRNA levels of *CD36* were increased by 3.19-fold ($P < 0.05$) in FM group compared to CT group, and this increase occurred in placentas with male fetuses; 3) mRNA levels of *DGAT1* were increased by 1.49-fold ($P < 0.05$) in FM group compared to the group without FM, regardless of the gender of fetuses; 4) mRNA levels of *PLIN1* were 2.22-fold higher ($P < 0.05$) in females compared to males; mRNA levels of *PLIN1* were 8.01-fold higher ($P < 0.05$) in FM group with female fetuses than CT group and in contrast, this value was 5.42-fold lower ($P < 0.05$) in FM group with male fetuses than CT group.

CONCLUSIONS: Although majority of genes were not altered, expression of *CD36*, *DGAT1* and *PLIN1* were elevated in FM group compared to controls in a gender dependent manner, and thus, altered placental fatty acid transport and accumulation associated with these genes may be responsible for FM in obese women.

S-048

Abnormal MCA Dopplers in Diabetic Patients and the Association with Stillbirth. Allison Shannon†, Sarah Crimmins, Jerome Kopelman, Chris Harman, Ozhan Turan*. *University of Maryland Baltimore, Baltimore, MD, USA.*

INTRODUCTION: The utility of brain sparing in fetal monitoring is controversial. The benefit of a Doppler assessment in management of diabetic pregnancies is questionable; therefore, weekly non-stress tests and biophysical profiles are the gold standard for diabetic antepartum surveillance. We tested the hypothesis that brain sparing is associated with stillbirth and adverse intrapartum events in the diabetic population.

METHODS: This is a retrospective cohort analysis of diabetic and non-diabetic patients. Patients who delivered after 34 weeks were identified from our perinatal ultrasound database between 2008 and 2015. Patients with Doppler information within 14 days of delivery and known neonatal outcomes were used for the analysis. Pregnancies complicated by fetal growth restriction were excluded in the analysis. Neonatal outcomes were stratified as stillbirth and composite adverse intrapartum events (arterial pH<7.1, 5 minute APGAR score less than 7 and cesarean section for fetal indication).The middle cerebral artery pulsatility index (MCA-PI) was converted to its z-score to exclude the effect of gestational age. Brain sparing was defined as a two standard deviation decline in the MCA-PI. The risk of stillbirth was investigated in diabetic and non-diabetic populations. Descriptive statistics and odds ratios were calculated for outcome variables.

RESULTS: 643 women met the inclusion criteria. Of those, 473 (73.5%) did not have diabetes (controls) and 170 patients had diabetes (26.5%). In the control group, the risk of stillbirth was 1/448 with normal MCA-PI z-score and 2/25 with brain sparing ((p=0.008, OR 38.8 [CI 3.40, 444.5]). In diabetics, brain sparing did not predict stillbirth, (2/157 v. 1/13 with normal MCA-PI z-score and brain sparing respectively, (p=0.213, OR 6.4 [0.55, 76.5])). The presence of brain sparing did not stratify risk of composite intrapartum events in either the control group or in diabetics (OR: 1.03 0.33-3.2 and 1.1 0.3- 3.7 respectively).

CONCLUSIONS: When brain sparing is observed, the greatest risk for stillbirth occurs in non-diabetic women with a normal weight fetus. The plausibility of this finding is that current surveillance protocols for diabetics are much more aggressive than in the non-diabetic population. Therefore evidence of brain sparing may be used as a valuable tool for increased surveillance in an otherwise low risk population.

S-049

Adrenomedullin Blockade Restores Expressions of Lipid Homeostasis Enzymes in Adipose Tissue from Gestational Diabetic Women. Yuanlin Dong*, Ancizar Betancourt, Michael Belfort, Chandra Yallampalli. *Baylor College of Medicine/Texas Childrens Hospital, Houston, TX, USA.*

INTRODUCTION: Impaired maternal lipid metabolism in gestational diabetes mellitus (GDM) has adverse effects on fetal adiposity and growth, but its underlying mechanism is unclear. Phosphoenolpyruvate carboxykinase C (PEPCK-C) is the key enzyme in glucose and lipid metabolism, and peroxisome proliferator activated receptor γ (PPAR-γ) is required for PEPCK-C expression. We have previously shown that adrenomedullin (ADM) and its receptor levels were higher in GDM adipose tissue. In this study, we assessed whether the mRNA for PEPCK-C and PPAR-γ were altered in adipose tissue from GDM women, and if blockade of ADM restores PPAR-γ and PEPCK-C expressions.

METHODS: Omental fat biopsies were obtained from pregnant women during caesarian sections at term with normal glucose tolerance (NGT) or GDM (n=6 in each group). Tissues were incubated in DMEM in the presence of ADM or its antagonist, ADM22-52. The mRNA for PPAR-γ andPEPCK-C were measured by quantitative q-PCR and expressed relative to GAPDH.

RESULTS: mRNA for both PPAR-γ andPEPCK-C were abundant in adipose tissue from NGT pregnancies and the levels were lower in GDM women (PPAR-γ: 4.85 +/- 0.26 in NGT vs. 2.95 +/- 0.37 in GDM, p<0.05;PEPCK-C: 3.42 +/- 0.48 in NGT vs. 2.25 +/- 0.10 in GDM, p<0.05). Treatment of adipose tissue from NGT with ADM (100 nM for 24 h) decreased mRNA for both PPAR- γ (2.76 +/- 0.29 in CTL vs. 1.67 +/- 0.17 in ADM treated, p<0.05) and PEPCK-C (2.45 +/- 0.15 in CTL vs. 1.81 +/- 0.09 in ADM treated, p<0.05). In contrast, incubation of adipose tissue from GDM (n=3) with ADM**22-52** (100 nM for 24 h) elevated mRNA for both PPAR-γ (1.96 +/- 0.07 in CTL vs. 9.41 +/- 0.50 in ADM22-52 treated, p<0.01) and PEPCK-C (1.85 +/- 0.32 in CTL vs. 3.06 +/- 0.23 in ADM22-52 treated, p<0.05).

CONCLUSIONS: The mRNA levels of PPAR-γ and PEPCK-C in adipose tissue are lower in GDM and this may be associated with our previous report of elevated ADM and its receptors in GDM adipose tissue. Treatment with ADM antagonist restored mRNA levels of these lipid homeostasis factors in GDM, suggesting ADM system may play a role in pathogenesis of diabetic pregnancies. Our studies show possible usefulness of ADM antagonist to improve re-esterification of the lipolytic fatty acids in dyslipidemia conditions of GDM.

S-050

Identifying Fetal Growth Disorders Using Ultrasound in Women with Diabetes. Annie M Dude†, Lynn M Yee*. *Feinberg School of Medicine, Northwestern University, Chicago, IL, USA.*

INTRODUCTION: Performance of third trimester ultrasound for estimate of fetal weight is common yet the test characteristics of ultrasound in this population are not well established. We evaluated the diagnostic performance of third trimester ultrasound to diagnose disorders of fetal growth among women with four different types of diabetes mellitus (DM).

METHODS: This is a retrospective cohort of nulliparous women with gestational or pre-existing DM who delivered term, singleton gestations at a single academic institution (2010-15). Clinical, demographic,

sonographic, and outcome data were abstracted for women who had an US for fetal growth assessment within 5 weeks of delivery. Large-for-gestational age (LGA) or small-for-gestational age (SGA) were defined as an US estimated fetal weight > 90% or < 10%, respectively. We characterized the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of ultrasound to detect LGA and SGA infants for the entire cohort, as well as by type of DM (gestational DM A1 and A2, type 1 DM, and type 2 DM). Finally, we compared the areas under the curve (AUC) for receiver – operating characteristic (ROC) curves for different types of DM.

RESULTS: Of 877 women with DM, 521 (59.5%) had an ultrasound within 5 weeks of delivery and were eligible for study inclusion. In this population, 3 (0.6%) screened positive for SGA and 64 (12.3%) delivered an SGA neonate. In contrast, 129 (24.8%) screened positive for LGA and 61 (11.7%) delivered an LGA neonate. The sensitivities, specificities, PPVs, and NPVs of ultrasound to detect SGA and LGA are shown below (table). The ROC curves did not differ significantly for different types of DM (p = 0.68, figure). Adding type of DM to a predictive model did not significantly improve its ability to detect LGA fetuses (p = 0.07).

**Figure(s) will be available online.*

CONCLUSIONS: Ultrasound in women with DM at term has a high specificity but poor sensitivity for SGA, and a low PPV for LGA as well. The classification capability of US to correctly classify fetuses with regard to growth abnormalities does not differ significantly by type of DM.

S-051

Perinatal Outcomes of Twin Gestations with and without Gestational Diabetes Mellitus. Lynn M Yee,[1] Aaron B Caughey,[2] William A Grobman,[1] Yvonne W Cheng*.[3] *[1]Northwestern University Feinberg School of Medicine, Chicago, IL, USA; [2]Oregon Health & Science University, Portland, OR, USA; [3]California Pacific Medical Center, San Francisco, CA, USA.*

INTRODUCTION: Existing data suggest obstetric outcomes for women with twin gestations who have gestational diabetes mellitus (GDM) may be comparable to those who do not have GDM, yet studies are limited by small sample sizes. The aim of this study was to utilize a large population-based cohort to examine differences in maternal and neonatal outcomes of twin gestations based on presence of GDM.

METHODS: This was a population-based retrospective cohort study of women giving birth to twin gestations in the United States between 2012 and 2014. Inclusion criteria were live births (>23 weeks) and available information on GDM status; women with pregestational diabetes were excluded. Women were categorized as either having had or not had GDM, and maternal and neonatal outcomes were assessed using bivariable and multivariable analyses. Multivariable logistic regression was utilized to assess the independent association of GDM with adverse maternal outcomes, whereas generalized estimating equation models were used to estimate associations with neonatal outcomes to account for clustering. Significance was set at p<0.001.

RESULTS: Of 173,196 women meeting inclusion criteria, 13,194 (7.6%) had GDM. Women with GDM were more likely to be older, of Hispanic or Asian race/ethnicity, married, college educated, privately insured, and obese than women without GDM. Women with GDM also were more likely to have had a prior cesarean delivery (CD) and to have conceived via assisted reproductive technology. After adjusting for potential confounders, women with GDM were more likely to have hypertensive disorders (18.0% vs. 10.2%; aOR 1.72, 95% CI 1.63-1.81) and to be delivered by CD (79.2% vs. 73.7%; aOR 1.17, 95% CI 1.10-1.25). In contrast, twins born to mothers with GDM had greater birthweights, lower odds of being very low birthweight, and lower odds of extreme prematurity. However, neonates born to mothers with GDM were more likely to receive ventilation >6 hours, NICU admission, and antibiotics.

CONCLUSIONS: Odds of maternal hypertension and CD are increased in twin gestations complicated by GDM. Although some neonatal outcomes are actually improved in the presence of GDM, this finding is balanced by the increased odds of adverse events such as NICU admission and ventilator support.

S-052

Periconceptional Maternal Dietary Patterns Are Associated with Embryonic Growth: The Rotterdam Periconception Cohort. Melek Rousian†,[1] Francesca Parisi†,[1] Anton H Koning,[2] Sten Willemsen,[3] Irene Cetin,[4] Eric A Steegers*,[1] Régine P Steegers-Theunissen.[1,5] *[1]Erasmus MC, University Medical Center, Rotterdam, Zuid-Holland, Netherlands; [2]Erasmus MC, University Medical Center, Rotterdam, Zuid-Holland, Netherlands; [3]Erasmus MC, University Medical Center, Rotterdam, Zuid-Holland, Netherlands; [4]Hospital Luigi Sacco, Center for Fetal Research Giorgio Pardi, Milano, Italy; [5]Erasmus MC, University Medical Center, Rotterdam, Zuid-Holland, Netherlands.*

INTRODUCTION: Knowledge about the influence of periconceptional nutrition on human embryonic growth is scarce. Therefore, our objective is to investigate associations between periconceptional maternal dietary patterns and embryonic growth.

METHODS: In a prospective periconceptional cohort study, 228 women with singleton ongoing pregnancies underwent longitudinal transvaginal three-dimensional ultrasound (3D-US) examinations between 6^{+0} and 12^{+6} weeks of gestation. Crown-rump length (CRL) and embryonic volume (EV) measurements were performed using the Barco I-Space Virtual Reality application in 135 strictly dated spontaneously conceived pregnancies and 93 pregnancies achieved after assisted reproductive technology (ART). Maternal dietary intakes were collected by food frequency questionnaires (FFQ) and validated by blood biomarkers. Principal component analysis was performed to identify dietary patterns. Associations between dietary patterns and CRL and EV trajectories were investigated using linear mixed models adjusted for potential confounders.

RESULTS: A median of five (range 1-7) first trimester 3D-US scans per pregnancy was performed. 991 out of 1162 datasets (85%) were of sufficient quality to perform CRL measurements and 899 (77%) for EV measurements. A 'fish-related dietary pattern' comprising high intakes of fish, olive oil and vegetables, and low intakes of meat was identified. In strictly dated spontaneous pregnancies, a strong adherence to this dietary pattern was associated with a 1.9 mm increased CRL at 7 weeks (+14.6%) and 3.4 mm increased CRL (+6.9%) at 11 weeks, whereas EV increased by 0.06 cm^3 at 7 weeks (+20.4%) and 1.43 cm^3 at 11 weeks (+14.4%), respectively. No significant associations were observed in ART pregnancies.

CONCLUSIONS: This study shows that strong adherence to a 'fish-related maternal dietary pattern' in the periconceptional period is positively associated with embryonic growth in strictly dated spontaneous pregnancies.

S-053

Pregestational Type 2 Diabetes Mellitus Induces Cardiac Hypertrophy in the Murine Embryo Through Cardiac Remodeling and Fibrosis. Penghua Yang†, Xi Chen, E Albert Reece, Peixin Yang*. *University of Maryland School of Medicine, Baltimore, MD, USA.*

INTRODUCTION: Cardiac hypertrophy is highly prevalent in patients with type 2 maternal diabetes (T2DM). Experimental evidence has implicated that pregnant women with T2DM and their children are both at an increased risk in cardiovascular diseases. Our previous study has revealed that maternal T2DM induces structural heart defects. The present study aims to determine whether maternal T2DM induces embryonic heart hypertrophy in a murine model of diabetic embryopathy.

METHODS: The T2DM embryopathy model was established by feeding 4-week-old female C57BL/6J mice with a high-fat diet (HFD) for 15 weeks. Cardiac hypertrophy in embryos at E17.5 was characterized by heart sizes and thicknesses of the right and left ventricle walls, and the interventricular septum, as well as the expression of β-myosin heavy chain (β-MHC), atrial natriuretic peptide (ANP), insulin-like growth factor 1 (IGF1), desmin (DES), and adrenomedullin (ADM). Cardiac remodeling was determined by collagen synthesis and fibronectin synthesis. Fibrosis was evaluated by the Masson staining and the expression of connective tissue growth factor (CTGF), osteopontin (OPN), and Galectin 3 (GAL3) genes. Furthermore, cell apoptosis was measured in the developing heart.

RESULTS: The thicknesses of the left ventricle walls and the interventricular septum of embryonic hearts exposed to maternal diabetes

were significantly thicker than those in the nondiabetic group. Maternal diabetes significantly increased β-MHC, ANP, IGF1 and DES expression, but decreased expression of ADM. Moreover, collagen synthesis was significantly elevated, whereas fibronectin synthesis was suppressed, in embryonic heart from diabetic dams, suggesting that cardiac remodeling is a contributing factor to cardiac hypertrophy. The cardiac fibrosis marker, GAL3, was induced by maternal diabetes. Furthermore, maternal T2DM activated the pro-apoptotic c-Jun-N-terminal kinase (JNK1/2) stress signaling and triggered cell apoptosis by increasing the level of cleaved caspase 3 and the number of TUNEL positive cells (10.4 ± 2.2% of the T2DM group vs. 3.8 ± 0.7% of the ND group, $P < 0.05$).
CONCLUSIONS: Maternal T2DM induces cardiac hypertrophy in embryonic hearts. Adverse cardiac remodeling including elevated collagen synthesis, suppressed fibronectin synthesis, profibrosis and apoptosis, is implicated as the etiology of cardiac hypertrophy.

S-054

Unscheduled Cesarean Section: Interval to Delivery. Corrie P Anderson,[1] Neil S Seligman,[1] Lisa Gray,[1] Loralei L Thornburg,[1] Richard Wissler.[2] *[1]Univ. Rochester Medical Center, Rochester, NY, USA; [2]Univ. Rochester Medical Center, Rochester, NY, USA.*
INTRODUCTION: To evaluate if a longer decision to delivery interval for unscheduled cesarean delivery increases the number of adverse events and to examine factors associated with longer times to cesarean delivery.
METHODS: A retrospective cohort study of unplanned cesarean deliveries at Strong Memorial Hospital from March 2011 to December 2013. Surgical, maternal and neonatal variables were collected. The primary exposure was interval to delivery categorized as ≤ 75 and > 75 minutes. Univariate analyses by delivery interval group were performed for maternal and neonatal outcomes. A secondary analysis was performed to examine intrapartum and temporal characteristics associated with a prolonged interval to delivery. P-values < 0.05 were considered significant.
RESULTS: Maternal antibiotic use (30%, p=0.021), chorioamnionitis (20%, p=0.015), and composite adverse maternal outcome (47%, p=0.005) were more likely in the ≤75 minute category. There were no significant differences in measured neonatal outcomes. Factors associated with shorter decision to delivery interval include active phase arrest (p=0.014), second stage arrest (p<0.001), repeat cesarean for rupture of membranes (p=0.001), night shift delivery (p=0.019), and part-time faculty status (p=0.001). Cesarean delivery was more likely to be initiated within the requested timeframe for urgent cesarean requests (within 1 hour, 59%, p=0.260).
CONCLUSIONS: Subjects were more likely to have a cesarean in ≤75 minutes if they were in labor. Adverse outcomes (antibiotic use and chorioamnionitis) were more common in this group likely indicating intrapartum events requiring expedited delivery. Night and weekend deliveries do not appear to be at risk for prolonged decision to delivery interval.

S-055

Recurrent Intrauterine Growth Restriction (rIUGR): Is the Placenta Pathology the Key to the Conundrum? Keren Rotshenker-Olshinka,[1] Sveta Terlezky†,[1] Letizia Shreiber,[2] Rivka Farkash,[1] Arnon Samueloff,[1] Sorina Grisaru Granovsky*.[1] *[1]Shaare Zedek HU, Jerusalem, Israel; [2]TAU, TA, Israel.*
INTRODUCTION: IUGR is a leading cause for perinatal morbidity/mortality; 20% recurrence. Among IUGR underlying processes, placenta disease is most relevant. We hypothesized unique rIUGR placenta histopathological features (HPf) and aimed to determine those that best describes rIUGR.
METHODS: Retrospective single center case-control, 2005-16. 34 placenta of 17 women who had ≥2 IUGR; birth weight <10th centile for gestational age(GA)(population based). Control: 59 GA matched placenta of healthy women,AGA fetuses, no IUGR risk factors.
Placenta HP performed by a single pathologist (Redline Classif 2015). Excluded: multifetal, intra uterine demise, thrombophilia. **Statistics**:Descriptive, univariate as appropriate.
RESULTS: Study groups differed significantly for birth and placenta weight, inherent to definition. IUGR HPf differed from control. Among statistically significant HPf, 3 were characteristics of rIUGR, **all placental vascular** lesions: **maternal** segmental/complete villous infarcts 17.6%, **fetal** villous capillary 11.8% and **chorionic plate**/stem villous thrombi 5.9%.

HPf	IUGR %	AGA %	P ***rIUGR sig**
Placental vascular			
Maternal stromal-vascular lesions			
Developmental	2.9	5.1	NS
Malperfusion			
Global/partial	5.9	8.5	NS
Villous infarcts	29.4	5.1	**0.018***
Loss of integrity	0	6.8	NS
Fetal stromal-vascular lesions			
Developmental			
Villous capillary	26.5	6.8	**0.011***
Delayed villous maturation	0	1.7	NS
Dysmorphic villi	8.8	0	**0.046**
Malperfusion			
Global/partial Obstructive lesions of umbilical cord	5.9	0	**0.027**
Segmental/complete Chorionic plate/stem villous thrombi	11.8	1.7	**0.058***
Loss of integrity	0	0	
Placental inflammatory-immune processes			
Acute MIR	2.9	15.3	NS
Acute FIR	0	8.5	**0.096**
Chronic villitis/intervillositis	0	1.7	NS
Immune/idiopathic Villitis of unknown etiology	5.8	3.4	NS
Other			
Cord complication	0	8.5	**0.096**
SUA	5.9	0	**0.027**
Meconium changes	20.6	16.9	NS
Hyper/hypocoiled	41.2	37.3	NS

Positive association found only between maternal HPf and hypertension p=0.015.
CONCLUSIONS: Significant vascular rather than stromal HPf are the underlying pathology for rIUGR. This may serve to define future risk groups and a platform for genetic fingerprinting of rIUGR.

S-056

Interventions for Postpartum Hemorrhage Requiring Transfusion. Audrey A Merriam†,[1] Cande V Ananth,[1,2] Yongmei Huang,[2] Jason D Wright,[1] Alexander M Friedman*.[1] *[1]Columbia University Medical Center, New York, NY, USA; [2]Joseph L Mailman School of Public Health, New York, NY, USA.*
INTRODUCTION: The objective of this study was to analyze use of medical, surgical, and radiological interventions for women experiencing postpartum hemorrhage requiring transfusion.
METHODS: Using an administrative database (Premier) that includes drugs, devices, and diagnosis and procedure codes, we identified a cohort of women who were diagnosed with PPH and required a blood transfusion in the setting of a delivery hospitalization between 2006-2014. We evaluated medical interventions (misoprostol, methylergonovine, carboprost), uterine tamponade, and uterine artery embolization utilized in this population. The incidence of the various interventions was analyzed temporally and by annualized hospital delivery volume quintile: 1st quintile 4-1309 deliveries per year, 2nd 1310-2187 deliveries, 3rd 2188-2942 deliveries, 4th 2943-4000 deliveries, and 5th 4001-9363 deliveries.

RESULTS: 21,255 patients were diagnosed with PPH and required a blood transfusion over the time period studied. From 2006-2008 to 2012-2014, use of misoprostol increased by >50% (from 29.3% to 45.2% of cases) while use of methylergonovine and carboprost was relatively stable.

Delivery Interval	2006-8	2009-11	2012-14	All Years
Methylergonovine	46.2%	45.2%	45.4%	45.5%
Carboprost	28.9%	28.7%	30.0%	29.3%
Misoprostol	29.3%	40.3%	45.2%	39.8%
Tamponade	3.8%	7.8%	10.3%	7.9%
Embolization	4.0%	3.9%	4.5%	4.2%

Use of uterine tamponade nearly tripled (from 3.8% to 10.3%). Uterine artery embolization was performed in 4.2% of cases. Rates of embolization and uterine tamponade were highest in the highest delivery volume quintile (7.6% and 12.4% of cases). Tamponade use was lowest in the lowest volume quintile (4.2% of cases). Rates of uterotonic agents were similar across varying hospital delivery volumes. Methylergonovine was the most commonly used medication for treating uterine atony across all hospital volumes, while use of misoprostol varied most.

CONCLUSIONS: Rates of interventions for PPH requiring transfusion vary by hospital volume, with larger volume hospitals utilizing embolization and tamponade more often. Uterine tamponade may be underutilized at lower volume and lower resource centers. Further comparative effective research may help in determining the most effective strategies in managing hemorrhage.

S-057

Neonatal Outcomes of Newborns Exposed to SSRI During Pregnancy: A Pharmacokinetic and Pharmacogenetic Analysis. Silvia Corti†, Paola Pileri, Chiara Mandò, Laura Pogliani, Emilio Clementi, Dario Cattaneo, Irene Cetin*. *University of Milan, Milan, Italy.*

INTRODUCTION: SSRIs (Selective Serotonin Reuptake Inhibitors) are the most frequent drugs to treat depression during pregnancy. SSRIs have direct potential effects on the developing embryo including increased risk of abortion, growth restriction, preterm birth, malformations and neonatal complications. The aim of our study was to investigate the contribution of SSRIs pharmacokinetics and pharmacogenetics during pregnancy on neonatal outcomes.

METHODS: We performed a case-control study: *cases* (n=43) were caucasian women with a diagnosis of depression and/or anxiety, treated with SSRIs for the whole pregnancy. *Controls* (n. 86) were caucasian women without a psychiatric diagnosis and not exposed to SSRIs during pregnancy. Exclusion criteria for both groups were other psychotropic drugs, anti-epileptics, drugs of abuse, alcohol addiction, maternal or fetal infectious diseases, fetal/neonatal chromosomal genetic abnormalities. Maternal and fetal blood samples were obtained at delivery to measure drug concentrations and to analyse genotype.

RESULTS: The population was homogenous for demographic, anthropometric, socio-economic and obstetric variables except for smoking and mean haemoglobin values before delivery. Obstetric features, were comparable. Newborns exposed to SSRIs during fetal life were significantly more likely to be LBW (birth weight<2500 g) (p=0.011), had significantly lower mean Apgar scores at 1' (p=0.006) and at 5' (p=0.023) and worse Apgar-1' distribution (p=0.017). Clinically these findings were associated to poor neonatal adaptation syndrome (PNAS) in 56% of newborns, respiratory distress syndrome or transient tachypnea of the newborn. The pharmacokinetic/pharmacogenetic analysis at delivery showed no striking differences in the frequencies of obstetric or neonatal complications between those with compared to those without any polymorphism. But for each drug, the worst adverse outcome was observed in infants born to the mothers with the most altered CYPs activity.

CONCLUSIONS: Newborns exposed to SSRIs are at increased risk of poor neonatal outcomes (LBW, low APGAR scores, PNAS). The pharmacokinetic/pharmacogenetic analysis showed that the degree of CYPs alterations, that depends on polymorphisms, may influence the severity of outcomes, more than their frequency.

S-058

Recurrence of Extreme Serum Analytes in Subsequent Pregnancies and Obstetrical Outcomes. Shelly Soni†,[1] David Krantz,[2] Meir Greenberg,[1] Nidhi Vohra*,[1] Burton Rochelson.[1] *[1]Northwell Health System, Manhasset, NY, USA; [2]Eurofins/NTD, Melville, NY, USA.*

INTRODUCTION: To evaluate if the presence of extreme serum analytes (≤5th or ≥95th %ile) recurs in subsequent pregnancies. Also, if extreme marker in prior pregnancy increases the risk of adverse outcomes in subsequent pregnancies.

METHODS: Retrospective review of patients with 2 consecutive pregnancies. Adverse outcomes were defined as indicated preterm delivery before 37 weeks due to preeclampsia or other complications. Patients with chronic medical diseases were excluded.

RESULTS: Maternal serum analytes were assessed in 926 patients in 2 consecutive pregnancies with outcomes available for 653 patients.

Presence of extreme analytes in a prior pregnancy increased the likelihood of extreme markers in a subsequent pregnancy. Patients with extreme markers in a prior pregnancy had a significantly increased incidence of preeclampsia and indicated preterm delivery in a subsequent pregnancy

	No extreme analyte in prior preg (N=670)	**1 extreme analyte in prior preg (N=268)**	**≥ 2 extreme analytes in prior preg (N=256)**	**P value**
≥1 extreme analytes in subsequent preg, n(%)	203 (30.3)	118 (44.0)	123 (48.1)	**< 0.0001**
≥2 extreme analytes in subsequent preg, n(%)	43 (6.4)	30 (11.2)	53 (20.7)	**< 0.0001**
	Outcomes			
	(N=338)	**(N=161)**	**(N=154)**	
Preterm preeclampsia in subsequent preg, n(%)	4 (1.2)	5 (3.1)	13 (8.4)	**0.0002**
Indicated preterm delivery in subsequent preg, n(%)	6 (1.8)	7 (4.3)	15 (9.7)	**0.0003**

Higher levels of AFP and Inhibin A, & lower levels of estriol in prior pregnancy were associated with adverse outcomes in subsequent pregnancy.

A substantial increase in the adverse outcomes in subsequent pregnancy was seen in the presence of extreme serum markers in prior pregnancy even when no extreme markers were present in the next pregnancy.

**Figure(s) will be available online.*

CONCLUSIONS: The presence of extreme serum markers in one pregnancy increases the likelihood of recurrence in subsequent pregnancy. A prior pregnancy with extreme markers predisposes subsequent pregnancies to adverse pregnancy outcomes. This suggests a maternal factor in the presence of extreme analytes.

S-059

The Effect of Uterine Balloon Tamponade on the Cases of Postpartum Hemorrhage. Gen Ishikawa, Hanae Kawabata, Akihito Nakai, Toshiyuki Takeshita. *Nippon Medical School, Bunkyo-ku, Tokyo, Japan.*

INTRODUCTION: Postpartum hemorrhage (PPH) is an important cause of maternal morbidity and mortality. Recently, efficacy of balloon tamponade has been shown by several studies. In this study, we examined the efficacy of Bakri Balloon retrospectively.

METHODS: Retrospective cohort of cases with PPH between 2013 and 2016, the cases which administered Bakri Balloon were enrolled in this study. The cases which needed no further alternative hemostat techniques enrolled in the successful group, whereas cases which administered further hemostat techniques enrolled in the unsuccessful group. Demographic data and outcomes were compared between groups.

RESULTS: In this study, 54 cases were administered Bakri Balloon. After exclusion of 2 cases for the reason of inadequate indication, 47 cases were recognized successful group and 5 cases received further hemostat techniques as unsuccessful group. Details of unsuccessful group were hemostasis via laparotomy (n=1), hysterectomy (n=4) and IVR (n=2): these data are including overlaps.

		Successful	Unsuccessful		
Age	(y)	35	35	*p*=0.827	1)
	(range)	21-46	26-44		
GA at delivery	(w, d)	37+5	38+5	*p*=0.084	1)
	(range)	33+3-41+2	37+2-40+5		
Delivery mode					
Cesarean/Vaginal	(n/n)	43/4	3/2	*p*=0.174	2)
Postpartum admit by ambulance	(n)	2 (4%)	3 (60%)	*p*=0.004	2)
Malposition placenta	(n)	20 (42%)	1 (20%)	*p*=0.619	2)

1) Mann-Whitney U, 2) Fisher's exact test

		Successful		Unsuccessful		
Inflation Volume	(mL)	150	(70-240)	140	(80-180)	*p*=0.623
Delivery-Insertion interval	(minute)	53.5	(18-503)	132	(50-215)	*p*=0.262
Blood loss prior to Bakri	(mL)	1035	(811-4300)	2500	(1925-4800)	*p*=0.082
Blood loss after Bakri	(mL)	154	(38-3391)	2633	(405-4500)	*p*=0.001
Blood Transfusion RBC	(unit)	3.5	(0-28)	38	(30-56)	*p*<0.001
FFP	(unit)	3.6	(0-40)	44.4	(28-56)	*p*<0.001
Serum Fibrinogen	(mg/dL)	306	(60-478)	120	(29-207)	*p*<0.001
Hospitalized date after Bakri	(day)	5	(3-19)	10	(7-17)	*p*=0.002

Mann-Whitney U test.

CONCLUSIONS: We showed the efficacy of Bakri Balloon in the case of PPH. Overall success rate was 90.3%, and in the cases of malposition of placenta, the rate was 95%. Adequate use of Bakri balloon might contribute to the less hospitalized period of PPH.

S-060

Universal MRSA Screening: Incidence in an Obstetric Population at an Academic Tertiary Care Center. Ann Lal, Thaddeus P Waters, Jean R Goodman. *Loyola University, Maywood, IL, USA.*

INTRODUCTION: Methicillin resistant staphylococcus aureus (MRSA) rates in the general population have been reported as 0.5-10%. Little data, however, has been collected on obstetric populations and the incidence of MRSA. Further clarification of MRSA rates in obstetric patients are needed, as well as maternal outcomes associated with MRSA positive status.

METHODS: This is a retrospective chart review of all pregnant women with a MRSA test performed at Loyola University Medical Center, from 2010-2014. Patients were obtained through the electronic medical record, using ICD-9 codes. At our institution, a MRSA swab is routinely collected as part of the patient's prenatal care at 35-37 weeks gestation or on admission to labor and delivery. Exclusion criteria for our study were an unknown MRSA status or known MRSA status, with delivery at an outside institution. Demographic information was collected. The incidence of MRSA was calculated. Delivery outcomes were collected, including: length of stay, endometritis and surgical site infection. Statistical analysis was performed with OpenEpi, version 3.01.

RESULTS: Of 3682 total patients during the study period, 82 were MRSA positive. The incidence of MRSA during the 4 year study period was 2.2%. MRSA was collected at average gestational age of 37.9 weeks. Length of stay was not significantly different between the study groups, 2.64 ± 1.47 for MRSA negative patients and 2.83 ± 1.1 for MRSA positive patients, p = 0.12. Endometritis rates were not significantly different between the groups, with 21 cases in the MRSA negative group and 0 in the MRSA positive group, p = 0.62. Surgical site infection rates were not significantly different between the 2 groups with 21 cases in the MRSA negative group and 1 in the MRSA positive group, p = 0.48.

CONCLUSIONS: The incidence of MRSA in the obstetric population is low, 2.2%. In our academic, tertiary care center, there were not significant differences in post-delivery outcomes, regardless of the MRSA status. Further information is needed regarding MRSA positive patients in an obstetric context, including what additional treatment was administered and its effect on maternal and neonatal outcomes.

S-061

Risk Factors for Primary Cesarean in Women with Premature Rupture of Membranes. Sasha M Davidson, Sadia Sahabi†, Catherine Wu†, Kafui A Demasio*. *Albert Einstein College of Medicine - Montefiore Medical Center, Bronx, NY, USA.*

INTRODUCTION: Women with premature rupture of membranes (PROM) and an unfavorable cervix are at risk for cesarean birth. This risk is 3 times greater for nulliparous women versus multiparous women in our cohort. The objective of this study was to determine risk factors associated with primary cesarean in nulliparous women with PROM and an unfavorable cervix.

METHODS: A randomized controlled trial was conducted from October 2014 to May 2016 where women with PROM, a Bishop score of ≤6, singleton pregnancy ≥34 weeks gestation, were randomized to 25 mcg of vaginal misoprostol or oxytocin as the initial induction agent. Parity and term versus preterm PROM were controlled by stratified block randomization. Intrapartum course, demographics, medical and obstetric risk factors were assessed. Primary outcome was cesarean section rate. Secondary outcomes of chorioamnionitis, maternal and neonatal morbidity were compared. Regression analysis and chi square were used to determine the association between maternal age, BMI, race, Bishop score, duration of labor induction, diagnosis of chorioamnionitis, abnormal fetal tracing, and physician level of experience, with a primary cesarean birth for women with PROM.

RESULTS: There were 290 women with PROM and 230 met criteria and were randomized. There were 152 nulliparous women with PROM and the cesarean birth rate was 30% (p .009) among this group. The median age in this population was 24 years old. Median BMI was 27. Significant factors associated with cesarean delivery were maternal age (p .008 OR of 4.3) and clinical diagnosis of chorioamnionitis (p 0.03). No other variables were significantly associated with mode of delivery.

CONCLUSIONS: Suspected chorioamnionitis and young maternal age were associated with primary cesarean birth in women with PROM. Understanding the risks associated with primary cesarean may provide an opportunity to decrease cesarean rates in this population.

S-062

Re-Engineering the Interpretation of Electronic Fetal Monitoring (EFM): Using the Fetal Reserve Index (FRI) to Anticipate the Need for Emergent Operative Delivery (EOD). Robert D Eden*,[1] Mark I Evans,[1,2] Shara M Evans,[1] Barry S Schifrin.[1] *[1]Fetal Medicine Foundation of America, New York, NY, USA; [2]Mt. Sinai School of Medicine, New York, NY, USA.*

INTRODUCTION: EODs, even with normal outcomes, expose mothers, fetuses, staff, and other patients to higher complications and added stress. We evaluated risk factors associated with EODs in patients undergoing planned trials of labor at term using the "fetal reserve index," (FRI) a metric which scores maternal, obstetrical, fetal, and EFM risk factors. Preliminarily, the FRI has shown high statistical discrimination for fetuses with neurologic injury.

METHODS: We retrospectively evaluated the clinical antecedents of EOD in 300 consecutive term, patients in labor with singleton, vertex, normal entry EFM, and normal neonatal outcomes. There were no other exclusions. The FRI applies color codes (Green/Yellow/Red) from quantitative scores from the onset of monitoring. We define Point A" when the fetus demonstrates significant compensatory responses to hypoxia/ischemia, strongly suggesting intervention. "Point B" is indicates fetal

neurological damage having occurred. FRI and Point A were ascertained blindly by different investigators. We compared the FRI with the ACOG Categories I-III.

RESULTS: Demographics, BW, and clinical outcomes were similar. 1,5 min Apgars & pH were lower (p<.001), but WNL. 75/300 CSs (25%) of which 51 (17%) were EOD; only 5 (1.6%) reached Point A, none Point B. 250/300 (84%) showed ACOG Category II; none reached Category III. 73/300 (24.3%) reached Red Zone of which 47/73 (64.4%) had EOD. 0/249 non EOD. (X2 =193.5, p<.00001) 4 patients had non fetal indications for EOD.

	EOD	Non-EOD	X2	SENS	47/51	92.2%
RED	47	26	153.6	SPEC	223/249	89.6%
G + Y	4	223	p<.0001	PPV	47/73	64.4%
				NPV	223/227	98.2%

EOD cases averaged 1.06hrs in Red zone. Controls: 0.05hrs (p<.0001).

CONCLUSIONS: The FRI facilitates earlier and more accurate prediction of fetal compromise compared to ACOG Category III (too rare, extreme) or Category II (too common, insensitive). Our data suggest that using the FRI prospectively as an indication for intrauterine resuscitation might achieve a lowering of EOD deliveries with resultant decreases in cost, morbidity, and disruption.

S-063

Preterm Birth and Arsenic Levels: A Pilot Study. Jasmine D Johnson†,[1] Shannon Robinson†,[1] Lisa Smeester,[4] Rebecca Fry,[3] Neeta Vora*.[2] *[1]University of North Carolina, Chapel Hill, NC, USA; [2]University of North Carolina, Chapel Hill, NC, USA; [3]University of North Carolina School of Public Health, Chapel Hill, NC, USA; [4]University of North Carolina School of Public Health, Chapel Hill, NC, USA.*

INTRODUCTION: Arsenic is a toxic metal that can cross the placental barrier from mother to fetus and has been linked to adverse reproductive outcomes such as preterm birth. We designed a retrospective case-control study that examined levels of arsenic in amniotic fluid in preterm birth subjects and term birth matched controls.

METHODS: Leveraging a retrospective cohort examining spontaneous preterm birth (sPTB), arsenic was measured in amniotic fluid supernatant (AFS) by Inductively-Coupled Plasma Mass Spectrometry. The AFS was obtained from singleton fetuses without structural abnormalities who underwent second trimester (15-24 weeks) genetic amniocenteses at UNC-Chapel Hill. AFS from women who had sPTB [(<37 weeks); n=21] was matched to AFS from women who had term birth [(>37 weeks); n=21] by fetal sex, maternal age, gestational age at amniocentesis, and medication exposure.

RESULTS: Statistical analysis of dichotomous categories (preterm birth/term birth) using a student's t-test did not show a significant difference between arsenic levels in the amniotic fluid of fetuses that delivered preterm compared to term (p=0.24). When arsenic levels were examined with gestational age as a continuous variable, no significant correlation was seen using the Pearson Coefficient test (p=0.79; r=0.04).

CONCLUSIONS: In this cohort, there was no difference in arsenic levels in second trimester AFS samples of fetuses delivered preterm compared to term. Given that there were detectable levels of arsenic in all the AFS samples, further research regarding effects of metals on fetal and maternal outcomes is needed.

S-064

Evaluating Hospitals' Comparative Effectiveness in Managing Shoulder Dystocia Using Data Envelopment Analysis. Chester Chambers,[1] Maqbool Dada,[1] Edith D Gurewitsch Allen*.[2] *[1]Johns Hopkins University, Baltimore, MD, USA; [2]Johns Hopkins University, Baltimore, MD, USA.*

INTRODUCTION: Performance-based payment increases the need for rigorous metrics and benchmarking. Rates of brachial plexus injury (BPI) at any given hospital will vary depending on a number of factors including delivery volume, rates of cesarean sections, preterm deliveries, and shoulder dystocia (SD). This confounds the ability to use the absolute rate of neonatal BPI to assess quality. Data Envelopment Analysis (DEA) is an operations research technique designed to compare relative performance of healthcare delivery units. We studied whether DEA could objectively compare performance across a diverse range of hospitals relative to rates of SD and BPI.

METHODS: We queried public Health Services Cost Review Commission metrics from all hospitals in Maryland for 2014. A DEA model was developed using delivery volume, total vaginal deliveries and rate of SD as quantitative inputs. [1 – BPI:SD ratio] was the desired output. Relative weights of each variable were determined for each hospital. Subtracting weighted inputs from output, DEA produces a single measure of relative efficiency for each unit for objective comparison.

RESULTS: Variance between units suggests 4 ranges of comparative effectiveness in resolving SD without BPI: Hospitals A-D are efficient (DEA=1), whereas U & V are least efficient

**Figure(s) will be available online.*

Differences in efficiency were discernible between hospitals otherwise comparable for such inputs as low overall delivery volume with high cesarean section rate (A & D vs P), being teaching hospitals (C & E vs T) and having only a Level 1 nursery (F vs M).

CONCLUSIONS: DEA is sufficiently robust to benchmark hospitals' comparative effectiveness in resolving SD without BPI, accounting for disparate resources. The range of DEA results further directs where efforts to improve performance related to BPI associated with SD might be tailored relative to weighted inputs and output of targeted units. The DEA scoring system produces an objective metric by which to track both efficiency and improvements.

S-065

Disparities in Trial of Labor Among Women with Twin Gestations in the United States. Lynn M Yee,[1] Aaron B Caughey,[2] William A Grobman,[1] Yvonne W Cheng*.[3] *[1]Northwestern University Feinberg School of Medicine, Chicago, IL, USA; [2]Oregon Health & Science University, Portland, OR, USA; [3]California Pacific Medical Center, San Francisco, CA, USA.*

INTRODUCTION: Recent clinical trial data suggest similar neonatal outcomes for twins of women who have a cephalic presenting twin regardless of whether they undergo planned vaginal or cesarean delivery, yet the rate of twin cesarean deliveries remains high, and it remains uncertain which factors contribute to women with twins undertaking a trial of labor (TOL). Thus, the aim of this study was to examine clinical and demographic factors associated with TOL among women with twin gestations eligible for a vaginal delivery.

METHODS: This was a population-based case-control study of women giving birth to twin gestations in the United States between 2012 and 2014. Inclusion criteria for the analysis included live births greater than 23 weeks gestation and a cephalic presenting twin. Women were categorized as either having had or not had a TOL, and clinical and demographic characteristics associated with this approach were evaluated using chi-square tests, Wilcoxon rank sum, and multivariable logistic regression analysis.

RESULTS: A total of 108,772 women met inclusion criteria. A minority (33.9%) of women underwent TOL. Women who had a greater gestational age at delivery (35.6 vs 35.2 weeks, p<0.001; aOR 1.06, 95% CI 1.06-1.07) were more likely to have a TOL. In contrast, several demographic factors were associated with decreased likelihood of TOL, including maternal age >35 years (aOR 0.74, 95% CI 0.71-0.77) and being Hispanic (aOR 0.67, 95% CI 0.65-70) or Asian (aOR 0.25, 95% CI 0.22-0.29) compared to non-Hispanic white. Clinical factors associated with decreased likelihood of TOL included nulliparity (aOR 0.60, 95% CI 0.58-0.62), prior cesarean delivery (aOR 0.10, 95% CI 0.09-0.10), obesity (aOR 0.86, 95% CI 0.84-0.89), diabetes (aOR 0.93, 95% CI 0.88-0.98), and having conceived via assisted reproductive technology (aOR 0.93, 95% CI 0.88-0.99).

CONCLUSIONS: In this large population of women with twins who were eligible for a TOL, factors such as maternal age, non-white race/ethnicity, infertility treatment, and parity are associated with decreased likelihood of undergoing trial of labor. Addressing such disparities in management of women with twin gestations may be one avenue to avoid unnecessary cesareans and promote health equity.

S-066

Serum Procalcitonin Levels as a Marker for Discontinuation of Antibiotics in Acute Pyelonephritis in Pregnancy. Manuel E Rivera-Alsina*,[1] Jessica Prussa†,[1] Gabbrielle C Rivera†,[2] Diana M Martinez,[3] Christine C Rivera.[1] *[1]Methodist Health System Dallas, Dallas, TX, USA; [2]MIT, Boston, MA, USA; [3]Hospital del Maestro, San Juan, Puerto Rico, United States Minor Outlying Islands.*

INTRODUCTION: Asymptopmatic Bacteriuria in Pregnancy progresses 30-50% of the time to Acute Pyelonephritis in Pregnancy. This could lead to sepsis and other complications in pregnancy. For the clinicians therapeutic actions include starting antibiotics quickly. This action and how long we use antibiotics, impacts antibiotic resistance. Procalcitonin (PCT) is a biomarker that helps us decide if we need to use antibiotics, and help us monitor the need for further therapy. These action is paramount for good antibiotic stewardship.

METHODS: Retrospective COHORT, at Methodist Health System Dallas, was studied betrween June 2013 and December 2015. The study was approved by the Institutiona; Review Board. The study population included 36 patients admitted with the diagnosis of Acute Pyelonephritis and followed with PCT as a biomarker for infection and cure, and 16 patients admitted with Acute Pyelonephritis and followed with Urine cultures and marker for infection and cure. All laboratory studies were conducted at Methodist Dallas Medical Center Laboratory. Serum PCT levels greater or equal to 0.05 ng/ml were considered positive for infection, levels below 0.05 ng/ml were considered negative for infection.

RESULTS: All 52 patients diagnosed with Acute Pyelonephritis had serum PCT levels greater than 0.05 ng/ml (Positive for infection), and positive Urine cultures. In the study group (36) PCT levels became negative (PCT less than 0.05 ng/ml) after 47hrs on antibiotics. In this group antibiotics were stopped and patients followed with PCT levels and Urine Culture as outpatients. In the non PCT group (16) antibiotics continues until 48 hrs afebrile (71 hrs). The study group had no recurrences in 6 weeks of follow up, the non PCT group had 2 recurrences within 6 weeks of follow up.

CONCLUSIONS: Our findings support expansion of our study, using serum PCT as a biomarker for early discontinuation of antibiotics and follow up in patients with Acute Pyelonephritis. Further studies are needed to evaluate the impact of this clinical marker as it relates to curtailing antibiotic resistance.

S-067

Reverse Syphilis Testing Compared to Traditional Testing in Pregnancy for Diagnosis of Syphilis in Pregnancy in High Burden Regions: A Cost Effectiveness and Decision Analysis. Ahizechukwu C Eke,[1] Israel T Agaku,[2] Uzoamaka A Eke,[3] Jeanne Sheffield.[1] *[1]Johns Hopkins University School of Medicine, Baltimore, MD, USA; [2]Centers for Disease Control and Prevention (CDC), Atlanta, GA, USA; [3]Wayne State University School of Medicine, Detroit, MI, USA.*

INTRODUCTION: To evaluate whether reverse syphilis testing algorithm is a cost effective screening strategy when compared to traditional diagnostic testing in pregnancy.

METHODS: A decision analytic model was used to estimate the economic impact of reverse syphilis testing versus traditional testing on congenital syphilis from a societal perspective. Our primary outcome was the annual cost-benefit per person tested. Baseline probabilities and cost estimates were derived from published literature. We conducted sensitivity analyses using both deterministic and probabilistic models. Cost estimates reflect 2016 U.S. dollars.

RESULTS: Reverse syphilis testing was the preferred cost-effective strategy. Annual net benefit from reverse syphilis testing was $21,043 per person tested, while traditional testing had a net benefit of $ 15,257 per person tested. Compared with traditional testing, the reverse syphilis testing algorithm was more cost effective, resulting in an incremental benefit of 4.4 quality-adjusted life-years (QALYs) and an incremental cost-effectiveness ratio of 451 per QALY gained. Monte Carlo simulations of 10 million trials selected reverse testing as the optimal strategy, being cost effective and cost-saving.

Probability estimates	**Base case**	**Range**
Prevalence of syphilis in pregnancy	0.05	0.01-1.0
Sensitivity of Rapid Plasma Reagin	87%	81-98%
Specificity of Rapid Plasma Reagin	95%	85-99%
Sensitivity of FTA-ABS test	92%	87-100%
Specificity of FTA-ABS test	97%	84-100%
Sensitivity of TPPA test	97%	95-100%
Specificity of TPPA test	96%	96-100%
Cost Estimates	**Base case**	**Range**
RPR test kit	$10	$1-15
FTA-ABS test kit	$12	$6-20
TPPA test kit	$20	$10-25
Preterm birth, neonatal care	$13,704	$3,328-190,849
Congenital syphilis, neonatal care	$12,610	$6,240-18,351
Term delivery, neonatal care	$2,087	$1,408-2,516

CONCLUSIONS: Our analysis provides evidence suggesting that reverse syphilis testing is a cost-effective strategy compared to traditional testing.

S-068

Antepartum Rubella Infection and Pregnancy Outcomes. Courtney Olson-Chen†,[1] Dongmei Li,[2] Timothy Dye*,[1] Dzhamala Gilmandyar.[1] *[1]University of Rochester Medical Center, Rochester, NY, USA; [2]University of Rochester Medical Center, Rochester, NY, USA.*

INTRODUCTION: Information on active rubella virus infection in pregnancy during the post-elimination era is sparse. While rubella is known to be associated with congenital anomalies, the determinants of rubella infection and adverse maternal and perinatal outcomes are less well understood. We sought to investigate these outcomes in the present time.

METHODS: A retrospective cohort study was performed using deidentified data from the Perinatal Data System in Upstate New York collected between January 1, 2004 and December 31, 2014. The presence of rubella infection in pregnancy was documented by hospital staff. Maternal characteristics were analyzed using chi-square tests, Student's t-tests, and Wilcoxon rank sum tests based on variable type and distribution. Pregnancy outcomes including preterm delivery (PTD), chorioamnionitis (chorio), abruption, and small for gestational age were evaluated by chi-square tests. A multivariate logistic regression analysis generating adjusted Odds Ratios (aOR) was performed to examine the association between rubella infection during pregnancy and adverse outcomes after adjusting for maternal age, race, ethnicity, income, education level, tobacco use and PTD.

RESULTS: We identified 101 cases of rubella in pregnancy out of 724723 delivery records. Rubella infection was significantly more common in women of Hispanic ethnicity (OR 1.9, 95%CI 1.03-3.59), low income (OR 1.53, 95%CI 1.03-2.26), low education (OR 3.65, 95%CI 1.38-9.68) and tobacco users (OR 1.85, 95%CI 1.18-2.9). Rubella infection was also more likely in women with hepatitis B infection (OR 12.2, 95%CI 3.0-49.5). Women with rubella infection in pregnancy were more likely to have chorio than those without rubella infection (aOR: 4.26; 95%CI 1.35-13.47). No significant differences in other adverse pregnancy outcomes were observed in women with rubella, though power was limited given the small sample size.

CONCLUSIONS: Despite the availability of a vaccine, cases of rubella infection during pregnancy still occur. Rubella is more common among women of sociomedical risk. The odds of chorio during labor is higher in women with rubella in pregnancy, but other adverse outcomes do not appear to be increased.

S-069

Fetal Nicotine Exposure Increases Brain Hypoxic-Ischemic Injury in Neonatal Rats: The Role of miRNA-210. Lei Wang†, Jun Ke†, Yong Li, Qinyi Ma, Chiranjib Dasgupta, Xiaohui Huang, Lubo Zhang, DaLiao Xiao*. *Loma Linda University School of Medicine, Loma Linda, CA, USA.*

INTRODUCTION: Fetal nicotine exposure increases the risk of neurodevelopmental disorders and neurobehavioral deficits in postnatal life. Our previous studies have demonstrated that perinatal nicotine exposure increases brain vulnerability to hypoxic-ischemic (HI) injury in neonatal rats. However the underlying mechanisms remain unknown. The present study tested the hypothesis that perinatal nicotine exposure exacerbated brain vulnerability to HI injury in neonatal rats through up-regulation of miR-210 expression.

METHODS: Nicotine was administered to pregnant rats via subcutaneous osmotic minipumps. Experiments of HI brain injury were performed in 10-day-old pups.

RESULTS: Perinatal nicotine exposure significantly increased miRNA-210 expression in neonatal brain as compared with the saline control groups. Intracerebroventricular administration of a miR-210 inhibitor (miR-210-LNA) significantly decreased HI-induced brain infarct size and reversed the nicotine-increased vulnerability to brain HI injury in the neonate. In addition, nicotine significantly attenuated brain-derived neurotrophic factor (BDNF) and tropomyosin-related kinase isoform B (TrkB) protein abundance in the neonatal brain, which were also reversed by the treatment of miR-210-LNA in the neonatal brains.

CONCLUSIONS: These data suggest that perinatal nicotine exposure enhances miR-210 expression in neonatal brains and the enhanced miR-210 may play a causal role in perinatal nicotine-induced developmental programming of ischemic sensitive phenotype in the brain.

S-070

Life-Course Differences in Liver Transcriptome Programming in Offspring of Obese (MO) Rats. Consuelo Lomas†,[1] Claudia J Bautista,[1] Luis A Reyes-Castro,[1] Guadalupe L Rodríguez-González,[1] Laura Cox,[2] Peter W Nathanielsz,[3] Elena Zambrano*.[1] *[1]Instituto Nacional de Ciencias Médicas y Nutrición SZ, Mexico City, Mexico; [2]TBRI, San Antonio, TX, USA; [3]University of Wyoming, Laramie, WY, USA.*

INTRODUCTION: MO predisposes F1 to metabolic disorders. Aging liver undergoes changes associated with impairment of hepatic metabolism. Mechanisms (s) whereby MO affects liver and aging are poorly understood. Several signaling pathways are implicated in aging. We have presented life course changes in male F1 and now compare changes in female F1. We hypothesized MO produces sex specific diet and aging liver transcriptome changes.

METHODS: F0 female rats ate control (C) or obesogenic diet (MO) from weaning through lactation. After weaning their F1 ate C diet. At 110 and 650d F1 liver was collected to determine F1 transcriptomics for differentially expressed genes (DEG) by age and diet. One-way ANOVA for all four groups of RNAseq within sex, M±SE Log2.

RESULTS: MO-induced liver injury was analyzed by serum, structure, protein and gene expression assays, and found differences between male and female F1 (data not shown). RNA-seq show dietary effects at 110 and 650d Fig 1 (A, B), KEGG pathways identified DEG related to metabolic pathways (314), OxPhos (39), insulin signalling (37) and proteasome (10) in males. In contrast with females at 110d, no relevant KEGG pathway enrichment was observed; but at 650d KEGG we found OxPhos (99), insulin signaling (85) and proteasome (43). Aging effect in Controls showed more total DEG in males (4,192) than in females (474) (Fig 1C), whereas MO in aging differed between males (72%DEG up) and females (98%DEG down) (Fig 1D).

**Figure(s) will be available online.*

Figure 1. RNA-seq; DEG in male and female F1. Dietary effects at **A)** 110 and **B)** 650d, aging effect in **C)** control and **D)** MO. M ± SE, n=5-6 male and female. F1 non-littermates. Genes considered differentially expressed if $p<0.05$ vs reference within sex.

CONCLUSIONS: MO programs sex-specific changes associated with liver dysfunction observed in F1. The adult liver of male MO adult F1 shows global down regulation of genes that are required for normal function of the transcription process.

S-071

Maternal Obesity (MO) Accelerates Male (M) Offspring (F1) Aging in Proteasome, Proteolysis and Autophagy Signaling Pathways. Consuelo Lomas†,[1] Luis A Reyes-Castro,[1] Lilia Vargas,[1] Carlos A Ibañez-Chavez†,[1] Laura A Cox,[2] Peter W Nathanielsz*,[3] Elena Zambrano.[1] *[1]Instituto Nacional de Ciencias Medicas y Nutricion, Mexico City, Mexico; [2]TBRI, San Antonio, TX, USA; [3]University of Wyoming, Laramie, WY, USA.*

INTRODUCTION: Human and animal F1 of high BMI (MO) mothers age faster than F1 of control (C) normal BMI mothers (1,2). Little is known of mechanisms of programming on aging. Autophagy, proteolysis and the proteasome are three major aging pathways. In our well-established model of rat MO (3) we evaluated the extent MO accelerates gene expression changes normally observed in these pathways as animals age. We hypothesized that livers would show similar differentially expressed genes (DEG) between MOF1 young adult post natal day (PND) 110 vs. PND 110 CF1 as seen with normal aging between PND 110 CF1 to PND 650 CF1. Our CF1 live to PND 850, MOF1 die soon after PND 650.

METHODS: F0 female rats ate control (C) or obesogenic diet (MO) from weaning through lactation. After weaning F1 males ate C diet with livers collected at PND 110 and 650 to determine F1 DEG by age and diet. One-way ANOVA for all four groups for RNAseq, M±SE Log2.

RESULTS: 110d MO F1 show impaired hepatic lipid function, increased NAFLD, OS markers and serum lipid, increased in MO at 650d. We found DEG in natural aging (PND C 110 vs C 650) with 97% down regulated as well as DEG between PND 110 F1 C and MO livers 95% down-regulated (Fig 1A). We used KEGG to identify candidate pathways related to premature aging in F1 from MO (Fig 1B). Autophagy, proteasome and proteolysis pathways show similarities in down regulated genes in 110d MOF1 to those in CF1 at PND 650 indicating premature aging (Fig 1C-E).

**Figure(s) will be available online.*

Fig 1. A) DEG , B) Three KEGG pathways from down regulated genes; C) Atg3, D) Psma1 and E) Ube2a. $P < 0.05$ data not sharing a letter. n=5-6 non-sib rats. Genes considered DEG with a P value $p < 0.05$ vs reference group.

CONCLUSIONS: In these three key aging pathways DEG between F1MO and CF1 are similar to DEG between PND 110 CF1 and PND 650 CF1.

1. Reynolds, BMJ. 2013. 347:f4539.
2. Klimek P., Gerontology. 2014;60):502.
3. Zambrano E. 2010. J physiol; 588(10):1791.

S-072

Gestational Diabetes Programs Offspring Adiposity. Omonseigho Talton†,[1] Keenan Bates†,[1,2] Kylie Hohensee†,[3] Laura Schulz*.[4] *[1]University of Missouri, Columbia, MS, USA; [2]University of Missouri, Columbia, MS, USA; [3]University of Missouri, Columbia, MS, USA; [4]University of Missouri, Columbia, MS, USA.*

INTRODUCTION: Gestational diabetes has been shown to predispose offspring to multiple facets of metabolic syndrome. As the incidence of gestational diabetes mellitus (GDM) rises globally, studies outlining the mechanisms through which GDM programs offspring health are much needed. We developed a model of GDM in which dams exhibit glucose intolerance and reduced insulin response to glucose challenge only during pregnancy, without accompanying obesity. We hypothesized that the offspring of GDM dams would display insulin resistance and obesity.

METHODS: Female C57B6 mice were fed a high fat high sucrose diet (HFHS) one week prior to mating and throughout gestation (4 weeks total). At 5, 11, 20, and 28 weeks, mice were placed in metabolic cages that recorded activity, food intake and metabolism for three days. One cohort of the offspring were sacrificed at 19 weeks, and half of the offspring in the second cohort were placed on HFHS at 23 weeks. All offspring in the second cohort were sacrificed at 31 weeks. Weight, body composition, glucose tolerance, liver triglycerides, serum IL-6, insulin and leptin were assessed in offspring.

RESULTS: Compared to offspring of control dams, male offspring of GDM dams exhibited increased body fat percentage at 12 (p=.01), and 21 (p=.05) weeks of age, while female offspring of GDM dams showed higher body fat percentage at 21 weeks on the chow diet (CD) (p=.01) and 28 weeks on HFHS (p=.03). Male offspring of GDM dams had a higher

respiratory quotient (RQ) than controls during the 12, 20, 28 CD and 28 HFHS light and dark cycles. Higher RQ indicates that carbohydrates rather than lipids are being metabolized. Male offspring of GDM dams also had lower total meters walked during the 12 and 20 week light cycles, and during the 28 week HFHS dark cycle. Offspring of GDM dams did not differ from controls in regards to weight, glucose tolerance, liver triglycerides, serum leptin, insulin, or IL-6 levels at 19 weeks. At 31 weeks there was improved glucose clearance in male (p=.004) and female (p=.03) offspring of GDM dams on the chow diet.

CONCLUSIONS: Maternal high fat diet consumption and glucose intolerance without obesity during gestation lead to increased adiposity in adult offspring, but not glucose intolerance and insulin resistance.

S-073

Antenatal Steroids Do Not Affect Splicing or DNA Methylation of the Glucocorticoid Receptor Gene in Cord Blood T-Cells. J Carpenter,[1] K Jablonski,[4] J Koncinsky,[3] M Varner,[1] L Joss-Moore*.[2] *[1]Univ. of Utah, Salt Lake City, UT, USA; [2]Univ. of Utah, Salt Lake City, UT, USA; [3]Univ. of Utah, Salt Lake City, UT, USA; [4]George Washington Univ., Washington, DC, USA.*

INTRODUCTION: Women at risk for preterm delivery (PTD) routinely receive glucocorticoids (GCs). GCs influence immune cell number/function via altered gene expression. These alterations in expression, or "programming" effects, relate to alternative exon usage. Alternative 5' exon usage of the glucocorticoid receptor (GR) gene influences GR expression. In CD4+ T-cells, GCs increase GR expression. Expression of GR alternative exon transcripts is regulated by cell-type specific DNA methylation. We hypothesized an association between antenatal GCs and: 1) altered levels of GR exons 1D, 1B, and 1C transcripts in cord blood CD4+ T-cells, 2) altered 5' GR DNA methylation in cord blood CD4+ T-cells, and 3) changes in the proportions of cord blood immune cell types.

METHODS: This was an ancillary to the NICHD MFMU Network Antenatal Late Preterm Steroids (ALPS) trial. Women at high risk for PTD (34.0-36.5 wks) were randomized to betamethasone (BMZ) or placebo. Flow cytometry was performed on cord blood from delivery and CD4+ T-cells isolated. The Illumina Methylation450 Chip was used to determine CpG methylation in the 5' region of the GR gene (41 CpGs) in CD4+ T-cells. Expression of GR exons 1D, 1B, and 1C mRNA transcripts in the CD4+ T-cells was determined using real-time RT-PCR. A p-value of 0.05 was considered significant.

RESULTS: Demographic/clinical characteristics of the 51 women (27 BMZ, 24 placebo) were similar between treatment groups. BMZ was not associated with an increase in GR exon 1D, 1B, or 1C mRNA transcripts, or with changes in GR 5' DNA methylation. Percentages of CD4+ and CD8+ T-cells did not differ between BMZ and placebo. BMZ was associated with an increase in granulocytes (median 51.6% vs. 44.7%, p=0.03) and a decrease in lymphocytes (median 36.8% vs. 43.0%, p=0.04), vs. placebo.

CONCLUSIONS: BMZ was not associated with altered GR transcript levels or changes in DNA methylation in cord blood CD4+ T-cells. Our small sample size is limiting given the diverse clinical scenarios within treatment groups. Differences in GR transcript expression or DNA methylation within treatment groups cannot be excluded, but changes may depend on individual clinical condition.

S-074

Simulated Shift Work in the Pregnant Sheep Disrupts Maternal Rhythms and Metabolism. Tamara J Varcoe,[1] Kathryn L Gatford,[1] Hong Liu†,[1] Timothy R Kuchel,[2] David J Kennaway*.[1] *[1]University of Adelaide, Adelaide, SA, Australia; [2]SAHMRI, Gilles Plains, SA, Australia.*

INTRODUCTION: Maternal shift work during pregnancy is associated with adverse pregnancy outcomes in humans, but effects on the children and their long-term health have not yet been reported. In our studies in rats, simulated shift work exposure throughout gestation severely disrupted normal circadian profiles in the mother and fetus, and also programmed poor glucose homeostasis and increased adiposity of offspring as adults (Varcoe et al. *PLoS ONE*, 6, e18504, 2011; Varcoe et al. *PLoS ONE*, 8, e53800, 2013). We are now using a large animal model, with gestation length and maturity at birth more similar to human, to test the hypothesis that maternal and progeny outcomes worsen with increasing duration of shift work in pregnancy.

METHODS: Merino ewes entered pen housing in a light-proof facility 3 d after timed mating to Merino rams near equinox. Ewes were randomised to be housed in 12L:12D photoperiod throughout pregnancy (Control), or were subjected to twice-weekly phase shifts of lighting and feeding time (simulated shift work, SW), throughout the first third (mating–week 7), first and second third (mating–week 14), or all of pregnancy. In early and late pregnancy (weeks 7 and 18), we measured maternal central (activity, circulating melatonin, cortisol and glucose) and peripheral rhythms (skeletal muscle expression of Clock genes) every 4 h for 72 h, and maternal glucose tolerance by intravenous glucose tolerance test (0.25 g glucose/kg, IVGTT). Lambs were weighed at birth (n=9-11/group).

RESULTS: Exposure to simulated shift work profoundly disrupted maternal central and peripheral rhythms in early and late pregnancy. Melatonin rhythms rapidly phased-shifted in response to the 12 h changes in light onset, but Clock gene expression rhythms remained abnormal 24-48 after phase shifts. At both stages of pregnancy, ewes currently housed in SW conditions took longer for blood glucose to return to fasting concentrations during IVGTT ($P<0.05$), but had similar glucose tolerance and insulin secretion, compared to ewes housed in control lighting. Despite these changes during pregnancy, gestation lengths and lamb birth weights were similar in SW and control groups.

CONCLUSIONS: Simulated shift work profoundly disturbs circadian rhythms and mildly impairs metabolic control during pregnancy in sheep. Long-term effects on progeny are currently under investigation.

S-075

Neonatal Heat-Shock Proteins in Pregnancies Complicated by Gestational Diabetes and Preeclampsia. Ana Mrkaic,[1] Barak Rosenn,[1] Ivana Stojanovic,[2] Samir Tivari.[3] *[1]Mount Sinai West Hospital, New York, NY, USA; [2]Medical Faculty, University of Nis, Nis, Serbia; [3]Rutgers University, Newark, NJ, USA.*

INTRODUCTION: Heat shock proteins (Hsp) are evolutionary conserved molecules with a pivotal role in cell survival. Their release is triggered by a variety of stressors and their presence in the extra-cellular space is considered a marker of cell damage. We hypothesized that cord blood concentrations of Hsp27 and Hsp70 is increased in pregnancies complicated by gestational diabetes (GDM) and preeclampsia (PIH).

METHODS: Pregnant women admitted for delivery at >28 weeks were divided into four groups, 30 in each group: healthy patients delivered vaginally (VAG), healthy patients delivered by C-section (CS), patients with PIH, and patients with GDM. Cord blood was collected at birth and frozen at -80°c and later assayed for concentrations of Hsp70 and Hsp27 using ELISA. Concentrations of Hsp and maternal characteristics were compared between the 4 groups using t-test, Chi square, Kruskal-Wallis, and Wilcoxon rank sum, as appropriate.

RESULTS: There were no differences between groups with respect to maternal age, gravidity, or ethnicity, and there were no statistically significant differences in the concentrations of Hsp70 or Hsp27 related to maternal age, BMI, weight, or gestational age. Hsp70 concentrations were positively associated with maternal intra-partum glucose levels ($\rho = 0.4122$, $p<0.05$). Gestational age, maternal BMI, and Hsp concentrations in the 4 groups are presented in the table. Concentrations of Hsp70 were significantly higher in the GDM group compared to the VAG and CS groups, but concentrations of Hsp27 were not statistically different amongst the groups.

	GDM[a]	PIH[b]	VAG[c]	CS[d]	P-value
Gestational Age (Mean (SD))	37.79 (2.42)	37.71 (2.47)	39.34 (1.48)	38.64 (2.74)	<0.05
BMI (kg/m^2)	30.6 (5.01)	32.93 (6.97)	27.29 (3.26)	33.02 (7.17)	<0.05
Weight (kg) (Mean (SD))	78.15 (13.32)	88.48 (18.28)	74.39 (8.67)	89.54 (20.19)	<0.05
Hsp27 (ng/ml) (Median [Q1-Q3])	0.84 [0.34-1.43]	0.86 [0.58-3.29]	0.88 [0.52-1.57]	0.71 [0.37-1.25]	>0.05
Hsp70 (ng/ml) (Median [Q1-Q3])	0.07 [0.03-0.20][a,c/a,d]	0.04 [0.02-0.08]	0.02 [0.00-0.07]	0.02 [0.01-0.04]	>0.05

CONCLUSIONS: In pregnancies complicated by GDM, neonatal Hsp70 is elevated and may serve as a sensitive marker for prenatal damage of fetal tissue.

S-076

POMC, MC4R and HNF4A Methylation Are Associated with Metabolic Components in Obese Children. Eun Jin Kwon,[1] Young Ah You,[2] Hae Soon Kim,[3] Eun Ae Park,[3] Su Jin Cho,[3] Young Ju Kim.[1] *[1]Ewha Womans University, Seoul, Korea; [2]Ewha Womans University, Seoul, Korea; [3]Ewha Womans University, Seoul, Korea.*

INTRODUCTION: To investigate whether the associations between the DNA methylation of proopiomelanocortin (POMC), melanocortin 4 receptor (MC4R) and hepatocyte nuclear 4 alpha (HNF4A) genes and metabolic components in Korean children.

METHODS: We analyzed DNA methylation of metabolic-related genes in blood from 41 obese and 79 normal children collected between 7 and 9 years of age by pyrosequencing. Serum triglyceride (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-c), insulin and glucose levels were measured using an automatic analyzer. Analysis of covariance (ANCOVA) analyses was used to assess the association between the DNA methylation status and metabolic indices.

RESULTS: In obese children, TG and insulin levels were increased, and HDL-c levels were decreased than normal-weight children ($P < 0.01$). Moreover, the methylation status of *HNF4A* were significantly higher in obese compared to normal-weight children. We found a significant correlation between methylation status of *POMC* and *MC4R* and HDL-c levels, between methylation status of *MC4R* and *HNF4A* and TC and insulin levels. TG levels was marginally significant associated with methylation status of *MC4R* ($P = 0.09$), TC levels were associated with methylation status of *POMC* and *HNF4A* ($P = 0.05$, respectively), In addition, HDL-c levels were related to methylation status of *POMC* and *HNF4A* ($P = 0.07$, respectively). In carbohydrate metabolism, insulin levels were related to methylation status of *MC4R* and *HNF4A* ($P < 0.05$, respectively).

CONCLUSIONS: These results suggest that *POMC, MC4R* and *HNF4A* methylation have a body mass index-independent association with metabolic indices in children. These findings provide evidence for identifying epigenetic modifications of altered metabolic indices and may be useful for risk assessment.

S-077

Impaired Ischemia Reperfusion Responses in Adult Male and Female Hearts of Offspring (F1) of Obese Rats. Carlos Ibáñez†,[1] Francisco Correa,[2] Gabriela Lira-León,[1] Luis A Reyes-Castro,[1] Francisco J Roldan,[2] Alejandro Silva-Palacios,[2] Mabel Buelna,[2] Cecilia Zazueta,[2] Peter W Nathanielsz,[3,4] Elena Zambrano*.[1] *[1]Instituto Nacional de Ciencias Medicas y Nutricion SZ, Mexico City, Mexico; [2]Instituto Nacional de Cardiologia Ignacio Chavez, Mexico City, Mexico; [3]University of Wyoming, Laramie, WY, USA; [4]Texas Biomedical Research Institute, San Antonio, TX, USA.*

INTRODUCTION: Maternal obesity (MO) predisposes F1 to cardiovascular disease (CD) that can be studied by ultrasound and the isolated heart.

METHODS: Female (F0) Wistar rats ate chow (C) or obesogenic diet (MO) from weaning through pregnancy and lactation. Non-sib male (M: n=5) and female (F: C n=8, MO n=7) F1 were weaned to chow. At postnatal day (PND) 550, basal echo function was determined. 2 d later hearts underwent 20 min *in vitro* global ischemia with 30 min reperfusion, fat depots dissected and total adipose tissue/body weight calculated. Insulin and glucose were measured.

RESULTS: Echocardiogram at rest was normal. Relative heart weight (M C=3.3±0.6, MO=4.2±0.6*; F C=3.3±0.5, MO=3.4±0.05, g/kg $p<0.05$), adiposity index and thoracic fat were higher in M MO F1 than C. F MO and C were similar. C M hearts recovered 78% function and C F 83% after 30 min reperfusion but MO M hearts only 28% and MO F hearts 52% of function, respectively. Heart rates (HR) were similar between genders during reperfusion. Fig 1.

**Figure(s) will be available online.*

Fig. 1: Left ventricular pressure (LVP) in F1 male (a) and female (b); HR F1 male (c) and female (d). M ± SEM t-test, n=5-8. C (circles), MO (triangles); * MO vs C, $p<0.05$.

CONCLUSIONS: There were no observable differences in echo evaluation at rest. Following the challenge of ischemia-reperfusion, MO hearts showed higher susceptibility to reperfusion damage in both sexes. The increased thoracic fact may play a local role. In addition, blood parameters indicated generalized insulin resistance (data not shown) which impairs cardiac function.

S-078

Antenatal Glucocorticoids Exposure Induces Left Ventricular Hypertrophy in the Adult Offspring in Sheep. Won Joon Seong, Angela G Massmann, Jie Zhang, Jorge P Figueroa*. *Wake Forest School of Medicine, Winston-Salem, NC, USA.*

INTRODUCTION: Exposure to glucocorticoids (GC) in the perinatal period is associated with several cardiometabolic alterations. We and others have shown elevations in blood pressure and increased vascular reactivity. The aim of the present study was to determine if the relatively minor elevation in blood pressure we observe can induce end organ damage.

METHODS: Pregnant sheep were treated with two IM doses of betamethasone (Beta, 0.17 mg/kg) or vehicle (V) 24-h apart at 80 days gestation and allowed to deliver at term. We harvested heart tissue from 18 mo sheep of both sexes treated with either vehicle (V; 8 females, 10 males) or Beta (9 females; 13 males). A slice of the heart cut across the ventricles at the junction of the upper 1/3 with the bottom 2/3 of the anterior aspect of the ventricular mass was obtained. High definition pictures were taken and Left (L) and right (R) ventricular and septal (S) thickness were obtained and analyzed with SigmaScan Pro. Data are expressed as Mean±SEM and were analyzed by ANOVA and two sample t test.

RESULTS: Although there was a trend for higher body weight in males, no significant differences were observed when analyzed by sex or treatment. We found a significant increase in left ventricular thickness in both males and females. L/S: L to S thickness ratio; R/S R to S ratio; L/R L to R ratio.The increase in wall thickness was restricted to the left ventricle. When ventricular thickness was normalized by septal thickness the significant Beta effect was still present. (*$p<0.05$ vs V).

**Figure(s) will be available online.*

CONCLUSIONS: Our data show that prenatal exposure to a single course of GC at 0.55 gestation has long-term effects on ventricular

growth. This increase in left ventricular thickness may be the result of the increase afterload, despite the relatively small magnitude. However, an alternative mechanism is that it may be the ventricular response to an abnormal visceral adipose tissue function. We suggest that an elevation in aldosterone either locally produced in the ventricle or from systemic origin may be a contributing factor. This hypothesis will be tested in future studies. HL 68728 and HD 04784.

S-079

A Potential Mechanism for Developmental Programming of Adult Cardiac Disease: Increased Apical Pericardial Fat (PCF) in 5.7 Year (Yr: Human Equivalent 20 Yr) Old Male but Not Female IUGR Baboon. Anderson H Kuo†,[1] Cun Li,[2] Peter W Nathanielsz,[2] Geoffrey D Clarke*.[1] *[1]University of Texas Health Science Center San Antonio, San Antonio, TX, USA; [2]University of Wyoming, Laramie, WY, USA.*

INTRODUCTION: IUGR is a common complication of pregnancy world-wide. Epidemiological studies show increased adult cardiac disease risks, metabolic dysfunction, and obesity in adults who were IUGR at birth. We demonstrated biventricular cardiac function decline in young adult IUGR baboons vs. age-matched normal birth weight baboons but the mechanism(s) remain unknown. Obesity is a well-recognized risk factor in cardiac disease. However, all fat depots are not equally implicated. PCF has a greater influence on cardiac function than fat at remote sites (PMID: 27391045) and associates with decreased right ventricular mass and end systolic volume (PMID: 27311062). PCF more closely predicts poor cardiac function than intramyocardial fat (PMC4788448). To assess whether coexistent PCF local fat may contribute to poor cardiac health in baboons who were IUGR, we quantified PCF by MRI in male control (CTL) and IUGR baboons.

METHODS: Pregnant baboons ate *ad lib* (CTL) or 70% *ad lib* diet in pregnancy and lactation with the result that their offspring were IUGR. The decrease in birth weight was moderate - approximately 11% in males and females. 3T MRI was used to quantify PCF with CMR 42 software (Circle Cardiovascular, Calgary, AB): IUGR (N=8Male, 8Female, 5.7 y; human equivalent 20 y) and age matched CTL (N=8Male, 8Female, 5.6 y).

RESULTS: Apical PCF thickness normalized for body surface area was higher in male IUGR (Fig 1) vs. male CTL baboons (20.0 ± 3.6 vs 12.2 ± 1.5 mm/m^2 M ± SEM, p = 0.04) with no difference in females (IUGR 21.6 ± 1.4 vs CTL 19.9 ± 3.3 mm/m^2).

**Figure(s) will be available online.*

Fig. 1 Cardiac apical fat thickness normalized for body surface area. M ± SEM. p **< 0.05.** n= 8 per group.

CONCLUSIONS: Increased apical PCF is seen in male but not female IUGR baboons. This increased local cardiac fat may act as a source for local distribution of inflammatory cytokines and other harmful adipose tissue products directly to the myocardium and increase the risk for cardiac disease.

S-080

Developmental Programming: Ectopic Lipid Accumulation in Liver and Muscle Likely Contributes to Insulin Resistance in Prenatal Testosterone-Treated Female Sheep. Vasantha Padmanabhan*, Muraly Puttabyatappa†. *University of Michigan, Ann Arbor, MI, USA.*

INTRODUCTION: Prenatal exposure to excess testosterone (T) disrupts reproductive and metabolic systems in the female sheep resulting in a polycystic ovary syndrome (PCOS) phenotype. The metabolic disruptions induced by prenatal T excess include peripheral insulin resistance (IR), reduced adipocyte size, dyslipidemia and tissue-specific changes in insulin sensitivity with muscle and liver but not adipose tissue being insulin resistant. The dyslipidemia in prenatal T-treated sheep, in the face of the reduced adipocyte size, could lead to ectopic accumulation of lipids in insulin target tissues, thus negatively impacting insulin sensitivity and contributing to the development of IR in this model.

Objective: To determine if the insulin resistant state of muscle and liver in prenatal T-treated sheep are associated with ectopic accumulation of lipids.

METHODS: To test this and determine if such perturbations are programmed by androgen or insulin (T excess induces maternal hyperinsulinemia), control, prenatal T- (100mg T propionate twice a week from days 30-90 of gestation), prenatal T plus androgen receptor antagonist, flutamide (15mg/kg/day)-, and prenatal T plus insulin sensitizer, rosiglitazone (0.11mg/kg/day)-treated female sheep were studied at 21 months of age. Tissue accumulation of lipids was assessed by triglyceride (TG) assay and oil red O staining and analyzed by one-way ANOVA followed by Tukey's test.

RESULTS: Oil red O staining showed increased ($p<0.05$) presence of lipid droplets in liver and intramuscular fat cells in prenatal T-treated group. Prenatal T excess also increased liver and muscle TG content ($p<0.05$). Neither androgen antagonist nor insulin sensitizer co-treatment prevented the ectopic fat accumulation.

CONCLUSIONS: Prenatal T-treatment leads to ectopic accumulation of lipids in liver and muscle that potentially arises from the reduced ability of the smaller adipocytes to store fat. The increased buildup of lipids in liver and muscle in this well-validated model of PCOS phenotype may contribute to the development of impaired insulin sensitivity in these insulin target tissues. Lack of effects of anti-androgen and insulin sensitizer to prevent ectopic lipid accumulation suggests potential mediation by estrogen, considering gestational T excess also increases fetal estradiol levels.

Support: NIH P01 HD44232.

S-081

Rescue of the Developmental Programming of Cardiovascular Dysfunction with the Mitochondria-Targeted Antioxidant MitoQ. AM Spiroski†,[1] Y Niu,[1] KL Skeffington,[1] MP Murphy,[2] DA Giussani*.[1] *[1]University of Cambridge, Cambridge, United Kingdom; [2]MRC Mitochondrial Biology Unit, Cambridge, United Kingdom.*

INTRODUCTION: Previous work suggests that maternal treatment with vitamin C in hypoxic pregnancy prevents the programming of cardiovascular dysfunction via nitric oxide (NO)-mediated mechanisms (Giussani *et al.*, *PLOS ONE* **7(2)**:e31017, 2012). However, the efficacious antioxidant dose of vitamin C used in animal paradigms is toxic to humans. MitoQ, a mitochondria-targeted antioxidant which improves NO bioavailability and ageing-associated endothelial dysfunction in mice (Gioscia-Ryan *et al. J Physiol.* **592(12)**:2549, 2014) has high therapeutic efficacy and low oral toxicity (Smith & Murphy. *Ann NYAS* **1202(1)**:96, 2010). We hypothesised that MitoQ would be a suitable alternative candidate for preventing the programming of cardiovascular dysfunction in adverse pregnancy.

METHODS: Pregnant Wistar dams were exposed to normoxia (N; 21% O_2) or (hypoxia (H; 13% O_2) from 6-20 days gestation ± MitoQ (NM and HM, respectively) provided at 200μM in drinking water. Offspring were maintained in normoxia to 4 months of age. One male per litter was selected for either conscious *in vivo* cardiovascular assessment or *ex vivo* cardiac Langendorff analysis. For *in* vivo assessment, offspring were instrumented with femoral vascular catheters and a flow probe placed in the contralateral leg. Basal and stimulated *in vivo* cardiovascular function was determined using the α_1-adrenergic agonist phenylephrine (PE) and the NO-donor sodium nitroprusside (SNP) 4-5 days post-operatively.

RESULTS: Despite similar basal arterial blood pressure (Fig. 1A), offspring of hypoxic pregnancy had greater femoral blood flow (B), enhanced pressor (C) and femoral vasopressor (D) responses to PE, a significantly enhanced reactive hyperaemic response (E) and altered cardiac baroreflex sensitivity (F). Offspring of hypoxic pregnancy also showed significant isolated cardiac systolic (G) and diastolic (H) dysfunction. Maternal treatment with MitoQ was protective on all outcome measures.

CONCLUSIONS: Maternal MitoQ intervention prevents the programming of cardiovascular dysfunction in pregnancy complicated by developmental hypoxia.

Supported by *The British Heart Foundation.*

**Figure(s) will be available online.*

S-082

Embryonic Development Is Associated with Periconceptional Maternal One-Carbon Metabolism and Fetal Size: The Rotterdam Periconception Cohort. Francesca Parisi, Melek Rousian, Anton K Koning, Sten P Willemsen, Eric A Steegers, Règine P Steegers-Theunissen. *Erasmus MC, Rotterdam, Netherlands.*

INTRODUCTION: The periconceptional period is crucial to improve pregnancy and future health outcomes. We studied associations between embryonic development and periconceptional maternal one-carbon (I-C) metabolism, and subsequent fetal size.

METHODS: 234 singleton ongoing strictly dated pregnancies without congenital malformations were enrolled before 8 weeks of gestation in a prospective periconception cohort between 2010 and 2014. Longitudinal transvaginal three-dimensional ultrasound (3D US) scans were performed from 6^{+0} to 10^{+2} weeks of gestation. Embryonic development was defined using internal and external morphological criteria of the Carnegie classification in a virtual reality system. Maternal serum vitamin B12 and plasma total homocysteine (tHcy) were assessed at enrollment. Z-scores were calculated for mid-pregnancy estimated fetal weight (EFW) and birth weight (BW). Associations between Carnegie stages, I-C biomarkers and fetal size parameters were investigated using linear mixed models.

RESULTS: We performed a median of three 3D US scans per pregnancy, resulting in 600 good quality datasets for the Carnegie stage annotation (80.5%). Vitamin B12 was positively associated with embryonic development (β=0.001 (95% CI: 0.000; 0.002), p< 0.05), with a 1.4-day delay in embryonic development in case of low (-2 standard deviation (SD), 73.4 pmol/l) compared to high concentrations (+2SD, 563.1 pmol/l). tHcy was negatively associated with embryonic development (β =-0.08 (95% CI: -0.14; -0.02), p<0.01), with high concentrations (+2SD, 10.4 µmol/l) resulting in a 1.6-day delay in embryonic development compared to low concentrations (-2 SD, 3.0 µmol/l). Embryonic development was positively associated with EFW (β=0.69 g (95%CI: 0.51; 0.86), p<0.001). Positive associations were detected between embryonic development and BW in males (β=0.37 g (95%CI: 0.04; 0.70), p<0.05). In females, embryonic development was negatively associated with BW (β= -0.36 g (95%CI: -0.62; -0.10), p≤0.01).

CONCLUSIONS: Periconceptional maternal I-C biomarkers are associated with embryonic development. We suggest that first trimester embryonic morphological assessment combined with sex-specific strategies could better define normal development and predict fetal growth later in pregnancy.

S-083

Characterisation and Identification of the Placental Androgen Receptor Isoforms and Its Relationship to Fetal Growth. Vicki L Clifton*, Ashley Meakin, Zarqa Saif. *Mater Medical Research Institute-University of Queensland, Brisbane, QLD, Australia.*

INTRODUCTION: The male fetus continues to grow normally in adverse maternal environments during pregnancy often only being growth restricted in an environment of multiple complications. We have previously identified that males may continue to grow normally in complicated pregnancies by instituting a state of glucocorticoid resistance in the placenta. However the mechanism that drives continued growth in males remains unknown. Unlike the adult, both cortisol and testosterone increase in response to a maternal stress during pregnancy in both male and female fetuses raising the question of whether continued male growth may be mediated by sex-specific differences in placental androgen receptor (AR) expression. Recent studies report there are different isoforms of the AR that regulate sensitivity to androgens in cancer cells. We sort to identify which AR isoforms are present in the human placenta and if there is an association with factors that regulate fetal growth.

METHODS: Placentae from pregnancies complicated by asthma (n=41) were compared to healthy pregnancies (n=23). Western blot analysis was used to identify the AR isoforms in the human placental cytosolic and nuclear fractions. AR and IGF-1 mRNA were measured using qPCR. Data was analysed using SPSS v17.

RESULTS: We identified 11 proteins that specifically bind to an anti-AR antibody as indicated by a preabsorption control. The proteins ranged from molecular weight (MW) 150 kDa to 37 kDa. Several proteins have been previously reported in other organs which include the full length AR (AR FL), 100 kDa, AR -75, 55 kDa, and AR-45. All isoforms were downregulated in male placentae of asthmatic pregnancies relative to healthy pregnancies (Mann-Whitney U test, P<0.05). AR- 45 was the most abundantly expressed protein all placentae (Mann-Whitney U test, P<0.05). AR mRNA and AR-45 protein were positively correlated with IGF-1 mRNA (Spearmans, P<0.05) in only male placentae relative to female placentae.

CONCLUSIONS: These data demonstrate for the first time there are several AR isoforms present in the human placenta which may be central to regulating fetal growth. Continued male growth in adverse conditions may be dependent on the expression of different AR isoforms regulating an increase in IGF-1.

S-084

Maternal Obesity (MO) Up-Regulates 11β-Hydroxysteroid Dehydrogenase Type 1(11βHSD1) and the Mineralocorticoid Receptor (MR) in the Late Gestation Baboon Fetal Frontal Cortex (FC). Shanshan Yang,[1,2,3] Diana Castro-Rodriguez,[2,3] Peter W Nathanielsz,[2,3] Cun Li*.[2,3] *[1]The First Affiliated Hospital of Harbin Medical University, Harbin, Heilongjiang, China; [2]Texas Biomedical Research Institute, San Antonio, TX, USA; [3]University of Wyoming, Laramie, WY, USA.*

INTRODUCTION: We previously showed that the glucocorticoid receptor (GR) is up regulated in the FC of fetuses of MO mothers. We have now investigated the 11βHSD system and MR to determine if there is further evidence for increased local production of cortisol and activity via MR.

METHODS: Female baboons, similar age and weight were randomly assigned to control (CTR, Purina Monkey diet containing 12% energy fat, 0.29% glucose, 0.32% fructose energy 3.07 kcal/g. n = 25) or MO diet (n = 19; 45% energy fat, 4.62% glucose, 5.64% fructose, and 2.32% sucrose, energy 4.03 kcal/g and free access to high-fructose sodas) for at least 9 months before pregnancy. Diets were maintained through pregnancy. Fetal FC was collected at Cesarean section under general anesthesia at 90% gestation. MR, 11β-hydroxysteroid dehydrogenase type 1 and 2 (11βHSD1 and 2) were measured by Immunohistochemistry (IHC) with Image J quantification of stained fraction. Analysis Student's t-test: $P < 0.05$.

RESULTS: % area stained for MR and 11βHSD1 were greater in gray (GM) and white matter (WM) of MO fetal FC, while GM 11βHSD2 protein decreased ($P < 0.05$).

**Figure(s) will be available online.*

Figure 1. MR, 11βHSD1 and 11βHSD2 images and protein expressed as % area stained in brain FC of 0.9 gestation control fetuses -mothers fed normal diet (CTR, n=25, F=13; M=12) or maternal obese fetuses, mother fed a high energy diet (MO, n=19, F=9; M=10) Data are expressed as mean ± SEM. * $p < 0.05$.

CONCLUSIONS: The observed changes would tend to increase local cortisol production in the FC potentially contributing to the observed programming of offspring of MO mothers to stressful, anxiety and depressive mood.

S-085

Behavioral Changes in Adult Male Baboons Exposed to Synthetic Glucocorticoids (sGC) in Fetal Life Indicate Increased Stress and Accelerated Aging. Hillary F Huber†,[1] Thad Q Bartlett,[2] Cun Li,[1] Susan L Jenkins,[1] Kenneth G Gerow,[3] Peter W Nathanielsz*.[1] *[1]University of Wyoming, Laramie, WY, USA; [2]The University of Texas at San Antonio, San Antonio, TX, USA; [3]University of Wyoming, Laramie, WY, USA.*

INTRODUCTION: Mothers with threatened premature delivery receive sGC to accelerate fetal lung development, reducing neonatal mortality and morbidity. There are few investigations of long-term effects in nonhuman primates. We conducted noninvasive behavioral studies in a male baboon model (*P. hamadryas*, ages 9-13 yrs) with two hypotheses: 1. Adult GC baboon males exhibit decreased walking speed, a biomarker of aging. 2. Adult GC baboon males show increased aggressive behavior, an indicator of stress.

METHODS: Mothers received 3 courses of 2-day IM injection of betamethasone (175μg/kg day, sGC group) versus saline (CTR group) at 0.6, 0.64, and 0.68 gestation. Behavioral observations (n=5 GC, 5 CTR) were conducted in Observer XT (v10), including aggression (e.g. biting), dominance (e.g. mounting), and self-directed behavior (e.g. hair pulling). Behavior frequencies were compared between GC and CTR with *t*-tests. Walking speed (n=5 GC, 29 CTR) was measured with a grid and stopwatch system, with linear regression to test if GC walk at expected speed for age.
RESULTS: GC walked at speeds below the regression line describing the normal speed-age relationship. The slope for CTR was -1.84, while for GC it was more steeply negative at -5.92. GC exhibited increased frequency of one dominant behavior (receive present, $p<0.01$) and decreased frequency of three submissive behaviors (flee, $p=0.03$; present, $p=0.1$; receive mount, $p=0.03$). GC did not show increased aggression or self-directed behavior.
CONCLUSIONS: Adult male baboons exposed to prenatal GC display behavioral changes indicative of increased stress and accelerated aging. Walking speed is associated with morbidity and mortality and the GC males show signs of walking slower for their age than CTR. Heavier weight decreases speed, and GC males are heavier than CTR. We expected to see increased aggression in adulthood as a marker of prenatal stress, but instead saw alterations to dominance-related behavior, also consistent with amplified stress. Since stressful experiences are known to accelerate aging, these two sets of behavioral findings may be intertwined. GC treatment during pregnancy is effective, but exploration of long-term effects is necessary to prevent and treat unwanted outcomes. (HD-OD011183).

S-086

Offspring Sex and Maternal Diet Impact the Effects of Maternal Obesity on Offspring Neurobehavior. Larissa H Mattei†,[1] Rachel Zeuner†,[2] Ingy Khattaby†,[3] Diana W Bianchi,[1] Andrea G Edlow*.[1] [1]*Tufts Medical Center/Tufts SOM, Boston, MA, USA;* [2]*Tufts SOM, Boston, MA, USA;* [3]*Medisys Health Network, Queens, NY, USA.*
INTRODUCTION: Maternal obesity (MATOB) is associated with increased risk of neurodevelopmental morbidity in offspring, including autism spectrum disorder and anxiety. Using a mouse model of maternal diet induced obesity, we evaluated the effects of pregnancy diet and offspring sex on social behavior and anxiety of offspring.
METHODS: Female (F) C57BL/6 mice were fed a 60% high-fat diet (HFD) or a 10% fat control diet (CD) for 12 wks prior to mating. In pregnancy, obese dams continued on HFD (HFD/HFD), or transitioned to CD (HFD/CD). Lean dams remained on CD (CD/CD). Offspring were weaned to CD at 3 wks. Male (M) and F offspring underwent neurobehavioral testing at 4 and 11 wks (juvenile/adult). Social behavior was evaluated with 3-chamber social interaction test (3ChSI). Anxiety-like behavior was evaluated with open field test (OF). 25-40 offspring/sex/diet group were evaluated.
RESULTS: HFD/HFD offspring demonstrated aberrant social behavior compared to CD/CD, spending significantly more time near a novel mouse in juvenile/adult life ($p<0.01$, Fig 1). Significant differences persisted in adult Ms only ($p=0.009$).
**Figure(s) will be available online.*
Pregnancy diet significantly affected social behavior; HFD/CD adult offspring had no preference for novel mouse vs empty cage. HFD/HFD Ms had significantly increased anxiety compared to CD/CD in juvenile and adult OF (Fig 2), with increased freezing at 4 wks ($p<0.01$) and slower velocity at 11 wks ($p<0.01$).
**Figure(s) will be available online.*
CONCLUSIONS: MATOB is associated with aberrant social behavior and increased anxiety in juvenile and adult offspring, with significant effects persisting into adulthood in Ms only. Striking differences in social behavior of HFD/HFD vs HFD/CD offspring highlight the impact of maternal diet.

S-087

Maternal Protein Restriction (MPR) in Pregnancy and/or Lactation Impacts Sperm Aging without Affecting Fertility in Male Rat Offspring (F1). Guadalupe L Rodríguez-González†,[1] Claudia C Vega,[1] Luis A Reyes-Castro,[1] Lourdes Boeck,[1] Carlos Ibáñez†,[1] Peter W Nathanielsz,[2,3] Fernando Larrea,[1] Elena Zambrano*.[1] [1]*Instituto Nacional de Ciencias Medicas y Nutricion SZ, Mexico City, Mexico;* [2]*University of Wyoming, Laramie, WY, USA;* [3]*Texas Biomedical Research Institute, San Antonio, TX, USA.*
INTRODUCTION: Nutrient restriction in development has programming effects on male fertility via increased reactive oxidative stress (ROS). We determined effects of MPR in pregnancy and/or lactation on a male reproductive aging. .
METHODS: We studied male F1 of rats fed control (C) (20% casein) or restricted (R) (10% casein) isocaloric diet in pregnancy (first letter) and/or lactation (second letter) - CC, RR and CR. After birth all rats ate C diet. At postnatal day (PND) 110 and 850 male F1 were euthanized and epidiymal tail and vas deferens sperm obtained to measure: 1) ROS, 2) superoxide dismutase, 3) sperm quality (concentration, viability), 4) Fertility rate.
RESULTS: At both ages ROS was higher in RR and CR vs CC. SOD activity was reduced only by PND 850. Sperm concentration was reduced at PND 110 in RR, whereas CR viability was reduced at both ages and only at PND 850 in RR. In CC and RR, ROS was not affected by age while in CR it was slightly decreased at PND 850. In CC, SOD activity did not change with age but was reduced in RR and CR. Sperm quality decreased in all groups, however reduction was greater in RR and CR. No changes were observed in fertility (Figure 1A – 1E).
**Figure(s) will be available online.*
Fig 1. Sperm at different PND: A) ROS, B) SOD, C) concentration, D) viability; E) fertility. M ± SEM, n=4-6, $p<0.05$ data not sharing a letter on same maternal diet. Open - CC , closed - RR, striped bar CR. * $p<0.05$ vs CC at same age.
CONCLUSIONS: We reported MPR only in pregnancy increases testicular and sperm OS leading to premature aging of male F1 reproductive capacity (1). In contrast, MPR during pregnancy and/or lactation increases ROS and reduces sperm quality but not fertility showing the complexity of programing effects on fertility. 1) Age (Dordr). 2014;36, 9721.

S-088

Effect of Very Advanced Maternal Age on Early Neonatal Outcomes After Assisted Reproductive Technology. Amir Shamshirsaz,[1] Amirhossein Moaddab,[1] Haleh Sangi-Haghpeykar,[1] Sara Arian,[1] Susan Ramin,[1] Zhoobin Heidari-Bateni,[1] Hadi Erfani,[1] Karin Fox,[1] Steven Clark,[1] Michael Belfort,[1] Gary Dildy,[1] Laurence McCullough,[2] Frank Chervenak,[2] Alireza Shamshirsaz.[1] [1]*Baylor College of Medicine, Houston, TX, USA;* [2]*Weill Medical College of Cornell University/New York Presbyterian Hospital, New York, NY, USA.*
INTRODUCTION: To assess early neonatal outcomes between assisted reproductive technology (ART) pregnancies in women aged <45 versus ≥45 years of age.
METHODS: In a population-level analysis study, all live births by ART identified on birth certificate data between 2011 and 2014 were extracted (n[thinsp]=[thinsp]101,494) using data from the CDC-NCHS. We investigated and compared neonatal outcomes on the basis of conditions routinely listed on birth certificates. Risks of various outcomes were compared between neonates born to women who received ART <45 years with those infants born to women ≥45 years of age. Outcomes of interest included gestational age at delivery, birth weight, APGAR at 5 and 10 minutes, immediately assisted ventilation, assisted ventilation>6 hours, NICU admission, surfactant therapy, use of steroids, antibiotic therapy, seizures, chromosomal disorders, Down's syndrome, anencephaly, gastroschisis, spina bifida/meningomyelocele, omphalocele, congenital diaphragmatic hernia, and cyanotic congenital heart disease.
RESULTS: Between 2011 and 2014, ART pregnancies in women aged ≥45 years comprised 5.4% of total live births secondary to ART in the U.S. The risk of preterm delivery and low birth weight did not significantly change with advanced maternal age. Although risk for NICU admission

was higher in offspring of women ≥45 years of age compared to women <45 years (28.28% vs. 25.77%, RR: 1.10, CI: 1.05-1.15), these infants were less likely to undergo immediate assisted ventilation (RR: .88, .81-.96). Women ≥45 years at the time of ART was not associated with increased risk of conditions like chromosomal disorders, anencephaly, gastroschisis, neural tube defects, omphalocele, congenital heart defects, or cyanotic heart defects.

CONCLUSIONS: Early neonatal outcomes were similar between ART pregnancies in women aged ≥45 years and women aged <45 years. However, these data should be interpreted with caution because of potential confounding by higher rates of donor eggs used in older women, the exact rates for which we were unable to ascertain from the available data.

S-089

Ten-Year Trend in Hypertensive Disorders in Pregnancy in the United States. Amir Shamshirsaz, Amirhossein Moaddab, Alireza Shamshirsaz, Christina Davidson, Gary Dildy, Michael Belfort, Steven Clark. *Baylor College of Medicine, Houston, TX, USA.*

INTRODUCTION: To evaluate national trends in the incidence of chronic hypertension (CHTN), gestational (pregnancy induced and preeclampsia) hypertension (GHTN), and eclampsia in pregnant women in U.S. between 2005-2014.

METHODS: We used live births data from the CDC-NCHS using the VitalStats online data access.We calculated and compared incidence rate of CHTN, GHTN, and eclampsia in pregnancies resulting in a live birth.

RESULTS: There were 40,922,512 live births in the U.S. The overall incidence (cases per 1,000 live birth deliveries) of CHTN, GHTN, and eclampsia over the study period were 12.9, 42.9, and 2.9, respectively. At the national level, rates of CHTN and GHTN increased significantly over the study period. The national rate of CHTN increased from 10.3 in 2005 to 15.8 in 2014 ($p<0.001$) and the rate of GHTN increased from 39.8 in 2005 to 50.8 in 2014 ($p=0.001$). However, the national rate of eclampsia was unchanged. (Figure 1).

**Figure(s) will be available online.*

State-by-state trends in all conditions are depicted in Figure 2.

**Figure(s) will be available online.*

Statistically significant increasing trends for CHTN were observed in all but 5 states. California had the lowest rate of CHTN and GHTN. Delaware and Kentucky had the highest rate of CHTN and GHTN, respectively.

CONCLUSIONS: Rates of both CHTN and GHTN increased significantly in the U.S. between 2005-2014. However, no associated increase in the rate of eclampsia was seen. Using eclampsia rate as a surrogate of good obstetric care in hypertensive women, these data support the value of current practice recommendations for hypertensive disease, and suggest broad compliance with such recommendations. Our state-specific data may assist state and regional organizations in directing quality initiatives toward the management of hypertensive disease in states where it is most needed.

S-090

Effect of Very Advanced Maternal Age on Maternal Outcomes After Assisted Reproductive Technology. Amir Shamshirsaz,[1] Amirhossein Moaddab,[1] Haleh Sangi-Haghpeykar,[1] Sara Arian,[1] Hadi Erfani,[1] Zhoobin Heidari-Bateni,[1] Susan Ramin,[1] Karin Fox,[1] Frank Chervenak,[2] Laurence McCullough,[2] Steven Clark,[1] Michael Belfort,[1] Gary Dildy,[1] Alireza Shamshirsaz.[1] *[1]Baylor College of Medicine, Houston, TX, USA; [2]Weill Medical College of Cornell University/New York Presbyterian Hospital, New York, NY, USA.*

INTRODUCTION: To compare maternal characteristics and outcomes between women with assisted reproductive technology (ART) <45 years of age and ≥45 years of age.

METHODS: In a population-level analysis study, all live births by ART procedures identified on birth certificate data between 2011 and 2014 were extracted (n[thinsp]=[thinsp]101,494) using data from the Centers for Disease Control and Prevention's National Center for Health Statistics. We investigated and compared maternal outcomes on the basis of conditions that appear on the birth certificates. Risk of various maternal outcomes were compared between women who received ART <45 years of age and those receiving this procedure ≥ 45 years including gestational hypertension, gestational diabetes, induction of labor, augmentation of labor, mode of delivery, use of antibiotics, anesthesia, chorioamnionitis, perineal laceration, uterus rupture, unplanned hysterectomy, transfusion, premature rupture of membranes, and admission to ICU.

RESULTS: Of the 101,494 reported ART pregnancies, 95,972 (94.6%) live infants were delivered by women less than 45 years old and 5,522 (5.4%) live infants were delivered by women ≥45 years. Most live births secondary to ART occurred in multiparous women. ($P<.001$) Among medical and obstetrical complications, gestational hypertension (RR: 1.46, CI: 1.37-1.55), gestational diabetes (RR: 1.34, CI: 1.30-1.49), eclampsia (RR: 1.50, CI: 1.11-2.01), unplanned hysterectomy (RR: 3.48, CI: 2.49-4.86), ICU admission (RR: 2.02, CI: 1.54-2.66), and maternal transfusion (RR: 1.50, CI: 1.24-1.82) were more frequent in women ≥45 years. The risk for these conditions remained significantly higher even after adjusting for potential confounders including demographic, lifestyle, health, and socioeconomic characteristics.

CONCLUSIONS: Despite the low absolute risks, women aged 45 years and older are faced with more medical and obstetrical complications and an increased risk for maternal morbidity compared to their younger counterparts, even after adjusting for several factors. This risk should be considered when counseling patients.

S-091

Use of a Novel Decision Aid for Prenatal Aneuploidy Screening: A Pilot Study. Laura Carlson†,[1] Sally Harris,[2] Emily Hardisty,[1] Neeta L Vora*.[1] *[1]University of North Carolina at Chapel Hill, Chapel Hill, NC, USA; [2]University of North Carolina at Chapel Hill, Chapel Hill, NC, USA.*

INTRODUCTION: Decision aids are known to improve knowledge and decisional conflict surrounding important screening and treatment decisions, including aneuploidy screening. Prior decision aids studied for prenatal use did not include cell-free DNA. In a pilot study, we aimed to evaluate a novel iPad-based decision aid (DA) incorporating cell-free DNA prior to initiating a randomized controlled trial.

METHODS: English and Spanish-speaking women at less than 22 weeks gestation with a singleton pregnancy were eligible. Women were excluded if they had previously undergone aneuploidy screening in the current pregnancy.

The DA was constructed with input from MFM physicians and genetic counselors at a 10th grade reading level. A modification of a validated knowledge questionnaire and low-literacy decisional conflict scale (DCS) questionnaire were administered to assess these domains. All patients completed the knowledge questionnaire, followed by self-administration of the DA where they indicated their testing preference . They then had genetic counseling and repeated the knowledge questionnaire and DCS. A questionnaire soliciting feedback on the DA was administered to all participants. Analyses were performed using t-test and ANOVA as appropriate.

RESULTS: Demographic characteristics that were collected included age, gestational age, parity, education level, employment, primary language, and history of prior genetic counseling. Mean knowledge score was 66% prior to aid completion and 77% following aid use. Mean knowledge improvement was 1.2 questions, though the difference in pre- and post-knowledge was not statistically significant ($p=0.07$). Mean knowledge change did not differ by primary language, education, or prior genetic counseling.

Mean DCS was 3.2 of 40, indicating a low level of decisional conflict, and did not differ by primary language, education, or history of prior genetic counseling. Seven women modified their screening or testing plan following genetic counseling. Women in general felt that the app was easy to navigate and understand.

CONCLUSIONS: This DA showed a trend toward improved patient knowledge in this pilot study, though our study was not powered for detection of this outcome. Decisional conflict was low. One-third of women ultimately changed their testing preference following genetic counseling.

S-092

Cell-Free Fetal DNA Screening: How It Has Affected the Choices of Women with Advanced Maternal Age. Zainab Al-Ibraheemi†, Barak Rosenn*, Natalie Porat†, Dyese Taylor†, Heather Fisher, Meredith Kalberer†. *Mount Sinai West, New York, NY, USA.*

INTRODUCTION: Cell-free fetal DNA (cffDNA) has recently been adopted as a method of screening pregnant women for specific fetal aneuploidies. Despite this being a limited screening test, many women opt to forgo the accuracy and additional information available through invasive diagnostic procedures to avoid their associated risks. The purpose of this study was to investigate recent trends in screening and testing for aneuploidy in pregnant women of advanced maternal age (AMA).

METHODS: This was an IRB approved retrospective cohort study that included all women who were to be 35 years or older at delivery (AMA) and were referred in their first trimester to our genetic division for consultation between January 2010-December 2015. In addition to nuchal translucency (NT) screening, all patients were offered cffDNA screening, chorionic villus sampling (CVS), or amniocentesis. The proportion of patients choosing each of the 3 options was determined in 6 month intervals over the entire period, and logistic regression was used to examine trend over time.

RESULTS: A total of 8,476 patients were referred for genetic counseling during the study period, of whom 5188 (61%) were AMA. Of these, 810 (15.8%) had an invasive procedure [640 (12.3%) amniocentesis and 170 (3.3%) CVS], 2,791 (54%) had cffDNA, 1,587 (30.5 %) chose not to have testing, and 37 women (0.7%) had both cffDNA and invasive testing. The percentage of patients opting for invasive procedures declined significantly over time from 38% in 2010 to 2% in 2015 (p< .0001), at an average of 29% (95% confidence interval 27%, 31%) reduction every 6 months. The rate of women opting for cffDNA rose precipitously from 28% in 2012, when it was first offered, to 91% in 2015 (p <.0001), at an average of 66% (95%CI 57%, 76%) every 6 months

**Figure(s) will be available online.*

CONCLUSIONS: Screening for aneuploidy with cffDNA has been widely adopted by AMA women and is expected to result in the continuing decline of invasive testing. It is very likely that future generations of MFM sub-specialists will not have the opportunity to acquire the necessary skills to perform these procedures, when needed.

S-093

Umbilical Vein Flow Calculation Methods: Correlation with Each Other and Umbilical Artery Pulsatility Index. Diane Gumina,[1] Nicholas Behrendt,[1,2] Mary Pinter,[1] Allison Gillan,[1] Henry Galan,[1,2] John Hobbins*.[1] *[1]University of Colorado School of Medicine, Aurora, CO, USA; [2]Colorado Fetal Care Center, Aurora, CO, USA.*

INTRODUCTION: Reduction in umbilical vein flow (UVF) is an early marker of pathologic fetal growth restriction (FGR), and in many cases precedes umbilical artery Doppler abnormalities. The UVF is calculated using the time-averaged maximum velocity (TAMAX) and the area of the vein. Previously published UVF studies determined the area of the vein by measuring the diameter from a longitudinal segment of a free loop of cord. This diameter is then used to calculate area ($a=\pi r^2$). As ultrasound has advanced, many ultrasound machines are now capable of calculating the area of an ellipse directly. As the shape of blood vessels can vary, we hypothesized that generating an area from a cross-sectional view of the umbilical vein would produce more accurate results than the traditional area calculation.

METHODS: In this prospective observational study, 49 patients identified as FGR (estimated fetal weight <10th%) were followed serially between the gestational ages of 24 and 38 weeks. Umbilical vein flow was calculated using the formula: UVF= (TAMAX cm/s)(vein area cm2)(60)(0.5). Area was calculated using either the diameter of vein measured from a longitudinal view or calculated by a GE E10 Voluson ultrasound machine using the area ellipse function in a cross-sectional view. Each UVF calculation was also compared to the umbilical artery pulsatility index (PI). Results were correlated using a Spearman correlation.

RESULTS: UVF calculated from both area measurement methods agreed with each other when correlating calculated values (r=0.7845, p=<0.0001) and calculated values normalized by estimated fetal weight (kg) (r=0.7356, p=<0.0001). The ultrasound area function showed a greater correlation to umbilical artery PI than the traditional calculation (r=-0.5374, p=<0.0001 vs. r=-0.4504, p=<0.0001).

CONCLUSIONS: There was a strong correlation between both methods. However, the ellipse function allows for the analysis of actual vessel shape as opposed to a theoretical calculated shape. The ellipse function method correlates better with umbilical artery PI indicating that it is a more sensitive method for determining umbilical vein flow.

S-094

Sex Specific Weight Elevation in Adult Progeny of Mothers with Pregestational Diabetes. Rolanda L Lister,[1] Francine Hughes,[2] Etoi Garrison,[1] Bin Zhou.[3] *[1]Vanderbilt University Medical Center, Nashville, TN, USA; [2]New York University, New York, NY, USA; [3]Albert Einstein College of Medicine, Bronx, NY, USA.*

INTRODUCTION: Maternal diabetes is a well-recognized risk factor for childhood obesity, metabolic syndrome and cardiovascular disease in adulthood. Moreover, children of diabetic mothers are more likely themselves to develop Type 2 diabetes mellitus. The objective is to compare the adult weight of male and female progeny exposed to pregestational maternal diabetes and euglycemic controls in a murine mode.

METHODS: Hyperglycemia was induced in wild type 8-week old CD-1 female mice with a one time intraperitoneal injection of 150 mg/kg of streptozotocin (STZ) prior to mating. Both groups were mated. The offspring were designated diabetic males (n=9), diabetic females (n=9), control males (n=9) and control female(n=8). Adult weights were measured at 8 months of age. Student t-test was used for statistical analysis. P<0.05 was considered significant.

RESULTS: Only adult male progeny exposed to maternal diabetes exhibited significantly increased weight (65.03+/-6.32 grams grams) as compared to controls (53.9+/- 11.2; P=0.018). There were no significant weight differences in the adult female progeny born to diabetic dams (52.5 +/- 16.6 grams) versus euglycemic dams (66+/- 17.77 ; P=.111).

CONCLUSIONS: Elevated adult weight was observed in male progeny of diabetic dams. More exploration needs to be done to elucidate the mechanism for these observed sex specific differences in adult male weight gain.

S-095

Effects of Pregnancy and Obesity on Vitamin D (D) Status and Metabolism in a Baboon Model. Eugenia Mata-Greenwood,[1] Hillary F Huber,[2] Cun Li,[2] Peter W Nathanielsz.[2] *[1]Loma Linda University, Loma Linda, CA, USA; [2]University of Wyoming, Laramie, WY, USA.*

INTRODUCTION: Human studies suggest that obesity correlates with vitamin D insufficiency which contributes to obesity-related disorders. Our aim was to characterize vitamin D status and metabolism in a baboon model of obese pregnancy.

METHODS: We studied lean and obese non-pregnant baboons and lean and and obese pregnant baboons at 0.9 gestation. Plasma 25-hydroxy and 1, 25-dihydroxy-vitamin D metabolites were analyzed using ELISA. CYP24a1 (vitamin D inactivation enzyme via 24 hydroxylation), CYP27b1 (activating enzyme via 1α hydroxylation), and vitamin D receptor (VDR) mRNA and protein were studied by real-time PCR and immunoblotting.

RESULTS: Pregnancy was associated with a significant increase in plasma bioactive vitamin D (1, 25-$(OH)_2$-D , 710 ± 8 pM), levels compared to non-pregnant baboons in both lean and obese groups (560 ± 17 pM, p<0.05). Pregnant obese baboons had lower plasma levels of vitamin D metabolites than control non-obese baboons (165 ± 17 vs. 244 ± 47 nM for 25-OH-D; 669 ± 20 vs. 710 ± 8 pM for 1, 25-$(OH)_2$-D Pregnancy significantly decreased maternal renal expression of CYP27b1 and CYP24a1. Obesity did not affect renal expression of VDR, CYP27b1 or CYP24a1 in non-pregnant baboons. In contrast, obesity further reduced maternal renal expression of CYP27b1, CYP24a1 and VDR. Placental expression of CYP24a1 was increased and that of chromatin-bound VDR was decreased in obese compared to non-obese pregnancies.

CONCLUSIONS: Pregnant non-obese baboons show increased vitamin D bioactivation and placental uncoupling of vitamin D-dependent regulation of VDR and CYP24a1 compared with non-pregnant baboons as observed in healthy pregnant women. Obesity decreased vitamin D status especially in pregnant baboons, suggesting that vitamin D dysregulation can be an important feature in this model (HD021350).

S-096

Targeting Interventions to Prevent Adult Consequences of Impaired Fetal Growth. Carol A Wang,[1] Wei Ang,[1] Scott White†,[1] Melanie K White†,[1] David Mackey,[2] Stephen J Lye,[3] Craig E Pennell*.[1] *[1]The University of Western Australia, Perth, Western Australia, Australia; [2]The University of Western Australia, Perth, Western Australia, Australia; [3]Mount Sinai Hospital, Toronto, ON, Canada.*

INTRODUCTION: There is a large body of evidence from epidemiological observations, animal experiments and human genetic association studies that early life events shape an individual's health. Primary prevention of the metabolic syndrome requires the identification of individuals at high risk as early as possible to provide the opportunity for interventions during the window of developmental plasticity.

Aim: To identify genetic variants that influence fetal growth trajectories and the metabolic syndrome in adults.

METHODS: A genome wide association study (GWAS) of longitudinal fetal femur length (FL), head circumference (HC) and abdominal circumference (AC) between 18-38 weeks was performed in the Raine cohort (n=1377) to identify gene regions associated with fetal growth. Significant GWAS gene regions were assessed in the ExomeChip data (n=1246) through burden test and SKAT approach. Analyses were restricted to nonsynonymous variants (ns), with weights assigned to each variant based on MAF. Significant regions were then tested against 18-, 20- and 22-year adult outcomes.

RESULTS: After multiple testing corrections, exonic (ns) variants within LPHN3, SAMD3, and PTPRB were associated with AC growth; variants within FIG4 were associated HC growth; variants in PDZD2 were associated with FL growth. Further analyses suggested significant associations between these genes and adult metabolic outcomes. Additionally, these genes were also observed to influence adult outcomes at the extremes of birth weight. Results are summarised in the table.

**Figure(s) will be available online.*

CONCLUSIONS: The combination of traditional whole genome and exome SNP data identified five novel genes associated with both impaired fetal growth and the adult metabolic syndrome. These data offer the potential to identify those at birth at the highest risk of adult disease based on individual growth and genetics.

S-097

Risk Factors for Neonatal Hypoxic-Ischemic Encephalopathy of Unknown Origin. Christopher Novak†, Hattan Arif, Ernest Graham*. *Johns Hopkins Hospital, Baltimore, MD, USA.*

INTRODUCTION: Hypoxic-ischemic encephalopathy (HIE) in the neonate at birth may be associated with an intrapartum sentinel event, in which case the cause is known, or may be of unknown origin. We sought to identify risk factors associated with HIE of unknown etiology.

METHODS: This is a retrospective cohort study of all neonates admitted to our NICU with suspected HIE treated with whole-body hypothermia from January 2007 through June 2016. All neonates were ≥ 35 weeks gestation. Those with an intrapartum sentinel event were compared to those without a sentinel event. A sentinel event was defined as an event occurring immediately before delivery that could result in fetal hypoxia, including uterine rupture, placental abruption, umbilical cord prolapse, shoulder dystocia or maternal cardiac arrest.

RESULTS: During this period, there were 203 neonates admitted with suspected HIE and treated with whole-body hypothermia, of which 79 (38.9%) experienced a sentinel event and 124 (61.1%) did not. Of the 203 neonates, 76 (37.4%) were born within our institution and the remainder were transferred to our institution from across our state. Placental histopathology was performed for 25/28 (89.3%) of inborn neonates with sentinel events and for 43/48 (89.6%) inborn neonates without sentinel events. Placental histopathology was not performed for neonates born at outside institutions. Neonates who experienced a sentinel event were more likely to have a nonreassuring fetal heart rate (FHR) tracing prior to delivery. There was no difference in birth weight, cord pH, initial neonatal pH, abnormal neonatal brain MRI, neonatal seizures, or neonatal death. Meconium was more likely to be present intrapartum in those neonates without a sentinel event. While there was no difference in intrapartum clinical chorioamnionitis, neonates without a sentinel event were more likely to have histologic chorioamnionitis or funisitis. On multivariate regression, the presence of meconium and histologic chorioamnionitis or funisitis did not remain significant in those neonates with unexplained HIE.

CONCLUSIONS: Neonates with HIE in the absence of sentinel events have comparable morbidity and mortality and do not differ in metabolic acidosis at delivery or have other identifiable risk factors when compared to those with sentinel events.

S-098

Assessment of the Global Sphericity Index and Cardiac Area as Indirect Indicators of Cardiac Dysfunction in Fetal Growth Restriction. Michael Zaretsky,[1,2] Greggory DeVore,[3] Diane Gumina,[1] Mary Pinter,[1] John Hobbins*.[1] *[1]University of Colorado School of Medicine, Aurora, CO, USA; [2]Colorado Fetal Care Center, Aurora, CO, USA; [3]University of California, Los Angeles, Los Angeles, CA, USA.*

INTRODUCTION: Recent studies suggest that abnormal ventricular and atrial shape is associated with fetal growth restriction (FGF). Changes in ventricular shape have been reported in adult and pediatric patients as a marker for cardiac dysfunction. However few studies have applied this concept to the fetus. We hypothesize that cardiac dysfunction associated with FGR will result globular heart shape and increased heart size. This study compares the global sphericity index (GSI) and cardiac area (CA) measured in fetuses with FGR against a control group of fetuses that were appropriate for gestational age (AGA).

METHODS: In 43 fetuses with estimated fetal weights (EFWs) below the 10th percentile; GSI was calculated from the four-chamber view (4CV) of ventricular end-diastole. GSI ratios were obtained from the epicardial borders at the widest transverse diameter (TL) and the longest basal/apical length (BAL) of the 4CV. In the same fetus, CA was calculated using the same two TL and BAL. Normative CA and GSI data from 200 AGA fetuses were used to generate Z-scores for our cohort and a student's t-test was used to determine statistical significance.

RESULTS: Using a 90th percentile threshold, one would expect a 10% incidence of increased cardiac size. However, 45% (20 fetuses) of our FGR cohort had CA> 90th percentile based on EFW. Average Z-score for CA were significantly increased in the FGR group when compared to the controls (1.059 ± 0.17 vs. -0.005 ± 0.07; p<0.0001). A GSI threshold of 1.08 is analogous to the 5th percentile in existing normative data. 25.5% (11 fetuses) in our FGR group had GSI's below this threshold, and average FGR Z-scores were significantly decreased when compared to controls (-0.316 ± 0.09 vs. 0.003 ± 0.07; p=0.020) indicating that these fetal hearts are more globular in shape.

CONCLUSIONS: Fetuses within our FGR cohort have significantly larger and more globular-shaped hearts than AGA controls, suggesting varying degrees of cardiac dysfunction. Computation of the GSI and CA are easy to obtain from the BAL and TL and should be considered as a screening tool prompting further evaluation of cardiac function in FGR fetuses.

S-099

Impact of Late-Onset Hypoxemia During the Final Third of Gestation on Adrenocortical Expression of Steroidogenic Genes in the Ovine Fetus. A Martin†,[1] D Myers,[1] BJ Allison,[2] KL Brain,[2] DA Giussani,[2] C Ducsay*.[3] *[1]Univ. Oklahoma HSC, Oklahoma City, OK, USA; [2]Cambridge Univ., Cambridge, United Kingdom; [3]Loma Linda Univ., Loma Linda, CA, USA.*

INTRODUCTION: We previously reported that early-onset gestational hypoxemia from ~40 dG through near-term (~140 dG) results in dramatic adaptive changes in the fetal hypothalamo-pituitary-adrenocortical axis, which suppress fetal adrenocortical activation (PMID:16099825). There

is reduced expression of key rate limiting enzymes for cortisol synthesis (CYP17, CYP11A1) and of the ACTH receptor (MC2R). Here, we determined the effect of late-onset gestational hypoxemia from 105 to 138 dG to establish the role of timing of the hypoxic insult on fetal adrenal steroidogenic enzyme expression.

METHODS: Chronically catheterized ewes carrying male singleton fetuses were exposed to normoxia (n=9) or hypoxia (10% inspired O_2, n=8) for the last third of gestation (105-138 dG; term~145 dG) in isobaric chambers (PMID: 26660546). At 138dG, quantitative real time PCR (qRT-PCR) was used to measure CYP17, CYP11A1, HSD3B2, StAR, MC2R and Cyclophilin (housekeeping gene) in fetal adrenal glands. Data expressed as mean±SEM.

RESULTS: Maternal PaO_2 was reduced in hypoxic pregnancy (N=106±2; H=47±1 mmHg, $p<0.05$). This level of maternal hypoxemia yields fetal PaO_2 values of 11.5±0.6 relative to 20.9±0.5 mmHg in controls (PMID: 26926316). Fetal adrenocortical mRNA for CYP11A1 and CYP17 was elevated in hypoxic pregnancy, while MC2R, HSD3B2, StAR, and Cyclophilin expression remained unchanged (Table 1).

TABLE 1.

Effects of hypoxemia on adrenal genes (fg mRNA/100 ng RNA; *p<0.05 *vs.* Normoxia)

Gene	Normoxia	Hypoxemia
CYP11A1	38.3 ± 2.4	56.0 ± 3.9*
CYP17	54.7 ± 6.8	88.9 ± 7.0*
MC2R	3.9 ± 0.3	4.4 ± 0.3
HSD3B2	159.7 ± 10.5	205.6 ± 15.6
StAR	76.2 ± 10.4	89.6 ± 6.7
Cyclophilin	20.0 ± 0.3	205.6 ± 15.6

CONCLUSIONS: In marked contrast to early-onset gestational hypoxemia, which reduces fetal adrenal steroidogenic gene expression, late-onset gestational hypoxemia significantly increased fetal adrenocortical CYP11A1 and CYP17 expression. Combined, past and present data show that the fetal adrenal gland adopts differential strategies to withstand early- versus late-onset gestational hypoxemia, significantly influencing the potential programming outcome. *(Supported by the British Heart Foundation and NIH grants HD31226 and HD083132)*.

S-100

Use of Doppler Ultrasound (US) in Evaluating Uterine and Umbilical Artery Blood Flow in the Hypoxic (HPX) Pregnant Guinea Pig. Shifa Turan, Graham W Aberdeen, Loren P Thompson*. *Univ. of Maryland, Baltimore, MD, USA.*

INTRODUCTION: Placental insufficiency is a leading cause of fetal hypoxia (HPX) in pregnancy complications. We have developed a HPX pregnant guinea pig (GP) model of placental insufficiency where trophoblast invasion of the uterine spiral arteries is reduced by mechanisms incompletely understood. This study proposes to evaluate the effects of HPX on placental perfusion by measuring *in vivo* uterine artery (UtA) and umbilical artery (UmbA) blood flow by pulse wave Doppler US. We hypothesize that chronic HPX decreases maternal and fetal blood flow as a contributing factor in placenta perfusion.

METHODS: Pulse wave Doppler US was performed on normoxic (NMX; N=6) and HPX (N=8) pregnant GPs at term (65d) under light anesthesia. Pregnant GPs were exposed to HPX (10.5%O_2) at 25d gestation (time of trophoblast invasion) until term. Doppler indices (resistance, RI; pulsatility, PI) were obtained from 3 consecutive waveforms of right (R) and left (L) UtA and UmbA of each fetus (NMX; N=17, HPX; N=17). After the exam, placentas/fetuses were excised from anesthetized GPs and weighed.

RESULTS: Maternal (~175bpm) and fetal (~193bpm) heart rates were similar between NMX and HPX. HPX increased ($P<0.05$) Doppler indices in both R (RI: 0.38±0.06 vs 0.73±0.05; PI: 0.56±0.14 vs 1.6±0.22) and L UtA (RI: 0.48±0.04 vs 0.76±0.06; PI: 0.76 ±0.12 vs 1.89±0.26, NMXvsHPX). Qualitatively, diastolic notching of UtA waveforms was observed in 4/8 HPX GPs compared to 0/8 in NMX controls. HPX had no effect on UmbA Doppler indices (RI: 0.63±0.03 vs 0.62±0.02; PI: 1.08±0.09 vs 1.05±0.09, NMXvsHPX). Chronic HPX reduced ($P<0.05$) fetal body (FBW: 101±4vs78±4g), heart (by 25.4%) and liver wt (by 32.7%) but had no effect on absolute brain or placental wt compared to NMX controls. Placenta (0.050±.001 vs .070±.003) and fetal brain wts (0.026±.001vs 0.033±.001) normalized to FBW were significantly increased with HPX. Chronic HPX increased ($P<0.01$) mean arterial blood pressure in HPX vs NMX sows (41.9±1.5mmHg vs 59.8±2.0mmHg).

CONCLUSIONS: Doppler US, used to assess maternal/fetal blood flow in the pregnant GP, identified that HPX impaired vascular remodeling of the uteroplacental circulation exhibiting increased vascular resistance and decreased compliance, but had no effect on the fetal side. The response to chronic HPX may contribute to elevated maternal blood pressure, reduced perfusion of compensated placentas and asymmetric fetal growth restriction. (NIH-HL126859-LPT).

S-101

Variability of MRI Based Volumetric Measurements of Fetal Brain. Anat Lavie*, Maya Dvir, Daphna Link, Dafna Ben Bashat, Gustavo Malinger, Liat Ben-Sira, Ariel Many. *Tel Aviv University, Tel Aviv, Israel.*

INTRODUCTION: We aimed to assess the variability of magnetic resonance imaging (MRI) based volumetric measurements of fetal brain in typically developed fetuses.

METHODS: MRI data of 28 apparently normal fetuses between 27 to 37 weeks of gestation that were referred by the US unit of the prenatal diagnostic center for fetal MRI were collected retrospectively and included in this study.

Data was acquired using a 3D Fast Imaging Employing STeady-state Acquisition (FIESTA) sequence of the fetal brain and body (TR/TE=3/1.3sec, Matrix=256x256, 4mm slice thickness) and was used for volumetric measurements. Manual segmentation of the whole brain and the ventricular system were performed using AnalyzeDirect software by two independent qualified students and validated by a senior pediatric Neuroradiologist. Inter-observer variability was evaluated.

RESULTS: Figure 1 represents correlation between gestational age and total brain volume, excluding ventricles and CSF. Figure 2 represents the ventricles volume. Inter-observer agreement was excellent.

**Figure(s) will be available online.*

Mean gestational age was 32±2 weeks. Mean brain volume was 177117±4580 mm^3 and mean ventriclular volume was 7746±2563 mm^3. A large variability of fetal brain volumet was observed for all gestational ages both for total brain volume (up to 1.9 time fold) and for ventricular volume (up to 3.4 time fold).

CONCLUSIONS: This study shows a large variability of brain volumes in typically developed fetuses in MRI. This variability is significantly larger then that observed in normal growth charts of head circumference in US.

Further studies with larger sample size are needed in order to provide normal MRI reference volumetric data of the fetal brain and to establish whether this parameter can aid in identification of certain brain pathologies such as microcephaly or macrocephaly.

S-102

Prophylactic Maternal Creatine Supplementation in a NHP Model of Birth Asphyxia. Meredith A Kelleher†,[1] Stacey Ellery†,[2] David W Walker,[2] Hayley Dickinson,[2] Peta L Grigsby*.[1] [1]*Oregon National Primate Research Center, Oregon Health & Science University, Beaverton, OR, USA;* [2]*Department of Obstetrics & Gynecology, Monash University, Melbourne, VIC, Australia.*

INTRODUCTION: Perinatal asphyxia, leading to hypoxic-ischemic encephalopathy, can result in significant long-term motor, sensory, cognitive and behavioural deficits. The creatine-phosphocreatine shuttle maintains cellular ATP, particularly under hypoxic conditions. Creatine supplementation during pregnancy is proposed as a therapy for perinatal hypoxic-ischemic insults. We have previously demonstrated that maternal dietary creatine supplementation significantly reduces mortality and multi-organ morbidity in a rodent model of birth asphyxia. We aimed to study the effect of maternal creatine supplementation on creatine levels and neuroprotection after umbilical cord occlusion (UCO) in the non-human primate (NHP).

METHODS: At ~105days gestation (dGA) (term ~165d) Rhesus macaques (n=4) had fetal ECG electrodes, and amniotic fluid and maternal femoral catheters implanted. Maternal blood pressure (BP), fetal heart rate and uterine contractility were continuously monitored. From 115dGA NHPs received vehicle (n=2) or creatine orally (0.3g/kg/day for 8 days, followed by 0.075g/kg/day until delivery; n=2). Maternal blood, urine and amniotic fluid was sampled regularly to assess creatine levels, basal metabolic status, renal and hepatic function. At 147-148dGA a creatine-treated and control fetus underwent 12min UCO to induce hypoxic insult before delivery.
RESULTS: Dietary creatine increased maternal plasma, amniotic fluid and neonatal CSF creatine levels by ~60%. Preliminary analysis suggests that creatine treatment had no affect on maternal health parameters, including BP and uterine activity. The UCO infant that did not receive gestational creatine had lower Apgar scores, increased measures of hypoxia/metabolic acidosis, displayed abnormal wrist flexion, reduced forelimb motor coordination and a reduced suckling reflex compared to the creatine supplemented UCO infant.
CONCLUSIONS: This pilot study suggests that maternal dietary creatine may reduce neonatal morbidity following hypoxia at birth in the rhesus monkey. Future studies will aim to establish the safety of maternal creatine supplementation and long-term developmental outcomes of neonates following hypoxic-ischemic insults during development.

S-103

An Innovative Fetoscopic Technique for Closure of Large Non-Cystic Meningomyelocele/Myeloschisis Lesions. Michael A Belfort*,[1] William E Whitehead,[2] Alireza A Shamshirsaz,[1] Olutoyin A Olutoye,[3] Zhoobin Bateni,[1] Sundeep Keswani,[4] Timothy Lee,[4] Jimmy Espinoza,[1] Oluyinka O Olutoye,[4] Magdalena Sanz Cortes,[1] Darrell L Cass.[4] *[1]Baylor College of Medicine/Texas Children's Fetal Center, Houston, TX, USA; [2]Baylor College of Medicine/Texas Children's Fetal Center, Houston, TX, USA; [3]Baylor College of Medicine/Texas Children's Fetal Center, Houston, TX, USA; [4]Baylor College of Medicine/Texas Children's Fetal Center, Houston, TX, USA.*
INTRODUCTION: In-utero neurosurgical repair for non-cystic flat meningomyelocele/myeloschisis lesions is not standardized. Varied techniques are in use for watertight closure and are performed via an open hysterotomy. We have developed a novel in-CO2 fetoscopic (ENDO) approach using a simple unified skin closure and fetoscopically created relaxing incisions without need for patches or extensive dissection.
METHODS: Retrospective case-control: 6 ENDO cases with 6 open surgery (OPEN) controls. In ENDO cases lateral relaxing incisions were made using diathermy. The defect was covered by suturing the block of tissue so released in the midline without any dissection or foreign material. OPEN cases had usual neurosurgical closure. Parametric and non-parametric tests as appropriate. MOMS trial outcome data used as reference. $p < 0.05$.
RESULTS: Demographics were similar. Gestational age at delivery was 36+/-3 in ENDO and 36+/-1 weeks in OPEN. No baby delivered < 30 weeks. 5/6 ENDO and 4/6 OPEN had myeloschisis. Neurosurgery time was significantly longer in ENDO than OPEN (119+/-40 vs. 40+/-13 minutes; $p < 0.001$). Blood loss (ml) was less in ENDO (50[25-300] vs. 120[50-180]; $p = 0.03$). Complication rates were similar. There were no perinatal losses. 5/6 (83%) ENDO and 5/5 OPEN had reversal of hindbrain herniation (P=NS), and 0/6 ENDO and 0/5 OPEN had repair dehiscence at birth. 3/6 ENDO delivered vaginally vs. 0/6 OPEN. Neurological outcomes were similar in terms of diagnosis of hydrocephalus and/or death, need for treatment for hydrocephalus, and functional neurological level.
CONCLUSIONS: Our novel fetoscopic technique is effective in closing large non-cystic meningomyelocele/myeloschisis lesions without the need for open hysterotomy, extensive dissection or the use of patches. Equivalent fetal/neonatal outcome as in open hysterotomy can be achieved with the distinct and important additional benefits of vaginal delivery and lower immediate and long term obstetric risk.

S-104

Time Series Analysis of Electroencephalogram Signal Using Simple Device for Getting EEG and Fluctuation of Hormone Levels with a Menstrual Cycle. Eri Okuzumi†*,[1] Yasue Mitsukura.[2] *[1]Graduate School of Integrated Design Engineering, 3-14-1, Hiyoshi, Kohokuku, Yokohama, Kanagawa, Japan; [2]Faculty of Science and Technology, 3-14-1, Hiyoshi, Kohokuku, Yokohama, Kanagawa, Japan.*
INTRODUCTION: Women tend to become emotionally and physically unstable in the luteal phase of a menstrual cycle. Therefore, it is very important for women to know own luteal phase. Generally, the main way to detect the luteal phase is the blood test. However, it would be a heavy burden on subjects physically. Then, in this paper, we propose the method of detecting the luteal phase using human feelings obtained by electroencephalogram (EEG). We use a simple EEG device which allows us to measure EEG signal very easily and safely compared with the blood test. Furthermore, EEG is appropriate method because a menstrual cycle is governed by female hormones which activates the brain. We also investigate the relationship between EEG signal and fluctuation of hormone levels. In this paper, we obtain two female hormones, estradiol and progesterone, using saliva check.
METHODS: We used KANSEI analyzer that outputs 5 KANSEI values as a percentage every second from EEG data. KANSEI indicates human feelings. These 5 KANSEI values include like, interest, concentration, drowsiness, and stress. Firstly, factor analysis was applied to 5 KANSEI values to find what KANSEI value is effective to distinguish the luteal phase. Secondly, Support Vector Machine (SVM) was applied to classify the luteal phase using the KANSEI values chosen by factor analysis. Finally, we applied correlative analysis to investigate the relationship between the secretion amount of two female hormones, estradiol and progesterone, measured by saliva check and EEG signals obtained for the same duration ofsaliva check.
RESULTS: Stress, concentration and drowsiness had large contribution amount for a menstrual cycle by factor analysis. These 3 KANSEI values were classified with SVM, the average of classification accuracy achieved 90.1%.Thus, we found that there is high correlation beyond 70% between EEG signal and the secretion amount of estradiol.
CONCLUSIONS: We could show the relationship among a menstrual cycle, EEG signals and hormone levels. Wewill apply a time series analysis between EEG signal and fluctuation of hormone levels and build a statistical model. Our final goal is to construct the system that is able to specify own menstrual cycle precisely only by EEG.

S-105

Regulation of Innate Lymphoid Cells by Human Papillomavirus' Oncoproteins. Laura F Núñez Castro†, Damián O Muzzio†, Kristina MT Hilz†, Christine Lamb†, Marek Zygmunt*. *University of Greifswald, Greifswald, Mecklenburg-Vorpommern, Germany.*
INTRODUCTION: Cervical cancer is the second most common cancer in women worldwide; human papillomavirus (HPV) infection is the main risk factor for developing this disease. HPV has shown several strategies for evading the immune system. HPV expresses different viral proteins, of which E6 and E7, when activated, are able to reduce $CD4^+$ lymphocyte activation, Th1 immune response and inhibit IL-18 triggered IFN-γ production in human peripheral blood mononuclear and NK cells. Additionally, after infection has taken place, E6 promotes pro-angiogenic cytokines, favoring tumor growth.
Recently described innate lymphoid cells (ILCs) are hematopoietic cells, which play an important role in maintaining epithelial integrity. ILCs originate from a common lymphoid progenitor and differentiate into ILC1, 2 or 3. ILC3s, for example, need RORγt for development. It has been shown that the expression of RORγt can be regulated, allowing one single cell population to have different functions. $ROR\gamma t^{dim}$ cells are IFN-γ producers while $ROR\gamma t^{high}$ cells produce IL-22.
Here we raised the question, whether HPV's viral oncoproteins modify cytokine's expression in ILCs assuring tumor formation and immune evasion.
METHODS: Hela cell line was used for our experiments. Production of E6 and E7 was confirmed through PCR. Isolated PBMCs were cultivated

for 3 days either with IL-18, E6-E7 or anti-E6/7 in the presence of Hela or HEK 293 to assess the effect of HPV's viral oncoproteins on ILCs. Hela's supernatant was collected and used in a cell culture with lymphocytes stimulated with IL-18 or/and anti-E6/7. ILC's profiles were determined using flow cytometry.

RESULTS: RORγt^{dim}ILC3s treated with Hela's supernatant produced less IFN-γ,when E6 and E7 were blocked with specific antibodies. Recombinant E6 and E7 induced production of IFN-γ within ILC3s compared to non-treated controls. Treatment with E6 and E7 also increased the amount of activated CD69^{+}RORyt^{dim}NCR^{-}ILC3s. Furthermore, E6 and E7 protected RORγt^{dim}ILC3s against cell death.

CONCLUSIONS: E6 and E7 increased IFN-γ's production in ILC3s from healthy donors. Further studies are needed to evaluate if E6/E7 induce IFN-γ's secretion during tumor development.

S-106

Identification of Somatic Genetic Alterations in Ovarian Clear Cell Carcinomas with Next Generation Sequencing. Yusuke Shibuya,[1] Sakae Saito,[2] Kaname Kojima,[2] Bin Li,[1] Hideki Tokunaga,[1] Masao Nagasaki,[2] Jun Yasuda,[2] Nobuo Yaegashi.[1] *[1]Tohoku University, Sendai, Miyagi, Japan; [2]Tohoku Medical Megabank Organization, Sendai, Miyagi, Japan.*

INTRODUCTION: Ovarian clear cell carcinoma (OCCC) is the most refractory subtype of ovarian cancers. OCCC arises from endometriosis and is more prevalent in Japanese than Caucasians (25% and 5% of all ovarian cancer, respectively). Frequent somatic mutations in the *ARID1A* (60%) and *PIK3CA* (40%) are reported for OCCC, but these mutations seem to be insufficient for explaining the characteristics of OCCC. The aim of this study is to discover the novel genomic alterations causing OCCC.

METHODS: With institutional approval, paired genomic DNAs of 48 OCCC tumors and corresponding non-cancerous tissue were extracted from the formalin-fixed, paraffin embedded specimen collected between 2007 and 2015. All specimens underwent genotyping by exome sequencing and SNP arrays. Exome library was prepared with Sure Select Human All Exon V6. Copy number analysis was performed with Japonica array (SNP array optimized for Japanese population).

RESULTS: The 48 OCCCs are divided into 5 clusters based on the mutation spectra and the each cluster shows significant similarity to the distinct COSMIC mutation signature. Frameshift or stop gain changes in the *ARID1A* (66.7%) and nonsynonymous and hot-spot mutations in the *PIK3CA* (50%) are found. Copy number analysis discloses partial trisomy of long arm of chromosome 8. Some oncogenic genes were significantly amplified.

CONCLUSIONS: We found several somatic genetic alterations, either novel or reported, in OCCC. We are comparing between clinical features and investigating gene ontology analyses of those genes. Next step is to characterize the biological properties of those genes by the experiments using cultured OCCC cells.

S-107

Bartholin's Gland Carcinoma, a Retrospective Review. Gary Altwerger†, Samantha Margulies, Gulden Menderes, Jon Black, Babak Litkouhi, Dan-Arin Silasi, Masoud Azodi, Alessandro Santin, Peter E Schwartz, Elena Ratner*. *Yale University School of Medicine, New Haven, CT, USA.*

INTRODUCTION: Bartholin gland carcinomas are rare malignancies diagnosed in 5 percent of all vulvar malignancies. Limited data exists on the treatment of Bartholin's gland carcinoma. Management of this carcinoma, as well as factors predicting recurrence will be characterized here.

METHODS: A retrospective review of the Tumor Registry was conducted. All Bartholin gland carcinomas from January 2000 to September 2016 were included. Baseline demographic data were collected. Details about the patient's stage, chemotherapy, radiation, surgical resection and survival were obtained.

RESULTS: Twelve patients were found to have Bartholin's gland carcinoma. The most common histologic sub-type was squamous cell carcinoma at 58%, the second most common was adenoid cystic carcinoma at 17%. Six patients were lost to follow up prior to treatment. The remaining six patients were diagnosed at a median age of 57. Fifty percent of the patients presented with advanced stage disease (III-IV). The most common surgery was a partial radical excision (67%). Inguinal lymphadenectomies were done in 83% of the cases. Negative surgical margins were achieved in 67% of the cases. Chemoradiation was given in 67% of the cases. Cisplatin was infused in 50% of the patients. The 5-year progression free survival was 83%, and the 10- year overall survival rate was 83%. Recurrence was seen in 17% of the cases. Eighty percent of the cases with 5-year progression free survival were found to have negative margins.

**Figure(s) will be available online.*

CONCLUSIONS: The mainstay of treatment for Bartholin's gland carcinoma is chemoradiation with either radical local excision or radical vulvectomy. This treatment provides patients with an excellent overall survival. The 83% 5-year progression free survival is most strongly correlated with obtaining negative margins at primary surgery. 5-year progression free survival is also correlated with the use of cisplatin and radiation. Negative margins along with cisplatin/XRT are important in the treatment of Bartholin's gland carcinoma.

S-108

The Impact of Tumor Fragments in the Lumen of Fallopian Tubes on Recurrence and Survival in Type I and Type II Endometrial Cancers. Jonathan D Black†,[1] Rachel Passarelli†,[1] Margaret Whicker†,[1] Benjamin Albright†,[2] Stefan Gysler†,[1] Lingen Lu,[1] Gulden Menderes†,[1] Gary Altwerger†,[1] Babak Litkouhi,[1] Elena Ratner,[1] Dan-Arin Silasi,[1] Masoud Azodi,[1] Alessandro Santin,[1] Schwartz Peter.[1] *[1]Yale School of Medicine, New Haven, CT, USA; [2]Hospital of the University of Pennsylvania, Philadelphia, PA, USA.*

INTRODUCTION: Type I endometrioid adenocarcinomas are estrogen dependent, slow growing tumors and Type II carcinomas (i.e. FIGO grade 3, serous carcinoma, clear cell carcinoma) are non-estrogen dependent and more aggressive. The objective of this study was to evaluate the impact on disease recurrence and death of tumor fragments (floaters) within the lumen of the fallopian tube.

METHODS: A single institution retrospective review of 1100 consecutive endometrial cancer cases from January 2005 to December 2010. Pathology reports were reviewed and subjects identified based on the presence of floaters within the lumen of the fallopian tube. Univariate and multivariate analyses were completed using standard logistic regression models and Cox Regression models. Interaction tests were also completed.

RESULTS: There were 619 cases of Type I disease and 256 cases of Type II disease. Twenty-one cases (2.4%) of floaters were identified. There was an increased likelihood of having floaters present in Type II vs. Type I cancers (3.1% vs. 2.1%, respectively, NS). They were equally common in Stage III/IV disease (Type I: 6.2% and Type II= 7.0%, NS) and two times more common in Type I cancer in Stage I/II disease (Type I= 1.3% and Type II= 0.6%, p=0.008). When floaters are present in Type II cancers there is an increased risk of recurrence (HR=8.66 , CI 3.50-21.48,p<0.0001) and death (HR=5.27, CI 2.15-12.90, p=0.0003). There is not an increased risk of recurrence (HR=0.67, CI 0.09-4.82, p=0.692) or death (HR=1.54, CI 0.49-4.85, p=0.459) in Type I cancers with floaters present.

CONCLUSIONS: The presence of floaters is more common in Type II endometrial cancers. However, in early stage disease they are more common in Type I cancers. It does not appear that floaters play a role in the recurrence rate or death rate in patients with Type I disease. In type II disease, it is more likely the aggressiveness of the disease combined with the advanced stage at presentation that results in an increased risk of recurrence and death and not the presence of floaters. Further pooled-data studies are warranted.

S-109

New Medical Therapeutics for Ectopic Pregnancy. Roxanne Hastie†, Natalie Hannan, Louie Ye, Tu'uhevaha J Kaitu'u-Lino, Stephen Tong*, The University of Melbourne. *University of Melbourne, Heidelberg, VIC, Australia.*

INTRODUCTION: Ectopic pregnancy represents a serious gynaecological emergency that can erode the maternal vasculature and cause fatal haemorrhage. While methotrexate injections can resolve small ectopic pregnancies, most are too large and require surgery. We

have previously shown that the combination of methotrexate & gefitinib is more efficacious at resolving an ectopic pregnancy than methotrexate alone. However, combination methotrexate & gefitinib is yet to prove efficacious at resolving larger ectopic pregnancies. Our objective was to identify a more potent therapeutic than methotrexate & the combination methotrexate & gefitinib to treat ectopic pregnancy.
METHODS: Twelve chemotherapeutics were screened in JEG3 and HTR8 placental cell lines using an MTS viability assay. Vinorelbine**,** a vinca alkaloid, was a clear outlier with surprising efficacy. We confirmed the potency of vinorelbine using the xCELLigence system and flow cytometry. In vivo, JEG3 xenografts were implanted subcutaneously in to SCID mice, and vinorelbine, methotrexate, combination methotrexate & gefitnib or vehicle were administered intravenously, with placental tumour volume measured over 14 days. The effect of vinorelbine exposure on human fallopian tubes was assessed ex-vivo to rule-out damage for ongoing fertility. Fallopian tubes were collected at the time of hysterectomy & treated with vinorelbine. Further assessment of vinorelbine on subsequent fertility is currently under way in-vivo, whereby mice have been treated with vinorelbine and then mated four weeks post treatment, with pregnancy outcomes to be recorded at day E18.5.
RESULTS: Vinorelbine is highly efficacious at reducing placental cell viability in-vitro, with 10 nM of Vinorelbine reducing cell viability significantly more than 100,000 nM of methotrexate. Additionally, in vivo vinorelbine induced a significant decrease in JEG3 xenograft tumour volume, tumour weight and circulating hCG, beyond both methotrexate alone & combination methotrexate & gefitinib treatments. Excitingly, vinorelbine at a dose of 5mg/kg induced complete placental tumour regression. Treating human fallopian tubes ex vivo with vinorelbine did not did not alter the protein expression of apoptotic markers. Further investigation in to the effects of vinorelbine on subsequent fertility is currently underway.
CONCLUSIONS: This data suggests that Vinorelbine is highly efficacious at inducing placental cell death beyond current therapeutic options.

S-110

Uterine Gene Expression in a Murine Model of Menstruation Largely Mimics Human Endometrial Gene Expression in Women with Abnormal Uterine Bleeding. Jörg Müller,[1] Ralf Lesche,[1] Andrea Wagenfeld,[1] Alison Murray,[2] Moira Nicol,[2] Lucy Whitaker,[2] Jackie Maybin,[2] Thomas M Zollner,[1] Hilary OD Critchley*,[2] *[1]Bayer Pharma AG, Berlin, Germany; [2]University of Edinburgh, The Queen's Medical Research Institute, Edinburgh, United Kingdom.*
INTRODUCTION: Abnormal uterine bleeding (AUB) is common and has a significant negative impact on quality of life. Causes of AUB include leiomyoma (steroid dependent benign tumours) or disorders of endometrial origin (AUB-L and AUB-E respectively). The mechanisms involved in AUB are only partially understood and a robust *in vivo* animal model is required to drive forward our understanding of endometrial physiology and pathology, with the aim of developing new treatments for these significant disorders.The objectives of the study were to validate the murine model of simulated menses by comparing the gene expression in the human endometrium (E) from women with AUB-E/AUB-L and mouse uterus (U) across the peri-menstrual phase to identify common and potentially different mechanisms which drive uterine bleeding.
METHODS: E biopsies taken from women complaining of AUB and U samples from mice across an artificial menstrual cycle. Human and mouse RNA was profiled on whole genome microarrays. Cycle stages of human E samples were defined based on cycle stage, E histology, serum estradiol (E2) and progesterone (P) levels. Artificial menstrual cycle phases of ovariectomized mice were defined by E2 and P supplementation and bleeding pattern.
RESULTS: Principle component analysis of human and mouse gene expression data show cyclic pattern according to cycle stages, indicating that gene expression mirrors physiological changes during the menstrual cycle and similar biological mechanisms are involved in the human E and mouse U. For example, decidualisation (e.g. PRLR) and P response (e.g. FKBP4, SGK1) marker are highly expressed in mid to late secretory phase of human E and correspondingly in the decidualised mouse U. Marker for inflammatory response (e.g. IL1B, IL6, TNF), angiogenesis (e.g. VEGF) and coagulation (e.g. F2R, PLAU) are concordantly highly expressed in human menstrual and murine bleeding phases.
CONCLUSIONS: This study emphasizes the value of the mouse model of menstruation for basic research, target validation and development of novel therapies for women complaining of AUB and heavy menstrual bleeding.

S-111

ID4 Allelic Variant Is Associated with Endometriosis and May Affect Mesothelial Epithelial to Mesenchymal Transition. Colin Bergstrom, Terry K Morgan. *OHSU, Portland, OR, USA.*
INTRODUCTION: Endometriosis affects approximately 10% of reproductive age women and is a leading cause of pelvic pain and infertility. This common disease is familial and genome wide association studies have suggested a potential risk locus called inhibitor of DNA binding (ID)-4 [rs6907340]. The ID4 minor allele variant (mav) is especially interesting to our group, because this tumor suppressor gene may be involved in the BRCA pathway and the epithelial-mesenchymal transition (EMT) process.
METHODS: Retrospective case:control study of all endometriosis cases diagnosed by tissue biopsy at OHSU from 2003-2010. Inclusion criteria required white non-Hispanic race (for allelic variant analysis), documented stage of disease severity (ASRM, stage 1 or 2 [mild], stage 3 or 4 [severe]), history of infertility (yes or no), and at least five years of documented clinical outcomes to evaluate for disease persistence and *de novo* presentation of breast cancer or adnexal cancer (ovary or fallopian tube). This yielded 180 cases for analysis. Negative controls were white non-Hispanic women with archived tissue biopsies for DNA and no history of endometriosis (n=177). DNA was extracted from FFPE tissue blocks and ID4 allelic discrimination was performed using Taqman. All samples were tested in duplicate and only reproducible genotypes were included for analysis. We also immunostained a series of pelvic peritoneal biopsies for cytokeratin 7, E-cadherin, and N-cadherin, from endometriosis cases homozygous for the ID4 mav compared with negative controls.
RESULTS: As expected, infertility was more common in cases of severe endometriosis (12/52, 23%) than cases of mild endometriosis (7/128, 5%), Fisher exact p=0.001. The ID4 minor allele frequency in white controls was 0.40 (expected 0.39). The frequency was increased in endometriosis (0.45) and more so in severe disease cases (0.47), yielding an odds ratio of 1.6 [0.99-2.75], p=0.05. Immunohistochemical analysis of peritoneal biopsies suggested mesothelial cells from cases may be more likely to lose E-cadherin staining and gain N-cadherin signal, consistent with EMT.
CONCLUSIONS: Although the functional significance of the ID4 rs6907340 allelic variant is unknown, we observed significant differences in allele frequency related to the severity of endometriosis and perhaps susceptibility to EMT.

S-112

PreImplantation Factor* in Endometriosis: A Potential Role in Inducing Immune Privilege for Ectopic Endometrium. Martin Mueller†*,[2,4,6] Marco Sbracia,[1] Brett McKinnon,[2] Fabio Scarpellini,[1] Daniela Marconi,[3] Gabriele Rossi,[3] Cedric Simmilion,[2] Michael Mueller,[2,4] Eytan R Barnea.[5] *[1]CERM, Rome, Italy; [2]University of Bern, Bern, Switzerland; [3]Università degli Studi di Roma Tor Vergata, Rome, Italy; [4]University Hospital Bern, Bern, Switzerland; [5]BioIncept LLC (*PIF proprietary), Cherry Hill, NJ, USA; [6]Yale University School of Medicine, New Haven, CT, USA.*
INTRODUCTION: Endometriosis is a chronic inflammatory condition with privileged inflammatory microenvironment and T regulatory $FoxP3^+$ cells are central. PreImplantation factor (PIF) is a peptide with immune modulatory function.
METHODS: Human tissues with endometriosis (n=25) and without (10) was used for IHC (anti-PIF and -FoxP3). We used FITC-PIF flow cytometry to detect FoxP3-PIF binding in PMBC. We used primary

endometrial stromal cells from women with and without endometriosis and immortalized cell lines. Whole transcriptome expression array was used in ectopic epithelial cells.

RESULTS: We report that PIF re-expresses in the epithelial ectopic cells (Fig. 1A+B) in close proximity to FoxP3$^+$ stromal cells (Fig. 2D). Synthetic PIF (sPIF) increases cell viability of epithelial eutopic (..) and decreases viability of epithelial ectopic (-) cells.

**Figure(s) will be available online.*

sPIF modulates multiple pathways including T regulatory signaling (Array). PIF interacts with FoxP3$^+$ cells and modulates cell viability diversely depending on cell source and presence of inflammatory mediators

**Figure(s) will be available online.*

CONCLUSIONS: Our finding represent a novel PIF-based mechanism in endometriosis and hold potential of a novel therapeutics.

S-113

Pro-Inflammatory Effects of IL-33 In Endometriosis. Jessica E Miller†,[1] Stephany P Monsanto,[1] SooHyn Ahn,[1] Kasra Khalaj,[1] Bruce A Lessey,[2] Steven Young,[3] Asgi T Fazleabas,[4] Chandrakant Tayade.[1] *[1]Queen's University, Kingston, ON, Canada; [2]Greenville Health System, Greenville, SC, USA; [3]University of North Carolina, Chapel Hill, NC, USA; [4]Michigan State University, Lansing, MI, USA.*

INTRODUCTION: Interleukin-33 (IL-33) is categorized as a pro-inflammatory, danger signal (or alarmin). As such, aberrant concentrations have been associated with conditions including Alzheimer's disease, asthma, recurrent pregnancy loss and pre-eclampsia. Higher levels of IL-33 have been detected in the plasma and peritoneal fluid of endometriosis patients; however, the role of IL-33 in the pathophysiology of endometriosis is unknown. We hypothesize that IL-33 perpetuates inflammation in endometriosis patients.

METHODS: Levels of IL-33 in plasma from endometriosis patients were compared to healthy controls using an ELISA (R&D Systems). Then, endometrial epithelial carcinoma cells (EECC), human umbilical vein endothelial cells (HUVECs) and endometriotic epithelial cell line (12Z) were treated with rIL-33 (Miltenyi Biotec) to understand the effect of IL-33 on the proliferation, apoptosis, angiogenesis, and cytokine profile. Finally, C57BL/6 mice were induced with endometriosis by explanting endometrial fragments from a donor mouse and then treatment mice were injected intraperitoneally biweekly with 1ug of mouse rIL-33 (Affymetrix eBioscience) and control mice with PBS. Weekly blood collections will undergo multiplex cytokine analysis. Tissues will undergo staining to compare collagen deposition, angiogenic factors and inflammation status.

RESULTS: Plasma concentrations of IL-33 were significantly higher in endometriosis patients compared to controls. *In vitro* data indicated IL-33 initiates the production of pro-inflammatory cytokines in EECCs, HUVECs and 12Zs and anti-proliferative effects in EECCs and HUVECs. Finally, mice treated with rIL-33 presented with larger, cyst-like lesions and splenomegaly compared to controls. Further analysis is in progress.

CONCLUSIONS: We support previous reports demonstrating high levels of IL-33 in the plasma of endometriosis patients compared to controls. Preliminary results in both *in vitro* and *in vivo* endometriosis models indicate a pro-inflammatory role of IL-33 in endometriosis.

S-114

Elucidating the Polarization of THP-1 Cells by Interleukin-17A Induced Cytokines from Peritoneal Endometriotic Epithelial Cells. Soo Hyun Ahn†,[1] Kasra Khalaj†,[1] Asgerally T Fazleabas,[2] Chandrakant Tayade*.[1] *[1]Queen's University, Kingston, ON, Canada; [2]Michigan State University, East Lansing, MI, USA.*

INTRODUCTION: Endometriosis is a chronic inflammatory gynecological disease affecting millions of women of reproductive age world-wide. Menstrual effluents, the source of endometriotic foci, initiate sterile inflammation in pelvic cavity through recruitment of macrophages and neutrophils. These cells in turn produce cytokines not only crucial for neovascularization and implantation of endometriotic foci in ectopic locations, but also for development of chronic pelvic pain. Interleukin-17A (IL-17A) is a proinflammatory cytokine elevated in the peritoneal fluid of patients with mild endometriosis. It has been found to indirectly induce polarization of monocytes into M2 lineage and to induce migration of monocytes in rheumatoid arthritis. With our previous findings that suggest the involvement of IL-17A in creating inflammatory milieu, we investigate the role of IL-17A-induced factors in the polarization of monocytes into a macrophage phenotype that are tolerant of endometriotic foci development.

METHODS: Cell surface expression of IL-17RA on 12Z and THP-1 cells was conducted using flow cytometry. To investigate the indirect role of IL-17A in the polarization of monocytes in endometriosis, 12Zs were treated with **5, 50 and 100ng/ml IL-17A, and PBS (negative control)** for 24 hours in the standard cell incubator. Each conditioned media (CM) was added into THP-1 cells that were pre-incubated in serum free media for 24 hours. After 6 hours of incubation in CM, the total RNA was extracted from THP-1 cells for subsequent qPCR analysis for expression of M1 or M2 associated genes.

RESULTS: Flow cytometry confirmed the expression of IL-17RA on both cell lines. IL-17A induces G-CSF, GM-CSF and Gro-α, IL-6 and IL-8 expression in dose dependent manner from 12Z cells, which seem to be mediated through phospho-ERK1/2 (confirmed by western blot). Preliminary qPCR analysis for IL-6, IL-10, IFN-γ,TNF-α, IL-17A, IL-23, IL-17RA, IL-17RC and COX-2 show increased mRNA expression of **IL-10,IFN-γ, IL-17, IL-23** as well as both the receptors in THP-1 cells treated with 50ng/ml IL-17A CM from 12Zs compared to PBS.

CONCLUSIONS: Understanding the mechanism behind the regulation of sterile pelvic inflammation by the immune system in women with endometriosis will elucidate novel therapeutic targets to treat not only pain symptoms, but also in hope eradicate disease.

S-115

The Baboon Model for Investigation of Endometriosis-Associated Pain. Arne Vanhie†,[1] Stan Kivai,[2] Daniel Chai,[2] Erik Omolo,[2] Galo Mary,[2] Nicholas Kiulia,[2] Atunga Nyachieo,[2] Cleophas Kyama,[2] Jason Mwenda,[2] Thomas D'Hooghe.[1] *[1]Leuven University, Leuven, Vlaams-Brabant, Belgium; [2]Institute of Primate Research, Karen, Nairobi, Kenya.*

INTRODUCTION: Endometriosis is a chronic gynecological disease associated with pelvic pain and infertility. The baboon model for endometriosis is considered the best model for endometriosis research. However the baboon model has not been validated for study of endometriosis-associated pain. Therefore we compared the behavior of baboons before and after induction of endometriosis to assess changes in the behavioral pattern that may indicate endometriosis-associated pain.

METHODS: The behavior of 5 female olive baboons (*Papio anubis*) was monitored during the menstrual, follicular and luteal phase of 11 menstrual cycles (3 baseline and 8 after induction of endometriosis). Endometriosis was induced by laparoscopic seeding of autologous menstrual endometrium. Baboons were housed in neighboring single cages allowing visual contact but with sufficient spacing to avoid physical contact. Direct observation was done using focal sampling through video recording of spontaneous behavior during 3 observation units of 15 minutes per individual per day (before, during and after feeding). Behavior was quantified in terms of frequency (the number of times a behavior occurred during the observation unit) and duration (the total time in seconds the behavior lasted during the observation unit).

RESULTS: There were significant changes in behavioral pattern before and after induction of endometriosis. Resting and sitting upright increased (2x $p<0.001$) opposed to a decrease in vigilance ($p=0.001$) and being up on fours ($p<0.001$). Analysis for the different cycle phases showed that resting was unchanged during menstruation but increased in the follicular phase ($p=0.004$) and luteal phase ($p<0.001$), while vigilance decreased in all phases (menstrual $p=0.0014$, follicular $p<0.001$, luteal $p<0.001$). Activities suggestive for pain or discomfort such as abnormal locomotion and sleeping only occurred after induction of endometriosis.

CONCLUSIONS: The occurrence of specific behavior suggestive for pain or discomfort and the significant changes in behavior pattern may indicate the development of endometriosis-associated pain. These data suggest that the baboon model for endometriosis could be used to study endometriosis-associated pain, allowing assessment of this essential clinical outcome when testing therapeutic agents for endometriosis.

S-116

Treatment with Icon, Results in Regression of Red Lesions in a Non-Human Primate Model of Endometriosis. Graciela Krikun,[1] Demetra Hufnagel,[1] Laura G Goetz†,[1] Zhiwei Hu,[2] Atunga Nyachieo,[3] Thomas D'Hoogie,[4] Antoni Duleba,[5] Hugh S Taylor,[1] Charles J Lockwood*.[6] *[1]Yale University, SOM, New Haven, CT, USA; [2]Ohio State University College of Medicine, Columbus, OH, USA; [3]Institute of Primate Research, Nairobi, Kenya; [4]Leuven University, Leuven, Belgium; [5]University of California SD, La Jolla, CA, USA; [6]University of South Florida, Tampa, FL, USA.*

INTRODUCTION: The immunoconjugate molecule (Icon) targets tissue factor (TF), which is aberrantly expressed in the endothelium of vessels in ectopic endometrial tissue. Icon binds TF to activate NK cell cytolytic response against TF-bearing cells. We evaluated Icon as a novel treatment of endometriosis in non-human primates using an adenoviral vector delivery system. The ultimate goal of this study is to treat in humans with a non-steroidal compound which does not affect fertility.

METHODS: Female baboons (n=15) underwent surgical induction of endometriosis. After laparoscopic confirmation of endometriotic lesions 6-weeks post-surgery, the treatment group (n = 7) received weekly intraperitoneal injections of received weekly 20 mL intraperitoneal (I.P.) injections of 3.3×10^{10} attenuated adenoviral particles encoding Icon whereas controls did not. After 6-weeks post-induction and 12 weeks post-induction laparoscopy was conducted to assess the lesions.

RESULTS: Icon preferentially diminished highly angiogenic red lesions which are highly vascularized. Animals treated with Icon had decreased red lesion numbers (86% reduction) compared to controls (p=0.03). The surface area and volume per red lesion in Icon treated animals also decreased significantly after treatment (reduction of 80% and 75% respectively, (p=0.03). In the control group, volume and surface area per all lesion types were unchanged between laparoscopies.

CONCLUSIONS: Icon presents a novel treatment for endometriosis by targeting red vascularized lesions and their TF-expressing cells. We posit that Icon degrades extant and developing vessels thus preventing the required vasculogenesis to support the growth of endometriosis lesions. These results have wide-reaching implications for translating a novel endometriosis treatment towards clinical use without the side effects of hormonal treatments, preserving fertility and potentially improving long-term outcomes for women with endometriosis.

S-117

External Technical Confirmation of Panels of Plasma Biomarkers for Endometriosis. O Dorien†,[1] Yousef El Aalamat,[2] Arne Vanhie†,[1] Daniëlle Peterse†,[1] Bart De Moor,[2] Christel Meuleman,[1] Etienne Waelkens,[3] Amelie Fassbender,[1] Thomas D'Hooghe*.[1] *[1]KU Leuven, Leuven, Belgium; [2]KU Leuven, Leuven, Belgium; [3]KU Leuven, Leuven, Belgium.*

INTRODUCTION: One of the milestones of the biomarker clinical validation process is the replication of initial findings among multiple laboratories, with a clinical assay that replaces the biomarker discovery assay. We re-evaluated two panels of biomarkers with high sensitivity and specificity for the diagnosis of endometriosis [>80%, (Vodolazkaia et al. 2012)] in a different laboratory (Roche, Penzberg) and using partially different immunological assays.

METHODS: Of the 353 patient samples originally selected (Vodolazkaia et al., 2012), 136 were available from women with (n=99) and without (n=37) endometriosis. CA-125 and VEGF-A were measured on an Elecsys c601 instrument using commercially available and internal research assays, respectively (Roche Diagnostics GmbH, Penzberg, Germany). sICAM-1 was measured with an internal immunoassay using the IMPACT technology. Plasma levels of Glycodelin were determined with an internally developed ELISA assay, and Annexin V was measured using a commercially available ELISA kit (Sekisui Diagnostics GmbH). Statistical analyses were performed using univariate and multivariate (logistic regression) approaches.

RESULTS: The panel of CA-125, VEGF, Annexin V and Glycodelin showed an AUC of 0.89 with 80% sensitivity and 90% specificity to detect ultrasound-negative endometriosis during the menstrual phase of the cycle whereas CA-125, VEGF, Annexin V and sICAM-1 showed an AUC of 0.85 with 73% sensitivity and 90% specificity. For all endometriosis patients during the menstrual phase (ultrasound positive and ultrasound negative), the panel of CA-125, VEGF and Annexin V showed an AUC of 0.76 with 74% sensitivity and 60% specificity.

CONCLUSIONS: Ultrasound negative endometriosis can be diagnosed with 73-80% sensitivity and 90% specificity. These data, obtained using partially different assay technology in a different laboratory environment when compared to our initial study (Vodolazkaia et al., 2012), confirm the performance of this diagnostic model based on 4 different peripheral blood biomarkers obtained during the menstrual phase.

S-118

DNA Methylation Profiling in Endometriosis – RRBS Based Analyses in LCM Separated Endometrial Samples. Maik Obendorf,[1] Ralf Lesche,[1] Eva Simon,[1] Joern Toedling,[1] Kati Hasenbein,[2] Anne Kroker,[2] Arndt Schmitz,[1] Rene Wenzl,[3] Lorenz Kuessel,[3] Thomas M Zollner*.[1] *[1]Bayer AG, Berlin, Germany; [2]Vivantes Humboldt Hospital, Berlin, Germany; [3]Medical University of Vienna, Vienna, Austria.*

INTRODUCTION: Endometriosis is a benign estrogen dependent inflammatory condition, causing among other symptoms chronic pelvic pain, dysmenorrhea, dyspareunia, and subfertility. Even though increasing evidence is indicating the impact of epigenetics in the development of endometriosis, the common use of tissue homogenates or cultured cells might have hampered the detection of distinct pathophysiological alterations so far.We therefore aimed to profile DNA methylation patterns from different cycle phases in stromal and epithelial tissue fractions, separated by laser capture micro-dissection (LCM) from patient material.

METHODS: 40 eutopic and 19 ectopic endometrial specimen from patients with endometriosis and normal endometrium from 15 control donors were provided by the Vivantes Humboldt Hospital Berlin andthe Department of Gynecology and Obstetrics at the University Hospital in Vienna, with informed consent of all donors. The separation of epithelial and stromal endometrial cells was performed by LCM. Differences in DNA methylation were examined by Reduced Representation Bisulfite Sequencing (RRBS). Briefly, DNA was fragmented with MspI and bisulfite-converted sequencing libraries were produced using NuGEN Ovation® Ultralow Methyl-Seq Library Kit.

RESULTS: We have successfully adapted the RRBS technology for analysis of less than 10 ng input DNA and show the precision of our method using calibrator samples with known DNA methylation levels. After separation of all clinical samples into epithelial and stromal fractions by LCM we recorded a total of 148 DNA methylation profiles. To our knowledge, this represents the largest collection of methylation profiles at this tissue and sequence resolution. Differential methylation analyses showed profound differences between epithelial and stromal cells (e.g. EPCAM). Less pronounced differences were found when comparing eutopic samples from patients and controls and different cycle phases, respectively. Currently we are increasing the resolution of our analyses by deeper sequencing.

CONCLUSIONS: These results are expected to unveil the contribution of epigenetic regulation to the pathogenesis of endometriosis.

S-119

Dysregulated Lipid Mediator Profile in the Peritoneal Fluid of Endometriosis Patients. Matthias Keck, Thomas M Zollner, Frank Sacher*. *Bayer AG, Berlin, Germany.*

INTRODUCTION: Endometriosis as defined by the presence of glands and stroma outside the uterine cavity is affecting 5 –10% of the female population in the reproductive age. The most common symptom is pelvic pain (e.g. dysmenorrhea).

Phospholipids are known to modulate inflammation and pain perception and e.g. regulate a broad range of cell processes such as mitogenesis and monocyte chemotaxis. Endometriosis is an inflammatory disease accompanied by elevated pro-inflammatory cytokines and immune cell influx to the lesions and peritoneal cavity. Hence, our aim was to characterize the lipid profile in the peritoneal fluid of endometriosis patients vs. controls.

METHODS: Peritoneal fluid of informed and consenting endometriosis patients and controls were collected in course of a laparoscopy and were

stored at -80°C. Targeted metabolite profiling of all fluids was performed by using the LC-MS based Absolute IDQ p180 Kit (Biocrates Life Sciences AG). Multivariate data analysis was carried out by the Umetrics SIMCA-P software.

RESULTS: Endometriosis patients showed a distinct pattern of LPCs (lyso-phosphatidylcholines) & PCs (phosphatidylcholines) in the peritoneal fluid. A principal component analysis (PCA) revealed a clear separation of diseased vs. healthy women. Interestingly, the level of the pro-algesic lyso-phosphatidylcholines LPC 16:1 and LPC 18:1 is significantly higher in patients and might contribute to the pain symptoms of the disease.

CONCLUSIONS: The profile of bioactive phospholipids differs in endometriosis patients vs. controls and might contribute to the inflammation and pain associated with this disease.

S-120

Endometriosis and Ovarian Cancer: Shared Genetic Risk and Common Mechanisms. Grant W Montgomery,[1] Jenny N Fung,[1] Sarah J Holdsworth-Carson,[2] Jane E Girling,[2] Juliet D Franch,[3] Stacey L Edwards,[3] Joseph E Powell,[1] Peter AW Rogers.[2] [1]*University of Queensland, Brisbane, QLD, Australia;* [2]*University of Melbourne, Melbourne, VIC, Australia;* [3]*QIMR Berghofer Medical Research Institute, Brisbane, QLD, Australia.*

INTRODUCTION: Epidemiological studies have demonstrated associations between endometriosis and some histotypes of ovarian cancer. Overlap between endometriosis and ovarian cancer in epidemiological studies could be influenced by discovery of endometriosis lesions at or close to the time of diagnosis for ovarian cancer. Genetic studies in independent samples are not subject to the same ascertainment.

METHODS: Genetic overlap between endometriosis and ovarian cancer has been determined using genetic relatedness estimates and genetic risk scores from genome-wide association data. We analysed one region of overlap on chromosome 1p36.12 in endometrial samples collected from women at the Royal Women's Hospital (n=136). DNA samples were genotyped on Human CoreExome chips and RNA samples analysed using Illumina HT-12 v4.0 Beadchips. Chromatin confirmation capture libraries were constructed using *Nco*I and interactions between DNA fragments and gene promoters in the region quantitated by real-time PCR (qPCR). To validate observed interactions, promoter-driven luciferase reporter constructs were generated by insertion of DNA fragments containing the *LINC00339* or *CDC42* promoters and transfected into Ishikawa cells. Luciferase activity was measured 24 hr post-transfection.

RESULTS: Analysis of polygenic risk scores found evidence for shared genetic risk between endometriosis and all histotypes of ovarian cancer, except for the intestinal mucinous type. There was a significant effect of SNP rs3820282 at 1p36 on expression of the long non-coding RNA *LINC00339*. Chromatin conformation capture provided evidence for risk SNPs interacting with the promoters of both *LINC00339* and *CDC4* and luciferase reporter assays suggest the risk SNP rs12038474 is located in a transcriptional silencer for *CDC42* and the risk allele increases expression of *CDC42*.

CONCLUSIONS: Our results suggest that SNPs increasing endometriosis risk at chromosome 1p36 act through *CDC42* similar to results for ovarian cancer. However, further functional studies are required to rule out inverse regulation of both *LINC00339* and *CDC42*.

Lu et al., Hum Mol Genet. 2015 24: 5955-5964. Powell et al., Hum Mol Genet 2016 (in press).

S-121

MRI Assessment Is Not Predictive of Patient Symptoms from Uterine Fibroids. Alessandra J Ainsworth†,[1] Shannon K Laughlin-Tommaso,[1] Lisa E Vaughan,[2] Amy L Weaver,[2] Elizabeth A Stewart,[1] Gina K Hesley*.[3] [1]*Mayo Clinic, Rochester, MN, USA;* [2]*Mayo Clinic, Rochester, MN, USA;* [3]*Mayo Clinic, Rochester, MN, USA.*

INTRODUCTION: Symptomatic uterine fibroids are often treated with minimally invasive procedures where correlation of symptoms and uterine anatomy is essential for individualized treatment. This study aimed to investigate the agreement between self-reported symptoms and physician assessment based on MRI.

METHODS: We completed a retrospective review of patients undergoing evaluation and treatment of uterine fibroids from April 2013 to March 2014, who underwent MRI and completed required questionnaires to assess fibroid symptoms. MR images were reviewed by a gynecologist and radiologist who specialize in fibroid care. Physicians were blinded and asked to predict symptoms based on objective measures and subjective review. Objective measures included fibroid distortion of the uterine cavity and anatomic location. These measures contributed to the overall subjective review of MRI images that reflected expert opinion of predicted symptoms. Positive agreement was calculated to compare accurate prediction of reported symptoms and negative agreement calculated to reflect correct prediction of symptom absence.

RESULTS: Twenty-four MRIs were reviewed. The most commonly reported symptoms were heavy menstrual bleeding (21/23, 91%) and increased urinary frequency (18/24, 75%), while the least commonly reported symptoms were urinary retention (5/23, 22%) and dyspareunia (7/23, 30%). Heavy menstrual bleeding and increased urinary frequency reached a positive agreement of over 70%, while only abdominal contour achieved a negative agreement over 70% (table 1). The lowest positive agreement was predicted bowel symptoms and lowest negative agreement was predicted dyspareunia.

Patient Symptom vs. Subjective Assessment	Positive Agreement (%)	Negative Agreement (%)
Heavy Menstrual Bleeding	17/21 (81%)	1/2 (50%)
Dysmenorrhea	9/13 (69%)	4/11 (36%
Pelvic Pressure	11/16 (69%)	2/5 (40%)
Bowel Symptoms	3/11 (27%)	7/13 (54%)
Increased Urinary Frequency	14/18 (78%)	3/6 (50%)
Urinary Retention	2/5 (40%)	10/18 (56%)
Dyspareunia	4/7 (57%)	5/16 (31%)
Abdominal Protrusion	7/11 (64%)	11/13 (85%)

CONCLUSIONS: Factors other than uterine anatomy appear to influence fibroid symptoms. This presents a challenge for patient counseling and anatomy-based staging systems for uterine fibroids.

S-122

Clinical Limitations of the International Federation of Gynecology and Obstetrics (FIGO) Classification of Uterine Fibroids. Shannon K Laughlin-Tommaso,[1] Elizabeth A Stewart,[1] Matthew R Hopkins,[1] Kathleen R Brandt,[2] Gina K Hesley*.[2] [1]*Mayo Clinic, Rochester, MN, USA;* [2]*Mayo Clinic, Rochester, MN, USA.*

INTRODUCTION: The *International Federation of Gynecology and Obstetrics* (FIGO) classification of fibroids uses more than 9 categories based on fibroid location. Our goal was to determine the feasibility of consistently applying the FIGO classification for women with symptomatic uterine fibroids.

METHODS: We classified fibroids for women who presented for clinical fibroid care and underwent magnetic resonance imaging (MRI) between April 2012 and April 2013. One to 3 fibroids from each MRI were selected and labeled, and then independently reviewed by 4 physicians with expertise in fibroid care (2 gynecologists, 2 radiologists). The number of unique stages assigned to the fibroids was recorded. The differences in staging were evaluated by whether they would alter surgical management of the fibroids or not. Fibroid volume was calculated using the prolate ellipsoid formula. Student t-test was performed to compare mean values.

RESULTS: We classified 42 fibroids in 23 uteri. The majority of fibroids (n=36, 86%) had at least 2 FIGO stages assigned; of these, 4 (11%) had 4 different assigned stages. One-fifth (n= 9, 21%) of these classification differences would have affected surgical management. The attached figure demonstrates a fibroid that was assigned 3 different FIGO stages that would have affected the surgical approach; a type 2 might have been approached hysteroscopically whereas types 3-6 or 4 would not.

**Figure(s) will be available online.*

Smaller fibroids were associated with differences in staging that would change management {mean volume 3 cm^3 (SD 2.3) vs. 27cm^3 (SD 36.9), p=0.03}.

CONCLUSIONS: FIGO classifications were not consistently assigned by expert physicians and would have resulted in changes in management. Further validation of the FIGO fibroid classification system should be conducted.

S-123

Silibinin Inhibits Progesterone Induced Rankl Expression, Cell Proliferation and Extracellular Matrix Deposition in Human Uterine Leiomyoma Cells. Deborah E Ikhena†, Shimeng Liu, Stacy Kujawa, Serdar Bulun, Ping E Yin*. *Northwestern University, Feinberg School of Medicine, Chicago, IL, USA.*

INTRODUCTION: Silibinin is a natural non-toxic polyphenolic flavonoid which has been reported to inhibit the effects of receptor activator of nuclear factor kappa-B ligand (RANKL); however, the underlying mechanism of its effect on RANKL is unclear. We previously demonstrated that progesterone stimulates RANKL expression in leiomyoma. Our goal here is to determine if silibinin inhibits progesterone induced RANKL expression, cell cycle proteins and extracellular matrix deposition.

METHODS: Tumors were obtained from pre-menopausal women aged 18-45 who did not report a history of menstrual irregularities. We isolated leiomyoma smooth muscle cells from fresh fibroid tissues and maintained them in primary culture (n=3). The cells were treated with vehicle or varying doses of silibinin (30, 60 or 90mM) for 24, 48, or 72 hours (h) respectively. Total RNA was extracted and RT-PCR was used to measure mRNA levels of RANKL, Cyclin D1 (a downstream target of RANKL and a cell cycle protein increased with cell proliferation) and Col1A2 and Col3A1 (markers of extracellular matrix deposition). Protein was extracted and proliferating cell nuclear antigen (PCNA) protein expression levels were measured at 48 and 72 hours.

RESULTS: In primary cells, silibinin reduced RANKL expression in a dose--dependent manner with the most significant change observed at 60 mM (up to 60%- decrease, $p<0.05$). Silibinin significantly decreased cyclin D1, Col1A2 and Col3A1 mRNA levels in a dose--dependent manner by up to 80% -change ($p<0.05$). Inhibition of RANKL, Cyclin D1, Col1A2 and Col3A1 expression by silibinin was observed as early as 24 h, peaked at 48 h and persisted till 72 h of treatment. Furthermore, silibinin treatment also led to a decrease in PCNA protein expression at 48 and 72 hours.

CONCLUSIONS: Silibinin is an effective inhibitor of RANKL expression. Silibinin also decreased cell proliferation and extracellular matrix deposition in leiomyoma smooth muscle cells. We postulate that these effects of silibinin on cell proliferation and extracellular matrix formation are mediated via suppression of RANKL activity. Silibinin has the potential to serve as a novel medical treatment option with no known side effects for uterine leiomyoma.

S-124

African Genetic Ancestry and Body Mass Index Interact to Modify Risk for Uterine Fibroids. Ayush Giri†,[1] Todd Edwards,[1] Katherine Hartmann,[2] Melissa Wellons,[3] Pamela Schreiner,[4] Digna Velez Edwards*.[2] *[1]Vanderbilt University Medical Center, Nashville, TN, USA; [2]Vanderbilt University Medical Center, Nasvhille, TN, USA; [3]Vanderbilt University Medical Center, Nashville, TN, USA; [4]University of Minnesota, Minneapolis, MN, USA.*

INTRODUCTION: African ancestry and obesity are important risk factors for uterine fibroids, and likely interact to provide the right conditions for fibroid growth. However, existing studies largely focus on main effects.

METHODS: We investigated whether the associations between genetically-inferred local ancestry (European compared with African) and imaging-confirmed fibroid status are modified by body mass index (BMI) in predominantly pre-menopausal African-American women from two independent sources: Vanderbilt University Medical Center bio-repository (BioVU) (539 cases and 794 controls) and Coronary Artery Risk Development in Young Adults study (CARDIA, 264 cases and 173 controls). Interactions were modeled in each data set with logistic regression adjusting for age, and genetic-principal components, followed by fixed-effects meta-analysis. Threshold for statistical significance was empirically estimated ($p=1.2x10^{-4}$).

RESULTS: The association between local European ancestry and fibroid risk was modified by BMI (continuous-interaction $p=3.75x10^{-5}$) in chromosome 6p24; the strongest association was found in the obese category (ancestry odds ratio (AOR)=0.51, $p=2.23x10^{-5}$) (Fig 1).
**Figure(s) will be available online.*
Analysis of genetic variants in this region showed similar evidence for interaction at an insertion/deletion marker in the *ADTRP* gene; strongest evidence was again found in the obese category (OR: 1.66, $p=1.72x10^{-6}$). We additionally report marginal evidence for interaction at a previously reported admixture mapping region in chromosome 2q31-32, which includes *TFPI*, an immediate downstream target gene for *ADTRP*.

CONCLUSIONS: Findings from our study provide an example of how modifiable and non-modifiable risk factors may interact to influence fibroid risk and suggest a biological role for BMI.

S-125

The Effect of Local Estrogen Therapy on Extracellular Matrix Biogenesis and Remodeling in Vaginal Tissue of Postmenopausal Women with Severe Pelvic Organ Prolapse. Tanya Tyagi†,[1] May Alarab,[2] Harold Drutz,[2] Stephen Lye,[1,2] Oksana Shynlova*.[1,2] *[1]Lunenfeld-Tanenbaum Res Institute, Toronto, ON, Canada; [2]Sinai Health Complex, Toronto, ON, Canada.*

INTRODUCTION: Pelvic organ prolapse (POP) affects nearly half of postmenopausal women. Current treatment options for POP include reconstructive pelvic surgeries with various vaginal implants and optional Local Estrogen Therapy (LET). We reported earlier that LET causes an activation of local immune response and leukocyte infiltration. Here we aim to analyze the effect of LET treatment on the expression (1) of genes participating in collagen/elastin biogenesis and biodegradation, and (2) on protein expression of chemotactic cytokines in vaginal tissues of postmenopausal women with severe POP.

METHODS: Postmenopausal women undergoing reconstructive pelvic surgery (POPQ=3-4) were recruited. Vaginal biopsies were collected from patients treated with LET (average duration 7.5 months, N=15) and untreated patients (N=17). Total RNA and protein were extracted; the expression of ECM structural and remodeling genes were analyzed by RT-qPCR, Luminex assays and immunohistology; cytokine proteins were analyzed by 40-plex Luminex assay.

RESULTS: We examined transcript levels of major vaginal collagens (COL1,3,5) and ECM maturation enzymes(LOXs, ADAMTS2, and BMP1). Expression of COL1,3,5 and BMP1 genes were significantly elevated ($p<0.05$) in vaginal tissues of POP patients treated with LET as compared to untreated POP patients. ECM remodelling enzymes matrix metalloproteases (MMPs) and their tissue inhibitors (TIMPs) were examined. MMP2 and TIMP2 mRNA levels were significantly up-regulated by LET in vaginal tissue ($p<0.05$), whereas MMP3 gene showed a significant ($p<0.05$) decrease in LET-treated tissue. Analysis of 40-plex Chemokine assay indicate that 11 vaginal chemokines involved in macrophage and T-cell infiltration were significantly ($p<0.05$) induced by LET in postmenopausal POP patients.

CONCLUSIONS: Estrogen activates local immune response in vaginal tissue of postmenopausal women with severe POP, causing significantly increased tissue chemokine levels and infiltration of immune cells, a major source of MMPs. We observed that LET increases MMPs /TIMPs, known regulators of tissue repair and regeneration. These changes in combination with observed increase in the expression of structural COL1,3,5 and proteins involved in maturation of collagen/elastin fibers support a beneficial role of estrogen in the remediation of pelvic floor tissue in POP patients.

S-126

Koch's Experimental Postulate Applied to Bacterial Vaginosis: Identification of a Single Organism as Sufficient to Elicit Clinical Features and Health Complications Associated with BV. Nicole Gilbert,[2] Amanda Lewis*.[1,2] *[1]Washington University School of Medicine, St. Louis, MO, USA; [2]Washington University School of Medicine, St. Louis, MO, USA.*

INTRODUCTION: Bacterial vaginosis (BV) is an "imbalance" of the vaginal microbiota linked with increased risks of vaginal, uterine, and placental infections caused by BV bacteria and other pathogens. However, despite thousands of reports describing the BV-associated microbiota and its risks, the mechanisms are largely unknown. Likewise, organism(s) responsible for the clinical features and complications associated with BV remain ill defined. We build new mouse models to better understand the roles of specific bacteria in the features and health complications associated with BV.

METHODS: We performed vaginal infection and co-infection in mice. In the nonpregnant model, we examined whether *Gardnerella vaginalis* or *Prevotella bivia* were sufficient alone or in combination to elicit clinical phenotypes of BV such as vaginal sialidase activity, mucus degradation, epithelial exfoliation, and the presence of clue-like cells. We also examined whether vaginal infection with *G. vaginalis* (in nonpregnant and pregnant mice) was sufficient to enhance host susceptibility to secondary infections of the upper reproductive tract. Comparisons were made between single- and co-infected groups using nonparametric statistical comparisons, most commonly the Mann-Whitney U-test.

RESULTS: While *Prevotella* established ~100-fold higher titer vaginal infections than *Gardnerella*, it failed to elicit an exfoliation response and did not boost sialidase levels over that observed in *G. vaginalis* mono-infections. We also report that vaginal infection with *G. vaginalis* was sufficient to enhance high titer uterine infections with *Prevotella*, a common cause of intrauterine infections in humans, with ~20-fold higher titers in co-infected compared to *Prevotella* mono-infected animals ($P<0.02$). In a timed pregnancy model of infection, *G. vaginalis* vaginal infection in pregnant mice led to greater a propensity of secondary vaginal, uterine and placental infection(s) common to human pregnancy.

CONCLUSIONS: Taken together, these results strongly suggest that *G. vaginalis* is part of the causal basis for both the mucosal damage and sensitization to secondary infections of the reproductive and urinary tracts that occurs in BV.

S-127

Longitudinal Lifestyle Monitoring in "Maternity Log Study" to Predict Preterm Birth. Daisuke Ochi†,[1] Takafumi Yamauchi†,[1] Yoshiki Tsunemoto†,[1] Yuki Harada,[2] Riu Yamashita,[2] Takahiro Mimori†,[2] Maiko Wagata†,[2] Osamu Tanabe,[2] Hirohito Metoki,[2] Nobuo Yaegashi,[3] Maternity Log Project Team,[2] Satoshi Hiyama,[2] Masao Nagasaki,[2] Junichi Sugawara*.[2] *[1]NTT DOCOMO, Inc., Yokosuka, Kanagawa, Japan; [2]Tohoku University, Sendai, Miyagi, Japan; [3]Tohoku University Graduate School of Medicine, Sendai, Miyagi, Japan.*

INTRODUCTION: Pregnancy related disorders, including preterm birth (PTB) are caused by complex interactions of genetic and environmental factors such as lifestyle and living environments. We have designed a prospective cohort study named "Maternity Log Study" to investigate unrevealed mechanisms of those disorders.

METHODS: Three hundred participants have been recruited by written informed consent at Tohoku University Hospital. We collected daily lifelogs of physiological data (body weight, blood pressure (BP), heart rate, daily step count, body temperature, sleep duration) and symptoms (morning sickness, abdominal pain, uterine contraction, bowel movement) as well as blood samples at several time points throughout pregnancy. We investigated potential lifelog predictors of PTB.

RESULTS: Heart rate in the morning after 24 weeks of gestational age was significantly different between the control and women with PTB (77.5±9.3 vs 88.4±11.2 bpm at 25 weeks, $p<0.001$). Caloric expenditure of the PTB group was lower than the control after 20 weeks (1676±271 against 1919±232 Kcal at 21 weeks, $p<0.01$). A PTB prediction model was generated from BMI change per week, caloric expenditure, bedtime, heart rate, age, diastolic BP in the evening, and the change in caloric expenditure. Cross-validation demonstrated the accuracy of 0.81 and 0.90 at 24 and 32 weeks of gestational age, respectively. The areas under Receiver Operating Characteristic curve were 0.908 and 0.913, respectively.

**Figure(s) will be available online.*

CONCLUSIONS: Combination of several daily maternal lifelogs might serve as a predictive marker for PTB. These findings may contribute to the development of wearable monitoring devices specific for pregnant women to predict onset of PTB.

S-128

Inhibition of DNA Methylation Rescues Chronic Hypoxia-Mediated Decrease in BK_{Ca} Channel Activity and Increase in Myogenic Contractility in Uterine Arteries of Pregnant Sheep. Xiang-Qun Hu,[1] Chiranjib Dasgupta,[1] Daliao Xiao,[1] Xiaohui Huang,[1] Shumei Yang,[2] Lubo Zhang*.[1] *[1]Loma Linda University School of Medicine, Loma Linda, CA, USA; [2]California State University, San Bernardino, CA, USA.*

INTRODUCTION: Previous studies demonstrated that long-term high altitude hypoxia during gestation resulted in a decrease in large-conductance Ca^{2+}-activated K^+ (BK_{Ca}) channel activity and an increase in myogenic contractility in uterine arteries of pregnant sheep, leading to maladaptation of uteroplacental circulation during pregnancy. The present study tested the hypothesis that chronic hypoxia triggers dysfunction of BK_{Ca} channel function in uterine arteries *via* heightenedDNA methylation.

METHODS: Resistance-sized uterine arteries were isolated from near-term pregnant sheep maintained at ~300 m above sea level. For *ex vivo* hypoxic treatment, uterine arteries from normoxic animals were treated with 21.0% O_2 or 10.5% O_2 for 48 hours in the absence or presence of a DNA methyltransferase (DNMT) inhibitor 5-aza-2'-deoxycytidine. The BK_{Ca} channel activity was determined with patch-clamp recording. Function of BK_{Ca} channels in the relaxation and pressure-induced myogenic constriction of uterine arteries were also determined.

RESULTS: Chronic hypoxia significantly reduced BK_{Ca} channel current density in uterine arteries. This suppression was prevented by 5-aza-2'-deoxycytidine. Accordingly, BK_{Ca} channel-mediated relaxations of uterine arteries was significantly impaired by chronic hypoxia. In accordance, pressure-dependent myogenic tone was increased by chronic hypoxia. Of interest, the impaired relaxations mediated by BK_{Ca} channels and heightened uterine vascular tone induced by hypoxia were ablated by inhibition of DNA methylation with 5-aza-2'-deoxycytidine.

CONCLUSIONS: Our data suggest that chronic hypoxia instigates dysfunction of BK_{Ca} channels *via* hypermethylation, leading to elevated uterine vascular tone in pregnant sheep.

S-129

Inhibition of DNA Demethylation Blocks Pregnancy-Mediated Increase in Large Conductance Ca^{2+}-Activated K^+ Channel Activity in Ovine Uterine Arteries. Xiang-Qun Hu, Limin Han, Lubo Zhang*. *Loma Linda University School of Medicine, Loma Linda, CA, USA.*

INTRODUCTION: The increase in large conductance Ca^{2+}-activated K^+ (BK_{Ca}) channel activity is of critical in the regulation of uterine vascular tone and blood flow during pregnancy. The activity of the BK_{Ca} channel in uterine arteries is largely regulated by the methylation status of KCNMB1 promoter and its expression levels. Previous studies demonstrated that pregnancy and estrogen caused a decrease in KCNMB1 promoter methylation in ovine uterine arteries. The present study tested the hypothesis that DNA demethylation of the KCNMB1 promoter plays a key role in pregnancy-mediated upregulation of BK_{Ca} channel activity in the uterine artery.

METHODS: Resistance-sized uterine arteries were isolated from nonpregnant and near-term pregnant sheep. For *ex vivo* hormonal treatment, uterine arteries from nonpregnant animals were treated with 17β-estradiol (E2β, Sigma) (0.3 nM) and progesterone (P4, Sigma) (100.0 nM) for 48 hours in the absence or presence of a ten-eleven translocation (TET) methylcytosine dioxygenases inhibitor fumarate. The expression of TET1 and KCNMB1 was determined with RT-PCR and Western blot. Knockdown of TET1 and KCNMB1 was achieved by transfection of uterine arteries with specific siRNAs.

RESULTS: Fumarate significantly inhibited BK_{Ca} channel current densities in uterine arteries from pregnant sheep. Treatment of uterine arteries from nonpregnant animals withestrogen and progesterone for 48 hours significantly increased BK_{Ca} channel current densities, which was ablated in the presence of fumarate. BK_{Ca} channel β1 subunit (KCNMB1) siRNAs signifciantly reduced the expression of KCNMB1 in the uterine arteries. In addition, TET1 siRNAs significantly decreased the expression of TET1. Of interest, knockdown of TET1 also decreased the expression of BK_{Ca} channel β1 subunit in the uterine arteries. Of importance, knockdown of either BK_{Ca} channel β1 subunit or TET1 in uterine arteries resulted in a substantial reduction of BK_{Ca} channel current densities.
CONCLUSIONS: Together, our data suggest that TET1-mediated demethylation plays an essential role in the regulation of BK_{Ca} channel activity in uterine arteries during pregnancy.

S-130

Validation of Microparticle Proteomics as a Means to Stratify the Risk of Spontaneous Preterm Birth. David Cantonwine,[1] Zhen Zhang,[2] Kevin Rosenblatt,[3] Brian Brohman,[4] Robert Doss,[4] Thomas McElrath*.[1] *[1]Brigham&Women's Hospital, Boston, MA, USA; [2]Johns Hopkins, Baltimore, MD, USA; [3]University of Texas, Houston, TX, USA; [4]Inc, Louisville, KY, USA.*
INTRODUCTION: We previously demonstrated that proteins associated with circulating microparticles (CMPs) exhibit a unique pattern at 10 weeks gestation among women who go on to experience spontaneous preterm birth (sPTB) <35 weeks (Cantonwine AJOG, 2016). Our present analysis validates these markers using a new cohort of individuals.
METHODS: Obstetrical outcomes in 75 singleton pregnancies with prospectively collected plasma samples obtained between 10-12 weeks were validated by physician reviewers for sPTB <35 weeks. These were matched to 150 uncomplicated singleton term deliveries. Controls were matched on gestational age at sampling (+/- 2 weeks), maternal age (+/- 2 years), race and parity. CMPs from these specimens were isolated and analyzed by multiple reaction monitoring mass spectrometry for known protein biomarkers selected from the previous study for their ability to predict the risk of delivery <35 weeks. We also examined the biological relevance of these analytes via a combined functional profiling/pathway analysis.
RESULTS: Cases and controls did not differ by BMI (26 vs 25 kg/m^2; p=0.37) or in vitro fertilization (17% vs 10%; p=.10) status respectively. Mean gestational age at delivery was 33 vs 39 weeks ($p<10^{-5}$). We observed that the CMP markers identified in the previous study again demonstrated distinct Kaplan-Meier curves for sPTB. Specifically, we found that for sPTB IC1, which is involved in the inhibition of complement activation, had a HR of 1.46 (95%CI 1.04-2.05) while PGRP2 which is involved in immune regulation (HR 1.45; 95%CI 1.11-1.90) and THBG which is involved in thyroid hormone function (HR 1.45; 95%CI 1.04-2.02) showed marked differences (figure).
CONCLUSIONS: Using an independent cohort, we validate a set of markers that, when obtained between 10-12 weeks, predict SPTB <35 weeks. These markers are components of plausible biologic pathways involving complement, immune, and thyroid function.
**Figure(s) will be available online.*

S-131

Does Gestational Diabetes Increase the Risk of Pregnancy Induced Hypertension in Twin Gestations? Mirella Mourad†, Gloria Too†, Cynthia Gyamfi-Bannerman, Noelia Zork*. *Columbia University, New York, NY, USA.*
INTRODUCTION: Gestational diabetes (GDM) is known to be associated with an increased risk for pregnancy induced hypertension (PIH) in singleton pregnancies. The data are mixed regarding the effect of GDM on the risk for PIH in twins. The objective of our study was to assess the rate of PIH in twin pregnancies complicated by GDM.
METHODS: This is a secondary analysis of a multi-center randomized trial in which twin gestations were assigned to weekly intramuscular injections of progesterone to reduce the rate of preterm birth. We included all twin pregnancies with and without GDM. Pre-gestational diabetics, chronic hypertensives, pregnancies complicated by twin to twin transfusion syndrome or congenital fetal anomalies were excluded. The primary outcome was the rate of PIH in twin pregnancies complicated by GDM as compared to those without GDM. Logistic regression analysis was used to evaluate the association between PIH and GDM after controlling for maternal age and BMI.
RESULTS: 621 twin pregnancies were included, 577 (93%) without GDM, 44 (7%) with GDM. The group with GDM had a significantly higher BMI and had a higher rate of advanced maternal age (AMA). The rate of PIH in the GDM group was significantly higher when compared to the non-GDM group (32% versus 18% p=0.022), however after adjusting for AMA and BMI, this association lost its statistical significance (aOR 1.3 (0.83 – 2.23), p=0.224)
**Figure(s) will be available online.*
CONCLUSIONS: In this prospective cohort of twin pregnancies, the rate of PIH did not differ significantly between gestational diabetics and non-gestational diabetics after adjusting for BMI and AMA status. PIH may not be a complication of GDM in twin pregnancies diagnosed using the same diagnostic criteria used for singletons. Future prospective studies evaluating the diagnosis of GDM in twins and its complications are warranted.

S-132

Relationship of Fat Distribution to Pre Pregnancy Uterine Artery Hemodynamics and Fetal Growth. Kylie Cooper,[1] Carole McBride,[1] Gary Badger,[2] Ira Bernstein.[1] *[1]University of Vermont, Burlington, VT, USA; [2]University of Vermont, Burlington, VT, USA.*
INTRODUCTION: Adipose tissue influences reproductive health including pregnancy outcomes. We evaluated the relationship of adipose distribution and body composition on pre pregnancy uterine blood flow and their independent effects on birth weight.
METHODS: Seventy-nine nulliparous women underwent assessment of body mass index and body composition via dual energy X-ray absorptiometry. Pre pregnancy uterine artery Doppler ultrasound was performed and hemodynamic indices were calculated. Additionally, subjects underwent measurement of cardiac output via Doppler echocardiogram and uterine index (the proportion of cardiac output received by the uterus) was determined. Patients were followed in subsequent pregnancy and birth weight and intrauterine growth restriction were documented. Correlation analysis and stepwise logistic regression were performed.
RESULTS: Gynoid fat mass (R=0.25, p=0.03; R=0.3, p=0.005) and percentage of gynoid fat distribution (R=0.24, p=0.03; R=0.22, p=0.05) were positively associated with uterine artery resistance index and pulsatility index. Gynoid fat mass was negatively associated with uterine index (R=-0.22, p=0.05). Stepwise regression did not identify adipose distribution as a significant independent predictor of birth weight.
CONCLUSIONS: In nulliparous women prior to pregnancy, gynoid fat mass was associated with increased measures of uterine artery resistance and diminished flow. When compared to other indices of body composition, gynoid fat plays a more significant role in determining uterine artery hemodynamics. This suggests that fat deposition patterns may play a role in regulation of uterine blood flow.

S-133

Greater Adenosine Monophosphate Kinase (AMPK) Activation During High-Altitude (HA) Pregnancy. Colleen G Julian,[1] Haemin Park,[2] Gabriel Wolfson,[1] Lorna G Moore.[3] *[1]University of Colorado Denver, Denver, CO, USA; [2]University of Colorado Denver, Denver, CO, USA; [3]University of Colorado Denver, Denver, CO, USA.*
INTRODUCTION: Reduced uterine artery (UtA) blood flow is an important contributor to the increased incidence of preeclampsia (PreE) and intrauterine growth restriction (IUGR) at high altitude (HA). Prior studies suggest that AMPK plays an important role in the regulation of uteroplacental blood flow at HA. Specifically, single nucleotide polymorphisms (SNPs) near the gene encoding the catalytic subunit AMPKa1 predicted to activate AMPK are associated with greater UtA diameter, blood flow and fetal growth at HA. **Objectives:** We sought

to determine whether (1) HA hypoxia activates AMPK in vascular and placental tissue during murine pregnancy, (2) HA increased the expression of AMPK activators (STK11 and MAP3K7), and (3) AMPK pathway gene expression levels in peripheral blood mononuclear blood cells (PBMCs) could serve as an index of those present in placenta.
METHODS: By western blot, we measured total and P-AMPKa, and two downstream AMPK targets (Raptor and tuberous sclerosis 2 (TSC2)) in placenta and thoracic aorta (TA) as a representative vascular tissue from gestational day (GD) 19.5 hypoxic (n=6) *vs*. normoxic (n=6) pregnant C57/BL6 mice. Expression levels of *STK11* and *MAP3K7*, were measured using RT PCR at GD 19.5 in UtA and placental tissue, and PBMCs of normoxic (n=4) and hypoxic (n=3) dams.
RESULTS: Compared to normoxic controls, placental and TA of hypoxic dams showed greater absolute and relative to total P-Raptor and P-TSC protein expression and greater P-relative to total AMPKa protein in hypoxic *vs*. normoxic tissues (P-AMPKa:AMPKa = 0.87 and 0.60, respectively). UtA *STK11* and *MAP3K7* expression levels were 4.0 (p=0.10) and 2.4-fold (p=0.09) greater, and placental STK11 and MAP3K7 expression levels 1.7-fold (p=0.002) and 1.4-fold (p=0.01) greater in hypoxic *vs*. normoxic dams. PBMC and UtA *STK11* gene expression levels were positively correlated in pregnant animals.
CONCLUSIONS: Our findings suggest that HA increases AMPK activation in placental and vascular tissue during pregnancy and support the potential use of PBMC expression profiles to identify biomarkers for processes occurring in the uterine vasculature.

Support: National Institutes of Health, American Heart Association.

S-134

Soluble Fms-Like Tyrosine Kinase-1 (Sflt-1) Adversely Impacts CGRP Family Peptide System in Omental Artery Smooth Muscle Cells. Madhu Chauhan, Uma Yallampalli, Yuanlin Dong, Chandra Yallampalli. *Baylor College of Medicine/Texas Childrens Hospital, Houston, TX, USA.*
INTRODUCTION: Elevated levels of soluble fms-like tyrosine kinase-1 (sFlt-1) contribute to vascular dysfunction in preeclampsia. Sensitivity of omental artery (OA) for potent vasodilators calcitonin gene-related peptide (CGRP), adrenomedullin (ADM) and adrenomedullin2 (ADM2) is elevated in human pregnancy. These peptides mediate their effects through calcitonin receptor like receptor (CRLR) whose ligand specificity is dictated by receptor activity modifying protein (RAMP) 1, 2 and 3. However, it is not known if sFlt-1 adversely affects the vascular function of these peptides in human pregnancy. The objective of this study is to: 1) Identify if CGRP, ADM and ADM2 increase cAMP synthesis in OA smooth muscle cells (HOASMC), 2) Assess the effects of sFlt-1 on the expression of CRLR, RAMP1, 2 and 3 mRNA in HOASMC, 3) Determine if sFlt-1 decreases cAMP synthesis in HOASMC; and if CGRP, ADM and ADM2 can inhibit the sFlt-1 induced decreases in cAMP levels.
METHODS: This study was approved by the Institutional Review Board at Baylor College of Medicine, Houston. HOASMC were isolated from normal pregnancyand used at passages 2-4. Cells were treated with or without sFlt-1 for 24 hrs in serum free DMEM and used for either mRNA or for cAMP generation in response to the treatments with peptides (10^{-7}M, 5 min) in presence of 100 μM of phosphodiesterase inhibitor isobutyl-1-methyl-xanthine. cAMP was measured by EIA (Cayman, USA) and mRNA by qRT-PCR. Data was analyzed by Prism GraphPad Software using unpaired t test or 1-way ANOVA. $P \leq 0.05$ was considered statistically significant.
RESULTS: 1) CGRP, ADM and ADM2 increased the synthesis of cAMP in HOASMC in the order of efficacy; CGRP>ADM=ADM2 ($P<0.05$), 2) sFlt-1 decreased cAMP synthesis in HOASMC ($P<0.05$), 3) CGRP and ADM but not ADM2 rescued the sFlt-1 induced decreases in cAMP levels in HOASMC ($P<0.005$), and 4) sFlt-1 increased CRLR mRNA and decreased RAMP1 mRNA ($P<0.05$), whereas RAMP2 and RAMP3 mRNA are not detectable in HOASMC.
CONCLUSIONS: CGRP, ADM and ADM2 increase cAMP synthesis in HOASMC in the order; CGRP>ADM=ADM2. sFlt-1 decreases the expression of RAMP1 and cAMP levels in HOASMC thus impairing the vascular effects of these peptides. Rescue of sFlt-1 mediated decreases in cAMP levels by CGRP and ADM in HOASMC suggest a potential protective role for these peptides in sFlt-1 mediated vascular dysfunction in human pregnancy.

S-135

Association of Interpregnancy Interval with Subsequent Perinatal Outcomes Following Pregnancies Complicated by Gestational Diabetes. Ashley N Battarbee†,[1] Lynn M Yee*.[2] [1]*The University of North Carolina at Chapel Hill, Chapel Hill, NC, USA;* [2]*Northwestern University Feinberg School of Medicine, Chicago, IL, USA.*
INTRODUCTION: Pregnancies complicated by gestational diabetes (GDM) are at increased risk for adverse perinatal outcome, and women with a history of GDM are at increased risk for development of type 2 diabetes (T2DM) later in life. Our objective was to evaluate the association of the interpregnancy interval (IPI) with recurrence of GDM or development of T2DM and other adverse perinatal outcomes in subsequent pregnancies.
METHODS: Retrospective cohort study of women who had a subsequent pregnancy following an index pregnancy complicated by GDM. The cohort was derived from all women with GDM seen in three large-volume practices from 2008-16. Women were stratified based on IPI < 18 months (m), 18 to 36 m, and > 36 m. Bivariable analyses were performed to determine the association between length of IPI and adverse perinatal outcomes. Multivariable logistic regression was performed comparing women with short or long IPI to the referent IPI group of 18 to 36 m.
RESULTS: Of 683 women with GDM in the index pregnancy, 143 (20.9%) had a subsequent delivery at this institution. Women with a short IPI (<18m) were more likely to have had A1GDM in the index pregnancy (73.9%) compared to those with 18-36m IPI (67.4%) and IPI >36m (44.8%, p=0.02). Long IPI was associated with both greater likelihood of subsequent gestational hypertension or preeclampsia (12.3% for <18mo, 14.3% for 18-36mo, and 37.9% for >36mo, p<.01) and of recurrent GDM or development of T2DM (66.2% for <18mo, 73.5% for 18-36mo, and 93.1% for >36mo, p=.02) in the subsequent pregnancy (Table). There were no statistically significant differences in preterm birth or birthweight between the IPI groups. After controlling for the type of GDM in the index pregnancy, neither short nor long IPI interval was independently associated with the development of gestational hypertension/preeclampsia or recurrent GDM/T2DM.
CONCLUSIONS: There is no evidence for an association between IPI after an index pregnancy complicated by GDM and subsequent adverse perinatal outcome.
**Figure(s) will be available online.*

S-136

Sphingosine 1-Phosphate Receptor Characterization in Term Diabetic and Normal Human Placentas. Luckey C Reed†,[1] Diana Villazana-Kretzer†,[1] Robert Walton†,[1] Sarah Estrada†,[1] Peter G Napolitano†,[1] Nicholas Ieronimakis*.[2] [1]*Madigan Army Medical Center, Tacoma, WA, USA;* [2]*Madigan Army Medical Center, Tacoma, WA, USA.*
INTRODUCTION: Vascular tone in the placenta is tightly regulated by molecular and mechanical factors. Spingosine-1-phosphate (S1P) is a potent bioactive sphingolipid that has been implicated in multiple disease processes to include hypertension, diabetes ,and preeclampsia. S1P signaling is mediated by five distinct g-protein coupled cell surface receptors. Receptors 1-3 have been shown to be highly expressed in the vasculature and play key roles in vascular tone, endothelial junction integrity, and inflammation. Despite increasing focus in S1P signaling with disease and pharmacological targeting of this pathway, its role in the human placenta is not well characterized. The purpose of this study is to further characterize the function of S1P receptors in physiological term human placentas compared to placentas from diabetic women.
METHODS: We investigated the expression of S1P receptors in term non-labor human placenta obtained from healthy pregnancies and those complicated by diabetes. Tissue from each placenta was processed for molecular analyses of S1P receptors.
RESULTS: Immunofluorescence analysis showed that the expression of S1P receptors appears to be highly specific, with distinct expression

patterns observed in each placental compartment and anatomical structure. S1P1 staining was predominantly in the smooth muscle cells (arrows), as compared to S1P2 and S1P3 (arrowheads), which were localized to the syncytiotrophoblasts. Interestingly, in the diabetic placentas we see the same localization pattern, however with greater staining intensity for S1P1 and S1P3.

**Figure(s) will be available online.*

CONCLUSIONS: To the best of our knowledge, this is the first study to characterize the expression of S1P receptors in human term placentas from both healthy pregnancies and those complicated by diabetes. Our results suggest that S1P plays a role in the regulation of placental vascular signaling and may represent a novel target for the prevention of diabetes associated feto-placental vascular dysfunction.

S-137

Differential Effects of TNF-α on the Production of Prostaglandins and Prostamides by Human Amnion Explants. Hassendrini N Peiris†, Kanchan Vaswani, Sarah Reed, Murray D Mitchell. *University of Queensland, Brisbane, QLD, Australia.*

INTRODUCTION: An increase in intrauterine prostaglandin production is critical for the onset and progression of labor in women and indeed all mammalian species studied. Endocannabinoids can act as substrates for enzymes of the prostaglandin biosynthetic pathways and can be utilized to generate other related compounds such as prostamides. The related end products can be indistinguishable by radioimmunoassay. However, mass spectrometry is able to separate these compounds and allows the accurate and relative measurements of prostaglandins and prostamides to be made in a single sample. **Aim:** To use mass spectrometry to identify products of endocannabinoid and eicosanoid biosynthetic pathways produced by amnion upon exposure to an inflammatory stimulus (TNF-α; Tumour Necrosis Factor -α) with and without the addition of substrate (Anandamide; AEA.)

METHODS: Human amnion explants from term placentae (delivery by elective caesarean section due to cephalopelvic disproportion) were treated with TNF-α (10 ng/mL), AEA (10μM) or a combination of TNF-α and AEA. Standards and samples were subjected to an extraction in methanol/formic acid. Extraction solution was prepared containing internal standards (PGE_2-d4, $PGF_{2\alpha}$-d4, PGFM-d4, PGE_2-EA-d4 250fmol each). Standards and samples were measured by LC-MS/MS.

RESULTS: Amnion explants produced significantly more prostaglandins (PGE_2) when treated with an inflammatory agent (TNF-α). The addition of anandamide substrate significantly increased the production of PGE_2-EA ($p<0.05$) compared to the inflammatory agent alone. In the absence of anandamide substrate prostaglandins (PGE_2) represent >90% of PGHS-derivatives. However, in the presence of anandamide substrate prostamides PGE_2-EA represent >90% of PGHS-derivatives.

CONCLUSIONS: We provide evidence that there is differential regulation of prostaglandin and prostamide biosynthesis in human amnion in response to an inflammatory stimulus and substrate (AEA). Our data demonstrate that amnion responds by a differential drive through the prostaglandin biosynthetic pathways. Moreover, and importantly, this has been shown using the "gold standard" of measurement by mass spectrometric means. The possibility is raised that separation of these products might reduce variability in results and lead to potential uses for their measurement in the diagnosis of preterm labor.

S-138

The Effect of Melatonin on Antioxidant Enzymes in Trophoblasts of Lean and Obese Women. Kayla E Ireland†, Leslie Myatt*. *University of Texas Health Science Center at San Antonio, San Antonio, TX, USA.*

INTRODUCTION: Maternal obesity is associated with increased oxidative stress and decreased mitochondrial respiration in trophoblasts. We have previously shown that addition of melatonin, a potent antioxidant, improves mitochondrial respiration in trophoblasts isolated from placentas of obese women. We hypothesized that this effect of melatonin is due to altered expression of antioxidant enzymes.

METHODS: Villous cytotrophoblasts were isolated from placental tissue collected at term c-section without labor from either obese (early BMI >30) or lean (early BMI 18-25) women and then were synctyialized over 72 hrs in culture with or without addition of melatonin (100 μM) for the last 24hr. Expression of the antioxidant enzymes superoxide dismutase (SOD) 1 [cytosolic], SOD2 [mitochondrial] and glutathione peroxidase 4 (GPx4), normalized to βactin, were measured by western blot. The effects of melatonin on the expression of the antioxidant enzymes were analyzed with two-way ANOVA and t-test as appropriate.

RESULTS: Maternal clinical characteristics were similar except for BMI (obese n=7 36.9 ± 2.0 and lean n=4 21.6 ± 1.0). No adverse clinical outcomes were noted. In trophoblasts of lean and obese women, addition of melatonin resulted in no significant alteration in the expression SOD1 or SOD2. While expression of GPx4, which has a high preference for lipid hydroperoxides, was significantly greater in trophoblast of obese compared to lean women ($p< 0.05$), the addition of melatonin significantly reduced ($p< 0.021$) GPx4 expression to a level not significantly different from that in lean women. There was no effect of melatonin on GPx4 expression in trophoblast of lean women.

CONCLUSIONS: We have previously shown that respiratory parameters of trophoblast from obese women, particularly the decreased maximal mitochondrial respiration and spare capacity - which is the ability to respond to stress, could be significantly improved by addition of melatonin and had no effect of melatonin in trophoblast of lean women. GPx4 was significantly increased in trophoblast of obese women, probably as a response to the increased oxidative stress but was reduced, back to the levels of lean placentas, with the addition of melatonin, perhaps as a response to decreased oxidative stress and need for antioxidant enzymes. The primary effect of melatonin may not be via induction of antioxidant enzymes, but by another mechanism of reducing oxidative stress to which GPx4 appears to be secondarily responsive.

S-139

First Trimester Placenta Transcriptome and Variation Among the Sexes. Tania L Gonzalez†,[1] Alexander F Koeppel,[2] Bora Lee,[1] Tianyanxin Sun†,[1] Erica Wang,[1,3] Lindsay Kroener,[1,3] Charles R Farber,[4] Stephen S Rich,[2] Yii-Der Ida Chen,[4] Jerome I Rotter,[4] Stephen D Turner,[2] John Williams III,[1] Margareta D Pisarska*.[1,3] *[1]Cedars-Sinai Medical Center, Los Angeles, CA, USA; [2]University of Virginia, Charlottesville, VA, USA; [3]UCLA School of Medicine, Los Angeles, CA, USA; [4]LABiomed/Harbor-UCLA Medical Center, Torrance, CA, USA.*

INTRODUCTION: Sex differences exist in fetal growth and development. Females grow slower in the first trimester. Males are more likely to be born prematurely and require more intensive neonatal support. Most studies trying to define mechanisms use term placenta, but this does not allow study of early gestation conditions that may contribute to these outcomes. Thus, we aim to characterize the transcriptome of the first trimester placenta.

METHODS: With IRB-approved protocols, we used chorionic villus sampling (CVS) tissue obtained from 26 male (XY) and 23 female (XX) spontaneous, singleton pregnancies at weeks 11-13 of gestation. RNA extracted from villi was analyzed using RNA-seq. An average of 22.53 million 2 x 75 bp pair-ended reads were generated for each sample using an Illumina NextSeq 500. To find differences between sexes, the Benjamini-Hochberg False Discovery Rate procedure was used to estimate adjusted p-values for genes. Protein-coding genes with significant sex differences ($p<0.05$) were selected for enrichment analysis. RNA-seq results were verified with qRT-PCR for select genes.

RESULTS: We detected 50,160 expressed transcripts in the first trimester placenta. The first trimester placenta transcriptome shows modest sexual dimorphisms, with 56 significantly different protein-coding genes among the sexes: 21 genes on autosomes, 23 on the X, and 12 on the Y chromosome. The chromosome distribution of this subset was different from expected based on the published human distribution of protein-coding genes. The X chromosome was over-represented in both sexes. Enrichment analysis showed sex-different expression of genes involved in cell-to-cell signaling, cell growth and survival, immunity, neural development, and more. Pathways analysis found most autosomal genes did not have known upstream regulators from sex chromosomes.

CONCLUSIONS: There are significant sex-differences in the first trimester placenta, not just in XY genes, but also autosomal genes not known to be regulated by XY genes. This study is supported by the NICHD (R01 HD074368).

S-140

Time Course Analysis of RNA Quality From Human Placenta and Decidua Biospecimens Preserved By RNA*later* or Flash Freezing. Nicole M Martin, Katherine M Cooke, Caitlin C Radford, Lauren E Perley, Michelle Silasi, Clare A Flannery*. *Yale School of Medicine, New Haven, CT, USA.*

INTRODUCTION: Preservation of biospecimen quality is critical to the accuracy and reliability of genomic and proteomic assessments. RNA stability and integrity directly affects gene expression analysis by qRT-PCR. However, few studies analyze how sample processing and storage affects RNA quality in placenta and decidua. The purpose of this study was to assess the effect of sample preparation using RNA-stabilizing solution or liquid nitrogen for flash freezing, and time duration of storage on RNA quality.

METHODS: We assessed RNA quality in specimens from nine placentas, with multiple sampling of full-thickness placenta and decidua. Specimens were processed within 30 minutes of delivery, and 8mm punch biopsy aliquots were placed in RNA*later*® or liquid nitrogen and stored at -80ºC. RNA was extracted immediately from a fresh sample of each placenta and decidua specimen (baseline), and then from matched stored samples at 1 month and 8-10 months. RNA Integrity Number (RIN) and expression of housekeeping genes (β-actin, YWHAZ, and TOP1) were quantified for each sample, and analyzed using Friedman test with Dunn's multiple comparisons test.

RESULTS: RIN values were within ideal range (>8) for baseline placenta (8.7±0.2) and decidua samples (8.0±0.5). Placenta samples stored in RNA*later* for 1 and 8-10 months had similar ideal RIN values (8.4±0.5; 8.0±0.2; p=NS). However, flash frozen placenta specimens had lower RIN values at both time points relative to baseline (4.0±1.0, $p<0.05$; 2.4±0.03, $p<0.001$). Consistent with this, Ct values for housekeeping genes in RNA*later* samples were similar to baseline at both time points (p=NS). For flash frozen samples, Ct values were significantly higher at 1 month for YWHAZ ($p<0.01$) and TOP1 ($p<0.001$), and for all three genes at 8-10 months ($p<0.001$) relative to baseline. In contrast, decidua samples stored in RNA*later* and flash frozen had RIN values unchanged from baseline at both time points (p=NS).

CONCLUSIONS: For RNA stability from placenta, we found that RNA*later* was a better mode of preservation than flash freezing for an 8mm punch biopsy. However, for decidua, which is less dense than placenta, both modes yielded equal RNA integrity over time. Based on these findings, we recommend smaller sectioning for aliquots of placenta, to avoid potential inconsistencies in freezing.

S-141

Role of High-Mobility Group A1 Protein in Preeclampsia. Yuka Uchikura, Keiichi Matsubara, Yuko Matsubara, Takashi Sugiyama. *Ehime University Hospital, Toon, Ehime, Japan.*

INTRODUCTION: Extravillous trophoblast (EVT) cells can invade into uterine decidual spiral arterioles and regulate the remodeling of these vessels. Disturbed arterial remodeling can lead to the serious complications such as preeclampsia and fetal growth restriction. High-mobility group A1 (HMGA1) protein is known to play an important role in the proliferation of many kinds of cancer cells; however, the specific function of HMGA1 in trophoblast migration has not been reported to date.In this study, we investigated HMGA1 expression in extravillous cytotrophoblasts derived from a mouse model of preeclampsia and examined the relationship between HMGA1 and immortalized human trophoblast cell (HTR-8/SVneo) proliferation and migration.

METHODS: We investigated HMGA1 expressions in cytotrophoblast derived from preeclampsia model mouse, CD40-L mouse, using immunofluorescence analysis. Wound healing and transwell migration assays were also performed using HTR-8/SVneo (extravillous trophoblast) cells transfected with DNA or siRNA of HMGA1. The effect of extranuclear translocation of HMGA1 on the migration of extravillous trophoblastic cells was evaluated using deoxycholic acid (DCA).

RESULTS: HMGA1 was expressed in nucleus of trophoblasts derived from control mouse; in contrast, cytoplasmic expression was observed in CD40-L mouse.

Furthermore, overexpression of HMGA1 in the nuclei of HTR-8/SVneo cells stimulated cell proliferation and migration. Translocation of nuclear HMGA1 to cytoplasm treated with DCA reduced cell migration.

CONCLUSIONS: These findings demonstrate that proper subcellular localization of HMGA1 is important for its function in trophoblast cells, and suggest that aberrant cytoplasmic expression of HMGA1 contributes to the pathogenesis of preeclampsia through impairment of trophoblast migration.

S-142

Systems Biology Identifies Key Molecular Networks and Hub Factors in Placental Pathways of Preeclampsia. Nandor Than,[1,2,3,4] Roberto Romero,[1] Adi Tarca,[1,2] Katalin Kekesi,[5] Yi Xu,[1] Kata Juhasz,[3] Hamutal Meiri,[6] Sonia Hassan,[1,2] Tinnakorn Chaiworapongsa,[1,2] Offer Erez,[1,2] Manuel Krispin,[7] Graham Burton,[8] Chong Kim,[1,9] Gabor Juhasz,[5] Zoltan Papp.[4] *[1]NICHD,NIH,DHHS, Detroit, MI, USA; [2]Wayne State Univ, Detroit, MI, USA; [3]Hungarian Acad Sci, Budapest, Hungary; [4]Semmelweis Univ, Budapest, Hungary; [5]Eotvos Lorand Univ, Budapest, Hungary; [6]TeleMarpeh Ltd, Tel Aviv, Israel; [7]Corp, Irvine, CA, USA; [8]Univ Cambridge, Cambridge, United Kingdom; [9]Wayne State Univ, Detroit, MI, USA.*

INTRODUCTION: Preeclampsia (PE) has various subtypes that are characterized by a common terminal pathway: release of placental toxins that induce systemic inflammation, anti-angiogenic state, hypertension, proteinuria. In early-onset PE the failure of trophoblast invasion leads to placental ischemia and toxin release, while the terminal pathway is triggered by distinct mechanism in late-onset PE. Although the terminal pathway was described, gaps in understanding the preceding pathologic events of this heterogeneous syndrome exist, inhibiting early diagnosis and specific therapy.

METHODS: We ran placental RNA/tissue microarrays, RT-PCR, bisulfite-Seq, histopathology, ISH, IHC, maternal serum proteomics on early/late-onset PE samples. Studies with primary trophoblast and trophoblast cell lines included differentiation, proliferation, migration, invasion assays, gene knock-down/overexpression, luciferase assays, ELISA, and confocal imaging. Data was assessed with various systems-, evolutionary- and statistical analyses.

RESULTS: We identified dysregulated gene modules and hub factors in placental transcriptome separately associated with blood pressure or birth-weight. Functional assays showed that dysregulation of these hub factors leads to impaired trophoblast invasion or sensitizes the trophoblast to ischemia. Genomic, evolutionary and functional evidences showed that the regulatory region of one of these hub factor genes is key for deep trophoblast invasion in primates, and hypermethylation in this region correlates with placental/fetal disease. First trimester serum proteomics suggests early systemic inflammatory changes and links maternal-placental disease pathways.

CONCLUSIONS: Systems biology revealed novel disease pathways of distinct PE subtypes that may have important implications in early molecular phenotyping and personalized therapy of PE patients.

S-143

VEGFR-1 Is the Predominant Vascular Endothelial Growth Factor Receptor Mediating Human Fetoplacental Endothelial Cell Angiogenesis. Shuhan Ji†,[1] Hong Xin,[1] Emily J Su.[1,2] *[1]University of Colorado Denver School of Medicine, Aurora, CO, USA; [2]University of Colorado Denver School of Medicine, Aurora, CO, USA.*

INTRODUCTION: Proper fetoplacental blood flow is imperative for a healthy pregnancy outcome, and one key mediator of this is angiogenesis throughout gestation. Vascular endothelial growth factor A (VEGFA) plays a vital role in angiogenesis, primarily through binding to two related receptor tyrosine kinases (RTKs), VEGFR-1 (Flt-1) and VEGFR-2 (KDR/

Flk-1). Within the human placenta, the specific roles of these two receptors remain unelucidated. Our objective was to determine the role of VEGFR-1 and VEGFR-2 on primarily isolated human fetoplacental endothelial cell (EC) characteristics of angiogenesis, and we hypothesized that EC migration is mediated primarily through VEGFR-2 while proliferation is regulated through VEGFR-1.

METHODS: Human fetoplacental ECs were isolated and cultured from placentas of full-term, uncomplicated pregnancies immediately after delivery. ECs were serum-starved and treated with either VEGFR-1 blocker (5 mg/ml), VEGFR-2 blocker (0.2 mg/ml), or both. ECs were then subjected to western blot. They also underwent wound scratch and tube formation assays while treated with either vehicle or VEGFA (60 ng/mL). All experiments were performed in triplicate utilizing ECs from at least three separate subjects. Images were analyzed by ImageJ software. One-way ANOVA with Tukey post-hoc testing was utilized for statistical analysis. $P<0.05$ was considered significant.

RESULTS: There was no difference in proliferating cell nuclear antigen (PCNA) or caspase-3 expression regardless of treatment. Wound scratch assays demonstrated that EC migration was significantly inhibited in the setting of VEGFR-1 blockade ($p<0.05$). In contrast, there was no significant effect on migration with VEGFR-2 inhibition. Tube formation assays demonstrated similar findings with significantly decreased branch points ($p<0.005$) and total tube length with VEGFR-1 inhibition ($p<0.05$).

CONCLUSIONS: Inhibition of VEGFR-1, VEGFR-2, or both did not affect proliferation or apoptosis of human fetoplacental ECs. In contrast, migration appears to be primarily regulated through VEGFR-1.

S-144

Preconceptional and First-Trimester Utero(Placental) Vascularization Using Three-Dimensional Power Doppler Virtual Reality Ultrasound. Igna F Reijnders†, Annemarie G Mulders, Wendy P Koster, Anton H Koning, Régine P Steegers-Theunissen, Eric A Steegers*. *Erasmus University Medical Center, Rotterdam, ZH, Netherlands.*

INTRODUCTION: Success of implantation and pregnancy is determined by interactions between the endometrium, developing embryo and placenta wherein uterine vascularization plays an essential role. Noninvasive biomarkers for *in vivo* utero(placental) vascularization and function assessment are not yet available. We aim to develop and validate a methodology to assess preconceptional and first-trimester utero(placental) vascular volumes using three-dimensional (3D) power Doppler (PD) ultrasound (US) in a Virtual Reality (VR) system.

METHODS: Preconceptional (n=5) and first-trimester (9 (n=10) and 11 weeks of gestation (n=10)) 3D PD US images of utero(placental) vascularization are obtained from 25 women. Offline, 2 researchers measure total vascular volume (TVV), uterine vascular volume (UVV) (including uterine arteries), fetal vascular volume (FVV) and placental bed vascular volume (PBVV) on a desktop VR system with a V-Scope volume rendering application (Figure 1). Intra-observer agreement is determined to assess validity.

**Figure(s) will be available online.*

RESULTS: Median (range) age (years) and body mass index (kg/m^2) were respectively 33.4 (27.8-36.6) and 22.4 (27.8-32.7). 52% were nulliparous and 60% conceived after assisted reproduction. Intraobserver variability showed intraclass correlation coefficients >0.95, indicating good agreement. Figure 2 shows the utero(placental) vascularization indices.

**Figure(s) will be available online.*

CONCLUSIONS: Preconceptional and first-trimester utero(placental) vascular volumes can be reliable measured using 3D PD US on a VR desktop system. A prospective periconception cohort study will investigate this technique and predictive value of these noninvasive biomarkers for adverse placental-related outcomes.

S-145

Mechanisms Implicated in the Development of Acute Atherosis: A Role for Intravascular Inflammation and Lipid Metabolic Disturbances. Yeon Mee Kim,[1,2,3] Roberto Romero*,[3,4,5,6] Chong Jai Kim,[7] Piya Chaemsaithong,[8] Yi Xu,[3] Nardhy Gomez-Lopez,[3] Gaurav Bhatti,[3] Bo Hyun Yoon,[9] Offer Erez,[3,10] Sonia S Hassan,[3,10] Young-Ran Yoon.[2] *[1]Haeundae Paik Hospital, Inje U College of Medicine, Busan, Republic of Korea; [2]Kyungpook National U Graduate School & Hospital, Daegu, Republic of Korea; [3]Wayne State U, Detroit, MI, USA; [4]U of Michigan, Ann Arbor, MI, USA; [5]Michigan State U, East Lansing, MI, USA; [6]Wayne State U, Detroit, MI, USA; [7]U of Ulsan College of Medicine, Seoul, Republic of Korea; [8]The Chinese U of Hong Kong, Shatin, Hong Kong; [9]Seoul National U College of Medicine, Seoul, Republic of Korea; [10]Wayne State U School of Medicine, Detroit, MI, USA.*

INTRODUCTION: Acute atherosis (AA) is unique vascular changes of the spiral arteries (SA) and has been reported in preeclampsia, SGA neonates, fetal death and preterm labor. The mechanisms responsible for AA are poorly understood but may resemble those of atherosclerosis. We investigated whether inflammation and disorders of lipid metabolism are involved in AA.

METHODS: We performed laser-captured microdissection of the SA with (n=15) and without (n=10) AA. Analyses of gene expression related to lipid metabolism (ABCA1, ABCG1, APOE, CD36, and MSR1), inflammation (CASP1, CASP4, IFN-γ, IL-1α, IL-1 β, IL-6, IL-8, IL-18), the NLR-subset inflammasome (AIM2, NLRC4, NLRP1, NLRP3), and the NOD-like family (NOD1, NOD2) were performed using qPCR.

RESULTS: 1) mRNA gene expression involved in lipid metabolism (ABCA1, ABCG1, APO E: all $p<0.001$), and MSR1 (Macrophage Scavenger Receptor 1; $p=0.015$), was significantly higher in AA group than in the control group; 2) Among genes involved in inflammation, the mRNA expression of CASP1($p=0.04$), IL-1β ($p=0.003$), and IL-18 ($p<0.002$) were significantly higher in AA group than in the control group.

CONCLUSIONS: Targeted analysis of the wall of the SA (obtained by laser capture microscopy) demonstrated a clear increase in the transcription of genes involved in lipid metabolism and in the control of inflammation, specifically, the inflammasome. The mechanism whereby activation of the inflammasome occurs in the context of AA represents a new frontier in the investigation of preeclampsia.

S-146

Increased Lipid Deposition in the Spiral Arteries and Villous Trophoblast of Patients with Acute Atherosis: A Potential Explanation for the Increased Risk of Subsequent Cardiovascular Death of Mothers with Preeclampsia and Preterm Birth. Yeon Mee Kim,[1,2,3] Roberto Romero*,[3,4,5,6] Bomi Kim,[1] Joo-Yeon Kim,[1] Chong Jai Kim,[7] Jung-Sun Kim,[8] Sonia S Hassan,[3,9] Young-Ran Yoon,[2] Offer Erez.[3,9] *[1]Haeundae Paik Hospital, Inje U College of Medicine, Busan, Republic of Korea; [2]Kyungpook National U Graduate School& Hospital, Daegu, Republic of Korea; [3]Wayne State U, Detroit, MI, USA; [4]University of Michigan, Ann Arbor, MI, USA; [5]Michigan State U, East Lansing, MI, USA; [6]Wayne State U, Detroit, MI, USA; [7]U of Ulsan College of Medicine, Seoul, Republic of Korea; [8]Sungkyunkwan U School of Medicine, Samsung Medical Center, Seoul, Republic of Korea; [9]Wayne State U School of Medicine, Detroit, MI, USA.*

INTRODUCTION: Preeclampsia (PE) and preterm delivery (PTD) are risk factors for subsequent maternal cardiovascular disease and death later in life. Acute atherosis (AA) is a unique spiral arteries (SA) lesion; its morphologic features resemble those of atherosclerosis. We aimed to determine lipid accumulation in the SA, chorioamniotic membranes (CA), and villous trophoblast (VT) of placentas with AA.

METHODS: This cross-sectional study included 134 placentas; 57 with AA and 77 without; 50 patients had PE. Lipid deposition was diagnosed by oil red O (ORO). Semi-quantitative methods for ORO intensity in the SA and the percentage of the positive areas of ORO in the CA and VT were used.

RESULTS: 1) Lipid droplets were identified in the SA, stroma of the CA, and cytoplasm of the VT; 2) cases with AA had greater depositions of lipid in the SA ($p=0.003$) and the VT($p=0.04$) than in those without AA; 3) the

median percentages of lipid deposition in the SA and VT in the placentas of patients with preterm PE (p=0.002 and p=0.008, respectively) and of women with normal term pregnancies (all p<0.03) were greater than in patients with spontaneous PTD; 4) The median percentages of positive areas of lipid deposition in the CA was lower in placentas with AA than those without AA in patients with preeclampsia (p=0.017).
CONCLUSIONS: An excess lipid accumulation occurs in the endothelial and vascular walls of the SA. We report for the first time morphologic evidence of an excess deposition of lipids in the VT in patients with AA.

S-147

Alterations in Metabolomic Profiles of Human Placental Tissue Among Male and Female Fetuses. Anushka M Chelliah†,[1] Jacquelyn Walejko†,[2] Cheyenna Espinoza†,[1] Gustavo Vilchez†,[1] Arthur Edison,[3] Anthony R Gregg*.[1] *[1]Univ of Florida, Gainesville, FL, USA; [2]Univ of Florida, Gainesville, FL, USA; [3]Univ of Georgia, Athens, GA, USA.*
INTRODUCTION: Gender differences have been reported in neonatal outcomes in many studies suggesting an increased vulnerability of the male fetus. Metabolomic analysis has been used to study physiologic and pathologic differences among gender in various disease states in combination with genetic studies. To date, there is limited data on metabolomic differences of male and female fetuses at the level of the placenta. We aim to evaluate changes in metabolites of placental tissue between male and female fetuses immediately following delivery.
METHODS: Patients were identified, and consented in an IRB approved study. 26 placental specimens were collected from maternal surfaces of the placenta. Placental tissue was collected prospectively; 8 from a pregnancy with a male fetus and 18 from female fetuses following cesarean delivery. Two tissue specimens from the center and periphery of each placenta were collected and frozen in liquid nitrogen within 15min. Nuclear magnetic resonance spectroscopy (^{1}H-NMR) was conducted on a 600 MHz spectrometer to gain global metabolic profiles of placental samples. Significance of metabolites was determined using a one way MANCOVA corrected for individual variation of the area under the metabolite peak(s) of probabilistic quotient normalized spectra.
RESULTS: A metabolomics profile of five metabolites were noted to be significantly higher in placental tissue of male fetuses compared to female. These metabolites were independent of maternal subject variability. The metabolites noted to be significantly increased were lysine, acetate, choline, myo-inositol, and phenylalanine (p<0.05).
CONCLUSIONS: In our analysis, several metabolites were noted to be elevated in concentration of placental tissue of male fetuses. The increase in these metabolites are consistent with other studies suggesting possible protein breakdown at the level of the placenta in males. This is one of the only human studies looking at the metabolomic differences among gender within the human placenta. To date, there is limited data on placental metabolism and transport in relation to fetal gender, and understanding altered metabolism in this tissue will contribute to knowledge of placental function and pathology in the future.

S-148

Placental Fatty Acid Translocase (FAT/CD36) and Tranport Protein-4 (FATP-4) Are Less Expressed in the Human Preterm Than Term Placenta. AnnieBelle J Sassine†, Gavin R Sooranna†, Natasha Singh, Bronwen R Herbert, Suren R Sooranna, Michael A Crawford, Mark R Johnson*. *Imperial College London, London, United Kingdom.*
INTRODUCTION: Long-chain polyunsaturated fatty acids (LCPUFAs) are essential for fetal brain development. LCPUFAs have limited synthesis in the fetus and are transported across the placenta from the maternal blood by plasma membrane and cytoplasmic fatty acid-binding and transport proteins (FABPs and FATPs). An understanding of the maternal-fetal transport mechanism is important, especially in preterm pregnancies complicated by placental insufficiency.
METHODS: 100 placentae were obtained after elective caesarean sections following term (n=25) and preterm deliveries (n=75). mRNA levels of Heart-FABP (H-FABP), FATP-4, FAT/CD36, FABP plasma membrane (FABPpm), and GAPDH (housekeeping gene) were quantified by qPCR. Differences in the mean expression levels of FABP and FATPs relative to GAPDH between term and preterm placentae were assessed using independent t-tests with Stata/SE 14.1 software.
RESULTS: FABPpm and FATP-4 mRNA expression levels were two-fold higher in term than preterm placentae (p=0.045, p=0.009, respectively). H-FABP levels were not significantly different while FAT expression levels were 1.6 times higher in preterm than term placenta (p=0.012).

Genes	Term (n=25) Mean ± SE	Preterm (n=75) Mean ± SE	P-value
H-FABP	0.00026 ± 0.00004	0.00047 ± 0.00018	0.24
FABPpm/GOT2	0.609 ± 0.144	0.286 ± 0.069	0.045
FATP4	0.023 ± 0.004	0.011 ± 0.002	0.009
FAT/CD36	0.155 ± 0.028	0.246 ± 0.021	0.012

CONCLUSIONS: Our study shows that gene expression levels of some FATPs and FABPs were significantly different between preterm and term placentae. This indicates the possibility of altered phenotype in the preterm placenta to maintain normal fetal growth. Future experiments will include measurement of the genes' protein levels.

S-149

Metabolomic Differences Between Maternal and Fetal Surfaces of Human Placenta. Anushka Chelliah†,[1] Jacquelyn Walejko†,[2] Alexa Avecilla†,[1] Maureen Keller-Wood,[2] Arthur Edison,[3] Anthony R Gregg*.[1] *[1]Univ of Florida, Gainesville, FL, USA; [2]Univ of Florida, Gainesville, FL, USA; [3]Univ of Georgia, Athens, GA, USA.*
INTRODUCTION: The current data available on evaluation of the maternal and fetal surfaces of the placenta is limited and little is known about transport across the human placenta from a metabolomics perspective. We aim to evaluate changes in metabolites of placental tissue between the maternal and fetal surfaces immediately following delivery.
METHODS: Twelve gravid full-term, non-labored patients were identified at UF Health, and consented for participation in an IRB approved study. Placentas were collected immediately following cesarean delivery. Two tissue specimens from both maternal and fetal surfaces were collected and were frozen in liquid nitrogen within 15min. Nuclear magnetic resonance spectroscopy (^{1}H-NMR) was conducted on a 600 MHz spectrometer to gain global metabolic profiles of 48 placental samples. Significance of metabolites was determined using a one way MANCOVA corrected for individual variation of the area under the metabolite peak(s) of probabilistic quotient normalized spectra.
RESULTS: A persistent profile of four identified metabolites was noted to be significantly higher on the maternal surface of the placenta. These metabolites were independent of maternal subject variability. The metabolites noted to be significantly increased were ketones (Beta-hydroxybutyrate and acetate), aspartate, and choline (P<0.05).
CONCLUSIONS: In our analysis, several metabolites were noted to be elevated on the maternal surface of placental tissue compared to the fetal surfaces. The persistence of ketones and aspartate is consistent with ovine studies suggesting limited placental transport of these metabolites. Choline transporters are known to be present in the placenta, but there is little information demonstrating metabolite transport. This is one of the only human studies to confirm findings of metabolite transport previously demonstrated in animal models. To date, there is limited data on metabolic transport in the placenta, and the persistence of metabolites may be used to gain information on altered metabolism in this tissue and transport across this organ in the future.

S-150

Phthalate Exposure Alters First Trimester Placental Gene Methylation in Women. N Grindler†,[1] I Yang,[2] L Vanderlinden,[2] K Rajendiran,[3] K Kannan,[3] D Schwartz,[2] S Teal,[1] A Polotsky,[1] T Powell,[4] T Jansson.[1] [1]*University of CO, CO, USA;* [2]*University of CO, NY, USA;* [3]*NY Dept Health, Albany, NY, USA;* [4]*University of CO, Aurora, CO, USA.*

INTRODUCTION: We have shown that exposure to the common plasticizer, phthalate, alters the placental transcriptome. Epigenetic mechanisms control gene expression and we hypothesized that exposure to phthalates alters first trimester placental gene methylation.

METHODS: Placental tissue and maternal urine were collected from elective first trimester terminations of pregnancy (n= 52, GA= 7.7 weeks). The concentrations of 23 phthalate urinary metabolites were measured by high performance liquid chromatography/mass spectrometry. We compared high and low total phthalate (TP) levels based on quartile distributions. Placental DNA methylation was measured (Illumina's Methylation 850k) in 16 samples in the low and high TP groups. An epigenome-wide association analysis was performed to find differentially methylated positions (DMP) between high and low TP exposure groups. Enrichment analysis using candidate DMPs (nominal p-value < 0.005) was performed in Panther to identify key pathway and biological processes. Candidate genes from previous microarray analysis of the same samples were used to define methylation-gene expression relationships in the placenta ($p<0.05$; effect size > 5%). Subsequently, pathway analysis was performed to characterize the methylation-gene expression changes.

RESULTS: We identified 2214 DMPs, which correspond to 1461 unique annotated gene symbols, in the placentas for high vs low TP. Major pathways identified in enrichment analysis were chromatin assembly, mitochondrial transport, and transmembrane signal transduction. Unique candidate genes (133) were previously identified based on microarray data, corresponding to 1985 CpG sites. We identified 40 genes with significantly altered methylation and gene expression patterns in the high vs low TP groups. Of these, 17 had inverse relationships between gene methylation and gene expression. The enriched canonical pathway for arginine, serine, and glycine biosynthesis were among the key differentially expressed pathways.

CONCLUSIONS: In early pregnancy, phthalate exposure is associated with alterations in methylation of critical placental genes that were linked to gene expression changes in the expected direction. Future studies are needed to determine the functional consequences of these changes in gene expression.

S-151

Unraveling the Obesity Epidemic: Is the Early and Persistent Disruption of Placental Vascularity Playing a Major Role? Kathleen O'Neill,[1] Tami Stuart,[2] David Condon,[3] Kyoung Won,[3] Rebecca Simmons*.[2] [1]*UPenn, Philadelphia, PA, USA;* [2]*UPenn, Philadelphia, PA, USA;* [3]*UPenn, Philadelphia, PA, USA.*

INTRODUCTION: Obese women experience increased rates of pregnancy loss and growth and metabolic abnormalities in offspring. We have previously shown in a mouse model that pre-gestational and gestational exposure to maternal high-fat diet (HFD) decreased fetal and placental weight. The aim of this study was to 1) identify genes and pathways altered by obesity that may impact placental structure/function and fetal development and 2) determine the onset and tissue-specificity of obesity-induced changes in gene expression.

METHODS: Female C57BL/6J mice from 4-16 weeks were fed control or HFD. Four days post-coitum (dpc) blastocysts were flushed from uterine horns and trophectoderm was dissected from the abembryonic pole. cDNA from control or HFD-derived pooled trophectoderm was generated and utilized for gene expression profiling with the GeneChip Mouse Exon 1.0ST array. In a separate cohort, embryos were isolated at 6.5 dpc. RNA was isolated from individual epiblasts (EBs) and ectoplacental cones (EPCs) and was used to generate RNA-Seq libraries for 4 male and 4 female embryos from HFD and control fed dams. Differentially expressed genes with FDR<.05 were identified and pathway analysis was performed with IPA. Finally, microvessel density was measured using mecA staining in the placentas of male and female embryos 12.5 dpc.

RESULTS: Exposure to a HFD altered expression of multiple genes and pathways in the trophectoderm and EPC. Of significance to our previous findings of altered placental and fetal growth, expression of genes involved in angiogenesis and vascular development including *angpt2*, *epas1*, *fgfr1*, *fzd5*, *hand2*, and *pdgfa* was increased in the trophectoderm and EPC of HFD derived embryos. Immunohistochemical staining at 12.5 dpc revealed significantly decreased microvessel density in the placentas of HFD male embryos.

CONCLUSIONS: Obesity results in the early and persistent altered expression of genes involved in angiogenesis and vascular development in cells fated to develop into the placenta. The differential expression of these genes may be functionally significant given the impaired establishment of vascular networks we detected in the early placentas of embryos from obese mice and may contribute to understanding the mechanism underlying the adverse reproductive and offspring outcomes associated with obesity.

S-152

Studies of Lipid Transport and Metabolism in Primary Human Trophoblast Cells Using ^{13}C-Fatty Acids. Veronique Ferchaud-Roucher*,[1] Thomas Jansson,[2] Theresa L Powell.[3] [1]*University of Colorado, Denver, CO, USA;* [2]*University of Colorado, Denver, CO, USA;* [3]*University of Colorado, Denver, CO, USA.*

INTRODUCTION: Transplacental delivery of lipids is critical for fetal growth and development. Syncytiotrophoblast fatty acid (FA) uptake is dependent on the transport capacity of the plasma membrane and intracellular metabolic processes including the formation of complex lipids such as triglyceride (TG) and phospholipid (PL). Little is known about placental lipid transport and metabolism including what form fatty acids are transferred into fetal circulation. We hypothesized that FA uptake into PHT cells and incorporation into lipid classes varies with chain length and saturation.

METHODS: Villous cytotrophoblasts were isolated from five term placentas. At 66h in culture, differentiated PHT cells were treated with a mixture of uniformly labeled ^{13}C-palmitic acid (PA, 95µM), ^{13}C-oleic acid (OA, 95µM), ^{13}C-linoleic acid (LA, 95µM) and ^{13}C-docosahexaenoic acid (DHA, 15µM) at maternal physiological concentrations. The isotopic enrichment of ^{13}C-FA was measured by GC-MS in total cellular lipids, in the lipid classes TG, PL, cholesterol ester (CE) and non-esterified FA (NEFA) over a 36h time course, and in culture media at 30h in culture.

RESULTS: Uptake of the four ^{13}C-FA into the total lipid fraction of PHT was linear the first two hours with LA and DHA (when accounting for the lower media concentration) taken up more rapidly than PA and OA (one way Anova $p<0.05$). The enrichment of labeled PA and OA in cellular TG and PL pools was greater than in NEFA and CE. Enrichment of ^{13}C-LA and DHA was similar in the four lipid classes. ^{13}C-LA was incorporated into cellular CE, TG and PL rapidly and reached a plateau at 80% enrichment from 6 to 36h. ^{13}C-LA and DHA were released from PHT in the form of highly enriched PL at 30h of incubation.

CONCLUSIONS: We have established a novel approach using stable isotope labeled FA species at maternal physiological concentrations to study FA uptake and metabolism in cultured PHT cells. Our findings suggest that PHT cells take up the four labeled FA rapidly but with preference for LA and DHA. In the cells, FA are stored as TG and preferentially incorporated into PL. Based on enrichments measured in the culture media, we speculate that PL could be a major lipid form for transfer of LA and DHA to the fetal circulation.

S-153

Folate Deficiency Alters Expression of Placental MicroRNAs In Vivo and In Vitro. Bernadette C Baker,[1] Susan L Greenwood,[1] Alexander EP Heazell,[1] Karen Forbes,[2] Rebecca L Jones*.[1] [1]*University of Manchester, Manchester, United Kingdom;* [2]*University of Leeds, Leeds, United Kingdom.*

INTRODUCTION: Low maternal folate is associated with adverse pregnancy outcomes, especially delivery of small for gestational age (SGA) infants. Features of placental dysfunction are evident in folate deficient teenagers. However, mechanisms linking low folate and placental

dysfunction are unknown. In other tissues folate influences microRNA (miRNA) expression. We hypothesised that placental dysfunction related to maternal folate deficiency is associated with altered miRNA expression.
METHODS: An unbiased miRNA array (Exiqon) compared term placental miRNA expression in folate deficient (RBC folate <450nM, n=7) and sufficient (RBC folate >800nM, n=7) mothers. Individual miRNAs were assessed by QPCR. Bioinformatic analyses were carried out using Ingenuity Pathway Analysis. Primary trophoblasts were cultured in folate deficient (1nM) or physiological (25nM) media for 114hr and analyses of trophoblast function were performed. Trophoblasts were transfected with specific miRNA target inhibitors or non-targeting controls. Affymetrix microarrays were performed.
RESULTS: 16 placental miRNAs were upregulated in folate deficient women ($p<0.05$); bioinformatic analysis predicted gene targets of these miRNAs, including genes known to be altered in placentas from SGA pregnancies, e.g. MYC, CDK6, TP53. Trophoblasts cultured in folate-deficient conditions exhibited significantly elevated apoptosis and reduced system A activity, consistent with observations in placentas of folate-deficient teenagers. Two miRNAs upregulated in placentas from folate-deficient women, miR-30e-3p and miR-34b-5p, were significantly altered in folate-deplete trophoblasts, confirming a direct effect of folate on trophoblast miRNA expression. Inhibition of these miRNAs had no effects on trophoblast apoptosis or system A. Gene array and *in silico* analysis identified functional pathways affected by these folate-sensitive miRNAs, including cell signalling, cell survival and oxidative stress.
CONCLUSIONS: These data demonstrate miRNAs are differentially expressed in placentas exposed to low folate conditions *in vivo* and that miRNAs are regulated by folate depletion *in vitro*. Investigation of the functional consequences of altered folate-sensitive miRNAs and their target genes is underway and may explain how altered miRNAs contribute to placental dysfunction and SGA.

S-154

A Novel Marker of Neonatal Respiratory Disorders: Umbilical 25-Hydroxyvitamin D (25(OH)D). Yumiko Ito, Hiroyuki Tsuda*, Kenji Imai, Tomoko Nakano, Tomomi Kotani, Fumitaka Kikkawa. *Nagoya University Graduate School of Medicine, Nagoya, Aichi, Japan.*
INTRODUCTION: Maternal vitamin D deficiency is associated with lung dysfunction in the infants, such ad asthma, and respiratory distress syndrome (RDS) . Placenta previa is also known ad a risk factor of neonatal respiratory disorders. The aim of this study was to investigate the association between the concentration of 25-hydroxyvitamin D (25(OH) D) in cord blood and the outcome of neonatal respiratory function, such as RDS and transient tachypnea of the newborn (TTN) in placenta previa.
METHODS: Forty-two placenta previa cases and 88 control cases without fetal or maternal complications at 31-38 weeks of gestation from cases treated in Nagoya University Hospital in the period from November 2011 to December 2015 were registered. All cases were singleton pregnancies and delivered by Caesarean section. The 25(OH)D levels in umbilical vein blood were measured using ELISA. This study was approved by the Ethics Committee of Nagoya University Hospital.
RESULTS: The 25(OH)D levels were statistical significantly lower in cases of placenta previa (26.2 ± 15.6 ng/ml) than those in controls (34.6 ± 17.1 ng/ml; $p < 0.01$). Among placenta previa cases, the level of 25(OH) D in the cases complicated with RDS or TTN were significantly lower than the cases without them ($p < 0.05$).
CONCLUSIONS: Low 25(OH)D levels in the umbilical vein was associated with complication of neonatal respiratory disorders in mother with placenta previa. Vitamin D deficiency is well known to be the common problem all over the world (2007 Michael F et al, NEJM), as well in the pregnant women. Thus, it is suggest that vitamin D supplementation would be a protective factor against neonatal respiratory disorders via improvement of maternal vitamin D status.

S-155

Can the Anti-Inflammatory Effect of Progesterone Be Enhanced in Stretched IL-1β Stimulated Human Amnion Cells? Ananya Das†,[1] Suren Sooranna,[2] Mark R Johnson*.[2] [1]*Imperial College, London, London, United Kingdom;* [2]*Imperial College, London, United Kingdom;* [3]*Imperial College, London, United Kingdom.*
INTRODUCTION: The steroid hormone progesterone (P4) is used clinically to reduce preterm labour (PTL) in high-risk singleton pregnancies, however its molecular mechanisms remain poorly understood. Studies have suggested that the up-regulation of cAMP signalling components in the myometrium contribute to uterine quiescence during pregnancy and may have the ability to enhance P4 action, though less is known about its actions in the amnion.
METHODS: Human amnion epithelial cells, obtained from women undergoing term elective caesarean, were stretched for 2 hours and pre-treated with P4 (1 and 10μM) and forskolin (100μM), either alone or in combination followed by IL-1β treatment (5ng/mL) for 1 hour. qPCR was carried out using a Rotor-Gene™ (Qiagen Ltd) to observe Il-1β stimulated COX-2 mRNA expression. COX-2 was also detected at the protein level through western blotting (n=6).
RESULTS: The addition of both forskolin and 10μM P4 appeared to reduce IL-1β driven COX-2 expression at the protein level in unstretched amnion cells compared with amnion cells that were also subjected to 11% mechanical stretch. In unstretched amnion cells, similar trends were also observed where the combination of 1μM P4 and forskolin appeared to suppress IL-1β stimulated expression, compared with the addition of P4 alone. The combined treatment of forskolin and P4 appeared to be ineffective in repressing IL-1β driven expression when amnion cells were subjected to mechanical stretch.
CONCLUSIONS: These results suggest that the combination of cAMP and P4 may work more effectively to suppress IL-1β beta driven gene expression compared with P4 alone in human amnion cells. Further investigation is required to determine the mechanisms through which this may occur.

S-156

Pre-Eclampsia, Fetal Growth Restriction and Pre-Term Birth Are Not Associated with Placental Infection with Eukaryotic Microbiota. Susanne Lager†,[1] Marcus de Goffau,[2] Sharon J Peacock,[2] Julian Parkhill,[2] D Stephen Charnock-Jones,[1] Gordon CS Smith*.[1] [1]*University of Cambridge, Cambridge, United Kingdom;* [2]*Genome Campus, Hinxton, United Kingdom.*
INTRODUCTION: Sequencing of the 18S rRNA gene allows identification of the presence of eukaryotic microbiota (e.g. fungi and protozoa). We hypothesized that placental infection with eukaryotic microbiota may be a cause of pre-eclampsia, fetal growth restriction or pre-term birth. Therefore, we sought to investigate: 1) the sensitivity of 18S rRNA gene sequencing to detect eukaryotic microbiota in placental biopsies, 2) whether placental samples from women experiencing pregnancy complications had higher rates of detection of eukaryotic microbiota.
METHODS: Assay sensitivity was determined by spiking 500ng of placental DNA with known amounts of DNA from Plasmodium falciparum, Toxoplasma gondii, and Saccharomyces cerevisiae (1, 10, 100, 1000 or 10,000 genome copies). Samples of terminal villi were taken after removal of maternal decidua, washed in PBS and flash frozen for DNA extraction. DNA from 4 biopsies (one from each of 4 quadrants of the placenta) were pooled. Placental samples from severe pre-eclampsia (ACOG 2013 definition, n=50) or fetal growth restriction (customized birth weight percentile ≤3rd; n=50) were matched 1:1 with healthy controls by mode of delivery, sample collection time, gestational age, fetal sex, maternal BMI, maternal age & smoking. Placental samples from 100 pre-term births (24-36 weeks) were also studied. PCR amplification of the 18S rRNA gene (V9 region) was performed with a blocking primer in the reaction to reduce human 18S rRNA gene amplification. The PCR amplicons were sequenced (MiSeq, 250 base paired-end reads). Data analysis was performed with Muther and ARB software.

RESULTS: All three "spike in" eukaryotic microbial DNAs could be detected at 10 to 100 genome copies. This is equivalent to detecting 1 microbe for every 800 to 8000 human cells. Of the 300 samples studied (200 cases and 100 controls), only one had any signal indicative of eukaryotic microbiota. This demonstrated 14 reads from Saccharomyces cerevisiae (yeast), but this was close to the reliable detection limit.
CONCLUSIONS: (1) 18S rRNA sequencing is a sensitive method for detection of placental eukaryotic microbiota in placental DNA, (2) there was no association between pre-eclampsia, fetal growth restriction or pre-term birth and the presence of DNA from eukaryotic microbiota in the placenta.

S-157

Agreement Conform Current Operational Rules and Directives (ACCORD): A Novel Method to Reach Multidisciplinary Agreement. Stephanie MP Lemmens†,[1] Veronica A Lopes van Balen†,[1] Hubertina CJ Scheepers,[2] Raymond G De Vries,[3] Yvonne CM Roselaers,[4] Marc EA Spaanderman*,[2] *[1]Maastricht University, Maastricht, Limburg, Netherlands; [2]Maastricht University Medical Center, Maastricht, Limburg, Netherlands; [3]Academy of Midwifery Science, Maastricht, Limburg, Netherlands; [4]ROS Robuust, Eindhoven, Noord-Brabant, Netherlands.*
INTRODUCTION: The contemporary practice of medicine is increasingly relying on multidisciplinary collaboration, which is almost impossible within a heterogeneous group of people with overlapping professional expertise but fundamental different views and perspectives. To ensure the process of reaching agreement to be relevant, efficient and fast, but also meticulous and widely supported enabling future professionals acceptance, we developed a novel strategy: the Agreement Conform Current Operational Rules and Directives-method (ACCORD). The ACCORD-method weighs the opinion of all participants on all pivotal topics within the given domain of care objectively and transparent.
METHODS: The ACCORD-method uses a four-step bottom-up approach and takes the judgment of all participants into account by structurally consulting them. First, an expert summarizes current guidelines, highlights inconsistencies between guidelines and formulates pivotal questions. Second, a flowchart on essential topics of care is created and translated into statements. Third, all participants rank these statements by their level of agreement on a 1 (disagree) to 10 (agree) Likert-scale. Finally, the mean and standard deviation (SD) of each statement is presented and discussed by a group of representatives and final recommendations for daily practice are formulated.
RESULTS: In total 14 surveys were sent to 137 participants containing 507 questions that had to be answered by ranking 681 statements. Based on the statement mean and SD, only 15% of all statements were directly accepted, 2% rejected and 8% inconclusive. The vast majority, 75% of statements had to be discussed, which resulted in acceptance, acceptance in a modified form or rejection of 29%, 19% and 27% of statements respectively. Agreement was reached on 92% of all statements and 98% of all questions were answered.
CONCLUSIONS: The ACCORD-method proved to be efficient in reaching multidisciplinary agreement, weighing available scientific evidence and the opinion of all involved professionals, especially if professionals with different views have to collaborate and guidelines are inconclusive.

S-158

Testosterone Supplementation Impairs Glucose Tolerance Mechanism in High Fat but Not Standard Diet Fed Male Rats. Amar More†, Jay Mishra†, Sathish Kumar. *University of Texas Medical Branch, Galveston, TX, USA.*
INTRODUCTION: Obesity is strongly linked to low testosterone (T) levels in men. However, how T replacement affects insulin actions in obese men remains unclear. We examined the high fat and regular diet fed rats to determine if castration-induced T deficiency and T replacement affects metabolic function including glucose tolerance and pancreatic insulin secretion.
METHODS: Three month old male SD rats were divided into control, castrated (for T deficiency) and castrated with testosterone replacement (subcutaneous 90 mg pellets, 90 day release) and fed either with a regular or a 45 kcal % high fat diet. Ten weeks later, all rats were assessed for oral glucose tolerance test. Pancreatic morphometry was assessed and gastrocnemius muscle was probed for insulin receptor (IR)-β expression.
RESULTS: On regular diet, T deficiency by castration did not affect fasting insulin and glucose levels but T replacement induced fasting hyperinsulinemia. Also, castration and T replacement on regular diet did not affect glucose and insulin responses following glucose tolerance test. On the other hand, in high fat diet, T deficiency by castrationdecreased fasting insulin (0.42±0.05; vs 0.583±0.05 ng/ml in control) and glucose levels (glucose: 114±3.69 mg/dl; vs 133.8±4.77 mg/dl in control), whereas T replacement reversed insulin (0.60±0.04 ng/ml) but not glucose levels (112±4.5 mg/dl). Castrated rats on high fat diet did not exhibit glucose intolerance but T replacement induced significant glucose intolerance with elevated glucose (glycemia fold AUC: 1.28±0.07) and decreased insulin responses (Insulin fold AUC: 0.48±0.04) compared to control. Pancreatic islet size was not altered by androgen status on regular diet. However, T replacement decreased pancreatic islet size on high fat diet. Gastrocnemius IR-β were significantly lower in control and T replaced high fat fed rats but was unaffected in regular diet fed rats.
CONCLUSIONS: This study shows that T supplementation to rats on high fat diet exhibits glucose intolerance and decreased pancreatic insulin secretion possibly due to compromised pancreas and skeletal muscle function.

S-159

Effect of LMWH in the Treatment of Recurrent Spontaneous Abortion on Liver Function. Yuan Gao, Chong Qiao*. *ShengJing Hospital, China Medical University, Shenyang, Liaoning, China.*
INTRODUCTION: Low molecular weight heparin(LMWH) is commonly used in the treatment of recurrent spontaneous abortion(RSA). Recently,we have found that some patients presented liver dysfuntion such as the elevation of transaminase after the use of LMWH for a period of time.Moreover,it seems to be positively relative to the dosage of LMWH and the using time.Therefore,we urgently need to explore the connection between the use of LMWH and the liver dysfuntion so that our patients will get the most proper regimen. **Objective:**To observe the effect of LMWH therapy on the liver function of RSA patients withabnormal uterine artery blood flow during pregnancy.
METHODS: A total of 60 RSA patients with abnormal uterine arteryblood flow during pregnancy admitted in Shengjing Hospital during October 2014 to October 2015 were recruited in the study. According to the different daily use of LMWH(in accordance with heparin sodium)dose, the patients were divided into small dosage group(one piece, 20cases), middle dosage group(two pieces, 20 cases), and large dose group(three pieces, 20 case). The liver function of three groups after continuous use of LMWH for two weeks and four weeks were recorded and compared.
RESULTS: (1)There was no significant difference in the liver function between small and middle dosage group after continuous use of LMWH for two weeks and four weeks($P > 0.05$). (2)The liver function of large dosage group after continuous use of LMWH for two weeks was significantly different($P < 0.05$).
CONCLUSIONS: Administration of large dosage LMWH in the treatment of RSA patients with abnormal uterine artery blood flow during pregnancy will affect the liver function. Therefore, the liver function should be monitored during the clinical application of LMWH.

S-160

Basal Plate Myometrial Fibers and Hypertensive Disorders of Pregnancy: A Case-Control Study. Ann A Wang†, Emily S Miller, Linda Ernst. *Northwestern University Feinberg School of Medicine, Chicago, IL, USA.*
INTRODUCTION: Basal plate myometrium (BPMYO), the pathological presence of myometrial fibers in the basal plate, was recently identified as a risk factor for placenta accreta in subsequent pregnancies. However, BPMYO's associations with complications in the index pregnancy have

not been well studied. Previous investigators have found myometrial fibers frequently located in proximity to poorly converted maternal spiral arteries, a finding associated with hypertensive disorders of pregnancy (HDP). Our objective was to determine whether the presence and degree of BPMYO are associated with HDP, given their association with abnormal maternal artery remodeling.

METHODS: This case-control study included women who delivered a liveborn singleton gestation between 2009 and 2016 whose placentas were sent for pathologic examination. Cases were defined as women with HDP (gestational hypertension, preeclampsia, or HELLP syndrome) as defined by ACOG. Controls were defined as women without HDP with placentas sent to pathology for prior history of malignancy, but without any malignant findings. The primary outcome was the presence of BPMYO. Secondary outcomes included the pathologic stage of BPMYO and the incidence of pathologically defined accreta (stage 3 or higher BPMYO). Each outcome was compared between cases and controls in bivariable and multivariable analyses.

RESULTS: Of the 306 women who met inclusion criteria, 230 (75%) had HDP. BPMYO was present in 99 (32%) of placentas. Compared to controls, cases were younger (p=.008), had higher BMI (p<.001), and were more likely to have diabetes (p<.001). Cases were more likely to be nulliparous (p=.004), to deliver preterm, (p<.001), and to have had a prior Cesarean (p=.002). There were no differences in the incidence of BPMYO, stage of BPMYO, or incidence of pathologically defined accreta between cases and controls (Table 1). These findings persisted after controlling for potential confounders (aOR for any BPMYO 2.09, 95% CI 0.95-4.64).

	Controls (n=76)	Cases (n=230)	p-value
Any BPMYO	23 (30.2%)	76 (33.0%)	0.65
BPMYO Stage			0.47
0	53 (69.7%)	154 (67.0%)	
1	18 (23.7%)	58 (25.2%)	
2	4 (5.3%)	7 (3.0%)	
3	1 (1.3%)	11 (4.8%)	
Pathologic Accreta	1 (1.3%)	11 (4.8%)	0.31

CONCLUSIONS: While BPMYO may be more common in the setting of abnormal placental vasculature, there is no significant association between BPMYO and HDP.

S-161

Adipokine Profiles in Preeclampsia and Visceral Fat Distribution. S Chandrasekaran,[1] H Hunt†,[1] HS Gammill,[1] EA Schur*.[2] *[1]UW, Seattle, WA, USA; [2]UW, Seattle, WA, USA.*

INTRODUCTION: Obesity affects one third of reproductive age women, and is associated with higher risks of developing preeclampsia (PE). The variation in development of PE among obese women could be due to differences in maternal fat distribution, since visceral fat (VF) has greater pro-inflammatory activity compared to subcutaneous fat (SC). We sought to evaluate the association of adipokine profiles with PE, analyzing markers specific to VF (visfatin, VN/resistin, RS) and those reflective of general adiposity (leptin, LT/ adiponectin, AN).

METHODS: We performed a case-control study among obese women with and without PE. Cases (N=36) and controls (N=29) were prospectively recruited, and 3rd trimester plasma samples were collected prior to onset of labor and, at time of PE diagnosis. Exclusion criteria included preexisting hypertension, diabetes, autoimmune disease, or spontaneous preterm labor. Samples of lean women with (N=25) and without PE (N=27) were also analyzed. Adipokines were measured via Luminex-based assays. Appropriate statistical transformations were applied to each marker, and Student T tests were performed.

RESULTS: Among obese women with PE (mean BMI=39±10 kg/m^2) compared to those without PE (mean BMI=35±4 kg/m^2), concentrations of VN, RS and LT were higher, and AN was lower. Among lean women with and without PE, findings were similar (table 1). Comparing obese women to lean women with PE, there were no significant differences in levels of VN and RS, whereas LT was increased (p=0.0002) and AN was decreased (p=0.0018).

CONCLUSIONS: VN and RS are significantly elevated with PE among obese and lean women, and might reflect the underlying state of inflammation associated with PE or a pre-existing risk. Due to the cross-sectional nature of the study that cannot be determined. Notably, these adipokines are thought to track most closely VF. This could imply that, regardless of initial BMI, fat distribution could influence PE pathogenesis. Further longitudinal studies throughout gestation are needed to clearly elucidate the role of visceral fat in the pathophysiology of PE.

Marker	Obese PE	Obese no PE	p value	Lean PE	Lean no PE	p value
Visfatin	58382	19737	<0.0001	61922	17436	<0.0001
Resistin	9159	6336	0.0022	8385	6083	0.002
Leptin	93611	58713	0.0003	53999	20161	0.0007
Adiponectin	1.74e+07	2.39e+07	0.036	3.46e+07	3.79e+07	0.53

S-162

Characterization of HO1, CPR, and BVR in the Serum and Placenta of Patients with Preeclampsia with Severe Features. Warren J Huber III†,[1] Paula Krueger,[2] Phinnara Has,[3] James Padbury,[2] Surendra Sharma,[2] Brenna Hughes*.[4] *[1]Women and Infants,Warren Alpert Medical School of Brown University, Providence, RI, USA; [2]Women and Infants,Warren Alpert Medical School of Brown University, Providence, RI, USA; [3]Women and Infants, Providence, RI, USA; [4]Duke University School of Medicine, Durham, NC, USA.*

INTRODUCTION: Heme Oxygenase-1 (HO1), Cytochrome P450 Reductase (CPR), and Biliverdin Reductase (BVR) catalyze the conversion of heme to bilirubin, a potent anti-oxidant. We hypothesized that enzyme levels would be elevated in serum and placenta of patients with severe preeclampsia (sPEC) and that full-length, membrane-bound HO1 and CPR would be present in the placenta; while a shortened, inactive form of HO1 and CPR would be present in the serum.

METHODS: Prospective cohort study of singleton gestations between 24 to 41'6 weeks diagnosed with sPEC (N=20) defined by the ACOG Hypertension in Pregnancy guidelines and gestational age-matched controls (N=20). Blood was collected pre-delivery and placenta was collected post delivery. Serum and placental levels of HO1, CPR, and BVR were quantified by ELISA assay. The molecular weights of HO1 and CPR in the serum and placenta were compared using Western blot. Serum and placental enzyme levels were analyzed with the Wilcoxon rank sum test.

RESULTS: Demographics were similar between the two groups. Serum levels of all three enzymes were significantly elevated in sPEC compared to controls: 33.5 vs 17.2 mg/ml (HO1), $p=0.02$; 53.9 vs 32.8 mg/ml, $p=0.03$ (BVR); and 15.8 vs 2.2 mg/ml, $p<0.001$ (CPR). In the placenta, only HO-1 was elevated when comparing sPEC to controls: 1.73 vs 1.4 µg/ml, $p<0.02$. Placental CPR and BVR levels were not elevated in sPEC. Western blot analysis revealed full-length forms of HO1 (~33 kDa) and CPR (~75 kDa) in the placenta; however, shortened, soluble forms of HO1 (~25 kDa) and CPR (~65 kDa) were found in the serum.

CONCLUSIONS: HO1, CPR, and BVR are elevated in the serum of women with sPEC; however HO1 and CPR are inactive, shortened fragments that are metabolically silent. In the placenta, only HO1 was elevated in sPEC. HO1 and CPR exist as the full-length, metabolically active form of the enzymes. Collectively, this data suggests that these enzymes are involved in the cellular protective mechanisms that respond to the inflammatory cascade potentiated in sPEC, but HO1 and CPR found in the serum is a shortened form of the enzyme.

S-163

CORM-A1 Treatment Leads to Increased Blood Carboxyhemoglobin in Pregnant CD-1 Mice. Karalyn E McRae†,[1] Nichole Peterson,[1] Graeme N Smith*.[1,2] *[1]Queen's University, Kingston, ON, Canada; [2]Kingston General Hospital, Kingston, ON, Canada.*

INTRODUCTION: Pre-eclampsia (PE) is a disorder affecting 5-7% of pregnancies, characterized by new-onset hypertension and proteinuria. While the etiology of PE is unknown, it is widely accepted that it is a result of impaired placental perfusion, which results in hypoxia and

oxidative damage in the placenta. At low doses, carbon monoxide (CO) has been shown to reduce inflammation, apoptosis, and increase vasodilation and angiogenesis in vessels. Carbon Monoxide Releasing Molecules (CORMs) are a class of pharmaceutical compounds composed of transition metal carbonyl complexes. This study aims to quantify the increase in carboxyhemoglobin (%COHb) following intermittent dosing with CORM-A1 (sodium boranocarbonate) in pregnant mice, determine fetal outcomes, and histological effect of CORM-A1.

METHODS: Female CD-1 mice (Charles River, USA) (5-7 weeks) were mated. Dams were treated with various doses of CORM-A1 (Sigma Aldrich, USA) by IP injection on E10.5 or daily E10.5-12.5. Blood was collected at specific intervals post-CORM injection via a submandibular bleed. Hemoglobin was measured using a Hemocue (Radiometer) and blood %COHb was measured using a head-space gas chromatograph CO analyzer (Peak Laboratories, USA). Data are presented as mean±SD. Analysis was performed by one-way ANOVA with post-hoc Dunn's test with significance of $p<0.05$.

RESULTS: Blood %COHb increased from 0.68%±0.09% at baseline (n=6) to 3.52%±0.81% at 15min post-CORM-A1 treatment (5mg/kg dose)(n=3). %COHb was significantly elevated at 15min post-injection, followed by a decline at each 15min interval post-injection back to baseline levels. Higher doses of CORM-A1 (10mg/kg E10-12) showed an increase in number of fetal resorptions compared to controls. There was no observable difference between treatment groups in maternal gestational weight gain, fetal or placental weight at E17.5.

CONCLUSIONS: Preliminary data indicates that a dose of 5mg/kg CORM-A1 can increase %COHb at 15 minutes post-treatment. The increase in fetal resorptions at higher doses suggests that a mechanism, such as hypoxia, may be leading to this fetal outcome. A more complete understanding of the mechanism by which CORM-A1 is acting on the placenta and fetus is required before CORM-A1 can be tested as CO-donor therapeutic.

S-164

Sphingosine 1-Phosphate and Increased Vasodilation in Pregnancy. Joren Manz†, Denise G Hemmings*. *University of Alberta, Edmonton, AB, Canada.*

INTRODUCTION: Sphingosine 1-phosphate (S1P) is a bioactive lipid produced by sphingosine kinase 1 and 2. S1P binds to receptors on the endothelium and generates nitric oxide (NO), a potent vasodilator. The role of S1P in the adaptive increased vasodilation responses found in normal pregnancy is unknown. However, S1P can also bind to vascular smooth muscle cells and induce constriction. Moreover, S1P can regulate endothelial permeability depending on its concentration and the receptors it binds to. Tumor necrosis factor alpha (TNFα) is a proinflammatory cytokine that increases in preeclampsia, increases permeability and can constrict arteries. S1P is produced in response to TNFα, but whether the vascular effects of TNFα are mediated by SIP is unknown. We hypothesized that S1P normally maintains the endothelial barrier in pregnancy and contributes to the adaptive vasodilatory response; however, elevated levels of TNFα will abnormally increase S1P levels leading to increased permeability, access of S1P to the vascular smooth muscle cells and overall constriction.

METHODS: Vascular tone and endothelial permeability were measured after co-infusion of S1P (1μM) or TNFα (10 ng/mL) with fluorescent 3kDa dextran inside pressurized uterine arteries isolated from pregnant and nonpregnant (NonP) mice. These responses were measured in the presence or absence of LNAME (NOS inhibitor; 100 μM) or SKII (sphingosine kinase 1 inhibitor; 10 μM).

RESULTS: Infused S1P did not constrict arteries from pregnant or NonP mice (1.97±2.37; 4.08±6.21%) but did so in the presence of LNAME to a greater extent in arteries from pregnant vs NonP mice (39.1±4.55; 22.0±11.5%). Infused TNFα did not induce constriction in arteries from pregnant or NonP mice (0.87±1.16; -2.90±0.562%). However, TNFα+LNAME constricted arteries from pregnant mice (29.9%,n=1) but had no effect on those from NonP mice (5.50±1.86). Blocking sphingosine kinase 1, an enzyme that produces S1P had no effect. Dextran leakage was increased in all co-treatments with LNAME; however LNAME alone had no effect on dextran leakage.

CONCLUSIONS: S1P maintains barrier function and plays an important role in the adaptive vasodilatory effects critical for normal pregnancy. TNFα may induce NO that modulates a TNFα-induced constriction response in arteries from pregnant mice but not in arteries from NonP mice. S1P may not play a role in these TNFα responses, although more work is needed to evaluate the role of sphingosine kinase 2.

S-165

Cardiac Remodeling and Preeclampsia: An Overview of Overlapping Circulating miRNAs. Chahinda Ghossein-Doha†,[1] Zenab Mohseni,[1] Leon de Windt,[2] Marc EA Spaanderman*.[1] [1]*Maastricht UMC, Maastricht, Limburg, Netherlands;* [2]*MUMC, Maastricht, Limburg, Netherlands.*

INTRODUCTION: During preeclamptic (PE) pregnancy the left ventricle (LV) remodels in a concentric way. This aberrant remodeling often persists after delivery and is thought to contribute to the increased risk of heart failure (HF) after PE. The concentric remodeling during PE may induce molecular signatures that may explain this increased risk. This signature may be evaluated in terms of microRNAs (miRNAs). This review evaluates existing literature on miRNA expression data in concentric remodeling on the one hand and PE on the other hand to generate a list of overlapping miRNAs.

METHODS: We have collected the data of the current literature on miRNAs during PE and during aberrant cardiac remodeling. First, data on miRNA expression in relation to cardiac remodeling was extracted. Next, data was extracted on miRNAs in relation to PE. Data on miRNA was stratified based on whether miRNA was isolated from humans, animals, tissue or the circulation. After extracting data on PE and cardiac remodeling, we compared both in order to extract the overlapping miRNAs between PE and concentric remodeling.

RESULTS: We found that nine miRNAs overlap between concentric remodeling and PE pregnancies (fig.1); miR-1, miR-18, miR-21, miR-29b, miR-30, miR-125b, miR-181, miR-195 and miR-499-5p. Five miRNAs where found to be up-regulated in both PE pregnancy and cardiac remodeling (miR-18, miR-21, miR-125b, miR-195 and miR-499-5p) and two miRNAs where down-regulated in both (miR-1 and miR-30). Two other miRNAs showed an up-regulation during PE while showing a down-regulation in cardiac remodeling (miR-29b and miR-181).

**Figure(s) will be available online.*

Fig.1: Overlapping miRNAs during cardiac remodeling and preeclampsia

CONCLUSIONS: This review revealed nine potentially relevant miRNA that should be validated in relation to cardiac adaptation during pregnancy. This approach may be an innovative step in finding relevant biomarkers for complicated pregnancy on the one hand and its relation with remote cardiovascular disease (CVD) on the other hand.

S-166

miRNAs Associated with Small for Gestational Age in Placenta and Maternal Plasma at Term. F Gaccioli†, S Gong, U Sovio, DS Charnock-Jones, GCS Smith*. *University of Cambridge, Cambridge, United Kingdom.*

INTRODUCTION: Placental miRNAs released into the maternal circulation may offer a non invasive method for detecting pregnancies with small for gestational age (SGA) fetuses. The objective of this study is to identify miRNAs differentially expressed in term placentas from pregnancies with SGA compared with appropriate for gestational age (AGA) fetuses. We further tested the hypothesis that placental miRNAs associated with SGA fetuses also differ in maternal plasma samples at 36 weeks of gestational age (wkGA).

METHODS: 55 SGA/AGA pairs were selected in our prospective cohort of 4,512 first pregnancies (POP study). SGA was defined as delivery of an infant small for gestational age (customized birth weight <5th percentile). AGA was defined as delivery of an infant with a birth weight percentile in the normal range (20-80th centile), no evidence of slowing in fetal growth trajectory and no evidence of obstetric complications. Total placental RNA and smallRNA libraries were prepared from placental biopsies collected from these patients. High-throughput sequencing (single read, 50bp) and bioinformatic analysis were used to identify miRNAs differentially

expressed between groups. 6 miRNAs identified in placental samples were further analyzed in plasma samples collected at 36wkGA from a subgroup of the same cohort (43 SGA/AGA pairs). An independent control cohort (N=37) was also investigated for a case-cohort methodological approach to test the predictive performance of the screening test.

RESULTS: smallRNA-seq analysis identified 20 miRNAs differentially expressed in term placentas from pregnancies with SGA and AGA fetuses (FDR<0.05). Consistent with their altered placental levels, two of these miRNAs (mir210 and mir150) were elevated in plasma samples collected at 36kGA from women carrying a SGA fetus (P=0.0005 and P=0.0104, respectively). Finally, receiver operating characteristic (ROC) curve analysis revealed poor screening performance for both miRNAs (Area under the curve was 0.60 for mir210, 0.53 for mir150 and 0.62 for their combination).

CONCLUSIONS: Using placental samples for patients participating in the POP study, we detected 20 placental miRNAs altered in women carrying a SGA fetus. mir210 and mir150 were also increased in 36wkGA plasma samples from SGA compared to AGA pregnancies. Although at present these 2 miRNAs show limited clinical usefulness, they could be measured in combination with other biomarkers to improve their screening performance.

S-167

Cardiomyopathy and Preeclampsia: Shared genetics? HS Gammill,[1,2] R Ch,[3] A Brewer,[3,4] JM Roberts,[5] R Shree,[1] E Tsigas,[4] K Ward*.[3] *[1]Univ Washington, Seattle, WA, USA; [2]Fred Hutch, Seattle, WA, USA; [3]Affiliated Genetics, Salt Lake City, UT, USA; [4]Preeclampsia Foundation, Melbourne, FL, USA; [5]Univ Pittsburgh, Pittsburgh, PA, USA.*

INTRODUCTION: Preeclampsia (PE), is associated with peripartum cardiomyopathy (CM), diastolic dysfunction and maternal cardiovascular disease (CVD). Recent data demonstrated shared genetic associations between peripartum CM and idiopathic dilated CM. We sought to determine whether CM gene mutations are also associated with PE.

METHODS: Subjects were participants in The Preeclampsia Registry and Biobank. After providing informed consent, subjects self-identified with prior PE completed a detailed questionnaire and provided medical records for diagnostic confirmation. Saliva samples were collected for DNA isolation. Whole exome sequencing (WES) was performed using Ion Proton Instrument with AmpliSeq Exome Capture Kit. Rare variants were considered (minor allele frequency of <0.1%). Missense variants were deemed "damaging" if so classified by any of 7 standard function prediction algorithms. Variants were defined as "truncating" if they caused a stop-gain, stop-loss, splicing, or frame-shift insertion or deletion. Results were compared with data from unrelated women with endometriosis (n=530) who underwent WES by the same methods (EndoC), as well as data from 33,000 subjects in the Exome Aggregation Consortium (ExAC). PE was not excluded in the population controls.

RESULTS: Of 190 PE subjects (170 confirmed/20 probable/awaiting additional records), 87% were Caucasian. 72% had ≥1 preterm PE delivery <37 weeks. Among PE subjects, WES demonstrated 203 rare, damaging/truncating variants in the 43 CM genes considered. 62% of women with PE carried ≥1 damaging/truncating variant in these 43 genes, and women with ≥1 mutation had an average of 1.8 mutations. As seen with peripartum CM, most mutations (56%) were found in the TTN gene. We observed excess TTN mutations in PE cohort (63%) vs 48% in EndoC (OR 1.8, 95% CI 1.3-2.5, p=6.9E-04). Pathogenicity of the observed TTN variants likely varies; the 5 variants with the highest association with PE are 12.5X more prevalent in PE cohort than EndoC cohort.

CONCLUSIONS: Women with PE are more likely to carry protein-altering mutations in genes associated with CM. These findings may have important implications for both PE directly and for later-life CVD, including as potential contributors to the clinical heterogeneity of both conditions. Further study is warranted.

S-168

Bone Mineral Density Is Decreased in Women Who Develop Preeclampsia. Carole A McBride†, Erin A Morris, Ira M Bernstein*. *UVM, Burlington, VT, USA.*

INTRODUCTION: There is growing evidence that bone is an active endocrine organ, affecting glucose homeostasis, energy expenditure, and reproduction. We evaluated the relationship of bone mineral density (BMD) with obesity, fitness (VO_2), arterial stiffness (PWV), and subsequent development of preeclampsia.

METHODS: Seventy-five healthy women (31 ± 4 yrs, BMI= 25 ± 6 kg/m^2), 21 with a history of prior preterm preeclampsia and 54 nulliparas, were recruited prior to pregnancy and evaluated in the follicular phase of their menstrual cycles (mean day 9 ± 3). Women were evaluated for physical fitness (VO_2 max), and PWV. Body composition was evaluated by DEXA scan. BMD z-score corrected for age and sex was calculated. All women subsequently conceived singletons. Pregnancy outcome data was collected. Correlations with BMDz and comparisons between women who developed preeclampsia (n=17) and those with healthy pregnancies (n=58) are made. Mean ± standard deviation with p<.05 are presented.

RESULTS: We identified no association of BMDz with prior preeclampsia or current PWV. BMDz was associated with future pregnancy outcome, with higher BMDz observed in women having healthy pregnancies compared to those who developed preeclampsia (mean = 1.07 ± 0.98 vs. 0.47 ± 0.95; p= 0.027). Women who developed preeclampsia had higher BMI (PE= 28.8 ± 6.5 vs. 24.0 ± 5.4 kg/m^2), however we observed no association between BMDz and BMI. Overall, increased BMDz was associated with lower pulse rate, (r= -0.31, p= 0.01), lower body fat % (r= -0.35, p= 0.002), higher lean body mass (r= 0.27, p= 0.02), lower android body fat % (r= -0.32; p= 0.03), and increased VO_2 (r= 0.43, p< 0.001). Subgroup analyses demonstrates that the correlative relationship observed with BMDz and both VO_2 and android fat were driven by those with healthy pregnancies, with no association in women who developed preeclampsia.

CONCLUSIONS: Our population had higher than average BMD. BMD appears to be decreased in women who develop preeclampsia compared to those with healthy pregnancies. Increased BMD in women with healthy pregnancies is associated with indices of fitness, consistent with an increase of BMD with weight-bearing exercise. However women who develop preeclampsia are heavier, yet have lower BMD. This may primarily reflect poor cardiovascular fitness or a difference in the regulation of bone turnover and endocrine processing that may indicate altered calcium metabolism.

S-169

Performance of the Fetal Medicine Foundation Preeclampsia Screening Test in Nulliparous Women: Results of the TEST Multicenter RCT. F Mone,[1] C Mulcahy,[2] P McParland,[1] F Breathnach,[2] J Morrison,[2] S Daly,[2] J Higgins,[2] A Cotter,[2] A Hunter,[2] E Tully,[2] P Dicker,[2] F Malone,[2] F McAuliffe*.[1] *[1]National Maternity Hospital, Dublin, Ireland; [2]Rotunda Hospital, Dublin, Ireland.*

INTRODUCTION: The Fetal Medicine Foundation (FMF) have devised a screening test which can predict the risk of developing preeclampsia from 11-weeks based on an unselected population. Its' performance in low risk women is unknown. Objectives were to determine; (i) the performance of the screening test in placental disease prediction in nulliparous women, and (ii) which components of the test are best predictors.

METHODS: 546 nulliparous women were randomized to; (1) 75mg aspirin from 11-14 weeks, (2) no aspirin and (3) aspirin depending on the screening test result. It was only in group 3 that results were prospectively revealed with the remainder calculated retrospectively. Screening test components included (i) maternal history, (ii) mean arterial blood pressure (MAP), (ii) PAPP-A and PLGF and (iii) uterine artery Doppler pulsatility index with calculation of preelampsia risk <42 weeks at a 1:8 cut off assessed using the FMF algorithm. The study was carried out by Perinatal Ireland and HRB Mother and Baby Clinical Trials Network.

RESULTS: The rate of placental disease was 15%, with any preeclampsia 4% (n=22), early onset pre-eclampsia 0.4% (n=2) and birthweight <10th centile 10% (n=57). The sensitivity and specificity for the FMF test in

detecting preeclampsia <42-weeks was 0.7 (0.46-0.87) and 0.06 (0.04-0.08) with an area under the curve (AUC) of 0.70. Preeclampsia prediction for individual groups is demonstrated in Figure 1. In terms of placental disease prediction sensitivities and specificities were 0.94 (0.91-0.95) and 0.06 (0.05-0.09) with and AUC of 0.66. Maternal risk factors and MAP at booking >88mmHg were the only significant predictors.
**Figure(s) will be available online.*
CONCLUSIONS: The FMF screening test performs only moderately well in nulliparous women. Maternal history and MAP in early pregnancy are the only markers, which appear to perform optimally in their detection of placental disease.

S-170

Abnormal Lymphatic Vessel Development and Difference of Lymphangiogenesis-Related Gene Expression Are Associated with Preeclampsia. Yun Ji Jung†, Yejin Park, Da Hee Yoon, Yong-sun Maeng, Yoo-na Kim, Joon Ho Lee, Young-Han Kim, Ja-Young Kwon*. *Institute of Women's Life Medical Science, Yonsei University College of Medicine, Seoul, Republic of Korea.*
INTRODUCTION: Preeclampsia (PE) is an invincible pregnancy induced disease that complicates pregnancy and places mother and fetus at high morbidity and mortality, characterized by dysfunctional remodeling of maternal vessels at the implantation site. Abnormal lymphagiogenesis has been observed in inflammatory bowel diseases in association with abnormal vasculogenesis and implicated as part of pathophysiology. However, study on placental lymphatic development is limited and controversial, and furthermore, it has not been evaluated in preeclamptic placenta. This study aims 1) to localize lymphatic vessels in the placenta and the membranes, 2) to compare the difference in lymphangiogenesis and 3) to compare the expression level of genes associated with lymphangiogenesis between normal and PE placenta.
METHODS: Fetal membranes and the chorionic plate were obtained from pregnancies with normal pregnancies (n=5) and PE (n=5). To localize lymphatic systems, immunofluorescence staining for LYVE1 and CD31 was performed. To compare the quality of lymphangiogenesis, the number of lymphatic vessels in six fields per section and the integrity of vascular structures were analyzed. Gene expression microarray analysis was performed to compare the placental expression of lymphangiogenesis-related genes between normal and PE.
RESULTS: No staining with LYVE1 was identified in fetal vessels in placental cotyledons of both groups. LYVE1-positive lymphatic vessels of normal pregnancy were present in abundance in decidua. In contrast, in decidua of PE showed a very low density of LYVE1-positive lymphatic vessels with small diameter, irregular and weak cell-to-cell junction. Interestingly, F4/80 -positive macrophages were significantly increased in chorionic membranes of PE as compared with normal. Comparative gene expression microarray analysis between normal and PE placenta showed the increased expression of immune cell recruitment and migration inducing factors in PE group, whereas immune suppressing factors decreased in PE group compared with their expression in normal group.
CONCLUSIONS: Lymphatic vasculature was present in the placental unit localized at decidua. The dysfunctional lymphatic system in the placenta of PE may in part contribute to the disease pathophysiology and this may related with macrophage recruitment.

S-171

Human Myometrial H_2S Biosynthesis Increases to Stimulate Myometrial Mcrovascular Endothelial Cell Angiogenesisduring Pregnancy. Honghai Zhang, Jennifer C Chen, Thomas J Lechuga†, Dong-bao Chen*. *University of California, Irvine, CA, USA.*
INTRODUCTION: Myometrial spiral artery expansion and remodeling *via* angiogenesis is a key mechanism for upregulating uterine blood flow during pregnancy. Hydrogen sulfide (H_2S), mainly synthesized from L-cysteine by cystathionine-beta synthase (CBS) and cystathionine-gama lyase (CSE), is a potent proangiogenic factor. However, it is unknown if pregnancy regulates myometrial angiogenesis.
METHODS: Myometrial tissues were obtained from hysterectomies from non-pregnant (NP) and late pregnant (>28 wks) women. CBS and CSE mRNA and protein were determined by qPCR and immunoblotting, respectively. H_2S production was measured by the methylene blue assay. Tissue sections were analyzed by immunofluorescence microscopy with antibodies of CBS, CSE, and endothelial marker CD31 for quantifying cellular CBS and CSE protein expression and angiogenesis. Primary myocytes and mcrovascular endothelial cells (hMMEC) were enzymatically isolated for *in vitro* angiogenesis assays.
RESULTS: Myometrial H_2S production was significantly higher in P *vs*. NP women in association with upregulated CBS but not CSE mRNA and protein and angiogenesis index. CBS and CSE proteins were localized in myocytes and microvessels. Treatment with a H_2S donor NaHS and VEGF significantly stimulated hMMEC proliferation, migration, and tube formation *in vitro (in vivo* angiogenesis*)*. Co-culture with primary myocytes also stimulated hMMEC migration *in vitro*, which was blocked by a specific inhibitor of CBS.
CONCLUSIONS: Pregnancy augments myometrial H_2S biosynthesis via CBS upregulation in myocytes and microvessels to stimulate myometrial angiogenesis (Funded by NIH RO1 HL70562).

S-172

Decidual Cell Regulation of CX3CL1: Implications for the Pathogenesis of Preeclampsia. Joseph Huang,[1,2] Chie-Pein Chen,[3] Longzhu Piao,[4] Frederick Schatz,[1] Ozlem Guzeloglu-Kayisli,[1] Umit Kayisli,[1] Li-Yen Shiu,[2] Chun-Yen Huang,[2] Nihan Semerci,[1] Charles J Lockwood*.[1] *[1]University of South Florida, Tampa, FL, USA; [2]E-Da Hospital, Kaohsiung, Taiwan; [3]Mackay Memorial Hospital, Taipei, Taiwan; [4]The Ohio State University, Columbus, OH, USA.*
INTRODUCTION: First trimester human decidua is dominated by decidual cells (FTDCs), natural killer (NK) cells and macrophages (MΦs). Shallow decidual trophoblast invasion with decreased utero-placental blood flow elicits subsequent preeclampsia (PE). FTDCs cultured with NK cell-derived interferon-gamma (IFN-γ) and either MΦ-derived tumor necrosis factor alpha (TNF-α) or interleukin-1 beta (IL-1β) synergistically enhance NK cell-recruiting IP-10 expression. Elevated IP-10 levels in first trimester human serum significantly predict later PE development. These findings are extended to include CX3CL1, also known as fractalkine, which mediates NK cell migration, adhesion and survival. Pleiotropic actions displayed by CX3CL1 in recruiting and activating NK cells prompted examination of the potential association between FTDC-expressed CX3CL1 and later PE development.
METHODS: Immunofluorescence staining localized CX3CL1 expression in first trimester decidua, preeclamptic and gestational age (GA)-matched term decidua. Enzyme-linked immunosorbent assays (ELISAs) assessed CX3CL1 protein levels in IFN-γ + IL-1β- or TNF-α-treated FTDCs, patients' serum and term decidua. Quantitative reverse transcription-polymerase chain reaction (qRT-PCR) evaluated CX3CL1 mRNA in IFN-γ + IL-1β- or TNF-α-treated FTDCs. The majority $CD56^{dim}CD16^{+}$ NK cells isolated from peripheral blood (pNK) were used in a CX3CL1-induced migration assay.
RESULTS: In first trimester human decidua, CX3CL1 is expressed primarily in decidual cells. Decidua from women with PE displayed higher CX3CL1 levels vs. GA-matched controls. However, no difference was found in CX3CL1 levels in first trimester serum from women eventually developing PE vs. controls. Incubation of FTDCs with IFN-γ + TNF-α or IL-1β synergistically enhanced CX3CL1 mRNA and protein expression. CX3CL1 elicited concentration-dependent-enhanced migration of pNK cells that peaked at 10 ng/mL, whereas 50 ng/mL inhibited migration.
CONCLUSIONS: These observations suggest that decidual cell-secreted CX3CL1 plays a role in the later development of PE rather than acts as an early predictor of PE.

S-173

The Impact of Hyperglycemia and Antiphospholipid Syndrome on Trophoblast Function. Daisy Leon-Martinez†,[1] Melissa J Mulla,[1] Christina S Han,[2] Lawrence W Chamley,[3] Vikki M Abrahams*.[1] *[1]Yale University, New Haven, CT, USA; [2]UCLA, Los Angeles, CA, USA; [3]University of Auckland, Auckland, New Zealand.*

INTRODUCTION: Diabetes and antiphospholipid syndrome (APS) are individually associated with increased risk of poor perinatal outcomes, in particular preeclampsia. One common mechanism by which both affect pregnancy is by altering placentation. Our prior research found that elevated glucose levels and antiphospholipid antibodies (aPL) independently disrupt trophoblast function by inducing anti-angiogenic factor and inflammatory cytokine secretion, notably IL-1β via uric acid-induced inflammasome activation. This study aimed to elucidate the effects of combination excess glucose and aPL on trophoblast function.

METHODS: The human first trimester trophoblast cells (Sw.71) were treated with glucose at 5mM (normoglycemic) and 25mM (hyperglycemic), in the presence and absence of aPL or IgG control (10μg/ml) (n=5). After 72hrs, supernatants were measured for pro-inflammatory IL-8 and IL-1β; inflammasome-related uric acid and caspase-1 activity; pro-angiogenic PlGF; and anti-angiogenic sFlt-1 and sEndoglin by ELISA and bioassays.

RESULTS: Compared to normoglycemic glucose levels, hyperglycemic levels significantly increased trophoblast secretion of IL-1β by 18.9-fold; uric acid by 1.3-fold; IL-8 by 3.4-fold; sFlt-1 by 3.0-fold; sEndoglin by 1.6-fold; and PlGF by 6.2-fold ($p<0.05$). Compared to hyperglycemic conditions alone, the presence of aPL, but not the IgG control, significantly augmented trophoblast secretion of IL-1β by 2.1-fold; uric acid by 1.7-fold; caspase-1 by 4.8-fold; and PlGF by 9.0-fold ($p<0.05$). In contrast the presence of aPL, but not the IgG control, significantly reduced the ability of excess glucose to induce trophoblast sFlt-1 by 54.5%; sEndoglin by 39.9% ($p<0.05$); and while not significant, IL-8 by 31.0%.

CONCLUSIONS: Trophoblast exposed to hyperglycemic conditions generated a pro-inflammatory and anti-angiogenic profile. The presence of aPL under hyperglycemic conditions further augmented the pro-angiogenic and inflammasome-mediated inflammatory responses while dampening the anti-angiogenic response. Thus, there may be counteracting effects when both diabetes and APS are concurrent. Further research is warranted so that we may better understand the mechanisms by which hyperglycemia and aPL in combination lead to poor perinatal outcomes.

S-174

Low Dose VEGF Protects, While IL-6 Amplifies TNFα-Induced Damage to Pregnancy-Derived UAEC Monolayers. Amanda C Hankes†, Mary A Grummer, Ian M Bird. *UW-Madison, Madison, WI, USA.*

INTRODUCTION: Pregnancy depends on a pregnancy-adapted increase in uterine artery endothelial vasodilation, which is dependent on Ca^{2+} signaling enhanced by increased gap junction communication at cell-cell contact points. Without such adaptation, diseases such as Preeclampsia (PE) occur. PE is an inflammatory condition characterized by a failure of pregnancy enhanced vasodilation and loss of endothelial monolayer integrity, resulting in hypertension, proteinuria, and edema. Many growth factors and cytokines are present during pregnancy but further altered in PE, including TNFα, VEGF, and IL-6 (linked with SGA). ***Our objective*** is to establish if different dosage combinations of TNFα, VEGF, and IL-6 will either enhance or worsen the P-UAEC cell-cell contact/monolayer integrity, so contributing to loss of vasodilation and onset of edema.

METHODS: Ovine P-UAEC were grown to confluence in 96-well ECIS (Electric Cell-Substrate Impedance Sensing) plates that measure monolayer resistance (higher resistance=better monolayer integrity). Cells were starved and treated alone or in combination with different doses of TNFα, VEGF, and IL-6 (0.1,1, and 10ng/mL) for 25 hours. Alternatively, cells were treated for 1 hr and Western blot analysis run to observe STAT phosphorylation (as an assay of IL-6 receptor signaling crosstalk).

RESULTS: We previously found TNFα decreases monolayer resistance (23% of control, $p<0.01$), but VEGF has no effect. Preliminary studies show low doses of VEGF combined with 10ng/mL TNFα increase resistance by 18% (for 0.1ng/mL VEGF) and 13% (for 1ng/mL VEGF, $p<0.05$). However, combination of 10ng/mL VEGF and TNFα decreases monolayer resistance even farther than just TNFα alone ($p<0.01$). Preliminary results also suggest IL-6 can further decrease monolayer resistance when combined with TNFα, but not alone. IL-6 can also potentiate STAT3 phosphorylation at y705 and s727 by VEGF or TNFα.

CONCLUSIONS: These results strengthen the theory that in PE, no single factor is responsible as many factors work together to signal the breakdown of junctional proteins, so causing monolayer permeability. VEGF is not effective by itself, and may be protective (low dose) or additive (high dose) to other factors effects (such as TNFα). Another potential modulator, IL-6, has no effect alone but is synergistic to TNFα mediated monolayer damage/permeability. Further studies of interactions of these factors are warranted to understand their values as biomarkers in prediction and treatment of PE.

NIHT32-HD041921,HD38843.

S-175

Elevated Complement Deposition and Altered CD46 Isoform Profiles in Preterm Delivery and Preeclampsia Placentas. Manu Banadakoppa, Meena Balakrishnan, Kjersti Aagaard, Chandra Yallampalli. *Baylor College of Medicine/Texas Childrens Hospital, Houston, TX, USA.*

INTRODUCTION: Pregnancy is associated with systemic elevation of products of complement (C) activation (C3a and C5a) with an exaggerated increase in pregnancies which are complicated by preeclampsia (PE) and preterm delivery (PTD). CD46, a cell surface regulator of C cascade is expressed in several isoforms due to differential splicing of mRNA. CD46 isoforms differentially regulate C activation; BC being 2 to 3 folds more efficient compared to C isoforms. However, local C activation and CD46 isoform expression at the fetal-maternal interface in the Placenta have not been previously studied. We sought to examine and relate level of C activation to CD46 isoform profiles in placentas from PE and PTD.

METHODS: Placental tissues from preterm delivery (PTD, n=23), early onset and/or severe PE (ESPE, n=13), preexisting hypertension (PHT, n=21), term delivery (control, n=25), and mild PE (MPE, n=17) were obtained from our PeriBank repository. C3b was measured by ELISA. CD46 isoform profiles were examined by qPCR and Western blot. The data were analyzed by one way ANOVA and Turkey's multiple comparison tests.

RESULTS: C3b deposited on placentas ranged from 6.5 to 251 ng/μg protein in healthy controls and 181 to 973 ng/μg protein in complicated pregnancies, with mean C3b levels higher (2 to 3 fold, $p<0.0001$) in PTD, ESPE, PTH, and MPE compared to term delivery controls. C3b levels were not different between complicated pregnancy groups except PTD and MPE (MPE 1.3 fold > PTD, $p<0.01$). Expression of CD46 isoforms were group specific with BC predominant in term delivery controls. Overall expression of CD46 decreased in ESPE, PTH, and MPE groups compared to PTD and term delivery controls.

CONCLUSIONS: When compared to term controls, C3b levels in PTD, PTH, ESPE, and MPE complicated pregnancies were significantly increased, indicating excess local C activation. This significantly correlated with both decreased expression of CD46 and isoform profiles in a disease specific fashion. Similar levels of C activation in all the complicated pregnancy groups with distinct CD46 isoform profiles suggests a relation between rate of C activation during gestation and disease manifestation and severity. These findings form the foundations of our current work on elucidating role of C regulators in the pathophysiology of pregnancy complications.

S-176

Is Home Blood Pressure Monitoring in Hypertensive Disorders of Pregnancy Consistent with Clinic Recordings? Helen Perry†, Elaine Sheehan, Basky Thilaganathan, Asma Khalil*. *St George's Hospital, London, United Kingdom.*

INTRODUCTION: Hypertensive disorders affect up to 10% of pregnancies, but the incidence is likely to increase due to increasing prevalence of obesity. Self-monitoring of blood pressure (BP) at home is preferable and more accurate to clinic recordings, so it recommended outside pregnancy. However, the data in pregnancy are scarce and many

unanswered questions remain regarding its implementation and predictive accuracy for adverse perinatal outcome. The aim of this study was to ascertain whether home BP recordings differ from those recorded in the clinic in women with hypertensive disorders of pregnancy.
METHODS: This was a prospective cohort study of hypertensive pregnant women undergoing home BP monitoring. Exclusion criteria included severe hypertension/preeclampsia, fetal growth restriction, maternal age less than 16 years or mental illness. Participants were provided with a Microlife® BP machine (validated in pregnancy hypertension) and a urine dipstick kit. They were taught how to take and record accurate BP readings and urinalysis. Participants were reviewed in clinic every 1-2 weeks and given information on reporting abnormal results and symptoms of pre-eclampsia. The data were tested for normal distribution and the paired T-test used to compare the paired measurements of systolic and diastolic BP recordings.
RESULTS: 78 women were included. The majority (n=61) were recruited in the third trimester. Overall, both systolic [mean (SD) 132.2 (14.04) vs 138.5 (14.44) mmHg; P<0.001] and diastolic [mean (SD) 85.03 (9.12) vs 87.06 (9.37); P= 0.037] BP recording were significantly lower at home vs clinic. In the second and third trimesters, there was a significant difference in home vs clinic systolic BP [mean (SD) 123.0 (12.25) vs 136.4 (14.74); P = 0.001 and 134.8 (13.33) vs 139.1 (14.58); P= 0.013, respectively), but not in diastolic BP (P=0.235 and P=0.145, respectively).
CONCLUSIONS: Our results are consistent with existing evidence outside pregnancy that home BP measurements are lower than those recorded in hospital. The finding of higher systolic readings in the second and third trimesters is consistent with non-pregnant studies which demonstrate greater differences in systolic compared to diastolic readings, and could be explained by the 'White Coat Hypertension' phenomenon. There were no adverse outcomes in our cohort and therefore it does not appear that the lower recordings at home are falsely reassuring.

S-177

Oocyte Cryopreservation in Transgender Men: A Case Series. Terrence D Lewis†,[1,2] Mae Wu Healyt†,[1,2] Alan H DeCherney,[2] Kimberly Moon,[3] Kate Devine,[3] Belinda J Yauger*.[1,2] *[1]National Institutes of Health, Bethesda, MD, USA; [2]Walter Reed National Military Medical Center, Bethesda, MD, USA; [3]Shady Grove Fertility Center, Rockville, MD, USA.*
INTRODUCTION: Over the past several years, gender reassignment hormone therapy for transgender populations has increasingly become an area of interest. With more patients seeking medical therapy, the need for appropriate fertility preservation counseling and options is paramount. Currently, for female to male (FtM) transgender patients, options include oocyte, embryo, or ovarian tissue cryopreservation. There is limited literature regarding recommendations for ovarian stimulation protocols for those previously exposed to androgens. More specifically, data is lacking regarding the ideal time off androgens prior to stimulation, the effect of longer androgen exposure on the response to stimulation and to potential outcomes such as pregnancy rates. Our objective is to report on two FtM patients and their oocyte cryopreservation (OC) cycles after initiating, and subsequently discontinuing, gender reassignment hormone therapy.
METHODS: FtM transgender patients who underwent oocyte cryopreservation at Shady Grove Fertility Science Center between 2014-2016 were included. Patient age, prior history of androgen exposure, ovarian stimulation protocol and outcomes, number of oocytes cryopreserved, and pregnancy rates were evaluated.
RESULTS: Two FtM patients underwent oocyte cryopreservation under an antagonist protocol with FSH and hMG. Both had previously been exposed to long-term androgen therapy, which was discontinued prior to OC. Stimulation cycles ranged from 10-13 days, with final oocyte maturation triggered with Lupron or human chorionic gonadotropin (hCG). Peak serum estrogen levels ranged from 902-4,993. The number of oocytes retrieved ranged from 5-29 with 2-17 M2's, which underwent vitrification. Neither patient has used their oocytes to attempt pregnancy.
CONCLUSIONS: FtM transgender patients can have good OC outcomes after long-term exposure to androgen therapy. More data is needed to further evaluate the ideal time off of androgen exposure prior to stimulation and the effect of longer androgen exposure. Long-term data is also needed to evaluate fertilization and live birth outcomes.

S-178

Cyclophosphamide and Its Metabolite Impact on Fertilization Through Mitochondrial Dysfunction. Roohi Jeelani†,[1] Mili Thakur,[1] Sara Aldaheri,[1] Hamid-Reza Kohan-Ghadr,[1] Robert Morris,[2] Husam Abu-Soud*.[1] *[1]Wayne State University, Detroit, MI, USA; [2]Karmanos Cancer Institue, Detroit, MI, USA.*
INTRODUCTION: Cyclophosphamide(CP) is a drug used to treat many gynecological cancers as well as various autoimmune diseases. Despite many advances, majority of women after this treatment may suffer from premature ovarian insufficiency and infertility. CP is metabolized in the liver to give stable toxic compound: acrolein. Recently, we have established that CP and acrolein exposure causes deterioration of oocyte quality through changes in microtubule morphology and chromosomal alignment. However, the effects on fertilization of these oocytes remains unknown. Our objective was to investigate the impact of oocyte deterioration and mitochondrial dysfunction on fertilization.
METHODS: Metaphase II mouse oocytes(n=282) were exposed for 45min to cyclophosphamide and acrolein (0-100μM) and compared to untreated controls. Generation of reactive oxygen species (ROS) was evaluated using the Cellular ROS Detection Assay Kit. The mitochondrial membrane potential was evaluated by the JC-10 Mitochondrial Membrane Potential Assay. Subsequently, outcomes of oocyte fertilization after incubation of the oocytes in the same compounds and time was determined by following cleavage rate and development to the morula and blastocyst stages at 24, 48 and 72h after insemination.
RESULTS: Treatment with these metabolites led to ROS overproduction and mitochondrial damage. Images of embryo morphology at 24 hours (2 cell stage), 48 hours (8 cell stage) and 72 hours (morula) and blastocyst rates after exposure to acrolein (0-25μM) and IVF were assessed. At 24 hours post insemination, the majority of the oocytes exposed to acrolein appeared granular and failed to fertilize compared to controls (63.3% vs. 93.3%), and the cleavage rate 24 hours post-fertilization was statistically significant in the different exposure groups (p<.05). The rates of embryo development at 48 hours were significantly lower in oocytes exposed to acrolein as compared to controls (56.7% vs. 93.3%, p<.05). Most treated zygotes exhibited fragmentation and a large perivitelline space. The arrested embryos were highly fragmented and atretic with a dark granular appearance.
CONCLUSIONS: In-vitro exposure to CP and its metabolites deteriorates oocyte quality through mitochondrial damage contributing to further generation of ROS and alteration of intracellular redox potential balance and ultimately fertilizability.

S-179

ZP1 and CD9 Play a Synergistic Role in Zona Pellucida Formation. Nicole Banks†,[1] Yangu Zhao,[2] Boris Baibakov,[2] Jurrien Dean*.[2] *[1]NIH, Bethesda, MD, USA; [2]NIH, Bethesda, MD, USA.*
INTRODUCTION: The mouse zona pellucida (ZP) is composed of 3 glycoproteins, ZP1, ZP2, and ZP3. Female mice lacking ZP1 have decreased fecundity and thinning of the ZP. To accumulate sperm in the perivitelline space and study an effect on zona penetration, we crossed *Zp1* null with *Cd9* null mice. CD9 is a tetraspanin membrane protein critical for efficient sperm-egg fusion but, heretofore, without a known role in ZP formation. Unexpectedly, we observed a synergistic defect in *Zp1*;*Cd9* null mice in which ovulated eggs had defective or absent ZPs.
METHODS: $Zp1^{tm/+}$ mice were crossed with $Cd9^{tm/+}$ mice to produce a double knockout line (DKO). DKO and $Zp1^{tm/tm}$ 8-week-old females were stimulated with 5 IU equine chorionic gonadotropin and 48 hours later with 5 IU of human chorionic gonadotropin (hCG). Ovaries were isolated 9 hours after hCG and fixed in 3% glutaraldehyde in 0.1 M sodium cacodylate. Tissues were embedded in plastic and 3 μm sections cut. Mounted sections were stained with periodic-acid Schiff's reagent and hematoxylin. $Zp1^{tm/tm}$, $Cd9^{tm/tm}$, DKO, and wildtype females were stimulated with gonadotropins and cumulus masses were isolated 12-14 hours after hCG and treated with hyaluronidase. Ovulated eggs were fixed in 2% paraformaldehyde and stained with wheat germ agglutinin and Hoechst, counted, and assessed by confocal microscopy.

RESULTS: Primary and secondary follicles had similar histology. The majority of pre-ovulatory follicles in the DKO mouse lacked a ZP, while all pre-ovulatory follicles in the *Zp1*$^{tm/tm}$ mouse had a ZP. The numbers of ovulated eggs are shown in the table below. Six of 25 imaged eggs from *Zp1*$^{tm/tm}$ mice had no ZP and 3 of 25 had a partial ZP. In the DKO line, 15 of 21 eggs had no ZP and 4 of 21 had a partial ZP. No absent or partial ZPs were observed in wildtype or *Cd9*$^{tm/tm}$ mice (n=5 in each group).

	Wildtype[b]	*Zp1*$^{tm/tm}$	*Cd9*$^{tm/tm}$	*Zp1*$^{tm/tm}$; *Cd9*^{tm}
Ovulated Eggs[a]	28.8 ± 6.3	22.2 ± 3.6	35.6 ± 3.4	8.4 ± 2.9
[a]mean ± s.e.m; [b]5 mice/group				

CONCLUSIONS: Mice lacking both ZP1 and CD9 have higher rates of ZP abnormalities than either *Zp1*$^{tm/tm}$ or *Cd9*$^{tm/tm}$ mice. This suggests that ZP1 and CD9 play a synergistic role in ZP formation. The zona proteins traffic through oocyte tethered to the endomembrane from which they are released at the cell surface. We propose that CD9, in the absence of ZP1, plays a role in helping to organize the zona proteins in the oolemma prior to their release to form the extracellular zona matrix.

S-180

Galactose and Its Metabolites Interfere with Normal Maturation and Function of Metaphase II Mouse Oocytes. Mili Thakur, Roohi Jeelani, Sarah Aldahaheri, Bernard Gonik, Husam Abu-Soud*. *Wayne State University, Detroit, MI, USA.*

INTRODUCTION: Although, female patients with classic galactosemia commonly suffer from hypergonadotropic hypoestrogenic infertility, rarely spontaneous pregnancies occur, indicating that some oocytes may be spared from the adverse effects of galactose and its metabolites. To understand the timing of the insult, whether it is pre or post fertilization, we sought to compare the effects of galactose and its metabolites on fertilization and embryonic development by comparing exposure of metaphase II oocytes and zygotes to these compounds.

METHODS: To determine the effect of D-galactose (2 μM), galactitol (11μM) and galactose 1-phosphate [Gal 1-P] (0.1 mM) (concentrations in patients on galactose-restricted diet) on pre fertilization gametes, metaphase II mouse oocytes (n = 120) were exposed for 4h (maximum effect on oocyte spindle), inseminated in vitro, and compared to controls. Outcomes of fertilization, cleavage, and development to the morula and blastocyst stages were compared at 24, 48 and 96h after insemination. To determine the same compounds on post fertilization development, 1-cell mouse embryos (n = 124) were exposed to identical concentrations for 4h and the effect on embryo development was studied until 120h.

RESULTS: Majority of the exposed oocytes appeared granular and demonstrated lower fertilization rate: galactose (37.5%), galactitol (30%) and Gal 1-P (25%) compared to controls (47.5%) at 24h. At 48h, significantly lower oocytes showed development when exposed to galactitol (5%), galactose 1-phosphate (5%) compared to control (37.5%). Similar trend was observed in oocytes exposed to D-Galactose (17.5%). After 96h, the rates of expanded blastocysts were significantly lower in all three treatment groups (0-2.5% versus 45% to control) (Fig 1A).

**Figure(s) will be available online.*

In contrast, the 1-cell embryos continued normal development despite exposure to same concentration of for the entire duration (120h) (Fig 1B).

CONCLUSIONS: Understanding the time and impact of the gametotoxic insult from galctose and its metabolites will pave the way to develop potential ways to intervene to extend the window of fertility in classic galactosemia.

S-181

Glucocorticoids in Assisted Reproduction-Should the Uterine Environment Dictate Use? Sarah Moustafa†,[1] Edwina Kisanga,[1] Robert N Taylor,[2] Shannon D Whirledge*.[1] *[1]Yale School of Medicine, New Haven, CT, USA; [2]Wake Forest School of Medicine, Winston-Salem, NC, USA.*

INTRODUCTION: Endometrial receptivity is a key factor determining success in assisted reproduction (ART), and the immune system plays a deciding role in establishing receptivity. The use of glucocorticoids in ART cycles has become common practice, where the anti-inflammatory activities of glucocorticoids are thought to provide a more favorable environment for implantation. However, clinical evidence to the utility of glucocorticoids in this capacity is not clear. Glucocorticoids possess both pro- and anti-inflammatory actions. In fact, glucocorticoids can exacerbate lipopolysaccharide (LPS) signaling, a risk factor for infertility. Our objective was to evaluate the impact of glucocorticoids on the immune response in decidualization, and in an *in vitro* model of bacterial infection.

METHODS: Primary endometrial stromal cells (ESC) were treated with 100 nM dexamethasone (Dex) and/or 100 ng/mL LPS in the absence and presence of 10 nM estradiol, 100 nM progesterone, and 0.5 mM dibutyryl cAMP. Morphological changes induced by decidualization were monitored under phase contrast microscopy and biomarkers were assessed. The transcriptional response was evaluated by gene expression pathway arrays. Cytokine production was assessed by 17-plex array.

RESULTS: LPS treatment substantially activated the TLR4 signaling pathway. Though glucocorticoid treatment alone did not induce TLR4 signaling, the presence of Dex with LPS resulted in the synergistic induction/repression of gene expression over the response to LPS alone. Moreover, cytokine production of IL-1β, IL-6, IL-17, IFN-γ, MIP1α, MIP1β, RANTES, and TNF-α were significantly higher in the presence of Dex and LPS. Interestingly, the presence of glucocorticoids during decidualization blunted production of the cytokines GRO-a, IL-6, IL-8, MCP-1, and IFN-g and increased VEGF, while the presence of LPS significantly induced almost all cytokines evaluated. Production of IP-10 was significantly higher in decidualized stromal cells exposed to glucocorticoids and LPS. Markers of decidualization *IGFBP1*, *PRL*, and *NOTCH1* were also altered by glucocorticoids and LPS.

CONCLUSIONS: Exposure to glucocorticoids in an infection model significantly changes the immune response in human primary ESC. This discovery suggests that immune pathologies should be accounted for prior to glucocorticoid therapy during ART.

S-182

Vitamin D Does Not Enhance Endometrial Stromal Cell Decidualization in Immortalized Human Endometrial Stromal Cells. Kathleen Jaeger, Arin Kettle-Oestreich, Maureen Schulte, Andrew Cusumano, Kelle Moley*. *Washington University in St. Louis, St. Louis, MS, USA.*

INTRODUCTION: Endometrial decidualization is the hormonally dependent response of the endometrium in preparation for pregnancy. Previous work in our lab suggests this process is influenced by modifiable lifestyle factors. Specifically, we have found that obese patients have decreased endometrial decidualization, in part due to impaired autophagy. Studies have demonstrated that vitamin D promotes autophagy and may positively influence fertility. Therefore, we hypothesized that vitamin D would promote endometrial decidualization in a mechanism dependent on autophagy.

METHODS: An immortalized human endometrial cell line was cultured in vitro and decidualization was induced by medroxyprogesterone acetate and cAMP in the presence or absence of vitamin D or an ethanol control. Cells were collected and quantitative RT-PCR was performed to evaluate markers of decidualization, prolactin (PRL) and insulin-like growth factor binding protein 1 (IGFBP1). Western blots were also performed to evaluate LC3B3, a marker of autophagic flux.

RESULTS: In this pilot study, vitamin D did not promote endometrial decidualization and had no effect on autophagic flux. In the qRT-PCR analysis, endometrial cells exposed to vitamin D had decreased endometrial receptivity by PRL and IGFBP1.

**Figure(s) will be available online.*

Western blots demonstrated that the control decidualized cohort had increased autophagic flux as expected; however, LC3B2 levels remained constant in both vitamin D control and decidualized cells indicating that vitamin D did not enhance autophagy in this group.

CONCLUSIONS: These data suggest that vitamin D does not promote endometrial decidualization. Experiments are ongoing to confirm these findings as well as evaluate the effect of vitamin D in a dose dependent manner. The clinical significance of the effect of dietary and modifiable lifestyle factors influencing endometrial decidualization and fertility

has wide reaching implications. As our lab previously demonstrated the deleterious effect of obesity on fertility, we are working to elucidate dietary factors that promote both decidualization and clinical fertility.

S-183

A Novel Approach to Optimizing Implantation in Young Patients Undergoing IVF-ICSI-PGS. Stephanie Baum†,[1] Moti Gulersen†,[1] Avner Hershlag,[2] Christine Mullin,[2] Matthew Cohen,[2] Tomer Singer*.[1] *[1]Lenox Hill Hospital/Northwell Health, New York, NY, USA; [2]Northwell Health, Manhasset, NY, USA.*

INTRODUCTION: The three most significant advances in assisted reproductive technology in the past decade have been the trend toward blastocyst transfer, Preimplantation Genetic Screening (PGS), and freeze-all cycles. We hypothesize that transferring a fresh blastocyst while biopsying the remaining blastocysts for PGS will neither decrease pregnancy rates nor increase miscarriage rates, as compared to a fresh blastocyst transfer where no embryos are biopsied or a frozen euploid blastocyst transfer.

METHODS: We performed a retrospective chart review of 477 cycles between 2014-2016. 75 cycles met inclusion criteria and were subdivided into 3 groups: 1. Fresh embryo transfer (ET)+PGS (Fresh ET+Freeze/PGS); 2. Fresh ET only; 3. Frozen euploid ET (FET/PGS). Inclusion criteria: age 38 or less undergoing the first blastocyst transfer after oocyte retrieval. Statistical analysis of continuous variables was performed by one-way ANOVA and categorical variables using Chi-square test. Primary outcome: clinical pregnancy (fetal heart rate detected by transvaginal ultrasound).

RESULTS: There was no significant difference between age, anti-mullerian hormone (AMH), and day 3 follicle stimulating hormone (FSH) amongst the 3 study groups. No significant difference was seen when comparing implantation and clinical pregnancy rate, though the implantation rate between "Fresh ET" and "FET/PGS" approached statistical significance.

	Overall (n=75)	Fresh ET +Freeze/ PGS (n=12)	Fresh ET (n=28)	FET/ PGS (n=35)	p-value
Age (mean±SD)	33.3±3.0	33.6±2.7	32.9±2.8	33.6±3.3	NS
AMH (ng/mL) (mean±SD)	4.3±3.0	3.6±2.6	4.5±3.2	4.5±3.3	NS
Day 3 FSH (IU/L) (mean±SD)	6.6±1.9	6.3±1.5	7.2±2.0	6.1±1.9	NS
Implantation rate (N(%))		8(66.7)	14(50.0)	25(71.4)	NS
Clinical pregnancy rate (N(%))		6(50.0)	13(46.4)	19(54.3)	NS

CONCLUSIONS: This novel approach of maximizing all usable embryos by transferring a fresh blastocyst while simultaneously biopsying remaining blastocysts allows young patients a shorter interval to pregnancy without compromising their chances of a live birth. Transferring an embryo immediately after stimulation allows for a thicker endometrial lining, decreases the financial burden of a subsequent frozen cycle, and increases cumulative pregnancy rates with transfer of a euploid embryo.

S-184

Organoid Cultures of Human Endometrial Glands: A Model for Investigating Early Pregnancy. Margherita Y Turco†,[1] Lucy Gardner,[1] Tereza Cindrova-Davies,[1] Jan J Brosens,[3] Hilary O Critchley,[2] Benjamin D Simons,[1] Myriam Hemberger,[1] Bon-Kyoung Koo,[1] Ashley Moffett,[1] Graham J Burton*.[1] *[1]University of Cambridge, Cambridge, Cambridgeshire, United Kingdom; [2]University of Edinburgh, Edinburgh, Scotland, United Kingdom; [3]University of Warwick, Coventry, Warwickshire, United Kingdom.*

INTRODUCTION: Human endometrium undergoes dynamic changes throughout the menstrual cycle and during early pregnancy. Secretions from the glands regulate implantation, and stimulate early placental development. Currently, no culture systems sustain growth and recapitulate gland function *in vitro.* Hence, we adapted the technique used to establish adult stem-cell derived organoids.

METHODS: Samples of proliferative and secretory phase endometrium and decidua were obtained with written informed consent and ethical approval. Samples were diced and digested in Dispase II/collagenase V. Fragments of the glands released were suspended in Matrigel drops and cultured in organoid Expansion Medium containing EGF, Noggin and R-spondin-1. Cultures were passaged by pipetting every 7-10 days or frozen for storage.

RESULTS: The cells self-organised into spheres with a pseudostratified columnar epithelial morphology, supported on the outside by basement membrane material and with an inner microvillous apical membrane that showed secretory activity. The organoids immunostained strongly for markers of the glandular epithelium (MUC-1, E-CADHERIN, CK7 and EPCAM). The organoids remained genetically stable in culture for over 6 months. Single cells from established organoids formed entire organoids containing both ciliated and secretory cells over 7-14 days, demonstrating clonogenic and bi-potent ability. The organoids were responsive to oestrogen and progesterone, upregulating expression of genes encoding uterine milk proteins, e.g. *PAEP* (glycodelin) and *SPP1* (osteopontin). Administration of hCG, placental lactogen and prolactin caused further upregulation and a hypersecretory phenotype, mimicking changes seen in early pregnancy.

CONCLUSIONS: The organoid technique provides a robust chemically defined method for establishing genetically stable 3-D cultures of human endometrial glands from non-pregnant and decidual samples that are responsive to sex steroids and pregnancy hormones. These will provide a powerful tool for investigating endometrial function during the cycle and early pregnancy, and for exploring pathologies such as endometrial carcinoma.

S-185

Uterine Natural Killer Cell Subpopulations and Their Proximity to Endometrial Arterioles Are Not Altered in Women with Recurrent Implantation Failure Following In Vitro Fertilisation. Premila Paiva†,[1] Wan Tinn Teh,[1,2,3] Leonie M Cann,[1] Cameron Nowell,[4] Jacqueline Donoghue,[1] Judith N Bulmer,[5] Catharyn Stern,[2,3] John McBain,[2,3] Peter A Rogers.[1] *[1]University of Melbourne, Royal Women's Hospital, Melbourne, VIC, Australia; [2]Royal Women's Hospital, Melbourne, VIC, Australia; [3]Melbourne IVF, East Melbourne, VIC, Australia; [4]Monash University, Parkville, VIC, Australia; [5]Newcastle University, Newcastle upon Tyne, United Kingdom.*

INTRODUCTION: Uterine natural killer (uNK) cells are potential regulators of decidual angiogenesis and spiral arteriole remodelling during early pregnancy. Altered numbers of CD56+ uNK cells have been associated with recurrent reproductive failure. However, variability in how tests are performed including the subjectivity of the staining and quantification methodologies, have questioned the reproducibility of the results reported so far. We aimed to investigate by immunohistochemistry and digital image analysis whether endometrial uNK cell subpopulations and their proximity to endometrial arterioles are altered in women with recurrent implantation failure (RIF) following in vitro fertilisation (IVF).

METHODS: Endometrial Pipelle® biopsies were collected 6 to 8 days post-luteinizing hormone (LH) surge from women with RIF (>6 transfers of good quality embryos or >2 transfers of embryos following pre-implantation genetic diagnosis; n=20) or women who had a successful pregnancy after IVF or otherwise (n=19). Endometrial expression of CD56+, CD16+ and the proximity of CD56+ cells to endometrial arterioles (i.e. within 100 μm or 100-200 μm), were investigated by immunohistochemistry and quantified using computer-assisted digital (ImageJ) image analysis.

RESULTS: Neither the density of CD56+ cells, CD16+ cells nor the proximity of CD56+ cells to endometrial arterioles was significantly altered in women with RIF compared to women with successful implantation following IVF or otherwise.

CONCLUSIONS: The lack of a difference in uNK cell density and/or subpopulations in women with RIF questions the validity of uNK cell testing in the clinical work-up prior to assisted reproductive procedures.

S-186

Development of an Endometrial Classifier for the Early Detection of Ectopic Pregnancy. Jessica Lentscher, Logan Peterson, Tim Clem, Richard O Burney, Greg E Chow*. *Madigan Army Medical Center, Tacoma, WA, USA.*

INTRODUCTION: Ectopic pregnancy is the leading cause of morbidity and mortality among women in the first trimester. Life threatening cases of ectopic pregnancy among deployed U.S. servicewomen have been described. A reliable diagnostic test for the early detection of ectopic pregnancy in cases of abnormal pregnancy of unknown location (PUL) is a critical gap. Studies investigating a serum marker for this indication have been unsuccessful. A semi-invasive, office-based diagnostic assay may reduce the interval for ectopic detection in cases of nonviable PUL. Herein, we report results of global gene expression profiling comparing the endometrial transcriptome of women with abnormal intrauterine pregnancy to that of women with ectopic pregnancy toward the development of a genomic classifier of pregnancy location in women with PUL.

METHODS: Endometrial samples were obtained by pipelle biopsy from 9 women with miscarriage scheduled for dilation and curettage and from 8 women with ectopic pregnancy at laparoscopy. Pregnancy location was histologically confirmed in all cases. Each sample was processed to high quality RNA and hybridized to gene arrays, and selected targets were validated by qRT-PCR. Independent component and regression analysis produced a classifier of highly informative genes that was tested in a leave-one-out approach.

RESULTS: Differential gene expression was observed in the endometria from women with miscarriage relative to that of women with ectopic pregnancy (139 up-regulated and 66 down-regulated genes with FC > 1.5). Principal component analysis revealed clustering of specimens by pregnancy location. In model test runs, the 25-gene classifier demonstrated 94% accuracy in the diagnosis of pregnancy location.

CONCLUSIONS: By including only women with histologically confirmed miscarriage and ectopic in the cohorts, this study compares rigorously defined groups for the paralleled gene expression profiling of endometrial samples. Samples evidenced clustering by pregnancy location. The endometrial genomic classifier developed using aggregate gene expression differences demonstrated excellent accuracy in the delineation of pregnancy location. Validation and reduction to minimum necessary informative genes represent next steps in classifier development.

S-187

Analysis of Follicular Growth and Oocyte Maturation in Cultured Murine Ovarian Tissue. Tomohiko Murase†, Akira Iwase, Phuoc Xuan Nguyen†, Umida Ganieva†, Ying Qin†, Natsuki Nakanishi†, Yukiyo Kasahara†, Takashi Nagai†, Ken Shimizu†, Chiharu Ishida†, Nao Kato†, Satoko Osuka, Tomoko Nakamura, Sachiko Takikawa, Maki Goto, Fumitaka Kikkawa. *Nagoya University, Nagoya, Japan.*

INTRODUCTION: Due to the remarkable progress of fertility preservation techniques, in recent years the autologous transplantation of frozen-thawed ovarian tissue has become possible. In the field of basic research, the development of ovarian follicles is being studied by adding various growth factors to human- or animal-derived ovarian tissue or isolated follicles. It has been reported that the early stages of follicular development can be promoted through the fragmentation of ovarian tissue. In this study, we fragmented murine ovarian tissue and evaluated the development of follicles and the maturation of oocytes after cultivation in the presence of various growth factors.

METHODS: This study was conducted with the approval of the Institutional Review Board. First, both ovaries of four-week-old murine females were removed, and each ovary was cut into four pieces. In the presence of each growth factor we cultivated ovarian tissue for 14 days, measured follicular surface area once a day, evaluated oocyte diameters at the time of oocyte release, cultivated the released oocytes for maturation, and evaluated the degree of maturation of these oocytes.

RESULTS: The larger follicular surface area became, the longer oocyte diameter became at oocyte release. Especially, oocyte diameter increased drastically when the follicular surface area was less than 25,000 μm^2. Moreover, oocytes at metaphase II were extruded from large follicles a lot significantly. In the groups to which GDF-9 or bFGF had been added, follicular surface area was significantly larger than in the other groups. However, in the groups to which plural factors for example, GDF-9 and bFGF had been added, no significant changes were observed compared to the control groups.

CONCLUSIONS: This is a new experimental system with which it is possible to get hold of follicle development and oocyte release through successive observation of ovarian tissue cultures, with which the correlation between the degree of follicle development, oocyte diameters at the time of release, and the degree of oocyte maturity is evaluated, and in which released oocytes are transferred into maturation medium to follow up the degree of maturation. This method is useful for evaluating which growth factors play a role in the late stages of follicular development.

S-188

Altered Gene Expression Indicative of Precocious Granulosa Cell Differentiation in the Fragile X Premutation Mouse. Xin Chen,[1] Carola Conca Dioguardi,[2] Monique Haynes,[3] Joshua Johnson*.[4] *[1]Nanfang Hospital, Southern Medical University, Guangzhou, China; [2]Vita-Salute San Raffaele University/IRCCS San Raffaele Hospital, Milan, Italy; [3]Yale School of Medicine, New Haven, CT, USA; [4]University of Colorado-Denver, Aurora, CO, USA.*

INTRODUCTION: Fragile X (FX) alleles result in disease in women and children. Between 1 in 113 and 1 in 250 women carry alleles with 55-199 CGG repeats in the *FMR1* gene 5' UTR (premutation carrier [PMC] alleles). PMC have increased fertility problems, altered ovarian function, and in some cases, early menopause, referred to as FX Primary Ovarian Insufficiency (FXPOI). In a mouse model, we have shown that significant oocyte and granulosa cell (GC) mitochondrial abnormalities arise in the presence of the PM, in a fashion that depends specifically upon repeat-bearing *Fmr1* PM RNA. We hypothesized that genes critical for granulosa cell (GC) differentiation would be altered in PMC mice compared to wild-type (WT) controls.

METHODS: RNAseq analysis was performed to compare the transcriptome between GC of small growing follicles of WT and FXPM mice (24 hours post-treatment with 100 mIU PMSG, n=3 unique samples per genotype). Raw data files were processed, fold differences in gene expression were calculated, and the expression of genes of interest was verified using qRT-PCR on separate samples.

RESULTS: Genes associated with cumulus GC differentiation *Areg, Btc, Ereg, Has2, Ptgs2/Cox2, Ptx3,* and *Tsg6/Tnfaip6* were all found to be upregulated more than 2.5-fold in immature PM GC compared to WT controls. All but *Btc* showed similar levels of upregulation after confirmatory qRT-PCR. Other genes indicative of mural/steroidigenic GC development, including *Btg2* and *Progesterone Receptor* (*Pgr*) were also upregulated approximately 3-fold in PM/+ granulosa cells. Accordingly, we found that the mitotic index of GC in growing follicles of all stages is reduced in FXPM mutants compared to WT controls.

CONCLUSIONS: Because collected GC were from immature follicles and were not from the peri-ovulatory follicles where differentiated mural and cumulus GC would be present, we interpret these findings as indicative of inappropriate, 'precocious' GC differentiation. We hypothesize that inappropriate 'precocious differentiation' contributes to FXPM pathophysiology and FXPOI.

S-189

Mass Spectrometry Analysis of Ovarian Autoimmunity in Spontaneous Primary Ovarian Insufficiency (POI) Patients. Satoko Osuka,[1,2] Akira Iwase,[1,2] Yukiyo Kasahara,[1,2] Tomohiko Murase,[1] Fumitaka Kikkawa.[1] *[1]Nagoya University Graduate School of Medicine, Nagoya, Aichi, Japan; [2]Nagoya University Hospital, Nagoya, Aichi, Japan.*

INTRODUCTION: Primary ovarian insufficiency (POI), commonly called premature ovarian failure (POF), is defined as primary hypogonadism in a woman under the age of 40 years. POI is one of the cause of intractable infertility. There are some known causes of POF, including chromosomal defects and iatrogenic factors. Moreover, not a few reports indicate the relationships between POI and autoimmune

diseases. In the current study, we analyzed the serum of POI patients with thyroid autoimmunity and tried to identify the autoantibodies and antigens for ovarian autoimmunity.
METHODS: We assessed the ovarian autoantibody in the serum of the POI patients. We compared the result of three groups: 1) POI patients with thyroid autoantibodies, 2) POI patients without thyroid autoantibodies, 3) women with normal menstrual cycle. We applied the serum of these patients as antibody for immunohistochemistry (IHC), immunoprecipitation (IP) and Western blot (WB). Normal human ovarian tissues were used for IHC, protein from human nonluteinized granulosa cells (HGrC1) were used for IP and WB. After that, we performed liquid chromatography tandem mass spectrometry (LC/MS/MS) of the IP products to identify the antigens with ovarian autoantibodies. Furthermore, we assessed the expression and localization of the identified protein in HGrC1 and human ovarian tissues.
RESULTS: IHC indicated the existence of ovarian autoantibodies in the serum of POI patients. In addition, the electrophoresis of the IP products and WB showed different band patterns between the patients group and normal group. By LC/MS/MS, several specific proteins were detected from the POI patients with thyroid autoantibodies group. We focused on POTE (prostate, ovary, testis and placenta) protein and confirmed the expression of POTE genes in human granulosa cells by RT-PCR. Moreover, IHC of human ovarian tissues by using anti POTE antibody showed the POTE protein localization in granulosa cells and oocytes.
CONCLUSIONS: The results of immunoassays indicated the presence of autoantibodies to ovaries in serum of POI patients. Furthermore, the results of mass spectrometry identified POTE protein as one of the antigen of the ovarian autoantibodies. The investigation of expression and function of POTE protein may help elucidate the pathogenesis of POI.

S-190

Transcriptomic Analysis of Laser Captured Human Primordial Follicles by RNA Sequencing: Bird's Eye View into Oocyte Aging. Shiny Titus†,[1] Biran Musul,[1] Sumanta Goswami,[12] Kutluk Oktay*.[1] *[1]New York Medical College, Valhalla, NY, USA; [2]Yeshiva University, New York, NY, USA.*
INTRODUCTION: Clinical and laboratory observations indicated that the DNA repair pathways are intimately involved in oocyte aging though numerous pathways may partake in this process. In-depth transcriptomic analysis methods from individual primordial follicles (pdf) can provide valuable information on pathways in oocyte aging. Here we sought to develop a single cell strategy to study transcriptomics in human pdf oocyte and gene expression changes that occur with aging.
METHODS: Ovarian tissues were obtained from organ donor cadavers (n=10). Tissues from those aged < 25 years were arbitrarily classified as "young", and those from age 35-40 years were classified as "old." The tissues were then fixed in OCT blocks and pdf oocytes were captured by laser capture dissection microscopy (LCM). RNA was then processed for RNA sequencing (RNA-seq) using next generation sequencing. The quality was analyzed by a bioanalyzer.
RESULTS: Nine of 10 samples had sufficient cDNA for sequencing. Of the samples subjected to RNA-seq, 7 showed homology (50-75%) to human reference genome. Key genes involved in DNA Double Strand Break (DSB) Repair, specifically BRCA1 (6.1 fragments per kilobase/million fragments mapped –FKPM- in young vs. 3.5 FKPM in old), MRE11 (7.0 in young vs. 3.8 in old), Rad51 (52.7 in young vs. 39.8 in old), showed lower expression with aging, confirming previous studies in GV oocytes. Also in accordance with previous laboratory data in GV oocytes, BRCA2 expression did not decline with age in human pdf oocytes (3.6 in young vs. 3.5 in old). Pdf oocytes expressed AMH receptors, which significantly increased with age (6.24 FKPM in young vs. 63.13 FKPM in old). In addition, we observed significant age-related changes in pathways involved in mitochondrial DNA integrity. This included TFAM, which is a transcription factor that preferentially binds to oxidatively, damaged DNA.
CONCLUSIONS: Using our unique single cell transcriptomics strategy utilizing LCM and RNA-seq, we have identified critical age-related changes in DNA DSB repair and mitochondrial health in human pdf oocytes. The data obtained from single cell transcriptomics approach will lead to discovery of pathways involved in reproductive aging. This approach may help in deciphering pathways that control and regulate early folliculogenesis.

S-191

ILCs Adopt a Tolerogenic Phenotype During Normal Pregnancies. Damián O Muzzio†, Jens Ehrhardt, Krüger Diana, Zygmunt Marek*. *University of Greifswald, Greifswald, Mecklenburg-Vorpommern, Germany.*
INTRODUCTION: The Th1/Th2/Th17 paradigm has been proposed to explain the impact of dysregulations of the immune homeostasis on pregnancy outcome. Recent discovery of innate lymphoid cells (ILCs) mimicking T helper function, cytokine secretion, capability of antigen presentation and expression of CD80 and CD86, forced us to re-evaluate this paradigm. Additionally, ILCs-regulated antibody secretion sheds new light on the regulation of the feto-maternal interface.
We hypothesized that ILCs adapt these mechanism to support pregnancy maintenance.
METHODS: In order to test our hypothesis, we applied a mouse model of Th1-mediated pregnancy loss. CBA/J females were paired either with BALB/c males for a normal pregnancy outcome (NP) or with DBA/2J males to induce disturbed pregnancies (DP). Non-pregnant CBA/J females were used as controls. Peritoneal cavity wash-outs (PerC), uterus, spleen, Peyer's patches (PP) and thymus were isolated and the ILCs compartment was analyzed by flow cytometry. Additionally, peripheral blood from pregnant and non-pregnant women was analyzed to evaluate ILCs in the course of healthy human pregnancy.
RESULTS: There was a significant switch towards a lower ILC1/ILC2 ratio ($P<0.05$) in the case of NP but not in mice with DP in splenic ILCs. Expression of MHCII was significantly reduced in NP mice as compared to DP mice ($P<0.05$). Additionally, mice with DP had higher levels of CD40L ($P<0.01$). Also, we observed lower percentages of $CD80^+$ ILCs and higher percentages of $DLL1^+$ cells in both groups of pregnant mice ($P<0.01$, $P<0.001$). In thymus, we found a decrease in the percentages of NCR^-ILC3s in both groups of pregnant mice ($P<0.01$). However, in the case of DP mice, higher percentages of ILC1s were observed in mice with DP ($P<0.01$). PP and PerC displayed higher percentages of ILC2s ($P<0.05$) in mice with DP compared to non-pregnant mice. NCR^-ILC3s percentage was also increased in mice with DP in PerC ($P<0.05$).
In human peripheral blood, the percentages of NCR^+ILC3s increased during the 1st trimester ($P<0.05$), while NCR-ILC3s in the 3rd trimester of pregnancy displayed a strong reduction ($P<0.01$). Finally, we showed in vitro that hCG promotes ILC2s in a dose dependent manner ($P<0.01$).
CONCLUSIONS: ILCs adopt a tolerogenic phenotype during NP, especially in organs where development and maturation of T and B lymphocytes take place. Thus, alterations in the ILCs functionality may impact on general immune homeostasis and compromise pregnancy wellbeing.

S-192

Umbilical Cord CD71+ Erythroid Cells from Neonates Born to Women Who Undergo Spontaneous Term or Preterm Labor Do Not Exhibit Immunosuppressive Functions but Enhance T-Cell Activation and Suppress CD8+ Regulatory T Cell Proliferation. Derek Miller†,[1,2,3] Roberto Romero,[1] Ronald Unkel,[1,2] Yi Xu,[1,2] Sonia S Hassan,[1,2] Nardhy Gomez-Lopez.[1,2,3] *[1]NICHD, Detroit, MI, USA; [2]Wayne State University, Detroit, MI, USA; [3]Wayne State University, Detroit, MI, USA.*
INTRODUCTION: Neonatal host defense against infection seems to be maintained by the temporal presence of immunosuppressive CD71+ erythroid cells (Nature. 2013;504(7478):158-62). Yet, their immunosuppressive function has not been proven. Immunosuppression is largely mediated by T cells; therefore, we evaluated the T-cell functionality of umbilical cord CD71+ erythroid cells. Also, we investigated whether the T-cell functionality of umbilical cord CD71+ erythroid cells was different between neonates born to women who underwent spontaneous preterm labor (PTL) and those born to women who underwent spontaneous labor (TIL).

METHODS: Umbilical cord blood was obtained from neonates born to women who underwent either PTL (n=8) or TIL (n=10). CD71+ cells were depleted from cord blood mononuclear cell suspensions using magnetic separation. Mock controls were also prepared using the CD71 isotype control. CD71-depleted cells and mock controls ($2X10^5$ cells per well) were stimulated with anti-CD3 and anti-CD28 (TCR stimulation) for 4 days. Unstimulated controls were also included. T-cell activation and regulatory T cell (Treg) proliferation were determined by immunophenotyping.
RESULTS: Depletion of cord blood CD71+ cells: 1) reduced the expression of CD69 (i.e. T-cell activation marker) by CD4+ and CD8+ T cells in PTL and TIL samples upon TCR stimulation; 2) reduced the proportion of CD62L+CD8+ T cells (i.e. effector CD8+ T cells) in unstimulated TIL samples, but did not have any effect on CD4+ and CD8+ T cells in unstimulated PTL samples; 3) increased the number of CD8+ Tregs in PTL and TIL samples with and without TCR stimulation; and 4) did not alter the number of CD4+ Tregs in PTL and TIL samples with and without TCR stimulation. Overall, no striking differences in T-cell functionality were observed between umbilical cord CD71+ erythroid cells from PTL and TIL groups.
CONCLUSIONS: Umbilical cord CD71+ erythroid cells from neonates born to women who undergo spontaneous term or preterm labor do not exhibit immunosuppressive properties; indeed, they enhanced T-cell activation and suppressed the proliferation of CD8+ Tregs.

S-193

Altered CD4 and NK Cell Profile with Inverse IFNγ and IL-10 Antiviral Response in HIV-1$^+$ Pregnancies. Alexander Cocker†,[1] Sarah Dermont,[2] Waheed Khan,[2] Nesrina Imami,[3] Mark Johnson*.[1] *[1]Imperial College London, London, United Kingdom; [2]Chelsea and Westminster Hospital, London, United Kingdom; [3]Imperial College London, London, United Kingdom.*
INTRODUCTION: HIV-1$^+$ mothers experience increased incidence of pre-term delivery and lower neonate birth weight in both resource rich and poor settings. Pre-term labour is linked to maternal inflammation and the activation of fetal lymphocytes; antiretroviral therapy (ART) treated HIV-1 infection is associated with chronic immune activation, potentially caused by persisting HIV-1 reservoir, and other viral co-infections. Parallels between HIV-1 infection and pre-term labour are apparent, therefore this study aims to use HIV-1 infection as a model, and determine differences in maternal lymphocyte composition and antiviral function in HIV-1$^+$ and HIV-1$^-$ pregnancies.
METHODS: Peripheral blood mononuclear cells (PBMC) were isolated and flow cytometric analysis performed to determine the expression of activation, differentiation and exhaustion markers. IFNγ and IL-10 ELISpot assays on PBMC were undertaken to measure responses against Flu and CMV antigens. Responses to Gag and Nef peptides were tested by ELISpot in HIV-1$^+$ individuals only. Statistical analysis was carried out using Prism version 6.0. Intergroup variation was assessed by unpaired two-tailed t tests, intragroup variation by Wilcoxon matched pairs test, and statistical significance defined as $p = <0.05$.
RESULTS: Phenotypic analysis showed increased frequency of exhausted CD4$^+$PD-1$^+$ effector memory T cells in HIV-1$^+$ women ($p = 0.0117$). CD11b and NKp30/NKG2A markers revealed a decrease of anergic NK cell subsets in HIV-1$^+$ mothers ($p = 0.0174$).There was a statistically significant increase in IFNγ response to Flu and CMV ($p = 0.0123$ and $p = 0.0005$ respectively), and a decrease in IL-10 response in the HIV-1$^+$ group. All HIV-1$^+$ women were IFNγ responders to Gag, and 7/8 (87.5%) were Nef responders.
CONCLUSIONS: Pregnancy may modify T-cell differentiation towards effector memory subset while maintaining fetal tolerance. Despite ART HIV-1 persists, as shown by Gag and Nef responses, and skews T cells to an exhausted profile. Differences in cell populations reflect prolonged activation and disrupted tolerance, confirmed by altered NK cell phenotype. Together these findings show the impact of viral persistence on innate and acquired immunity, and identify cell populations that may be integral in the cause of pre-term labour.

S-194

Hydroxychloroquine as Empiric Treatment for Recurrent Pregnancy Loss. Elizabeth Constance†, Angela Kelly, Neil Kamdar, Emily Kobernik, Kristian Seiler, John Randolph, Cosmas Van De Ven, Molly Moravek*. *University of Michigan, Ann Arbor, MI, USA.*
INTRODUCTION: Recurrent pregnancy loss (RPL) affects 5% of all couples, with no causative factor identified in up to 75% of patients. Hydroxychloroquine (HCQ), an anti-inflammatory medication typically prescribed for autoimmune disease, is being used as empiric therapy for unexplained RPL, but there is a paucity of data on outcomes. Our objective in this descriptive study is to examine outcomes in women using HCQ for unexplained RPL.
METHODS: Retrospective chart review of all women treated with HCQ for RPL at a single academic medical center from 2006-2016. Primary outcomes of interest were miscarriage and live birth rates. Data was analyzed using Fisher's exact test and Wilcoxon Rank Sum test as appropriate.
RESULTS: 30 women met study criteria for a total of 35 pregnancies. Overall miscarriage rate was 40% (14/35), and live birth 56% (19/34), with one ongoing pregnancy at 35 weeks gestational age. Miscarriage rate stratified by reproductive history is displayed in the table.

Pregnancy Outcomes by Reproductive History		
Previous Live Birth	**Number Previous Miscrriages**	**% Miscarriage on HCQ Treatment**
≥1 Previous Live Birth	2-3	30% (3/10)
	4-5	25% (1/4)
	6+	75% (3/4)
No Previous Live Birth	2+	44% (7/16)

Live birth was achieved in 12/27 (44%) of Caucasians and 7/8 (87%) of non-Caucasians ($p=0.05$). No statistically significant differences were found in demographic factors, BMI, substance use, autoimmune disease, reproductive history, or treatment to conceive between those who achieved live birth and those who did not. One third-trimester loss of an infant with multiple anomalies and one second-trimester uterine rupture with intrauterine fetal demise occurred. No adverse side effects from HCQ were reported.
CONCLUSIONS: Miscarriage rates on HCQ stratified by reproductive history (table) were consistent with established RPL data in untreated women. However, a trend toward increased effectiveness of treatment was noted in non-Caucasian women and a trend toward decreased effectiveness in the Caucasian population. Although sample size is low, this finding may indicate a benefit to individually tailored therapy. This warrants further investigation with large controlled studies in diverse populations to further characterize treatment effects.

S-195

Metformin Improves Endometrial Responsivity to Progesterone in Women with PCOS. Tugba Ensari,[1] Harvey J Kliman,[2] Lubna Pal.[2] *[1]Etlik Zubeyde Hanim Women's Health Education and Reseach Hospital, Ankara, Turkey; [2]Yale University School of Medicine, New Haven, CT, USA.*
INTRODUCTION: Polycystic ovary syndrome(PCOS) is one of the most common endocrine disorders, affecting 7% of the reproductive age women. Use of insulin sensitizing agents, such as metformin (M), is common in the management. While ovulatory dysfunction is a well-recognized contributor to infertility in women with PCOS, an unfavorable endometrial milieu and impaired receptivity are being increasingly appreciated. We hypothesized that M may have direct effects on endometrium.
METHODS: Women (n=15) meeting NIH criteria for PCOS who were users (n=7) and nonusers (n=8) of M were offered participation. Endometrial biopsies (EMBx) were performed following 7-10 days exposure to vaginal progestin(P). Endometrial dating was undertaken on H&E stained tissue based on Hendrickson and Kempson's Decision Tree for Endometrial Dating, and by IHC expression of cyclin E and p27 endometrial receptivity markers). A subset of patients (n=5) underwent EMBx before and after 3-month use of M in escalating dose to a target

of 2000mg daily, a single nonuser served as a prospective control. Cyclin E and p27 expression by IHC was related to histological findings and conventional dating and compared between M unexposed and exposed endometria. Persistence, and magnitude of nuclear glandular, stromal expression of cyclin E following P exposure was deemed to reflect glandular-stromal dyssynchrony(GSD), a morphological surrogate for impaired endometrial receptivity. Luteal nuclear cyclinE % reflected severity of the Glandular Developmental Arrest(GDA) with 20% expression taken as normal, between 20-50 as inappropriate and >50% as 'severe GDA'.

RESULTS: Evidence of GDA was noted in 11/15 endometrial samples including 7/10 deemed as normal by conventional dating by H&E. 8/11 (73%) of GDA endometria were from M non-users. All 4 samples that did not demonstrate GDA were from M users. M use was associated with a significantly lower likelihood of endometrial GDA ($p<0.05$).

CONCLUSIONS: Based on cyclin E, as a marker of GDA in P exposed endometrium, M use was found to improve endometrial responsivity to P. Our findings also suggest that histologically 'normal appearance' according to histologic assessment does not necessarily reflect normal endometrial development in women with PCOS. These data yield mechanistic information whereby metformin may improve endometrial receptivity in women with PCOS.

S-196

Does Preimplantation Genetic Screening (PGS) Improve Blastocyst Implantation Rates (IR)? Jessica Rubin†*,[1,2] Khalied Kaskar,[2] Terri Woodard,[1,2,3] William Gibbons.[1,2] *[1]Texas Children's Pavilion for Women, Houston, TX, USA; [2]Baylor College of Medicine, Houston, TX, USA; [3]MD Anderson, Houston, TX, USA.*

INTRODUCTION: Blastocyst IR is influenced by numerous factors. This study aims to determine if there are differences in blastocyst IR between fresh & frozen embryo transfers (ET) with & without PGS. A retrospective compilation of women undergoing autologous IVF cycles was compiled between June 2014 & April 2016. Patients were subdivided into age <35 & ≥ 35.

METHODS: Transfers were performed as blastocysts on 'day 5.' Indications for frozen ET without PGS included patient preference, elevated progesterone, or ovarian hyperstimulation syndrome & standard morphologic criteria prioritized selection order. In embryos with PGS, trophectoderm cells were biopsied at the blastocyst stage. Blastocysts were vitrified & biopsies sent for Next Generation Sequencing. Fresh ET data was included for comparison.

RESULTS: In the <35 frozen ET group, clinical pregnancy rate (CPR) & IR showed no difference with & without PGS. When all non-PGS (fresh+ frozen) cycles were included, there was no difference compared to the PGS group in CPR nor IR. In FET cycles in women ≥35, IR showed no change with & without PGS. However, the IR with PGS was higher than in fresh cycles because of embryo selection in women ≥35. This pattern did not change when all non-PGS (fresh+ frozen) cycles were included, and compared to PGS there was no change in CPR but there was an improved IR with PGS.

Table 1:Clinical pregnancy & implantation rate of day 5 fresh & frozen ET with & without PGS.

	Fresh ET		Frozen ET without PGS		Frozen ET with PGS	
Age	<35	≥35	<35	≥35	<35	≥35
# of Patient Cycles	35	10	16	15	31	7
Clinical Pregnancy Rate	24 (68.6%)	3 (30.0%)	7 (43.8%)	9 (60.0%)	15 (48.4%)	5 (71.4%)
Embryos Transferred (mean)	42 (1.2)	17 (1.7)	18 (1.1)	25 (1.7)	39 (1.3)	7 (1.0)
Cardiac Activity	26	3	7	10	18	5
Implantation Rate	61.9%	17.6%[a]	38.9%	40.0%	46.2%	71.4%[a]

[a]p=0.3.

CONCLUSIONS: Our data did not demonstrate improved CPR or IR in women <35 using frozen ET with & without PGS. Fresh ET pregnancy rates in women <35 were surprisingly high in light of our clinic's trend towards fewer fresh ET & may reflect small sample size. For women ≥35, PGS offers an advantage in embryo selection for ET.

S-197

Are Embryos That Reach Blastocyst on Day 5 or Day 6 More Likely to Be Euploid? Jessica Rubin†*,[1,2] Khalied Kaskar,[1] Paul Zarutskie,[1,2] William Gibbons.[1,2] *[1]Texas Children's Hospital Texas Children's Pavilion for Women, Houston, TX, USA; [2]Baylor College of Medicine, Houston, TX, USA.*

INTRODUCTION: The rate of embryo development is variable and limited data exists to correlate embryo developmental rate with ploidy. This study aims to determine if there are differences in euploid rates between embryos reaching blastocyst development on day 5 compared to day 6. A retrospective compilation of Next Generation Sequencing (NGS) blastocyst biopsy results for patients undergoing preimplantation genetic screening (PGS) was compiled between June 2014 and April 2016. Patients were subdivided into two groups, women age <35 and ≥ 35.

METHODS: All IVF candidates using autologous oocytes and electing for PGS were selected for inclusion. Donor oocytes were excluded. Trophectoderm cells were biopsied using laser on day of blastulation, either day 5 or day 6. Blastocysts were then cryopreserved using vitrification. Biopsy samples were sent for NGS.

RESULTS: Among all ages, 427 embryos were biopsied and 53.0% were euploid. Women <35 had 62.7% euploid on day 5 and 48.6% euploid on day 6 (p=.03). Women ≥35 had 47.4% euploid on day 5 and 40.0% euploid on day 6 (NS). For all ages, a significant difference was detected in euploid rate between day 5 and day 6 embryos (p=.02). A significant difference was detected for day 5 euploid embryos between women <35 and ≥35 years old (p=.05). A higher percentage of euploid embryos reached blastocyst on day 5 in women <35 compared to women ≥35 (36.9% vs 25.2%, p=.03).

PGS Results for Day 5 and Day 6 Embryos Following ART

	<35 years old		≥35 years old		All ages	
	Day 5	Day 6	Day 5	Day 6	Day 5	Day 6
Euploid (%)	94/150 (62.7%)[ab]	51/105 (48.6%)[a]	27/57 (47.4%)[b]	20/50 (40.0%)	121/207 (58.5%)[c]	71/155 (45.8%)[c]
Total euploid (%)	145/255 (56.9%)[d]		47/107 (43.9%)[d]		192/362 (53.0%)	

[a] p=0.3; [b] p=0.5; [c] p=0.2; [d] p=0.2.

CONCLUSIONS: As expected, the euploid rate of day 5 embryos was higher in women <35 compared to women ≥35. This data also supports that for women <35, a day 5 embryo is more likely to be euploid than a day 6 embryo suggesting that developmental delay is associated with higher aneuploidy rates. Application of this knowledge can help identify the ideal order to select embryos for transfer.

S-198

The Bottom Line of Fresh versus Frozen ART Cycles in PCOS Patients: Cost Analysis of an RCT. Jessica R Zolton†, Mae W Healy†, Alan H DeCherney, Micah J Hill*. *Eunice Kennedy Shriver National Institute of Child Health and Human Development, Bethesda, MD, USA.*

INTRODUCTION: "Freeze all" strategy has been associated with higher pregnancy rates, improved perinatal outcomes, and decreased ovarian hyperstimulation syndrome. Freeze all policies may provide PCOS patients the greatest opportunity to avoid potentially serious complications and maximize reproductive outcomes. A 2016 randomized control study found that in PCOS patients, the live birth rate following frozen transfer was 49% while the live birth rate was 42% following fresh transfer. However, the higher costs of a freeze all approach may limit its use. The goal of this study was to determine if fresh versus frozen embryo transfer in young women with PCOS is cost-effective based on cost per live birth modeling.

METHODS: A PubMed search was conducted to determine the average cost in the United States of in vitro fertilization with fresh embryo transfer and in vitro fertilization with a frozen embryo transfer (FET). Based on literature published from 2015-2016, the published cost of a fresh cycle with freezing of supernumerary embryos was $17,137 and the cost of IVF plus freeze all and subsequent FET was $19,234. In acknowledging the variation in prices, a second analysis was conducted utilizing a higher published cost model where a fresh cycle with freezing of supernumerary embryos was $19,850 and IVF with FET at $23,256. The cost per live birth was determined based on the RCT trial in PCOS patients undergoing fresh and frozen cycles. Sensitivity analyses were performed over a range of costs for fresh and FET cycle and range of live birth rates to determine the cost effectiveness of freeze all.

RESULTS: A freeze all cycle was cost effective in comparison to a fresh cycle when the total cost of freeze all cycle did not exceed $20,000. In the second model, a freeze all cycle with FET transfer was cost effective if the total cost did not exceed $23,500. The freeze all approach was only cost effective if it added less than 17% to the total price of an ART cycle. At published cost models, the live birth rate for freeze all cycle must exceed fresh ART cycles by 6-8% to be cost effective.

CONCLUSIONS: A freeze all approach may be cost effective for young PCOS patients in ART cycles, but only if freeze all adds less than 17% additional costs to the ART cycles and improves live birth by at least 6-8%.

S-199

Low BMI Is Associated with Poorer Infertility Treatment Outcomes: Analysis of 249,436 Treatment Cycles from 13 US Fertility Clinics. Anthony Santistevan, Karen Hunter Cohn, Keri H Kalmbach, Elizabeth Amador, Polaris Data Network, Erin F Wolff, Piraye Yurttas Beim*. *Celmatix, New York, NY, USA.*

INTRODUCTION: Few studies have examined the impact of low BMI on reproductive outcomes. Here, we study the the effect of BMI on fertility treatment outcomes in a multi-center retrospective analysis (13 clinics).

METHODS: We analyzed 249,436 treatment cycles from 113,809 patients undergoing timed intercourse (TI) with oral fertility medications (OM), intrauterine insemination (IUI) (with/without OM and/or gonadotropin stimulation (Gnd)), and IVF (excl. canceled cycles) between 2009-2015. Cox prop. hazards models with time-dependent covariates were utilized to model number of treatment cycles to ongoing pregnancy. Regression was utilized to compare antral follicle count (AFC) and anti-mullerian hormone (AMH) across BMIs. Models were adjusted for age, AFC, medication type, sperm motility, clinic, and diagnoses.

RESULTS: Women <18.5 BMI had reduced AFC (P=0.02) but similar AMH levels to women with normal BMI (P=0.12). BMI was correlated with the probability of achieving ongoing pregnancy in a protocol-dependent fashion (Fig1, P<0.001). Inflection points in success probabilities did not correspond with normal BMI boundaries. Also, underweight women undergoing IVF were at significantly increased odds of having cancelations or no embryos for transfer compared to women with normal BMI (OR=1.14, P=0.038, adjusting for age, bAFC).

Table 1. Modeled chances of achieving ongoing pregnancy in cycle 1 across BMI and cycle treatment type.

NIH Category	BMI	TI + Orals (n=30,067)	IUI/IUI + Orals (n=93,974)	IUI + Gnd (n=61,600)	IVF (n=63,795)
Under-weight	**< 18.5**	8.6%	6.9%	11.5%	50.4%
Normal	**18.5 - 24.9**	8.6%	8.6%	12.7%	50.8%
Over-weight	**25.0 - 29.9**	8.3%	10.0%	13.6%	50.0%
Obese I	**30 - 34.9**	7.8%	10.4%	14.1%	48.3%
Obese II	**35 - 39.9**	7.1%	10.0%	14.2%	45.5%
Obese III	**>= 40**	5.8%	7.8%	13.5%	39.3%

**Figure(s) will be available online.*

CONCLUSIONS: We show that traditional definitions of normal BMI do not translate to optimal BMI for reproductive outcomes and success with fertility treatments. These insights pave the way for greater personalization in patient management.

S-200

Risk Factors Associated with Complete Failure to Fertilize in IVF with Conventional Insemination. Andrew R Fisher†,[1] Maureen M Schulte†,[2] Stephanie Tsai,[2] Joan K Riley,[2] Emily Jungheim*.[2] *[1]Barnes Jewish Hospital, Saint Louis, MS, USA; [2]Washington University School of Medicine, Saint Louis, MS, USA.*

INTRODUCTION: Because abnormalities in fertilization are not uncommon, our center employs split conventional insemination-ICSI for couples with unexplained infertility, undergoing their first ART cycle. The objective of this study was to determine factors associated with complete failure to fertilize (CFF) with conventional insemination for cases with split conventional insemination-ICSI to better determine which couples with unexplained infertility may benefit from full ICSI.

METHODS: A retrospective cohort of 191 couples with unexplained infertility undergoing their first ART cycle between 2014 and 2015 using split conventional insemination-ICSI were identified. 25 of these couples had CFF with conventional insemination but normal fertilization with ICSI. Semen parameters were assessed after "swim-up" was performed to prepare the sperm for insemination. Standard bivariate statistics were used to identify factors associated with CFF. Significant factors were placed in a regression model to determine which were independently associated with CFF. Significant variables from the regression model were subjected to receiver operating characteristic (ROC) curves for CFF to determine what cutoff values were diagnostic for CFF.

RESULTS: Semen parameters including lower sperm concentration, count, and motility were all associated with increased risk of CFF with bivariate statistics. Younger female and male partner age were also associated with increased risk of CFF. After regression analysis, only lower sperm motility and younger female partner age remained significant. ROC curves demonstrated that female partner age younger than 31 years and sperm motility less than 60% were the most sensitive and specific values for predicting CFF. Categorizing patients around these values in our regression model, the OR associated with CFF in cases in which the female partner was younger than 31 was 3.4 (95% CI 1.4-8.3) and it was 3.3 (95% CI 1.3-8.7) in cases where the sperm motility was less than 60%. Couples with both of these factors had a RR of 4.4 (95% CI 2.2-8.8) for CFF.

CONCLUSIONS: Female partner age less than 31 and sperm motility less than 60% are associated with CFF in couples with unexplained infertility. It may be beneficial to use ICSI to inseminate all oocytes in such cases.

S-201

Elevated Progesterone Impacts Embryo Development During IVF. Amanda Kohlmeier, John Zhang, Jared Robins*. *Northwestern University, Chicago, IL, USA.*

INTRODUCTION: Elevated progesterone (P4) levels during IVF leads to poor endometrial receptivity. Controversy exists as to whether it may also impact embryo development. Because of the lowered implantation rate, IVF cycles with elevated P4 levels often do not have fresh embryo transfers; the embryos are frozen with a subsequent frozen embryo transfer. If embryonic development is impacted, cryopreservation may not be the best strategy. This research utilized morphometric parameters to determine if elevated P4 has an impact on embryonic development during IVF.

METHODS: Retrospective cohort study of patients undergoing IVF with low P4 (LP) (< 1.0ng/mL) and high P4 (HP) (≥1.8ng/mL) on the day of hcg. Inclusion criteria included cycles performed at a university-based IVF center between 1/1/2016 and 9/1/2016. All embryos were cultured in a time-lapse incubator from fertilization to embryo transfer/freeze. Data included age, protocol type, amount of FSH used, # oocytes/mature oocytes retrieved, fertilization rate, # reaching blastocyst stage, and morphometric parameters including time to PN appearance/fade, time to 2-5 cell development. Statics included student's t-test and chi-square.

RESULTS: There were 105 patients in the LP group and 17 patients in the HP group. There were no differences in regard to age, type of stimulation, or total units of gonadotropin. HP patients had a greater level of estrogen on day of hCG trigger (1664 pg/mL vs 2483pg/mL, p=0.005) and a greater number of eggs retrieved (7.7 v 11.7, p=0.01). Although no difference was noted in time to PN appearance, the time from fertilization to 5-cell embryo was 43.6h in the LP group vs 36.7h in the HP group, p=0.04 (see fig). Blastulation rates (defined as # blasts/#fertilized embryos) were significantly higher for the HP group (43.4% for LP vs 65.3%for HP, $p < 0.001$).

CONCLUSIONS: Patients with high P4 had higher levels of estrogen and more eggs retrieved. Embryos from the HP group exhibited quicker development from fertilization through cleavage and were more likely to become blastocysts. Although aggressive stimulation protocols may impact the endometrium and lower rates of implantation during fresh IVF, our data suggest that there is no adverse impact on embryonic development. In fact, cycles with elevated P4 exhibited enhanced embryo development. Therefore, aggressive stimulation with FET may be an optimal IVF protocol. Further, these data may explain the improved pregnancy rate some authors report with frozen embryos transfer.

S-202

Serum hCG Levels and Prediction of Live Birth in IVF Pregnancies. Lia A Bernardi, Angela K Lawson, John X Zhang, Randall B Barnes*. *Northwestern University Feinberg School of Medicine, Chicago, IL, USA.*

INTRODUCTION: First trimester ultrasound (US) findings are commonly used to counsel individuals on expected pregnancy outcomes after IVF. Serum hCG levels, which are performed earlier in gestation, also provide valuable predictive information regarding likelihood of live birth (LB). Therefore, the objectives of this study are to evaluate whether specific hCG rises in early IVF pregnancies are associated with LB and to determine whether these hCG parameters are as predictive of LB as the presence of fetal cardiac activity (FCA) on early US.

METHODS: This retrospective cohort study utilized data collected from 2002-2013 in an academic REI practice. Cycles where women underwent IVF with subsequent autologous fresh or frozen embryo transfer (ET), had a serum hCG >5 mIU/mL 8 or 10 days after ET, and had an US performed between 5 0/7 and 6 6/7 weeks that did not demonstrate a viable multiple gestation were analyzed. Multiple logistic regression was used to investigate the relationship between LB and these hCG variables: doubling from the first to second hCG in early pregnancy ("doubled"), reaching an hCG of 100 mIU/mL by 10 days after blastocyst or 12 days after cleavage stage ET ("reached 100") or the combination of doubling and reaching an hCG of 100 mIU/mL ("doubled and reached 100"). The model adjusted for age, year of ET, fresh or frozen ET, and the number of embryos transferred. Positive predictive values (PPV) of the hCG variables and the PPV of presence of FCA on early US on LB were examined.

RESULTS: 484 cycles (96.3% fresh, 3.7% frozen) were included. The mean age of the women was 35.6 ±3.9 years. The mean number of embryos transferred was 2.4 ±0.8 (8.9% blastocyst and 91.1% cleavage stage) and the LB rate was 70.9%. Both "doubled" (OR 3.6, 95% CI 2.2-5.8) and "doubled and reached 100" (OR 5.1, 95% CI 3.3-7.8) were significantly associated with odds of LB. However, the odds of LB were highest when hCG "reached 100" (OR 5.5, 95% CI 3.5-8.6). The PPV of LB was 76.5% for "doubled", 80.4% for "reached 100", and 82.8% for "doubled and reached 100". The PPV of presence of FCA on LB was 74.1%.

CONCLUSIONS: There was an association between hCG levels in early pregnancy and LB, with the odds of LB highest when hCG reached 100 mIU/mL by 10 to 12 days after ET. Given that the PPV of each hCG variable was higher than the PPV of FCA on early US, serum hCG levels in IVF pregnancies may allow for earlier and more accurate prediction of LB than US before 7 weeks.

S-203

Melatonin in Assisted Reproductive Technology (MIART) – Oral Melatonin Treatment During Ovarian Stimulation Does Not Affect Sleep – A Double-Blind Randomized Placebo Controlled Trial. Shavi Fernando†,[1,2] Euan Wallace,[1,2] Sarah Biggs,[1,3] Rosemary Horne,[1,3] Luk Rombauts*.[1,2,4] *[1]Hudson Institute of Medical Research, Melbourne, VIC, Australia; [2]Monash University, Clayton, VIC, Australia; [3]Monash University, Clayton, VIC, Australia; [4]Monash Surgical Private Hospital, Clayton, VIC, Australia.*

INTRODUCTION: Melatonin is increasingly used as an adjuvant to assisted reproductive technology (ART) because of its perceived benefits as an oxygen scavenger. It is largely considered to be sedative, with nocte dosing being standard. In this study, we aimed to determine whether high doses of melatonin, given twice daily (morning and evening) would affect subjective and objective measures of sleep quality and daytime sleepiness.

METHODS: One hundred and sixteen women having their first cycle of IVF were randomized into one of four groups (placebo, 2mg, 4mg and 8mg of melatonin). Trial medication was taken orally twice per day from Day 2 of their cycle until the night before their oocyte retrieval. During this time, each participant wore a Phillips Actiwatch2® (Philips Respironics, Pittsburg, USA) kept sleep diaries and completed the Karolinska sleepiness scale detailing their nighttime sleep activity and daytime sleepiness. This study was double-blinded.

RESULTS: Of the 116 participants who had actigraphy, 89 had complete data and were available for analysis (placebo (n=25), 2mg (n=22), 4mg (n=17), 8mg (n=25)). There was no significant difference in daytime Karolinska sleepiness score, wake after sleep onset time, sleep onset latency or sleep efficiency both between groups and before and after treatment. There was also no evidence of phase shift despite medication being given in the morning. There was a significant improvement in subjective sleep quality scores for all groups (including placebo).

CONCLUSIONS: This is the first randomized controlled trial to show that oral melatonin, at doses as high as 8mg twice per day given during ovarian stimulation, does not induce changes in nighttime sleep quality or quantity or daytime sleepiness in women undergoing ART.

S-204

Role of mTOR (Mammalian Target of Rapamycin) Signal Mechanism in the Treatment of Polycystic Ovary Syndrome (PCOS). Aylin Yaba Uçar*,[1] Mehmet Serif Aydin†,[2] Sami Agus†,[3] Elif Günalan†,[3] Ecem Yildirim†,[3] Bayram Yilmaz†.[3] *[1]Yeditepe University School of Medicine, Istanbul, Turkey; [2]Bezmialem University School of Medicine, Istanbul, Turkey; [3]Yeditepe University School of Medicine, Istanbul, Turkey.*

INTRODUCTION: Polycystic ovary syndrome (PCOS) is a common and complex endocrine disorder and is well associated with an increased prevalence of anovulatory infertility.The mammalian target of rapamycin (mTOR) gene product is a serine/threonine kinase that has been implicated in the control of a variety of cell behaviors as cell growth and proliferation, protein synthesis, ribosome biogenesis and autophagy. We showed before, phosphorylation of serine residue 2448 in mTOR has been shown to correlate with the activation status of mTOR and proliferation of granulosa cells, and mTOR signal pathway has functional role in granulosa cells

during successful folliculogenesis. We presented in our another study that mTOR has effective role in ovary with PCOS. In this study we suggested that mTOR signal pathway may have important role in treatment of PCOS. Therefore our aim is to suppress proliferation of granulosa cells and control hormon level so regulate folliculogenesis in PCOS ovary.

METHODS: PCOS was induced in 25 day old BalbC female mice by dehidroepiandrostenedion (DHEA) administration for 20 day, as evidenced by ovarian morphology, estrogen and progesteron hormon levels by ELISA. Immunohistological analysis revealed expression of mTOR and P-mTOR. TUNEL and follicle counting used to show difference between experimental groups. We showed mTOR signal pathway proteins using western blott and qRT-PCR. All of the data are eveluated by statistically.

RESULTS: Our findings provide the first evidence for the presence of mTOR signal in PCOS and Rapamycin treated mouse ovary. We detected ovulation and corpus luteum in PCOS mouse ovary after Rapamycin treatment. We showed that mTOR has very important and functional role during folliculogenesis and mouse reproductive hormonal control ($p<0.05$). Therefore mTOR signal pathway may be use as a potential therapeutic strategy for the treatment of PCOS.

CONCLUSIONS: We suggested that our project to light the way for dominant follicle selection and anovulatory female infertility beside treatment of PCOS.

Support: TÜBITAK#214S328.

S-205

The Effect of Semen Parameters on Intrauterine Insemination (IUI) Success. Emily C Holden†,[1,2] Ashley Papapetrou†,[3] Sara S Morelli,[1,2] Peter McGovern*.[1,2,3] *[1]University Reproductive Associates, Hasbrouck Heights, NJ, USA; [2]Rutgers-NJMS, Newark, NJ, USA; [3]St. Joseph's Regional Medical Center, Paterson, NJ, USA.*

INTRODUCTION: Intrauterine insemination (IUI) is often a first line treatment for couples with infertility. Total number of motile cells (TNMC) refers to the number of total motile sperm in a semen sample. TNMC is often calculated twice; from the initial semen sample and after processing. Although the predictive value of TNMC on IUI outcomes is controversial, many studies demonstrate better outcomes with post-wash TNMC greater than 10 million. Sperm morphology, using Kruger strict criteria, may also affect IUI outcomes. We calculated normal morphology TNMC (K-TNMC) by multiplying the Kruger morphology percentage by the initial TNMC (Kruger % x volume x concentration x motility %). We hypothesize that parameters in the initial semen analyses and/or in the processed IUI specimens predict clinical pregnancy after IUI treatment.

METHODS: A retrospective review of medical records was performed. Data were collected from 478 IUI cycles in 228 women, between January 1, 2009 through February 1, 2012. Female age ranged from 25-48. Clinical pregnancy was defined as an intrauterine pregnancy seen on ultrasonography. Overall clinical pregnancy rate (CPR) was 11.7%. Simple logistic regression and multiple logistic regression analyses were used to test for associations between CPR and female age, basal FSH, antral follicle count (AFC), cycle type, motility, Kruger normal morphology, TNMC, K-TNMC, days of IUI abstinence and post-processing TNMC.

RESULTS: Simple logistic regression analysis revealed that higher initial Kruger morphology score and K-TNMC were associated with increased CPR ($P=0.048$ and $p=0.01$, respectively). Higher AFC was also associated with higher CPRs ($P<0.01$). Multiple logistic regression showed that only K-TNMC ($P=0.001$) and AFC ($P=0.002$) remained significant predictors of success. No other parameters measured were significantly associated with CPR.

CONCLUSIONS: Contrary to previous literature, the TNMC of the processed IUI sample did not predicted IUI success. The initial semen analysis samples' morphologically normal total number of motile cells (K-TNMC) was a significantly useful predictor of IUI success. As this parameter-unlike the day of IUI processed sample TNMC- is available prior to initiating IUI treatments, it allows better treatment selection and patient counseling.

S-206

Melatonin and Women Quality of Life at a Climacteric Syndrome. Elena Usoltseva*. *South-Ural Medical University, Chelyabinsk, Russian Federation.*

INTRODUCTION: Epifiz plays a role of the regulator of reproductive function of women, in particular, defines time of menopause approach. Research purpose was to estimate women's quality of life with a climacteric syndrome in perimenopause at treatment by melatonin.

METHODS: The efficiency of treatment by melatonin 3 mg daily was estimated by Kupperman Index, and quality of life was estimated by SF-36 and WHQ questionnaires before treatment, in 1 and in 3 months of observation. Considered statistically significant distinctions at $p<0,05$, when comparing with indicators before treatment.

RESULTS: We have examined 70 women at the age of 53,6±5,5 years. Kupperman's index has decreased in 3 months of treatment: 25,8±9,7 vs 12,9±5,8 points, $p<0,001$. According to the SF-36 data physical and role physical functioning statistically significantly raised (fig. 1) , and according to WHQ results was revealed decrease of somatic symptoms, sleep problems, depressed mood and anxiety/fears (fig. 2).

**Figure(s) will be available online.*

Figure 1. Dynamics of patients quality of life according to the SF-36 general questionnaire at treatment by melatonin.

Note: FF – physical functioning, RFF – role physical functioning, B – pain, GH – general health, V – viability, SF – social functioning, REF – role emotional functioning, PsH – psychological health, PhC - physical component of health, PsC - psychological component of health (in points); * - $p<0,05$.

**Figure(s) will be available online.*

Figure 2. Dynamics of women's quality of life according to a WHQ special questionnaire at treatment by melatonin.

Note: DEP – depressed mood, SOM – somatic symptoms, MEM – memory/concentration, VAS – vasomotor symptoms, ANX – anxiety/fears, SEX – sexual behaviour, SLE – sleep problems, ATT – attractiveness (in points), * - $p<0,05$.

CONCLUSIONS: The pineal hormone melatonin is effective for climacteric syndrome treatment and improves some indicators of patients' quality of life.

S-207

CoQ10 Increases ATP and Oct4 While AMPK Activity and Oocyte Death Decrease During IVM. Mohammed Abdulhasan†, Quanwen Li, Jing Dai, Elizabeth E Puscheck, Daniel A Rappolee*. *Wayne State University, Detroit, MI, USA.*

INTRODUCTION: Improving *in vitro* maturation (IVM) is important to enable more efficient beef and milk production and elective oocyte freezing by young women who seek to preserve high oocyte quality. Hypothetically, the stress of multiple *in vitro* fertilization (IVF) techniques such as IVM is obviated by increasing adenosine triphosphate (ATP) available to mount a stress response and continue normal oocyte development in vitro without over-activating AMP-activated protein kinase (AMPK) which is associated with potency factor loss and anabolism and/or growth decrease in oocytes, 2-cell embryos, blastocysts and embryonic and trophoblast stem cells.

METHODS: Bovine oocytes were aspirated from slaughterhouse derived ovaries and cultured in optimized IVM media for 24hr with 0, 20, 40, or 60uM CoQ10 under oil. Oocytes were assayed for ATP by firefly luciferase based luminescence measurement using plate reader. Micrographs of oocytes were quantitated using Simple PCI DNN module for Oct4, pAMPK (AMPK activity), polarization by JC1 staining, and mitochondrial mass by mitotracker green staining.

RESULTS: Testing CoQ10 doses at 0, 20, 40, and 60um CoQ10, it was found that 40uM enables 1.9-fold more ATP after 24hr of oocyte in vitro maturation (IVM) than 0uM CoQ10. This was correlated with 4.3-fold less oocyte death at 40uM CoQ10 and 1.7-fold more mitochondrial charge polarization, and 3.1-fold more mitochondrial mass than at 0uM CoQ10. Hypothetically, stress depletes ATP and activates AMPK and it was found that increased ATP at 40uM CoQ10, is associated with 2.2-fold lower AMPK activation (i.e. AMPK thr172P), and 2.1-fold higher levels

of nuclear Oct4 stemness/potency protein than 0uM CoQ10. CoQ10 is hydrophobic and at all doses tested 50% was lost from media by ~12hr during 24hr IVM. But, replenishing CoQ10 at 12hr did not significantly diminish fraction of dead oocytes.
CONCLUSIONS: This suggests that CoQ10 may partition into oocytes as well as the oil overlay, or that maximal benefit occurs in the first 12hr. Altogether the data suggest that CoQ10 improves mitochondrial function in IVM and should improve many IVF/ART protocols where unwanted stress, higher AMPK activity and Oct4 potency loss are induced.

S-208

Testing of a New Tyramine-Substituted Hyaluronan Gel for the Culture of Embryonic Stem Cells. Nina Desai*, Arsela Gishto, Pavinder Gill. *Cleveland Clinic, Beachwood, OH, USA.*
INTRODUCTION: Embryonic stem cells have tremendous potential for regenerative medicine as well as tissue engineering. Early studies were performed using mouse embryonic fibroblast feeder (MEF) layers or Matrigel, an extracellular matrix (ECM) complex isolated from mouse tumor cells. More recently, there has been a movement away from use of feeder layers and animal derived ECM with the ultimate goal of xeno-free culture of stem cells. This study investigates the use of a tyramine substituted hyaluronan gel (HA) for the culture of embryonic stem cells.
METHODS: Mouse embryonic stem cell (mESC) line C56BL6/129SvJ was thawed and cultured on MEF feeder layers. The culture medium was ESC-Sure DMEM with 20% ESC-Sure FBS, 10 ng/ml LIF, 2.0 mM L-glutamine, 0.1 mM non-essential amino acids, 1.0 mM sodium pyruvate and 0.1 mM β-mercaptoethanol. After 1-2 passages on MEF feeder cells, the mESCs were seeded on HA gel coated wells. HA gel at concentrations of 1.0 and 1.5 mg/ml, either alone or with laminin (10 ug/ml) was used to coat wells. Wells were seeded with 5-10,000 cells. ESC cultures were stained for embryonic stem cell markers. Embryoid bodies were formed to confirm pluripotency and presence of all three germ layers.
RESULTS: Mouse ESC were cultured for over 50 passages on HA. Colonies displayed morphology characteristic of undifferentiated stem cells. Cultures were passaged when colony size was 100-120 μM . Optimal mESC attachment and proliferation was achieved with 1 mg/ml HA gel. Laminin did not provide any additional benefit. Mouse ESC stained positive for undifferentiated stem cell markers, Sox2, Oct4, SSEA1, as well as AP activity. Stem cells cultured on HA gel formed embryoid bodies with all three germ layers. Embryoid bodies stained positive for two endoderm markers (α-fetoprotein and pan cytokeratin), a mesoderm marker (smooth muscle actin) and an ectoderm marker (tubulin III).
CONCLUSIONS: The novel tyramine substituted hyaluronan hydrogel used in this study shows tremendous potential for feeder-free culture of stem cells. The unique properties of this modified HA hydrogel include easy cross-linking, ability to be shaped, transparency for accurate cell visualization and biocompatibility, allowing robust cell proliferation and attachment. Embryonic stem cell pluripotency was maintained after continuous passage on this chemically defined substratum. Moreover, this hydrogel can potentially be combined with other extracellular matrix proteins to create 3-D scaffolding for tissue engineering applications.

S-209

Human Endometrial Reconstitution Using W5C5$^+$, ICAM1$^+$ Cells and Side Population Cell Lines in a Xenograft Model. Nuria López-Pérez†,[1] Claudia Gil-Sanchis,[1] Amparo Faus,[1] Ana Díaz,[2] Hannes Campo†,[1] Antonio Pellicer,[1,3] Irene Cervelló,[1] Carlos Simón*.[1,4] *[1]Fundación Instituto Valenciano de Infertilidad, Paterna, Valencia, Spain; [2]Valencia University, Valencia, Spain; [3]Instituto de Investigación Sanitaria La Fe, Valencia, Spain; [4]Stanford University School of Medicine, Stanford, CA, USA.*
INTRODUCTION: The human endometrial tissue has high proliferative capability due to the presence of somatic stem cells (SSC). Nevertheless, the lack of consensuated specific SSC markers hinders the clinical translation of the field. The Side Population (SP) method has been used to isolate endometrial SSC. Other suggested candidates are W5C5$^+$ cells at perivascular location and ICAM1$^+$ cells. The aim of the present work was to elucidate the stem cell capabilities of W5C5, ICAM1 and SP cell lines in an animal model.
METHODS: Human endometrial cells were sorted out by flow cytometry based on the expression of W5C5 and ICAM1. Positive cells were supplemented with total endometrium, and NOD-SCID mice (n=33) were used for xenotransplantation under the kidney capsule using: W5C5$^+$, W5C5$^-$, ICAM$^+$, ICAM$^-$, ICAM$^+$W5C5$^+$, ICAM$^-$W5C5$^-$ and SP cells. The reconstitution rate (RR) (Masuda et al., 2007) was assessed after 60 days of injection with HE staining and capsule thickening evaluation. Immunofluorescence confirmed the reconstitution efficiency by the presence of vimentin, progesterone receptor and cytokeratin. Proliferation was assessed by Ki-67.
RESULTS: The endometrial RR showed 100% efficiency in W5C5$^+$ and SP injected mice. ICAM$^+$ and ICAM$^+$W5C5$^+$ cells showed a RR of 66 and 50% respectively. These findings suggest that supplemented W5C5$^+$ cells and SP lines have the optimal potential to generate endometrial-like tissue. RR of W5C5$^+$ cells alone decreases to 66%, confirming that supplemental cells are required as a "niche" provider for *in vivo* reconstitution. It is worth noting that the negative fractions alone also formed new tissue and in all cases the proliferating cells were located around blood vessels.
CONCLUSIONS: Our results suggest that W5C5$^+$ and ICAM1$^+$ cells have low efficiency for endometrial RR. Nevertheless SP cell lines, an heterogeneous cell population, are able to reconstitute endometrium efficiently and proliferating cells were located around blood vessels, probably stimulating the differentiation of surrounded cells to tissue formation.
Supported by PROMETEO II/2013/018. IC and CS contributed equally.

S-210

Syncytiotrophoblast Derived from Induced Pluripotent Stem Cells (iPS) of Patients with Preeclampsia Display Increased Sensitivity to External Stressors. Jie Zhou†,[1] Megan A Hollenbeck†,[2] Aihua Dai,[2] Yuchen Tian,[2] Toshihiko Ezashi,[2] Danny J Schust*.[1] *[1]University of Missouri, Columbia, MO, USA; [2]University of Missouri, Columbia, MO, USA.*
INTRODUCTION: Preeclampsia (PE) is the most serious form of hypertensive pregnancy. The pathophysiology of PE is complicated and remains enigmatic, although studies have documented increased levels of syncytiotrophoblast microvesicles (STBV) in the maternal circulation in PE at levels positively correlated with disease severity. Several cytokines, including TNF-α have been implicated in the pathogenesis of PE and can alter trophoblast microvesicle shedding. Distinguishing whether changes in TNF-α are a cause or an effect of the disorder is difficult and it may act in a feedback loop.
METHODS: Human iPSC (control or PE cord derived) were treated with BMP4, A83-01 and PD173074(BAP). Syncytiotrophoblast resulting from this protocol represents the leading-edge trophoblast formed during blastocyst implantation. Experiments were performed with or without TNF-α (10 ng/ml). Media were collected at day 8. STBV shed from BAP-Primed iPSC were analyzed with a Zetasizer Nano ZS system (Malvern Instruments). Cell number was used for normalization. Experiments were performed at least three times in each of 2 control and 2 patient lines.
RESULTS:
**Figure(s) will be available online.*
STBV release was lower in control lines versus PE cell lines at baseline (17.1±7.8 vs. 173.2±36.2 respectively; $P<0.05$) and after TNF-α treatment (82.2±22.1 vs. 185.4±6.10, respectively, $p<0.05$). When cell lines were treated with TNF-α, STBV release from control cell lines did not significantly change, while that from PE cell lines increased nearly 5 fold.
CONCLUSIONS: STBV shedding from BAP-primed PE cell lines is significantly more sensitive to external stress (TNF-α) than from control cell lines. Since the iPSC model represents immediate post-implantation placental syncytia, these results suggest that PE may begin to develop in the very earliest stages of pregnancy. Future experiments will include exposure to other relevant stressors and evaluation of simultaneous cell morphology changes using electron microscopy.

S-211

Effects of Single or Repeated Intranasal Administration of Umbilical Cord Stem Cells in Neonatal Rats with Hypoxic-Ischemic Brain Lesions. Byron Oppliger†,[1,2] Marianne Joerger-Messerli,[1,2] Martin Mueller,[1,2,3] Ursula Reinhart,[1,2] Philipp Schneider,[1,2] Daniel V Surbek,[1,2] Andreina Schoeberlein.[1,2] *[1]Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland; [2]University of Bern, Bern, Switzerland; [3]Yale University, New Haven, CT, USA.*

INTRODUCTION: Lately, there has been a significant increase in preterm-specific brain injuries that still remain an unresolved clinical issue. The majority of the infants born preterm with brain injuries develop non-cystic, diffuse white matter injury (WMI), characterized by an overall hypomyelination of the brain. Preterm brain injury is an important cause for long-term disability. To date, no cure has been found to treat such lesions. Intranasal delivery of Wharton's jelly mesenchymal stem cells (WJ-MSC) might be the ideal, non-invasive therapeutic approach to restore the damaged brain. Therefore, our goal is to find an optimal treatment regimen of intranasally delivered WJ-MSC to achieve a maximum recovery after brain injury.

METHODS: WJ-MSC (84'000 cells/µl) were delivered intranasally to Wistar rat pups that were previously brain-damaged (total $1*10^6$ cells). Rat pups received either one, two or three treatments, at two days intervals. Animals were sacrificed 7 days after the first application of the cells. Fixed brains were analyzed by immunohistochemistry and real-time PCR.

RESULTS: Treatment with WJ-MSC increased myelination and decreased astro- and microgliosis. Repeated intranasal delivery was not more effective than single treatment, as assessed by immunohistochemistry. However, multiple administrations increased significantly the expression of brain-derived neurotrophic factor (Bdnf) compared to single administration.

CONCLUSIONS: In conclusion, intranasal delivery of WJ-MSC to the newborn after preterm brain damage has a neuroregenerative potential, which is probably mediated by a decreased astro- and microgliosis and an increased expression of important neurotrophic factors like Bdnf. Intranasal delivery of stem cells to the brain is an efficient and non-invasive method for stem cell treatment of perinatal brain damage.

Financial support by Cryosave Switzerland, Mobiliar Jubiläumsstiftung, Switzerland and The Eagle Foundation, Switzerland.

Membership Listing

Table of Contents

Regular Members **305**
Associate Members **336**
In-Training Members **336**
Emeritus Members **340**
Honorary Members **344**

Regular Members

Aagaard, Kjersti
Baylor College of Medicine
OB/GYN
Division of Maternal-Fetal Medicine
One Baylor Plaza, MS-BCM611
Houston, TX 77030
Telephone: (713) 798-8467
Email: aagaardt@bcm.edu

Aberdeen, Graham W.
University of Maryland SOM
Dept. of Ob/Gyn & Repro. Sci.
655 West Baltimore Street
Rm. 11-027, F.C. Bressler Bld
Baltimore, MD 21201
Telephone: (410) 706-3390
Email: gaberdeen@fpi.umaryland.edu

Abrahams, Vikki M.
Yale University
Dept. of Ob/Gyn & Repro. Sciences
333 Cedar Street
LSOG 305C
New Haven, CT 06510
Telephone: (203) 785-2175
Email: vikki.abrahams@yale.edu

Adair, C. David
Univ. of Tennessee COM
Dept. of Ob/Gyn
Chattanooga Regl Obstetrical Consultants
902 McCallie Ave.
Chattanooga, TN 37403
Telephone: (423) 664-4460
Email: adair@rocob.com

Adams Waldorf, Kristina M.
University of Washington
Dept. of Ob/Gyn
Box 356460
Seattle, WA 98195-6460
Telephone: (206) 543-6712
Email: adamsk@u.washington.edu

Adamson, Geoffrey David
Advanced Reproductive Care, Inc.
20665 Fourth Street
Suite 201
Saratoga, CA 95070
Telephone: (408) 647-9809
Email: gdadamson@arcfertility.com

Adashi, Eli Y.
Brown University
272 George Street
Providence, RI 02906
Telephone: (401) 274-4032
Email: eli_adashi@brown.edu

Al-Bader, Maie
Kuwait University
Dept. of Physiology, Faculty of Medicine
P.O. Box 24923
Safat, 13110
Kuwait
Telephone: +965 25319501
Email: albader@hsc.edu.kw

Albrecht, Eugene D.
University of Maryland SOM
Dept. of Ob/Gyn & Repro. Sciences
3265 East Hill Road-Andover
Ludlow, VT 05149
Telephone: (410) 706-3391
Email: ealbrecht@fpi.umaryland.edu

Al-Hendy, Ayman
Georgia Regents University, Medical College of Georgia
Dept. of Obstetrics and Gynecology
1120 15th Street
BA-7300
Augusta, GA 30912
Telephone: (706) 721-3833
Email: AALHENDY@augusta.edu

Allen, Terrence
Duke University Hospital
Dept of Anesthesiology
Erwin Road
Durham, NC 27710
Telephone: (919) 812-7302
Email: terrence.allen@dm.duke.edu

Amato, Paula
Oregon Health & Science University
3303 SW Bond Ave
Mail Code CH 10F
Portland, OR 97239-4501
Telephone: (503) 418-3744
Email: amatop@ohsu.edu

Anchan, Raymond M.
Brigham & Women's Hospital, Harvard Medical School
Dept. of Ob/Gyn & Div. of Repro. Med.
Harvard Medical School
75 Francis Street
Boston, MA 02115
Telephone: (617) 732-4648
Email: ranchan@partners.org

Anderson, Matthew L.
Baylor College of Medicine
Obstetrics & Gynecology
One Baylor Plaza, BCM610
Houston, TX 77030
Telephone: (713) 798-5152
Email: matthew@bcm.edu

Anthony, Russ V.
Colorado State University
Dept. of Biomedical Sciences
1683 Campus Delivery
ARBL-Foothills Campus
Fort Collins, CO 80523
Telephone: (970) 491-2586
Email: russ.anthony@colostate.edu

Anumba, Dilly O.
University of Sheffield
Human Metabolism
The Jessop Wing, Tree Root Walk
Level 4
Sheffield, S10 2SF
United Kingdom
Telephone: 44-1142268317
Email: d.o.c.anumba@sheffield.ac.uk

Apa, Rosanna
Universita Cattolica S.Cuore
Dept. of Ob/Gyn
Largo Gemelli 8
Roma, 00168
Italy
Telephone: 39-06-3015-6771
Email: krimisa@libero.it

Archer, David F.
EVMS
Dept. of Ob/Gyn
The Jones Institute
601 Colley Avenue
Norfolk, VA 23507-1912
Telephone: (757) 446-7444
Email: archerdf@evms.edu

Armant, D. Randall
NICHD/NIH
Program
Reproductive & Adult Endocrinology
275 East Hancock Street
Detroit, MI 48201-1405
Telephone: (313) 577-1748
Email: d.armant@wayne.edu

Aubuchon, Mira
University of Missouri
MCRM Fertility
17300 N Outer Forty
Suite 101
Chesterfield, MO 63005
Telephone: (636) 778-9899
Email: mira.aubuchon@gmail.com

Aziz, Natali
Stanford University School of Medicine
Obstetrics and Gynecology
300 Pasteur Drive, Room HG332
Stanford, CA 94305-5317
Telephone: (209)480-2040
Email: naziz@stanford.edu

Azziz, Ricardo
Georgia Regents University
226 S. Stanley Drive
Los Angeles, CA 90211
Telephone: (706) 721-2304
Email: razziz@gru.edu

Bagchi, Indrani C.
University of Illinois
Dept. of Comparative Biosciences
3411 VMBSB
2001 S Lincoln
Urbana, IL 61802
Telephone: (217) 333-7986
Email: ibagchi@illinois.edu

Bagchi, Milan K.
University of Illinois
Dept. of Mol. & Int. Physiology
534 Burrill Hall
407 S Goodwin Ave., MC 114
Champaign, IL 61822
Telephone: (217) 352-0599
Email: mbagchi@life.illinois.edu

Bainbridge, Shannon A.
University of Ottawa
Interdisciplinary School, Health Science
Roger Guindon Hall., Rm. 3028
451 Smyth Road
Ottawa, ON K1H 8M5
Canada
Telephone: (613) 562-5800 ext. 8569
Email: shannon.bainbridge@uottawa.ca

Ballas, Jerasimos
Baylor College of Medicine
Dept. of OB/GYN
One Baylor Plaza
BCM-610
Houston, TX 77006
Telephone: (646) 207-8096
Email: jerryballas@gmail.com

Bates, Gordon Wright
University of Alabama at Birmingham
Dept. of Ob/Gyn
1700 6th Ave South
Room 10390
Birmingham, AL 35249-7333
Telephone: (205) 934-1030
Email: gbates@uabmc.edu

Batt, Ronald E.
5648 Broadway
Lancaster, NY 14086-2317
Telephone: (716) 686-0245
Email: rbatt@buffalo.edu

Baxi, Laxmi V.
100, Haven Ave.
9D
New York, NY 10032
Telephone: (917) 414 8418
Email: baxilax@gmail.com

Bdolah, Yuval
Hadassah Mt Scopus MC
Dept. of Ob/Gyn
PO Box 24035
Jerusalem, 91240
Israel
Telephone: 972-2-584-4956
Email: ybdolah@hadassah.org.il

Benfield, Rebecca D.
University of Nevada, Las Vegas
School of Nursing
Office: BHS 416
Mail Code: 3018
Las Vegas, NV 89154-3018
Telephone: (702) 895-5045
Email: rebecca.benfield@unlv.edu

Bennett, Kelly Angela
Vanderbilt University Medical Center
Dept. of Ob/Gyn
3418 Trimble Road
Nashville, TN 37215-3224
Telephone: (615) 343-6275
Email: kelly.a.bennett@vanderbilt.edu

Bennett, Phillip R.
Imperial College London
IRDB, Hammersmith Hospital Campus
Du Cane Road
London, W12 ONN
United Kingdom
Telephone: 02075942176
Email: p.bennett@imperial.ac.uk

Berenson, Abbey B.
UTMB
Dept. of Ob/Gyn
301 University Blvd
Division of Peds & Adol. Gyn
Galveston, TX 77555-0587
Telephone: (409) 772-2417
Email: abberens@utmb.edu

Berga, Sarah L.
Wake Forest School of Medicine
Dept. of Ob/Gyn
Medical Center Blvd.
1 Medical Center Boulevard
Winston-Salem, NC 27157
Telephone: (336) 716-4594
Email: sberga@wakehealth.edu

Berkowitz, Karen M.
Drexel University COM
Dept. of Ob/Gyn & Biochemistry/Molecular
245 N. 15th Street, MS 497
11th Floor Room 11103
Philadelphia, PA 19102-1192
Telephone: (215) 762-1941
Email: kberkowitz@drexelmed.edu

Bernardi, Lia Ann
Northwestern University
Obstetrics and Gynecology
676 N St Clair St.
Suite 1845
Chicago, IL 60611
Telephone: 312-926-8244
Email: lia.a.bernardi@gmail.com

Bernstein, Ira M.
University of Vermont COM
Dept. of Ob/Gyn
Smith 410, UVMMC
111 Colchester Avenue
Burlington, VT 05401-1435
Telephone: (802) 847-5112
Email: ira.bernstein@uvm.edu

Bianchi, Diana W.
National Institute of Child Health and Human Development
NICHD
Building 31, Room 2A03
31 Center Drive, MSC 2425
Bethesda, MD 20892-2425
Telephone: (301) 496-3454
Email: Diana.Bianchi@Nih.gov

Bird, Ian M.
University of Wisconsin-Madison
Perinatal Research Labs
202 S. Park Street
7E Meriter Hospital
Madison, WI 53715
Telephone: (608) 417-6314
Email: imbird@wisc.edu

Blakemore, Karin J.
Johns Hopkins University SOM
Dept. of Ob/Gyn
Johns Hopkins Hospital
600 N. Wolfe Street, Phipps 228
Baltimore, MD 21287-1228
Telephone: (410) 955-6207
Email: kblakem@jhmi.edu

Blumenfeld, Zeev
Technion- Israel Institute of Technology
Dept. of Ob/Gyn & Repro. Endo.
RAMBAM HCC
The B Rappaport Faculty of Medicine
Haifa, 31096
Israel
Telephone: 97-24-8256388
Email: bzeev@tx.technion.ac.il

Bocca, Silvina M.
The Jones Institute -EVMS
Dept. of Ob/Gyn
601 Colley Ave.
Norfolk, VA 23507
Telephone: (757) 446-7119
Email: boccas@evms.edu

Bocchi, Caterina
University of Siena
Ob/Gyn Section
Dept. Molecular & Developmental Medicine
Santa Maria Alle Scotte, Viale Bracci
Siena, 53100
Italy
Telephone: 39-057-758-6607
Email: caterina.bocchi@unisi.it

Bocking, Alan D.
University of Toronto
Dept. of Ob/Gyn
Mount Sinai Hospital
60 Murray Street Box 43
Toronto, ON M5G 1X5
Canada
Telephone: (416) 586-4800 ext 5635
Email: abocking@mtsinai.on.ca

Boniface, Jay J.
Sera Prognostics
Dept. of Research & Development
2749 East Parleys Way
Suite 200
Salt Lake City, UT 84109
Telephone: (801) 990-0593
Email: jboniface@seraprognostics.com

Bonney, Elizabeth Ann
University of Vermont
60 Winooski Falls Way #1209
Winooski, VT 05404
Telephone: (802) 236-9414
Email: ebonney@uvm.edu

Bouma, Jerry
Colorado State University
ARBL - 1683
Fort Collins, CO 80523-1683
Telephone: (970) 491-8738
Email: Gerrit.Bouma@colostate.edu

Branch, D. Ware
University of Utah
Dept. of Ob/Gyn
2B200
Salt Lake City, UT 84132
Telephone: (801) 581-8425
Email: dwbranch@gmail.com

Braun, Thorsten
Charite University of Berlin
Dept. of Ob/Gyn
Augustenburger Platz 1
Berlin, 13353
Germany
Telephone: 49-30-450-56-4072
Email: thorsten.braun@charite.de

Bruner-Tran, Kaylon L.
Vanderbilt University SOM
Dept. of Ob/Gyn
1161 2nd Ave.
MCN B-1100
Nashville, TN 37232
Telephone: (615) 322-6152
Email: kaylon.bruner-tran@vanderbilt.edu

Buhimschi, Catalin S.
The Ohio State University
Dept. of Ob/Gyn
395 W 12th Avenue, 5th Floor
Columbus, OH 43210
Telephone: (614) 293-4929
Email: catalin.buhimschi@osumc.edu

Bukowski, Radek
Yale University School of Medicine
330 Cedar Street
P.O. Box 208063
New Haven, CT 06520-8063
Telephone: (203) 785-5855
Email: radek.bukowski@yale.edu

Bukulmez, Orhan
University of Texas Southwestern Medical Center
Div of Repro Endocrinology & Infertility
Dept. of OB/GYN
5323 Harry Hines Blvd
Dallas, TX 75390-9032
Telephone: (214) 648-4747
Email: Orhan.Bukulmez@UTSouthwestern.edu

Bulun, Serdar E.
Northwestern University
250 E. Superior St
Suite 03-2306
Chicago, IL 60611
Telephone: (312) 472-3636
Email: sbulun@nm.org

Burd, Irina
Johns Hopkins University
Dept. of Ob/Gyn
600 N. Wolfe Street
Phipps 228
Baltimore, MD 21287
Telephone: (410) 955-8496
Email: iburd@jhmi.edu

Burkin, Heather
University of Nevada
Pharmacology
1664 North Virginia Street, CMM-307E
CMM-307E
Reno, NV 89557
Telephone: (775) 784-6289
Email: hburkin@medicine.nevada.edu

Burlingame, Janet M.
University of Hawaii
Dept. of Ob/Gyn
John A. Burns SOM
1319 Punahou St., Suite 824
Honolulu, HI 96814
Telephone: (808) 203-6543
Email: burlinga@hawaii.edu

Burney, Richard Owen
Madigan Army Medical Center
Dept. of Ob/Gyn
Att: MCHJ-OG
9040A Fitzsimmons Dr.
Tacoma, WA 98431-1100
Telephone: (650) 804-4091
Email: roburney@stanford.edu

Burton, Graham J.
University of Cambridge
Centre for Trophoblast Research
Physiological Laboratory
Downing Street
Cambridge, CB2 3EG
United Kingdom
Telephone: 44-0-1223-333856
Email: gjb2@cam.ac.uk

Bush, Mark R.
Conceptions Reproductive Associates of Colorado
271 West County Line Road
Littleton, CO 80129
Telephone: (303) 794-0045
Email: markbush@earthlink.net

Bustillo, Maria
South Florida Inst. for Repro. Medicine
7300 S.W. 62nd Place
4th Floor
Miami, FL 33143
Telephone: (305) 662-7901
Email: mbustillo51@gmail.com

Buxton, Iain L.
University of Nevada
Dept. of Pharmacology
School of Medicine
1664 N. Virginia Street, MS 31
Reno, NV 89557-0270
Telephone: (775) 784-4800
Email: ibuxton@medicine.nevada.edu

Buyuk, Erkan
Albert Einstein College of Medicine
1300 Morris Park Ave.
Block 634
Bronx, NY 10461
Telephone: (718) 430-3512
Email: erbuyuk@yahoo.com

Bytautiene, Egle
University of Texas Medical Branch
Dept. of Ob/Gyn
301 University Blvd.
MRB 11.138
Galveston, TX 77555
Telephone: (409) 747-5139
Email: egbytaut@utmb.edu

Cahill, Alison G.
Washington University
Dept. of Ob/Gyn, Division of MFM
660 South Euclid Avenue, Maternity Bldg.
Campus Box 8064
St. Louis, MO 63110
Telephone: (314) 747-0739
Email: cahilla@wustl.edu

Calhoun, Byron C.
1570 Summit Drive
Charleston, WV 25302
Telephone: (304) 388-1599
Email: calhounbc@earthlink.net

Cameron, Iain T.
University of Southampton
Faculty of Medicine
Mailpoint 801, South Academic Block
Southampton General Hosp, Tremona Road
Southampton, SO16 6YD
United Kingdom
Telephone: 44-023-8120-6581
Email: itc@soton.ac.uk

Caniggia, Isabella
Mount Sinai Hospital
Lunenfeld-Tanenbaum Research Institute
60 Murray Street, Box 40
Toronto, ON M5T 3L9
Canada
Telephone: (416) 586-4803
Email: caniggia@lunenfeld.ca

Caritis, Steve N.
University of Pittsburgh
Dept. of Ob/Gyn
300 Halket St.
Rm. 2229
Pittsburgh, PA 15213
Telephone: (412) 641-5403
Email: scaritis@mail.magee.edu

Carr, Bruce R.
UTSW Medical Center
Dept. of Ob/Gyn
5323 Harry Hines Blvd.
Dallas, TX 75390-9032
Telephone: (214) 648-4747
Email: bruce.carr@utsouthwestern.edu

Carson, Sandra Ann
American College of Obstetricians & Gynecologists
Education
409 12th Street, SW
Washington, DC 20024
Telephone: (202) 863-2550
Email: scarson@acog.org

Carvajal, Jorge Andres
Pontificia Universidad Catolica de Chile
Dept. of Ob/Gyn
Marcoleta 391
Santiago, 833-0024
Chile
Telephone: 56-2-2686-3034
Email: jccjccjcc@vtr.net

Casper, Robert F.
University of Toronto
Dept. of Ob/Gyn
655 Bay St
Suite 1101
Toronto, ON M5G 2K4
Canada
Telephone: (416) 972-0777
Email: casper@lunenfeld.ca

Castro, Lony C.
California University of Science and Medicine
California Univ of Science and Medicine
1405 W. Valley Blvd, Suite 101
Colton, CA 92324
Telephone: (909) 954-3138
Email: castrol@calmedu.org

Catalano, Patrick M.
Case Western Reserve/MetroHealth Medical Center
2500 MetroHealth Drive
Cleveland, OH 44109
Telephone: (216) 778-4262
Email: pcatalano@metrohealth.org

Catov, Janet M.
University of Pittsburgh SOM
Dept. of Ob/Gyn & Reproductive Sciences
300 Halket Street
Room 2315
Pittsburgh, PA 15213-3180
Telephone: (412) 641-6217
Email: catovjm@upmc.edu

Caughey, Aaron B.
OHSU
3181 SW Sam Jackson Pk Rd
Mail Code L - 466
Portland, OR 97239
Telephone: (503) 494-2999
Email: caughey@ohsu.edu

Cedars, Marcelle I.
UCSF
Dept. of Ob/Gyn & Fertility
499 Illinois Street
Suite 601
San Francisco, CA 94115
Telephone: (415) 353-9776
Email: Marcelle.Cedars@ucsf.edu

Cetin, Irene
University of Milano
Dept. of Ob/Gyn
Via GB Grassi 74
#1
Milano, 20157
Italy
Telephone: 00-39-025-031-9804
Email: Irene.Cetin@unimi.it

Chambers, Setsuko K.
Arizona Cancer Center
Div. of Women's Cancers
University of Arizona
PO Box 245024
Tucson, AZ 85724-5024
Telephone: (520) 626-0950
Email: schambers@uacc.arizona.edu

Chambliss, Linda Ruth
Creighton University SOM
Dept. of Ob/Gyn
4440 N. Dromedary Rd.
Phoenix, AZ 85018
Telephone: (602) 541-0693
Email: lrchambliss@yahoo.com

Chamley, Lawrence W.
University of Auckland
Dept of Ob-Gyn, Rm 502-201J
School of Medicine, FMHS
Private Bag 92019
Auckland, New Zealand
Telephone: 64-9 9235901
Email: l.chamley@auckland.ac.nz

Chan, Shiao-yng
National University Singapore
Dept of Obstetrics and Gynaecology, NUH
1E Kent Ridge Road,
NUHS Tower Block, Level 12
Singapore, Singapore 119228
Telephone: (656) 772-3507
Email: obgchan@nus.edu.sg

Chang, Judy C.
University of Pittsburgh
Dept. of Ob/Gyn & Reproductive Sciences
300 Halket Street
Pittsburgh, PA 15213
Telephone: (412) 641-1441
Email: jchang@mail.magee.edu

Chang, Justine C.
P.O. Box 385
Mountain View, CA 94042
Telephone:
Email: justine_chang5@hotmail.com

Chang, Peter L.
Beth Israel Ctr. for Inf. & Repro. Hlth.
Noble Fertility Center
137 East 36th Street
New York, NY 10016
Telephone: (212) 804-6666
Email: pchang2216@gmail.com

Chanrachakul, Boonsri
Samitivej Sukhumvitl Hospital
Dept. of Ob/Gyn
133 Sukhumvit 49
Klongtan Nua, Vadhana
Bangkok, 10110
Thailand
Telephone: (662) 022-2222
Email: boonsri@hotmail.co.uk

Chao, Conrad R.
University of New Mexico
Department of OB/Gyn
1 University of New Mexico
MSC 10 5580
Albuquerque, NM 87131
Telephone: (505) 272-6399
Email: cchao@salud.unm.edu

Charnock-Jones, Stephen
University of Cambridge
Dept. of Ob/Gyn
Box 223, Rosie Hospital
Robinson Way
Cambridge, CB2 0SW
United Kingdom
Telephone: 01-223-336-875
Email: dscj1@cam.ac.uk

Chaudhuri, Gautam
David Geffen SOM at UCLA
Dept. of Ob/Gyn
Molecular and Medical Pharmacology
10833 Le Conte Avenue, 27-117 CHS
Los Angeles, CA 90095-6928
Telephone: (310) 206-6575
Email: gchaudhuri@mednet.ucla.edu

Chauhan, Madhu Lata S.
Baylor College of Medicine
1102 Bates Avenue
Ste.1870
Houston, TX 77030
Telephone: (409) 692-4413
Email: mschauha@bcm.edu

Chelmow, David
VCU Medical Center
Dept. of Ob/Gyn
1101 E. Marshall Street
Box 980034
Richmond, VA 23298
Telephone: (804) 828-7877
Email: dchelmow@mcvh-vcu.edu

Chen, Dongbao
UC Irvine SOM
Dept. of Ob/Gyn
MFM, Zot 3230
Med Surge I, Build 810, RM140
Irvine, CA 92697
Telephone: (949) 824-2409
Email: dongbaoc@uci.edu

Chervenak, Frank A.
Weill Med. College of Cornell Univ.
Dept. of Ob/Gyn
Weill Cornell Medical Center
525 East 68th St., J-130
New York, NY 10065
Telephone: (212) 746-3046
Email: fac2001@med.cornell.edu

Cheung, Cecilia Y.
Oregon Health & Science University
Dept. of Obstetrics & Gynecology
3181 SW Sam Jackson Park Road
Mail Code L-458
Portland, OR 97239
Telephone: (503) 494-1254
Email: cheungce@ohsu.edu

Chien, Edward K.
710 Jefferson Ave #328
Cleveland, OH 44113
Telephone: 216-778-8586
Email: echien@metrohealth.org

Chishima, Fumihisa
Nihon University School of Medicine,
Department of Obstetrics and
Gynecology
30-1 Oyaguchi-kamimachi Itabashi-ku
Tokyo, 173-8610
Japan
Telephone: +81-3-3972-8111
Email: chishima.fumihisa@nihon-u.
ac.jp

Cho, SiHyun
Yonsei University College of Medicine
146-92 Gangnam-gu, Dogok-dong
Gangnam Severance Hospital
Department of Obstetrics & Gynecology
Seoul, 135-720
Korea
Telephone: +82-2-2019-3430
Email: sihyuncho@yuhs.ac

Choi, Suk-Joo
Sungkyunkwan University SOM
Dept. of Ob/Gyn
Samsung Medical Center
50 Ilwon-Dong, Gangnam-Gu
Seoul, 135-710
Korea
Telephone: 82-2-3410-3546
Email: drmaxmix.choi@samsung.com

Christman, Gregory M.
University of Florida
Dept. of OB/GYN
PO Box 100294, Room M302L
1600 SW Archer Road
Gainesville, FL 32611-0294
Telephone: (352)-273-7676
Email: gchristman@ufl.edu

Christy, Alicia Y.
National Institutes of Health
10817 Melvin Grove Ct
Kensington, MD 20895
Telephone: (301) 633-5112
Email: alicia.christy@nih.gov

Chwalisz, Kristof
AbbVie, Inc.
1 N. Waukegan Road, AP4A-3
Dept. R440
North Chicago, IL 60064
Telephone: (847) 938-0563
Email: kristof.chwalisz@abbvie.com

Ciarmela, Pasquapina
Polytechnic Univ. of Marche
Dept of Experimental & Clinical
Medicine
Via Tronto 10 A
Ancona, 60020
Italy
Telephone: 39-071-220-6270
Email: p.ciarmela@univpm.it

Cipolla, Marilyn Jo
University of Vermont
Dept. of Neurological Sciences
149 Beaumont Ave.
HSRF 416
Burlington, VT 05404
Telephone: (802) 656-9714
Email: marilyn.cipolla@med.uvm.edu

Clark, Erin A. S.
University of Utah SOM
Dept. of Ob/Gyn
30 N. 1900 E.
SOM, Suite 2B200
Salt Lake City, UT 84132
Telephone: (801) 581-8425
Email: erin.clark@hsc.utah.edu

Clifton, Vicki L.
Mater Medical Research Institute
Translational Research Institute
37 Kent St
Brisbane, QLD 4101
Australia
Telephone: 617 34437640
Email: vicki.clifton@mater.uq.edu.au

Coddington, Charles C.
Mayo Clinic
Dept. of Ob/Gyn
Charlton 3A
200 First Street, S.W.
Rochester, MN 55905
Telephone: (507) 284-4520
Email: coddington.charles@mayo.edu

Condon, Jennifer C.
Wayne State University
Dept. of Ob/Gyn
CS Mott Center
#339
Detroit, MI 48202
Telephone: 313 5772152
Email: jcondon@med.wayne.edu

Connell, Kathleen A.
University of Colorado Denver
12631 E 17th Ave
Aurora, CO 80045
Telephone: (303) 724-2038
Email: kathleen.connell@ucdenver.edu

Conrad, Kirk P.
University of Florida COM
Dept, Phys & Functional Genomics, OBGYN
1600 SW Archer Rd, M552
PO Box 100274
Gainesville, FL 32610-0274
Telephone: (352) 392-2798
Email: kpconrad@ufl.edu

Contag, Stephen A.
University of Maryland
Dept. of Ob/Gyn and Reproductive Science
22 South Greene Street
Room N6W104G
Baltimore, MD 21201
Telephone: (410) 328-6475
Email: contag@live.com

Cooke, Christy-Lynn
University of Alberta
Obstetrics & Gynaecology
Women & Children's Health Research Inst
232 HMRC
Edmonton, AB T6G2S2
Canada
Telephone: (780) 492-8562
Email: christyl@ualberta.ca

Cooper, Brian C.
Mid-Iowa Fertility
1371 NW 121st St.
Clive, IA 50325
Telephone: (515) 222-3060
Email: bcooper@midiowafertility.com

Copel, Joshua A.
Yale School of Medicine
Dept. of Ob/Gyn & Repro. Sciences
333 Cedar Street
PO Box 208063
New Haven, CT 06520-8063
Telephone: (203) 785-2671
Email: joshua.copel@yale.edu

Coulam, Carolyn B.
111 E Chestnut St
Apt 43K
Chicago, IL 60611
Telephone: (847) 869-7777
Email: cbcoulam@aol.com

Coustan, Donald R.
Women & Infants Hospital of RI
Division of Maternal-Fetal Medicine
Brown University SOM
101 Dudley Street
Providence, RI 02905-2401
Telephone: (401) 274-1122 ext: 47452
Email: dcoustan@wihri.org

Cracchiolo, Bernadette M.
UMDNJ-New Jersey Medical School
Dept. of Ob/Gyn
185 South Orange Ave.
Rm. E-506
Newark, NJ 07103
Telephone: (973) 972-5055
Email: cracchbm@njms.rutgers.edu

Critchfield, Gregory
Sera Prognostics, Inc
2749 East Parleys Way
Salt Lake City, UT 84109
Telephone: (801) 990-0525
Email: gcritchfield@seraprognostics.com

Critchley, Hilary Octavia Dawn
University of Edinburgh
MRC Centre for Reproductive Health
The Queens Med. Rsrch. Inst.
47 Little France Crescent
Edinburgh, EH16 4TJ
United Kingdom
Telephone: 44-131-242-6858
Email: hilary.critchley@ed.ac.uk

Croy, Barbara Anne
Queen's University
Dept. of Biomedical & Molecular Sciences
Room 924 Botterhell Hall
Kingston, ON K7L 3N6
Canada
Telephone: (613) 533-2859
Email: croya@queensu.ca

Daftary, Gaurang S.
Mayo Clinic
Dept. of Ob/Gyn, Div. of Repro. Endo.
200 First Street SW
Charlton 3-127
Rochester, MN 55905
Telephone: (507) 284 4520
Email: Daftary.Gaurang@mayo.edu

Damario, Mark A.
Center for Reproductive Medicine
991 Sibley Memorial Highway
Suite 100
St. Paul, MN 55118
Telephone: (651) 379-3110
Email:

Damewood, Marian D.
2680 Blackberry Road
Dover, PA 17315
Telephone: (717) 424-0733
Email: mdamewood19@gmail.com

D'Antona, Donato
University of Padua
Dip Salute Della Donna E Del Bambino
Via Giustiniani 3
Padova, 35128
Italy
Telephone: 39-049-8213458/3410/3411
Email: donato.dantona@unipd.it

David, Anna L.
University College London
Institute for Women's Health
86-96 Chenies Mews
London, WC1E 6HX
United Kingdom
Telephone: 44-20-7679-6499
Email: a.david@ucl.ac.uk

Davidge, Sandra T.
Women and Children's Health
Research Inst. - University of Alberta
232 HMRC, Dept. of Ob/Gyn
Edmonton, AB T6G 2S2
Canada
Telephone: (780) 492-1864 (lab)
Email: sandra.davidge@ualberta.ca

Davis, John S.
University of Nebraska Medical Center
Dept. of Ob/Gyn
983255 Nebraska Medical Center
Omaha, NE 68198-3255
Telephone: (402) 559-9079
Email: jsdavis@unmc.edu

De Groot, Christianne JM
VU University Medical Center
Dept. of Obstetrics
De Boelelaan 1117
8F-035
Amsterdam, Netherlands
Telephone: 31-20-444-4851
Email: cdegroot@me.com

De Haan, Harmen H.
Isala Clinics, loc. Sophia
Dept. of Ob/Gyn
PO Box 10400
Zwolle, 8000 GK
Netherlands
Telephone: 31-384-24-5604
Email: h.h.de.haan@isala.nl

DeCherney, Alan H.
National Institutes of Health
10 Center Drive, Room 1-3140
MSC 1109
Bethesda, MD 20892-1109
Telephone: (301) 496-5800
Email: decherna@mail.nih.gov

DeMayo, Francesco J.
NIEHS
111 T. W. Alexander Dr.
F191
Research Triangle Park, NC 27709
Telephone: (919) 541-0280
Email: demayofj@niehs.nih.gov

Depoix, Christophe L.
universite catholique de Louvain
IREC/obstetrique
Tour C. Bernard
Avenue Hippocrate 55
Woluwe-saint-Lambert, 1200
Belgium
Telephone: (322) 764-9421
Email: christophe.depoix@uclouvain.be

Desai, Mina
David Geffen SOM at Harbor-UCLA
Dept. of Ob/Gyn
1124 West Carson St.
Box 467, RB-3 Bldg.
Torrance, CA 90502
Telephone: (310) 974-9540
Email: mdesai@@labiomed.org

Desoye, Gernot
Medical University of Graz
Dept. of Ob/Gyn
Auenbruggerplatz 14
Graz, A-8036
Austria
Telephone: 43-316-385-14605
Email: gernot.desoye@medunigraz.at

Detti, Laura
University of Tennessee
Dept. of Ob/Gyn
853 Jefferson Ave.
Suite E100B
Memphis, TN 38163
Telephone: (901) 448-5859
Email: ldetti@uthsc.edu

Di Simone, Nicoletta
Universita' Cattolica del Sacro Cuore
Dept Obstet Gyn, Policlinico Gemelli
Largo Gemelli 8
Rome, 00168
Italy
Telephone: 00-39-06-301-54826
Email: nicoletta.disimone@virgilio.it

Diamond, Michael P.
Augusta University
1120 15th Street
BA-7300
Augusta, GA 30912
Telephone: (706) 721-3591
Email: mpdmd@aol.com

Dimitriadis, Evdokia
Hudson Institute of Medical Research
Centre of Reproductive Health
PO Box 5152, Clayton
Melbourne, VIC 3168
Australia
Telephone: 61-3-85722546
Email: evdokia.dimitriadis@hudson.org.au

diZerega, Gere S.
USC Keck School of Medicine
Dept. of Ob/Gyn
231 Bonetti Drive
Suite 240
San Luis Obispo, CA 93401
Telephone: (805) 595-1300
Email: dizerega@usc.edu

Dmowski, W. Paul
Institute for the Study and Treatment of Endometriosis
2425 W. 22nd Street
Suite #200
Oak Brook, IL 60523
Telephone: (630) 954-3636
Email: wpdmowski@teamrmi.com

Dodson, William C.
Penn State University
Dept. of Ob/Gyn, H 103
M.S. Hershey Med. Ctr.
PO Box 850
Hershey, PA 17033
Telephone: (717) 531-8478
Email: wdodson@psu.edu

Dong, Xuesen
Vancouver Prostate Centre
University of British Columbia
2660 Oak Street
Vancouver, BC V6H 3Z6
Canada
Telephone: (604) 875-4111 ext: 6302
Email: xdong@prostatecentre.com

Douglas, Nataki C.
Columbia University Medical Center
Dept. of Ob/Gyn
Div of Repro Endocrinology & Infertility
622 West 168th Street, PH 16-64
New York, NY 10032
Telephone: (212) 305-6337
Email: nd2058@cumc.columbia.edu

Drewlo, Sascha
Wayne State University SOM
Dept. of Ob/Gyn
C.S. Mott Center, Human Growth & Devlp
275 E. Hancock #295
Detroit, MI 48201
Telephone: (313) 577-1158
Email: sdrewlo@med.wayne.edu

Driscoll, Deborah A.
Univ. of Pennsylvania
Dept. of Ob/Gyn
3400 Spruce St.
5 Dulles
Philadelphia, PA 19104
Telephone: (215) 662-7503
Email: ddriscoll@obgyn.upenn.edu

Druzin, Maurice L.
Stanford University SOM
Dept. of Obstetrics and Gynecology
300 Pasteur Drive
G302
Stanford, CA 94305-5317
Telephone: (650)-725-8623
Email: druzin@stanford.edu

Ducsay, Charles A.
Loma Linda University
Center for Perinatal Biology
SOM
Loma Linda, CA 92350
Telephone: (909) 558-4325
Email: cducsay@llu.edu

Dudley, Donald J.
University of Virginia
University of Virginia, Dept of OB/Gyn
P.O. Box 800712
Charlottesville, VA 22908
Telephone: (434) 924-9700
Email: dd7ss@virginia.edu

Duncan, Francesca E.
University of Kansas Medical Center
Dept. of Anatomy and Cell Biology
3901 Rainbow Blvd (HLSIC 3071)
Kansas City, KS 66160
Telephone:
Email: fduncan@kumc.edu

Ealy, Alan D.
Virginia Tech
Dept. Animal and Poultry Sciences
3430 Litton-Reaves Hall (0306)
Blacksburg, VA 24061
Telephone: 540-231-4425
Email: ealy@vt.edu

Easterling, Thomas R.
University of Washington
Dept. of Ob/Gyn
1959 NE Pacific
Box 356460, BB667B
Seattle, WA 98195
Telephone: (206) 543-1521
Email: easter@u.washington.edu

Eaton, Jennifer L.
Duke University
Dept. of Ob/Gyn
Div of Repro Endocrinology & Infertility
5704 Fayetteville Road
Durham, NC 27713
Telephone: (919) 572-4673
Email: jennifer.eaton@duke.edu

Ecker, Jeffrey L.
Massachusetts General Hospital
Dept. of Ob/Gyn
Founders 4
Boston, MA 02114
Telephone: (617) 726-2770
Email: jecker@partners.org

Edlow, Andrea G.
Tufts University School of Medicine
800 Washington Street
Box 394
Boston, MA 02111
Telephone: (617) 636-1468
Email: aedlow@tuftsmedicalcenter.org

Elkind-Hirsch, Karen E.
Woman's Hospital
Research Department-Support Services
100 Woman's Way
Baton Rouge, LA 70817
Telephone: (225) 231-5278
Email: Karen.Elkind-Hirsch@womans.org

Elovitz, Michal A.
University of Pennsylvania
421 Curie Blvd
1354 BRB 2/3
Philadelphia, PA 19104
Telephone: (215) 573-0859
Email: melovitz@obgyn.upenn.edu

England, Sarah K.
Washington University SOM
Dept. of Ob/Gyn
425 South Euclid Ave.
Campus Box 8064
St. Louis, MO 63110-1010
Telephone: (314) 286-1798
Email: englands@wustl.edu

Eswaran, Hari
University of Arkansas COM
Dept. of Ob/Gyn
SARA Research Center
4301 W. Markham Slot 518
Little Rock, AR 72205
Telephone: (501) 686-5847
Email: eswaranhari@uams.edu

Euser, Anna G.
University of Colorado
Dept. of Ob/Gyn
12631 East 17th Ave.
Aurora, CO 80045
Telephone: (303) 724-2014
Email: anna.euser@ucdenver.edu

Evans, Mark I.
Comprehensive Genetics
131 East 65th St
New York, NY 10065
Telephone: (212) 288 1422
Email: Evans@compregen.com

Fassett, Michael J.
Kaiser Permanente West Los Angeles Medical Center
Dept. of Ob/Gyn
6041 Cadillac Avenue
Los Angeles, CA 90034
Telephone: (323) 857-3399
Email: michael.j.fassett@kp.org

Fazleabas, Asgerally T.
Michigan State University
Dept. of Ob/Gyn & Reprod Biolology
333 Bostwick Avenue NE
Room 4027 VanAndel Institute
Grand Rapids, MI 49503-2532
Telephone: (616) 234-0981
Email: asgi@hc.msu.edu

Feghali, Maisa
University of Pittsburgh/Magee-Womens Hospital of UPMC
OBGYN/RS - Maternal Fetal Medicine
300 Halket Street
Pittsburgh, PA 15213
Telephone: (412) 641-4462
Email: maisafeghali@gmail.com

Feltovich, Helen
Utah Valley Regional Medical Center
Dept. of MFM
Intermountain Healthcare
1034 North 500 West
Provo, UT 84604
Telephone: (801) 357-8152
Email: hfeltovich@gmail.com

Feng, Liping
Duke University Medical Center
Research Drive
234 Sands
Durham, NC 27710
Telephone: (919) 613-1459
Email: liping.feng@duke.edu

Ferrazzi, Enrico M.
Buzzi Children's Hospital University of Milan
Dept. of Ob/Gyn
Buzzi Children's Hospital
Via Castelvetro, 32
Milano, 20154
Italy
Telephone: 39-02-579-95369
Email: enrico.ferrazzi@unimi.it

Field, Nancy T.
University of California-Davis
Dept. of Ob/Gyn
4860 Y Street
Suite 2500
Sacramento, CA 95817
Telephone: (916) 734-6930
Email: ntfield@UCDAVIS.EDU

Figueroa, Jorge P.
Wake Forest SOM
Dept. of Ob/Gyn
Medical Center Boulevard
Winston-Salem, NC 27157-1066
Telephone: (336) 716-2351
Email: figueroa@wakehealth.edu

Flannery, Clare Ann
Yale SOM
Dept. of Ob/Gyn & Repro. Sciences
PO Box 208063
333 Cedar Street
New Haven, CT 06520
Telephone: (203) 737-5619
Email: clare.flannery@yale.edu

Flores, Idhaliz
Ponce Health Sciences University - Ponce Research Institute
Dept of Microbiology / Dept of ObGyn
PO Box 7004
Ponce, PR 00732
Telephone: (787) 840-2575
Email: iflores@psm.edu

Ford, Stephen P.
University of Wyoming
Dept. of Animal Science
Rm. 113, Animal Science
Molecular Bio. Bldg., Box 3684
Laramie, WY 82071-3684
Telephone: (307) 766-2709
Email: spford@uwyo.edu

Fowler, Paul A.
University of Aberdeen
Institute of Medical Sciences
Foresthill
Aberdeen, AB25 2ZD
United Kingdom
Telephone: 44-122-443-7528
Email: p.a.fowler@abdn.ac.uk

Frasch, Martin G.
University of Washington
Dept. of Ob/Gyn
1959 NE Pacific St
Box 356460
Seattle, WA 98195
Telephone: (206) 543-5892
Email: mfrasch@uw.edu

Frias, Antonio E.
Oregon Health & Science University
3181 SW Sam Jackson Park Rd
Mail Code: L458
Portland, OR 97239
Telephone: (503) 494-2121
Email: friasa@ohsu.edu

Fritz, Marc A.
University of North Carolina
Dept. of Ob/Gyn
Old Clinic Bldg.
CB 7570-4001
Chapel Hill, NC 27599-7570
Telephone: (919) 966-5283
Email: mafritz@med.unc.edu

Fujii, Eriko Y.
Nara Medical University
Dept. of Obstetric and Gynecology
840 Shijo-Cho
Kashihara City
Nara, 634-8522
Japan
Telephone: 81-744-29-8877
Email: perky.ef@gmail.com

Fukami, Tatsuya
ASO Iizuka Hospital
Dept. of Ob/Gyn
160-5 Rakuichi, Iizuka
Fukuoka, 8200074
Japan
Telephone:
Email: fukami1975@msn.com

Funai, Edmund F.
University of South Florida
12901 Bruce B Downs Blvd
MDC 02
Tampa, FL 33612
Telephone: (813) 974-4531
Email: edmund.funai@icloud.com

Furukawa, Yuichi
Northwestern University
Robert H Lurie Medical Research Center
Room 4-123
303 E Superior St
Chicago, IL 60611
Telephone: (312) 503-5281
Email: yufurukawa@oita-u.ac.jp

Gabbe, Steven G.
The Ohio State University Wexner Medical Center
Medicine Administration
410 West 10th Ave
168 Doan Hall
Columbus, OH 43210
Telephone: (614) 685-4418
Email: steven.gabbe@osumc.edu

Galan, Henry L.
University of Colorado Denver
Dept. of Ob/Gyn
12631 E. 17th Ave.
M/S B198-5
Aurora, CO 80045
Telephone: (303) 724-2032
Email: Henry.Galan@UCDenver.edu

Gammill, Hilary S.
University of Washington/Fred Hutchinson Cancer Research Center
Dept. of Ob/Gyn
Box 356460
Seattle, WA 98195-6460
Telephone: (206) 667-4053
Email: hgammill@uw.edu

Gantert, Markus
St. Franziskus-Hospital Ahlen
Wersegrund 6a
Muenster, D-48157
Germany
Telephone: 49-251-20308379
Email: markusgantert@googlemail.com

Gao, Haijun
Baylor College of Medicine
1102 Bates Ave
Ste.1870
Houston, TX 77030
Telephone: (832) 824-4196
Email: haijung@bcm.edu

Garcia-Velasco, Juan A.
IVI-Madrid / Rey Juan Carlos University
Dept. of Repro Endo & Infertility
Av. Del Talgo 68
Madrid, 28023
Spain
Telephone: 34-91-180-2900
Email: jgvelasco@ivi.es

Gargett, Caroline E.
Hudson Institute of Medical Research
The Ritchie Centre
Translational Research Facility Level 5
27-31 Wright Street
Clayton, VIC 3168
Australia
Telephone: 613-8572 2795
Email: caroline.gargett@hudson.org.au

Gelber, Shari E.
Weill Medical College
Dept. of Ob/Gyn
Cornell Univ.
525 East 68th Street, Box 122
New York, NY 10065
Telephone: (212) 746-3182
Email: shg7001@med.cornell.edu

Gibbons, William E.
Baylor College of Medicine
Dept. of Ob/Gyn
6651 Main Street
Suite F1050
Houston, TX 77030
Telephone: 832-826-7463
Email: gibbons@bcm.edu

Girard, Sylvie
University of Montreal - Sainte-Justine Hospital
Dept. of Ob/Gyn
Ste-Justine Hospital Research Center
3175 Cote Ste-Catherine
Montreal, QC H3T 1C5
Canada
Telephone:
Email: sylvie.girard@recherche-ste-justine.qc.ca

Girling, Jane E.
The University of Melbourne
University of Melbourne Dept. of Ob/Gyn
The Royal Women's Hospital
Cnr Flemington Rd and Grattan St
Parkville, VIC 3052
Australia
Telephone: 61-3-8345-3717
Email: jgirling@unimelb.edu.au

Giudice, Linda C.
UCSF
Dept. of Ob/Gyn & Reproductive Sciences
550 16th Street, Floor 7
Box 0132
San Francisco, CA 94143
Telephone: (415) 476-2564
Email: giudice@obgyn.ucsf.edu

Giussani, Dino A.
University of Cambridge
Physiology Development & Neuroscience
Downing Street
Cambridge, CB2 3EG
United Kingdom
Telephone: 44-122-3333-894
Email: dag26@cam.ac.uk

Glantz, John C.
University of Rochester Medical Center
Dept. of Ob/Gyn
Strong Memorial Hospital
601 Elmwood Ave., Box 668
Rochester, NY 14642-8668
Telephone: (585) 275-7480
Email: chris_glantz@urmc.rochester.edu

Gleicher, Norbert
Center for Human Reproduction,
Rockefeller University
21 E 69th Street
New York, NY 10021
Telephone: (212) 994-4400
Email: ykizawa@thechr.com

Goetzl, Laura
1529 Pine Street
Philadelphia, PA 19102
Telephone: (267) 908-2032
Email: goetzl@temple.edu

Goharkhay, Nima
Texas MFM
450 W Medical Center Blvd
Suite 300
1016 Point Isabel Lane
Friendswood, TX 77546
Telephone: (832) 680-9311
Email: ngoharkhay@gmail.com

Gokina, Natalia I.
University of Vermont
Dept. of Ob/Gyn
89 Beaumont Ave.
Given Bldg. C-209
Burlington, VT 05405
Telephone: (802) 656-1205
Email: natalia.gokina@uvm.edu

Goldberg, Jeffrey M.
Cleveland Clinic
Cleveland Clinic Dept of OB/GYN
9500 Euclid Avenue
Cleveland, OH 44195
Telephone: (216) 444-2242
Email: goldbej@ccf.org

Goldsmith, Laura T.
Rutgers - New Jersey Med. School
Dept. of Ob/Gyn & Women's Health
185 S. Orange Ave.
MSB-E569
Newark, NJ 07103
Telephone: (973) 972-5516
Email: goldsmit@njms.rutgers.edu

Golichowski, Alan M.
4042 Statesmen Drive
Indianapolis, IN 46250
Telephone: (317) 415-7744
Email: agolich@iupui.edu

Gomez-Lopez, Nardhy
Wayne State University SOM
Ob/Gyn & Immunology & Microbiology
C.S. Mott Center, Human Growth & Devlp
275 E. Hancock, Room 305
Detroit, MI 48201
Telephone: (313) 577-8904
Email: ngomezlo@med.wayne.edu

Gonik, Bernard
Wayne State University School of Medicine
Dept. of Ob/Gyn
3990 John R Street,
7 Brush North, Box 163
Detroit, MI 48201
Telephone: (313) 993-1375
Email: bgonik@med.wayne.edu

Gonzalez, Frank
Indiana University SOM
Dept. of Ob/Gyn
550 N. University Blvd
Suite 2440
Indianapolis, IN 46202
Telephone: (317) 948-3148
Email: gonzalef@iupui.edu

Goshen, Ran
Rango Science & Medicine Ltd.
3 Nissim Aloni St.
Apt. 2102
Tel Aviv, 6291917
Israel
Telephone: 972-52-456-4442
Email: ran@rango.co.il

Goulopoulou, Styliani
University of North Texas Health Science Center
Inst. Cardiovascular & Metabolic Dis.
3500 Camp Bowie Blvd
Fort Worth, TX 76107
Telephone: (817) 735-2973
Email: styliani.goulopoulou@unthsc.edu

Goyal, Ravi
Loma Linda University
Center for Perinatal Biology
11234 Anderson Street
Loma Linda, CA 92354
Telephone: (909) 253-1596
Email: rgoyal@llu.edu

Graham, Ernie M.
Johns Hopkins University
Dept. of Ob/Gyn
600 N. Wolfe St, Phipps 228
Baltimore, MD 21287-1228
Telephone: (410) 955-3187
Email: egraham5@jhmi.edu

Gravett, Michael G.
University of Washington
Dept. of Ob/Gyn
1959 NE Pacific St.
Box 356460
Seattle, WA 98195
Telephone: (206) 884-8228
Email: gravettm@uw.edu

Greaves, Erin
University of Edinburgh
MRC Centre for Reproductive Health
47 Little France Crescent
Edinburgh, EH16 4TJ
United Kingdom
Telephone: 0131 242 6196
Email: egreaves@ed.ac.uk

Green, Lucy R.
University of Southampton
Institute of Developmental Sciences
887 Southampton General Hospital
Tremona Rd.
Southampton, S016 6YD
United Kingdom
Telephone: 44-023-81-206373
Email: l.r.green@soton.ac.uk

Gregg, Anthony R.
University of Florida
Dept. of Ob/Gyn
1600 SW Archer Road
PO Box 100294
Gainesville, FL 32610
Telephone: (352) 273-7562
Email: greggar@ufl.edu

Grigsby, Peta L.
Oregon National Primate Rsch. Ctr.
Div of Repro & Developmental Sciences
505 NW 185th Ave.
Beaverton, OR 97006
Telephone: (503) 690-5286
Email: grigsbyp@ohsu.edu

Grobman, William A.
Northwestern University
Dept. of Ob/Gyn
250 East Superior St.
Suite 05-2175
Chicago, IL 60611
Telephone: (312) 472-4685
Email: w-grobman@northwestern.edu

Grotegut, Chad A.
Duke University
Dept. of Ob/Gyn
DUMC Box 3967
Durham, NC 27710
Telephone: (919) 668-0843
Email: chad.grotegut@duke.edu

Guarnaccia, Michael M.
4 Lindeman Ave
Closter, NJ 07624
Telephone: (646) 756-8282
Email: mmg2112@columbia.edu

Guller, Seth
Yale University SOM
Dept. of Ob/Gyn
333 Cedar Street
Rm. 339 FMB, PO Box 208063
New Haven, CT 06520-8063
Telephone: (203) 737-2532
Email: seth.guller@yale.edu

Gyamfi-Bannerman, Cynthia
Columbia University MC
Dept. of Ob/Gyn
622 West 168th Street
PH - 16
New York, NY 10032
Telephone: (212) 305-6293
Email: cg2231@cumc.columbia.edu

Habli, Mounira A.
University of Cincinnati
Dept. of Pediatric Surgery. MFM Division
Cincinnati Childrens Hospital
3333 Burnet Ave., MLC 11025
Cincinnati, OH 45229
Telephone: (513) 636-6259
Email: drmhabli@gmail.com

Halder, Sunil K.
Augusta University
Dept. of Ob/Gyn
1120 15th Street, MCG
Georgia Regents University,CB-2915B
Augusta, GA 30912
Telephone: (706) 721-8907
Email: shalder@gru.edu

Hallman, Mikko N.
University of Oulu
Dept. of Pediatrics
Institute of Clinical Medicine
Aapistie 5, Box 5000
Oulu, 90220
Finland
Telephone: 358-8-315-5100
Email: mikko.hallman@oulu.fi

Halvorson, Lisa M.
703 New Mark Esplanade
Rockville, MD 20850
Telephone: (301) 480-1646
Email: lisa.halvorson@nih.gov

Hansen, Thomas R.
Colorado State University
Dept. of Biomedical Sciences
ARBL 1683 Campus Delivery
Fort Collins, CO 80523-1683
Telephone: (970) 491-8081
Email: thomas.hansen@colostate.edu

Hanson, Mark A.
Southampton University
Institute of Developmental Sciences
Mailpoint 887, Southampton General Hosp.
Tremona Road
Southampton, S016 6YD
United Kingdom
Telephone: 44-023-8120-5255
Email: m.hanson@soton.ac.uk

Hartmann, Katherine E.
Vanderbilt University
Dept. of Ob/Gyn
2525 West End Avenue, Ste 600
Nashville, TN 37203
Telephone: (615) 322-4785
Email: katherine.hartmann@Vanderbilt.Edu

Hassan, Sonia S.
Wayne State University/Perinatology Research Branch
Dept. of Ob/Gyn
3990 John R, 4 Brush
Detroit, MI 48201
Telephone: (313) 577-5774
Email: shassan@med.wayne.edu

Hawkins, Shannon M.
Indiana University School of Medicine
Department of Obstetrics and Gynecology
550 N. University Blvd, UH 2440
Indianapolis, IN 46202
Telephone: (713) 865-6069
Email: thehawk02@gmail.com

Heikinheimo, Oskari M.
Helsinki Univ. Central Hospital
Dept. of Ob/Gyn
Katiloopisto Hospital
PO Box 610 (Sofianlehdonkatu 5a)
Helsinki, 00029-HUS
Finland
Telephone: 358-40-587-1070
Email: oskari.heikinheimo@helsinki.fi

Heitmann, Ryan J.
9701 166th Street Ct E
Puyallup, WA 98375
Telephone: (253) 968-3276
Email: ryan.j.heitmann.mil@mail.mil

Heller, Debra S.
Rutgers-New Jersey Medical School
Dept. of Pathology, UH/E158
185 S. Orange Ave.
UH E 158
Newark, NJ 07101
Telephone: (973) 972-0751
Email: hellerds@njms.rutgers.edu

Hellman, Kevin M.
6620 N. Whipple St.
Chicago, IL 60645
Telephone: (872) 226-7124
Email: khellman@uchicago.edu

Hellner, Karin
University of Oxford
John Radcliffe Hospital
Headley Way
Oxford, OX3 9DU
United Kingdom
Telephone: 00441865221021
Email: karin.hellner@obs-gyn.ox.ac.uk

Helmer, Hanns P.
Medical University Vienna
Dept. of Ob/Gyn
Waehringer Guertel 18-20
AKH-Wien, Ebene 8C
Vienna, 1090
Austria
Telephone: +431-40400-29380
Email: hanns.helmer@meduniwien.ac.at

Hemmings, Denise G.
University of Alberta
Dept. of Ob/Gyn
227 HMRC
Edmonton, AB T6G 2S2
Canada
Telephone: (780) 492-2098
Email: denise.hemmings@ualberta.ca

Hill, Meghan G.
University of Arizona
Dept. of Ob/Gyn, Division of MFM
1501 N. Campbell, 8th Floor
Tucson, AZ 85724
Telephone: (520) 626-6174
Email: meghanhill@obgyn.arizona.edu

Hirsch, Emmet
NorthShore University HealthSystem
Dept. of Ob/Gyn
2650 Ridge Avenue
Walgreen Bldg, Suite 1507
Evanston, IL 60201
Telephone: (847) 570-1546
Email: ehirsch@northshore.org

Hirshfeld-Cytron, Jennifer E.
Fertility Center of IL
Dept. of Ob/Gyn
851 Northwoods
Deerfield, IL 60015
Telephone: (612) 281-4451
Email: jhirshfeldcytron@gmail.com

Hobel, Calvin J.
Cedars-Sinai Medical Center
Dept. of Ob/Gyn
8635 West 3rd St.
Suite 160W
Los Angeles, CA 90048
Telephone: (310) 423-3365
Email: calvin.hobel@cshs.org

Holloway, Alison C.
McMaster University
Dept. of Ob/Gyn
1200 Main Street, West
Rm 3N52 Health Sciences Centre
Hamilton, ON L8N 3Z5
Canada
Telephone: (905) 525-9140 ext: 22130
Email: hollow@mcmaster.ca

Hornstein, Mark D.
Brigham & Women's Hospital
Dept. of Ob/Gyn
75 Francis Street
Boston, MA 2115
Telephone: (617) 732-4648
Email: mhornstein@partners.org

Hoskins, Iffath A.
NYU Medical Center
515 East 72nd St
Apt 17-H
New York, NY 10021
Telephone: 917-626-6301
Email: iffath.hoskins@nyumc.org

House, Michael D.
Tufts Medical Center
Dept. of MFM
Mother & Infant Research Institute
800 Washington Street #360
Boston, MA 02111
Telephone: (617) 636-3200
Email: mhouse@tuftsmedicalcenter.org

Hsu, Albert L.
Dartmouth-Hitchcock Medical Center
5 Low Road
Hanover, NH 03755
Telephone: (917) 670-9003
Email: scooberhsu@gmail.com

Hsu, Chaur-Dong
Hutzel Women's Hospital
Dept. of Ob/Gyn
3990 John R. Street, Box 158
Detroit, MI 48201
Telephone: (516) 572-6255
Email:

Huang, Gloria
Albert Einstein College of Medicine/
Montefiore Medical Center
Dept of OB/GYN & Women's Health
Division of Gynecologic Oncology
1695 Eastchester Road, Suite 601
Bronx, NY 10461
Telephone: (718) 405-8082
Email: gloria.huang@einstein.yu.edu

Huang, Hong-yuan
Chang Gung Memorial Hospital
Dept. of Ob/Gyn
5, Fu-Hsing Street
Kwei-shan, Tao-Yuan, 333
Taiwan
Telephone: 886-3-328-1200 ext: 8258
Email: hongyuan@cgmh.org.tw

Huang, S. Joseph
384 Engelwood Ct.
Powell, OH 43065
Telephone: (813) 974-1191
Email: sete94040@yahoo.com

Huang, Yingqun
5 Robby Lane
East Haven, CT 06512
Telephone: (203) 737-2578
Email: yingqun.huang@yale.edu

Hubel, Carl A.
Magee-Womens Research Institute
Dept. of Ob/Gyn & Repro. Sciences
204 Craft Avenue
A346
Pittsburgh, PA 15213
Telephone: (412) 641-6130
Email: chubel@mwri.magee.edu

Hughes, Francine
Albert Einstein College of Medicine
Dept of Ob/Gyn & WH
1300 Morris Park Avenue
Block Bldg. 631
Bronx, NY 10461
Telephone: (718) 430-2524
Email: francine.hughes@nyumc.org

Hurt, K. Joseph
University of Colorado SOM
Dept. of Ob/Gyn, Basic Repro Sciences
12700 East 19th Ave.
RC2-P15-3005 (Mailstop 8613)
Aurora, CO 80045
Telephone: (303) 724-5965
Email: k.joseph.hurt@ucdenver.edu

Hwang, Jong Yun
Kangwon Natl. Univ. Hospital
Dept. of Ob/Gyn
156 Baengnyeong-ro
Chuncheon-si
Kangwon-do, 200-722
Korea
Telephone: 82-33-258-2307
Email: stanfordhwang@gmail.com

Illsley, Nicholas P.
Hackensack University MC
Dept. of Ob/Gyn
David Jurist Institute for Research, 40
Room RC446
Hackensack, NJ 07601
Telephone: (551) 996-8122
Email: nillsley@hackensackUMC.org

Imbar, Tal
Hadassah Mt. Scopus - Hebrew Univ.
MC
Dept. of Ob/Gyn & Reproduction
PO Box 24035, Mt. Scopus
Jerusalem, 91240
Israel
Telephone: 972-2-584-4400
Email: talim@hadassah.org.il

Irwin, Juan C.
UCSF
Dept. of Ob/Gyn & Repoductive
Science
513 Parnassus Avenue
HSE 1619
San Francisco, CA 94143
Telephone: (415) 476-2039
Email: juan.irwin@ucsf.edu

Ishikawa, Gen
Nippon Medical School
Dept. of Ob/Gyn
1-1-5 Sendagi
Bunkyo-ku
Tokyo, 113-8602
Japan
Telephone: 81-3-5814-6212
Email: gen-ishi@nms.ac.jp

Ishikawa, Hiroshi
Chiba University, Graduate SOM
Reproductive Medicine
1-8-1 Inohana Chuo-ku
Chiba, 260-8670
Japan
Telephone: 81-43-226-2121
Email: ishikawa@chiba-u.jp

Ishimoto, Hitoshi
Tokai University SOM
Dept. of Ob/Gyn
143 Shimokasuya
Isehara, 259-1193
Japan
Telephone: 011-81-463-931121 ext2388
Email: ishimoto@is.icc.u-tokai.ac.jp

Itoh, Hiroaki
Hamamatsu University SOM
Dept. of Ob/Gyn
Maternal-Fetal and Neonatal Care Center
1-20-1 Handayama, Higashi-ku
Hamamatsu, 431-3192
Japan
Telephone: 81-53-435-2309
Email: hitou-endo@umin.ac.jp

Iwanaga, Ritsuko
University of Colorado SOM
Dept. of Ob/Gyn
12700 E. 19th Ave.
Anschutz Medical Campus
Aurora, CO 80045
Telephone: (303) 724-8475
Email: ritsuko.iwanaga@ucdenver.edu

Jacobsson, Bo
Gothenburg University
Dept. of Ob/Gyn
Institute of Clinical Science
Sahlgrenska University Hospital/ Ostra
Gothenburg, SE 416 85
Sweden
Telephone: +46-70-560-0162
Email: bo.jacobsson@obgyn.gu.se

Janát-Amsbury, Margit M.
University of Utah
OB/Gyn
30 N 1900 East, Ste. 2A200, Rm. 2A242
Salt Lake City, UT 84132
Telephone: (801) 213-2248
Email: margit.janat-amsbury@hsc.utah.edu

Jansson, Thomas
University of Colorado Anschutz Medical Campus
Department of Obstetrics & Gynecology
Research Complex-2; Mail Stop 8613
2700 East 19th Avenue, Room P15-3100C
Aurora, CO 80045
Telephone: (303) 724 8622
Email: thomas.jansson@ucdenver.edu

Jellyman, Juanita K.
Los Angeles Biomedical Research Institute at Harbor-UCLA
Dept. of Ob/Gyn
1124 West Carson Street
Torrance, CA 90502
Telephone: (626) 771-7366
Email: juanitajellyman@yahoo.co.uk

Jeyabalan, Arundhathi
University of Pittsburgh
Dept. of Ob/Gyn & Reproductive Sciences
300 Halket Street Rm 2225
Pittsburgh, PA 15213
Telephone: (412) 641-5256
Email: ajeyabalan@mail.magee.edu

Johnson, Donna D.
Medical University of South Carolina
Dept. of Ob/Gyn
96 Jonathan Lucas St. Box 250619
Charleston, SC 29425
Telephone: (843) 792-8355
Email: johnsodo@musc.edu

Johnson, Julia Virginia
University of Massachusetts Med. Sch.
Dept. of Ob/Gyn
UMass Memorial Medical Center
Jaquith 4, Room 4060
Worcester, MA 01605
Telephone: (508) 334-5369
Email: Julia.Johnson@umassmemorial.org

Johnson, Mark Richard
Imperial College
Dept. of Ob/Gyn
Chelsea and Westminster Hospital
369 Fullham Road
London, SW10 9NH
United Kingdom
Telephone: 44-208-846-7892
Email: mark.johnson@imperial.ac.uk

Johnson, Timothy R.B.
University of Michigan
Dept. of Ob/Gyn
1500 E. Medical Center Drive
Room L4000 Women's
Ann Arbor, MI 48109-5276
Telephone: (734) 764-8123
Email: trbj@umich.edu

Jones, Helen
Cincinnati Children's Hospital MC
Rep. Sci and Peds Surgery
MLC 11025
3333 Burnet Ave.
Cincinnati, OH 45229
Telephone: (513) 636-3774
Email: helen.jones@cchmc.org

Joss-Moore, Lisa A.
University of Utah
Dept. of Pediatrics/ Neonatology
295 Chipeta Way
Salt Lake City, UT 84108
Telephone: (801) 587-7486
Email: lisa.joss-moore@hsc.utah.edu

Jungheim, Emily Susan
Washington University
Dept. of Ob/Gyn
4444 Forest Park Avenue, Suite 3100, Cam
St. Louis, MO 63108
Telephone: (314) 286-2430
Email: jungheime@wustl.edu

Kaitu'u-Lino, Tu'uhevaha
University of Melbourne
Dept. of Ob/Gyn
Mercy Hospital for Women
163 Studley Road, Level 4
Heidelberg, VIC 3084
Australia
Telephone: 61-3-8458-4355
Email: t.klino@unimelb.edu.au

Kallen, Amanda N.
Yale School of Medicine
OB/GYN & Reproductive Sciences
333 Cedar Street
PO Box 208063
New Haven, CT 06510
Telephone: (860) 402-4217
Email: amanda.kallen@yale.edu

Karipcin, Sinem
Conceptions Florida
4425 Ponce de Leon Blvd. Suite 110
Coral Gables, FL 33146
Telephone: (203) 747-4302
Email: dr.sinemkaripcin@gmail.com

Karumanchi, Ananth
Harvard Medical School and Beth Israel Deaconess Medical Center
Dept. of Medicine
Beth Israel Deaconess Med. Ctr., RN 370D
330 Brookline Ave.
Boston, MA 02215
Telephone: (617) 667-1018
Email: sananth@bidmc.harvard.edu

Katz, Michael
San Francisco Perinatal Associates
San Francisco, CA
Telephone:
Email: mkatz@sfperinatal.com

Kaufman, David G.
University of North Carolina at Chapel Hill
Dept. of Pathology & Lab Medicine
School of Medicine
620 Brinkhous-Bullitt Bldg
Chapel Hill, NC 27599-7525
Telephone: (919) 966-1396
Email: uncdgk@med.unc.edu

Kay, Helen H.
Advocate Medical Group
130 N. Garland Court
Chicago, IL 60602
Telephone: (708)684-5340
Email: kay.helen.h@gmail.com

Keefe, David L.
New York University SOM
Dept. of Ob/Gyn
550 First Avenue
NBV 9N1A
New York, NY 10016
Telephone: (212) 263-0774
Email: david.keefe@nyumc.org

Keelan, Jeffrey A.
University of Western Australia
School of Women's & Infant's Health
King Edward Memorial Hospital
374 Bagot Rd, Subicao
Perth, WA 6008
Australia
Telephone: 61-8-9340-1880
Email: jeff.keelan@uwa.edu.au

Keller-Wood, Maureen
University of Florida
Dept. of Pharmacodynamics
PO Box 100487
Gainesville, FL 32610-0487
Telephone: (352) 273-7687
Email: kellerwd@cop.ufl.edu

Kemp, Matt
University of Western Australia
School of Women's and Infants' Health
35 Stirling Highway
Perth, 6156
Australia
Telephone: 61-401-58-9773
Email: matthew.kemp@uwa.edu.au

Kenny, Louise Clare
UCC
Irish Centre for Fetal &
Neonatal Translational Research
Cork University Maternity Hospital
Wilton, ROI
Ireland
Telephone: 353 (0)21 4205023
Email: l.kenny@ucc.ie

Khalil, Asma
Apartment 64
11 Sheldon Square
London, W2 6DQ
United Kingdom
Telephone: 00-44-791-740-0164
Email: akhalil@sgul.ac.uk

Khorram, Omid
Harbor-UCLA Medical Center
Dept. of Ob/Gyn
1000 W. Carson St.
Box 489
Torrance, CA 90502
Telephone: (310) 222-3867
Email: okhorram@labiomed.org

Kiesel, Ludwig
University of Muenster
Dept. of Ob/Gyn
Albert-Schweitzer-Campus 1, Building A1
Strasse 33
Muenster, 48149
Germany
Telephone: 49-251-83-48201
Email: ludwig.kiesel@ukmuenster.de

Kilby, Mark D.
University of Birmingham UK
Dept. of Ob/Gyn, Div. of MFM
Edgbaston
Birmingham, B15 2TG
United Kingdom
Telephone: 011-44-121-627-2778
Email: m.d.kilby@bham.ac.uk

Kim, Hoon
Seoul National University College of Medicine
Dept. of Ob/Gyn
Seoul Nat'l Univ. Hospital
28 Yungun-Dong, Chongno-Gu
Seoul, 110-744
Korea
Telephone: 82-2-2072-2388
Email: obgyhoon@gmail.com

Kim, J. Julie
Northwestern University SOM
Dept. of Ob/Gyn
303 E. Superior Street
Lurie 4-117
Chicago, IL 60611
Telephone: (312) 503-5377
Email: j-kim4@northwestern.edu

Kim, Yoon Ha
Chonnam Natl. Univ. Med. School
Dept. of Ob/Gyn
42, Jebong-ro, Dong-gu
Gwangju, 61469
Korea
Telephone: 82-62-220-6375
Email: kimyh@chonnam.ac.kr

Kliman, Harvey J.
161 Ford Road
Woodbridge, CT 06525
Telephone: (203) 785-3854
Email: harvey.kliman@yale.edu

Kniss, Douglas A.
Ohio State Univ. Wexner Medical Center
Dept. of Ob/Gyn
395 W. 12th Ave.
Fifth Floor, Faculty Office Tower
Columbus, OH 43210
Telephone: (614) 293-4496
Email: kniss.1@osu.edu

Kodaman, Pinar H.
Yale University SOM
Dept. of Ob/Gyn
150 Sargent Drive
2nd Floor
New Haven, CT 06511
Telephone: (203) 785-4708
Email: pinar.kodaman@yale.edu

Konje, Justin C.
University of Leicester and Sidra Medical and Research Center
Depart of Ob/Gyn
Sidra Medical and Research Center
PO Box 26999
Doha, Qatar
Telephone: 44(116) 252-5826
Email: jck4@le.ac.uk

Koos, Brian J.
UCLA Medical Center
Dept. of Ob/Gyn
David Geffen School of Medicine
10833 LeConte Ave., 22-167 CHS
Los Angeles, CA 90095-1740
Telephone: (310) 502-7848
Email: bkoos@mednet.ucla.edu

Krause, Bernardo J.
Pontificia Univ. Catholica de Chile
Neonatology
Marcoleta 391
Santiago, Chile
Telephone: (562) 354-8119
Email: bjkrause@gmail.com

Krause, Miriam S.
319 S Sherrin Ave
Louisville, KY 40207
Telephone: (502) 897-2144
Email: ms.krause@yahoo.de

Krikun, Graciela
Yale University SOM
Dept. of Ob/Gyn & Repro. Sciences
333 Cedar Street, LSOG 406
PO Box 208063
New Haven, CT 06510
Telephone: (203) 785-5951
Email: graciela.krikun@yale.edu

Ku, Seung-Yup
Seoul National University Hospital
Dept. of Ob/Gyn
28 Yonkeun-dong Chongno-gu
Chongno-gu
Seoul, 110-744
Korea
Telephone: 82-2-2072-1971
Email: jyhsyk@snu.ac.kr

Kumar, Deepak
CWRU, MetroHealth Medical Center-Case Western Reserve University
Dept. of Pediatrics
2500 MetroHealth Dr.
Cleveland, OH 44109
Telephone: (216) 778-5946
Email: dkumar@metrohealth.org

Kumar, Sathish
University of Texas Medical Branch
Dept. of Ob/Gyn
301 University Blvd.
Galveston, TX 77555
Telephone: (409) 747-6699
Email: kusathis@utmb.edu

Kuohung, Wendy
Boston University SOM
Dept. of Ob/Gyn
85 East Concord St.
6th Fl.
Boston, MA 02118
Telephone: (617) 414-5175
Email: wkuohung@bu.edu

Kuokkanen, Satu Maarit
Montefiore/ Medical Center/Albert Einstein College of Medicine
Obstetrics & Gynecology & Women's Health
1300 Morris Park Ave.
Block Building, 6th Floor Room 627
Bronx, NY 10580
Telephone: (718) 430-3152
Email: skuokkanen@verizon.net

Kutzler, Michelle Anne
Oregon State University
Dept. of Animal and Rangeland Sciences
College of Agricultural Sciences
112 Withycombe Hall
Corvallis, OR 97331
Telephone: (541) 737-1401
Email: michelle.kutzler@oregonstate.edu

Kwak-Kim, Joanne Y.
Rosalind Franklin Univ. of Medicine and Science
Dept. of Ob/Gyn
Division of Reproductive Medicine
830 West End Ct., Suite 400
Vernon Hills, IL 60061
Telephone: (847) 247-6900
Email: joanne.kwakkim@rosalindfranklin.edu

La Barbera, Andrew R.
American Society for Reproductive Medicine
1209 Montgomery Hwy
Birmingham, AL 35216-6822
Telephone: (205) 978-5004
Email: andrew.labarbera@gmail.com

Laivuori, Hannele
University of Helsinki
Medical Genetics
PO Box 63 (Haartmaninkatu 8)
Helsinki, 00014
Finland
Telephone: 358-50-4154871
Email: hannele.laivuori@helsinki.fi

Landon, Mark B.
Ohio State University
Dept. of Ob/Gyn
395 W 12th Avenue
Suite 572
Columbus, OH 43210-1267
Telephone: (614) 293-8513
Email: Mark.Landon@osumc.edu

Lang, Uwe
Medical University of Graz
Dept. of Ob/Gyn
Auenbrugger Platz
Graz, A 8036
Austria
Telephone: 43-316-385-17069
Email: ulgraz@yahoo.de

Lappas, Martha
University of Melbourne
Dept. of Ob/Gyn
Mercy Hospital for Women
4th Fl., 163 Studley Road
Heidelberg, VIC 3084
Australia
Telephone: 61-3-8458-4370
Email: mlappas@unimelb.edu.au

Laudanski, Piotr
Medical University of Bialystok
Dept. of Perinatology and Obstetrics
Ul. Marii Sklodowskiej-Curie 24a
Bialystok, 15-276
Poland
Telephone: 00-48-608-344-788
Email: plauda@umb.edu.pl

Laven, Joop S.E.
Erasmus Medical Center
Div. Reproductive Medicine
'S Gravendijkwal 230
Rotterdam, 3015 CE
Netherlands
Telephone: 31-107-03-3760
Email: j.laven@erasmusmc.nl

Layman, Lawrence C.
Augusta University
Dept. of Ob/Gyn
1120 15th Street
Section REI & Genetics
Augusta, GA 30912-3360
Telephone: (706) 721-3832
Email: lalayman@gru.edu

Leach, Richard E.
110 Sunnybrook Ave., SE
Grand Rapids, MI 49506
Telephone: (517) 884-6031
Email: richard.leach@hc.msu.edu

Learman, Lee A.
Florida Atlantic University
Charles E. Schmidt College of Medicine
777 Glades Road
Boca Raton, FL 33431
Telephone: (561) 297-4826
Email: llearman@health.fau.edu

Lee, Eun D.
Virginia Commonwealth University
Dept. of Ob/Gyn
1101 E. Marshall Street
Suite 11-028B
Richmond, VA 23298
Telephone: (804) 828-2423
Email: eun.lee@vcuhealth.org

Lee, Men-Jean
2111 Momi Way
Honolulu, HI 96822
Telephone: (808) 203-6530
Email: menjean.lee@gmail.com

Leitao, Mario M.
Memorial Sloan-Kettering Cancer Center
Dept. of Surgery
1275 York Avenue
H1314
New York, NY 10021
Telephone: (212) 639-3987
Email: leitaom@mskcc.org

Leslie, Kimberly K.
University of Iowa Hospitals & Clinics
Dept. of Ob/Gyn, Univ. of IA Hosp.
200 Hawkins Drive
Room 31140-A PFP
Iowa City, IA 52242
Telephone: (319) 356-1976
Email: kimberly-leslie@uiowa.edu

Lessey, Bruce A.
Greenville Health System
Dept. of Ob/Gyn
University Medical Group
890 West Faris Rd., Ste. 470
Greenville, SC 29605
Telephone: (864) 455-1600
Email: mbennefield@ghs.org

Levine, Lisa D.
University of Pennsylvania
3400 Spruce Street
2 Silverstein
Philadelphia, PA 19104
Telephone: (215) 662-2982
Email: lisa.levine@uphs.upenn.edu

Li, Cun
University of Wyoming
1000 E University Ave
Laramie, WY 82071
Telephone: (210) 258-9271
Email: cli5@uwyo.edu

Limesand, Sean W.
University of Arizona
Animal and Comparative Biomedical Scienc
4101 N. Campbell Ave.
Tucson, AZ 85719
Telephone: (520) 626-8903
Email: limesand@ag.arizona.edu

Liu, Huishu
Guangzhou Women & Children Medical Center
Dept. of Ob/Gyn
9 Jinsui Road, Guangzhou
Guangzhou, 510623
Peoples Republic of China
Telephone: 86-1-392-415-2738
Email: huishuliu@hotmail.com

Lobo, Rogerio A.
Columbia University
Dept. of Ob/Gyn
622 W. 168th Street
16th Floor Rm. 16-65
New York, NY 10032
Telephone: (212) 305-6337
Email: ral35@columbia.edu

Loch-Caruso, Rita K.
University of Michigan
Dept. of Environmental Health Sciences
School of Public Health 6618 Tower SPHI
1415 Washington Heights
Ann Arbor, MI 48109-2029
Telephone: (734) 936-1256
Email: rlc@umich.edu

Lockwood, Charles J.
The University of South Florida Morsani College of Medicine
VP/Deans, Dept. of Ob/Gyn
12901 Bruce B. Downs Blvd.
MDC 02
Tampa, FL 33612
Telephone: (813) 974-0533
Email: cjlockwood@health.usf.edu

Lopez Bernal, Andrés
University of Bristol
School of Clinical Sciences
St. Michael's Hospital, Level D, OB/GYN
Southwell Street
Bristol, BS2 8EG
United Kingdom
Telephone: 44-117-331-3161
Email: ogalb@bristol.ac.uk

Loret de Mola, J. Ricardo
SIU School of Medicine
Dept. of Ob/Gyn
PO Box 19640
Springfield, IL 62794-9640
Telephone: (217) 545-1523
Email: rloretdemola@siumed.edu

Lowery, Curtis Lee
University of Arkansas for Medical Sciences
Dept. of Ob/Gyn
4301 West Markham #518
Slot 518
Little Rock, AR 72205
Telephone: (501) 686-5847
Email: lowerycurtisl@uams.edu

Ludmir, Jack
Pennsylvania Hospital/Penn Medicine
Dept. of Ob/Gyn
800 Spruce Street
2 Pine East
Philadelphia, PA 19107
Telephone: (215) 829-3934
Email: jaludm@uphs.upenn.edu

Luisi, Stefano
University of Siena
Dept. of Ob/Gyn
Viale Bracci
Siena, 53100
Italy
Telephone: 39-057-758-6641
Email: stefano.luisi@unisi.it

Lumsden, Mary Ann
University of Glasgow
Reproductive & Maternal Medicine
Royal Infirmary
Level 2, New Lister Building
Glasgow, G31 2ER
United Kingdom
Telephone: 44-141-211-4704
Email: maryann.lumsden@gla.ac.uk

Lye, Stephen J.
Lunenfeld-Tanenbaum Res. Inst.
Lunenfeld-Tanenbaum Research Institute
Sinai Health System
25 Orde Street, Rm. 6-1004-1
Toronto, ON M5T 3H7
Canada
Telephone: (416) 586-8640
Email: lye@lunenfeld.ca

Ma, Kimberly K.
University of Washington
Obstetrics and Gynecology
1959 NE Pacific St., Box 356460
Seattle, WA 98195
Telephone: (206) 598-3588
Email: kkma@uw.edu

Macones, George A.
Washington University SOM
Dept. of Ob/Gyn & MFM
4911 Barnes-Jewish Hospital Plz
Campus Box 8064-6th FL. MAT Rm. 607
St. Louis, MO 63110-1031
Telephone: (314) 362-7139
Email: maconesg@wustl.edu

MacPhee, Daniel J.
University of Saskatchewan
Veterinary Biomedical Sciences
WCVM, Univ. of Saskatchewan
52 Campus Dr, Room 2330
Saskatoon, SK S7N5B4
Canada
Telephone: 306-966-7153
Email: d.macphee@usask.ca

Magee, Thomas R.
Charles R Drew University
Dept. of Health and Life Sciences
1731 E. 120th Street
Keck Annex, RM 5
Los Angeles, CA 90059
Telephone: (323) 357-3455
Email: thomasmagee@cdrewu.edu

Magness, Ronald R.
University of South Florida
Dept. of Ob/Gyn
12901 Bruce B. Downs Blvd.
MDC48
Tampa, FL 33612
Telephone: (608) 417-6498
Email: rmagness@health.usf.edu

Mahalingaiah, Shruthi
Boston University
85 East Concord St-6th Floor
Department of Obstetrics and Gynecology
Boston University School of Medicine
Boston, MA 02118
Telephone: (617) 414-7305
Email: shruthi@bu.edu

Mahendroo, Mala
UTSW Medical Center
Dept. of Ob/Gyn
5323 Harry Hines Blvd
Room F2.306
Dallas, TX 75235-9032
Telephone: (214) 648-3091
Email: mala.mahendroo@utsouthwestern.edu

Mainigi, Monica
University of Pennsylvania
Dept. of Ob/Gyn
8th Floor
Philadelphia, PA 19119
Telephone: (215) 662-2972
Email: mainigim@uphs.upenn.edu

Mak, Winifred
Yale University SOM
Dept of Repro Endocrin & Infertility
FMB329
333 Cedar Street
New Haven, CT 06511
Telephone: (203) 584-1638
Email: winifred.mak@yale.edu

Makino, Shintaro
Juntendo University
Dept. of Ob/Gyn
2-1-1, Hongo
Bunkyo-ku
Tokyo, 113-8421
Japan
Telephone: 81-3-3813-3111
Email: shintaro@juntendo.ac.jp

Maloyan, Alina
Oregon Health and Science University
3181 S.W. Sam Jackson Park Rd.
Portland, OR 97239-3098
Telephone: (513) 238-3783
Email: maloyan@ohsu.edu

Mando, Chiara
Via Plinio 28
Milan, 20129
Italy
Telephone: 00-39-02-50319882
Email: chiara.mando@unimi.it

Maniu, Adina
University of Maryland, Baltimore
Dept. of Ob/Gyn
11 S Paca Street
Suite 400
Baltimore, MD 21201
Telephone: (410) 328-5964
Email: admaniu@gmail.com

Manuck, Tracy
UNC-Chapel Hill
3010 Old Clinic Building
CB#7516
Chapel Hill, NC 27599
Telephone: (919) 966-1601
Email: tmanuck@med.unc.edu

Marbaix, Etienne
Universite Catholique de Louvain
Dept. of Pathology
Service D' Anatomie Pathologique,
T-1, C
Ave. Hippocrate, 10
Bruxelles, B-1200
Belgium
Telephone: 32-2-764-6755
Email: etienne.marbaix@uclouvain.be

Marconi, Anna Maria
University of Milano
Dept. of Ob/Gyn- DHS San Paolo
Via A di Rudini', 8
Milano, 20142
Italy
Telephone: 00-39-025-032-3064
Email: annamaria.marconi@unimi.it

Mari, Giancarlo
University of Tennessee Health Science Center
Dept. of Ob/Gyn
853 Jefferson Avenue
E102 Rout
Memphis, TN 38103
Telephone: (901) 448-2531
Email: gmari@uthsc.edu

Marsh, Erica E.
University of Michigan
Dept. of Ob/Gyn
676 N. St. Clair
Suite 1845
Chicago, IL 60611
Telephone: (312) 926-8244
Email: marshee@med.umich.edu

Martens, Mark G.
Jersey Shore Univ. Medical Center
Dept. of Ob/Gyn
1945 Route 33
Neptune, NJ 07753
Telephone: (732) 776-3790
Email: mmartens@meridianhealth.com

Maruyama, Tetsuo
Keio University SOM
Dept. of Ob/Gyn, Keio Univ Sch Med
35 Shinanomachi
Shinjuku-ku
Tokyo, 160-8582
Japan
Telephone: 81-3-5363-3578
Email: tetsuo@keio.jp

Matsubara, Keiichi
Ehime Univ. SOM
Dept. of Ob/Gyn
Shitsukawa
Toon, Ehime, 791-0295
Japan
Telephone: 81-89-960-5379
Email: keiichi@m.ehime-u.ac.jp

Matthews, Stephen G.
University of Toronto
Dept. of Physiology
1 King's College Circle
Toronto, ON M5S 1A8
Canada
Telephone: (416) 978-1974
Email: stephen.matthews@utoronto.ca

Mattison, Donald R.
Risk Sciences International
553 Colonial Drive
Hilton Head Island, SC 29926
Telephone: (613) 260-1424 x 211
Email: dmattison@risksciences.com

Maulik, Dev
UMKC School of Medicine
Dept. of Ob/Gyn
2301 Homes St.
#713
Kansas City, MO 64108
Telephone: (816) 404-5181
Email: dev.maulik@tmcmed.org

McElrath, Thomas Frederick
Brigham & Women's Hospital
Dept. of Ob/Gyn
Harvard Medical School
75 Francis St
Boston, MA 02115
Telephone: (617) 732-5452
Email: tmcelrath@partners.org

McGee, Elizabeth A.
University of Vermont Medical Center
Dept. of Ob/Gyn
111 Colchester Ave
251 SM4
Burlington, VT 05401
Telephone: 802-847-3450
Email: elizabeth.mcgee@vtmednet.org

McGinnis, Lynda K.
University of Southern California
1441 Eastlake Ave
NOR 5419
Los Angeles, CA 90033
Telephone: (323) 865-3013
Email: lynda.mcginnis@usc.edu

McGovern, Peter Gerard
Mount Sinai St Lukes Roosevelt Hospital
214 Terrace Avenue
Hasbrouck Heights, NJ 07604
Telephone: (201) 288-6330
Email: pmcgovern@uranj.com

McLean, Kelley C.
University of Vermont
Dept. of Ob/Gyn & MFM
University of Vermont Medical Center
111 Colchester Ave.
Burlington, VT 05401
Telephone: (303) 870-9691
Email: kelley.mclean@uvmhealth.org

Meczekalski, Blazej
Poznan University of Medical Sciences
Dept. of Gynecological Endocrinology
Fredry 10
Poznan, 61-701
Poland
Telephone: 48-61-841-9366
Email: blazejmeczekalski@yahoo.com

Mehendale, Ramkrishna
Rush University Medical Center
Dept. of Ob/Gyn
1725 W. Harrison
Suite 408
Chicago, IL 60612
Telephone: (312) 997-2229
Email: ramkrishna_mehendale@rush.edu

Mendelson, Carole R.
UT Southwestern
Dept. of Biochemistry
5323 Harry Hines Blvd
K3-106
Dallas, TX 75390-9038
Telephone: (214) 648-2944
Email: carole.mendelson@utsouthwestern.edu

Menon, K.M.J.
University of Michigan
Dept. of Ob/Gyn
1150 W. Medical Center Drive
6428 Medical Science 1
Ann Arbor, MI 48109-0617
Telephone: (734) 764-8142
Email: kmjmenon@umich.edu

Menon, Ramkumar
University of Texas Medical Branch
301 University Boulevard
OBGYN
Galveston, TX 77555-1062
Telephone: (409) 772-7596
Email: ra2menon@utmb.edu

Mercer, Brian M.
Case Western Reserve University
Dept. of Repro. Bio. & Ob-Gyn
MetroHealth Medical Center
2500 MetroHealth Dr., Ste. G267
Cleveland, OH 44109
Telephone: (216) 778-4876
Email: bmercer@metrohealth.org

Merhi, Zaher
5 Mill Pond Lane
New Rochelle, NY 10805
Telephone:
Email: zom00@hotmail.com

Merrill, David C.
Aurora Health Care
Aurora Women's Pavillion
8905 Lincoln Ave.
Suite 505
West Allis, WI 53227
Telephone: (414) 329-5647
Email: dave.merrill@aurora.org

Mesiano, Sam A.
Case Western Reserve University
Dept. of Reproductive Biology
MacDonald Women's Hosp. Rm8009
11100 Euclid Avenue
Cleveland, OH 44106-5034
Telephone: (216) 844-1553
Email: sam.mesiano@case.edu

Metz, Christine N.
The Feinstein Inst. for Med. Rsch.
350 Community Drive
Manhasset, NY 11030
Telephone: (516) 562-3403
Email: CMetz@NORTHWELL.edu

Meyer, Marjorie
University of Vermont
Dept. of Ob/Gyn
Smith 419
MCHV/FAHC
Burlington, VT 5401
Telephone: (802) 847-5066
Email: Marjorie.meyer@uvm.edu

Miller, Bradley T.
Reproductive Medicine Associates of Michigan, PLC
130 Town Center Drive
Suite 106
Troy, MI 48084
Telephone: (248) 619-3100
Email: bmiller@rmami.com

Minegishi, Takashi
Gunma University Graduate SOM
Dept. of Gyn. & Repro. Med.
3-39-22 Showa-machi
Maebashi
Gunma, 371-5811
Japan
Telephone: 81-27-220-8420
Email: tminegis@gunma-u.ac.jp

Mitchell, Bryan F.
University of Alberta
Dept. of Ob/Gyn
220 Heritage Medical Research Centre
227 HMRC
Edmonton, AB T6G 2S2
Canada
Telephone: (780) 492-8561
Email: brymitch@ualberta.ca

Mitchell, Murray D.
University of Queensland
Centre for Clinical Research
Building 71/918
RBWH Campus, Herston
Brisbane, QLD 4029
Australia
Telephone: 61-73-346-5016
Email: murray.mitchell@uq.edu.au

Miyoshi, Hiroshi
Hiroshima University Graduate School of Medicine
Dept. of Ob/Gyn
1-2-3 Kasumi, Minami-ku
Hiroshima, 734-8551
Japan
Telephone: 81-82-257-5262
Email: miyo36@hiroshima-u.ac.jp

Moalli, Pamela A.
Magee-Womens Research Institute
Dept. of Ob/Gyn/RS
204 Craft Avenue
Lab A320
Pittsburgh, PA 15213
Telephone: (412) 641-6052
Email: pmoalli@mail.magee.edu

Moley, Kelle H.
Washington University School of Medicine
BJC-IH Bldg 10th Floor
425 S. Euclid Avenue
St. Louis, MO 63110
Telephone: (314) 286-1765
Email: moleyk@wustl.edu

Monga, Manju
Baylor College of Medicine
Dept. of Ob/Gyn
One Baylor Plaza, Mail Stop 610
Houston, TX 77030
Telephone: (832) 826-7376
Email: monga@bcm.edu

Montgomery, Grant W.
The Institute for Molecular Bioscience
Institute for Molecular Bioscience
The University of Queensland
Brisbane, QLD 4072
Australia
Telephone: +61 7 3364 2612
Email: g.montgomery1@uq.edu.au

Moore Simas, Tiffany Anne
Univ. of Massachusetts Medical School/UMass Memorial Healthcare
UMMS/UMMHC
Dept of Ob/Gyn - Memorial Campus
119 Belmont Street - Jaquith 2.008
Worcester, MA 01605
Telephone: (508) 334-6678
Email: TiffanyA.MooreSimas@UMassMemorial.org

Moore, John J.
CWRU - MetroHealth
Dept. of Pediatrics
2500 MetroHealth Drive
249 Old Research Bldg.
Cleveland, OH 44109
Telephone: (216) 778-5946
Email: jmoore@metrohealth.org

Moore, Lorna G.
University of Colorado Denver
Dept. of Ob/Gyn
Anshutz Medical Campus, 12631 E. 17th Av
Mail Stop 8613, Research 2 Rm 3004
Aurora, CO 80045
Telephone: (303) 724-7474
Email: Lorna.Moore@ucdenver.edu

Moore, Robert M.
623 Oakhurst Drive
Brunswick, OH 44212
Telephone: (216) 496-7657
Email: rmm@case.edu

Moravek, Molly B.
University of Michigan
Center for Reproductive Medicine
475 Market Place, Bldg 1, Suite B
Ann Arbor, MI 48108
Telephone: (734) 972-5364
Email: mollymoravek@gmail.com

Morelli, Sara Sinha
Rutgers-New Jersey Medical School
185 South Orange Avenue
MSBE506
Newark, NJ 07103
Telephone: (917) 365-7034
Email: morellsa@njms.rutgers.edu

Morgan, Terry
Oregon HS University
Dept. of Pathology
3181 SW Sam Jackson Park Rd.
Mailcode: L471
Portland, OR 97239
Telephone: (503) 494-2771
Email: morgante@ohsu.edu

Morrison, Janna Leigh
University of South Australia
Sansom Institute for Health Research
P5-50 City East
GPO Box 2471
Adelaide, SA 5001
Australia
Telephone: 618-8302-2166
Email: janna.morrison@unisa.edu.au

Muneyyirci-Delale, Ozgul
SUNY Downstate Medical Center
Dept. of Ob/Gyn
450 Clarkson Avenue
Box 24, Rm. B3-492
Brooklyn, NY 11203
Telephone: (718) 270-2101
Email: ozgul.muneyyirci-delale@downstate.edu

Murtha, Amy P.
Duke University Medical Center
Dept. of Ob/Gyn
Box 3967, Div. of MFM
Trent Drive
Durham, NC 27710
Telephone: (919) 684-3225
Email: murth002@mc.duke.edu

Mutch, David G.
Washington University SOM
Div. of Gyn-Oncology
4911 Barnes Hospital Plaza
St. Louis, MO 63110
Telephone: (314) 362-3181
Email: mutchd@wudosis.wustl.edu

Myatt, Leslie
9435 SW View Point Terrace
Portland, OR 97219
Telephone: (503) 418-2781
Email: myattl@ohsu.edu

Myers, Dean A.
University of Oklahoma HSC
Dept. of Ob/Gyn
Suite 468, RP1, 800 Research Parkway
Ste. 468, Bldg. #1
Oklahoma City, OK 73104
Telephone: (405) 271-2286
Email: dean-myers@ouhsc.edu

Myers, Jenny
St. Mary's Hospital
Maternal-Fetal Health Rsch. Ctr.
University of Manchester
5th Floor (Research)
Manchester, M13 9WL
United Kingdom
Telephone: +44 161 7016963
Email: jenny.myers@manchester.ac.uk

Myers, Kristin
Columbia University
Mechanical Engineering
500 W 120th St, Mudd 200
New York, NY 10027
Telephone: (212) 854-2957
Email: kmm2233@cumc.columbia.edu

Mysorekar, Indira U.
Washington University SOM
Dept. of Ob/Gyn
660 South Euclid Avenue
St. Louis, MO 63110
Telephone: (314) 747-1329
Email: mysorekari@wudosis.wustl.edu

Nakajima, Steven T.
Stanford University
Fertility and Reproductive Health
1195 Fremont Ave., 1st Floor
Academic Office
Sunnyvale, CA 94087
Telephone: (408) 426-5483
Email: stnakajima@gmail.com

Napolitano, Peter G.
1305 Sequalish Street
Steilacoom, WA 98388
Telephone: (253) 968-3394
Email: doc.pete@ix.netcom.com

Narahara, Hisashi
Oita University
Dept. of Ob/Gyn
1-1 Idaigaoka, Hasama, Yufu
Oita, 879-5593
Japan
Telephone: 81-975-865-922
Email: naraharh@oita-u.ac.jp

Nathanielsz, Peter W.
University of Wyoming
Dept Animal Science
1000 E University Avenue
Laramie, WY 82071
Telephone: (210) 258-9549
Email: peter.nathanielsz@uwyo.edu

Nayak, Nihar R.
Wayne State University School of Medicine
Dept. of Ob/Gyn
275 E Hancock Ave
Detroit, MI 48201
Telephone: 313 577 8910
Email: nnayak@med.wayne.edu

Neal-Perry, Genevieve S.
University of Washington
Dept. of Ob/Gyn
1959 NE Pacific Street
Box 356460
Seattle, WA 98195-6460
Telephone: (206) 543-5231
Email: nealperr@uw.edu

Nelson, D. Michael
Washington University SOM
Dept. of Ob/Gyn
4566 Scott Avenue
Campus Box 8064
St. Louis, MO 63110-1094
Telephone: (314) 747-0738
Email: nelsondm@wudosis.wustl.edu

Newnham, John P.
University of Western Australia
School of Women's & Infant's Health
M550 University of Western Australia
35 Stirling Highway - Crawley
Perth, 6009
Australia
Telephone: 61-08-9340-1331
Email: john.newnham@uwa.edu.au

Nie, Guiying
Hudson Institute of Medical Research
Implantation & Placental Dvlp
Laboratory
27-31 Wright Street
Clayton
Melbourne, VIC 3168
Australia
Telephone: 61-3-9594-4380
Email: guiying.nie@Hudson.org.au

Nijhuis, Jan G.
Maastricht UMC
Dept. of Ob/Gyn
P. Debyelaan 25
PO Box 5800
Maastricht, 6202 AZ
Netherlands
Telephone: 31-43-387-4764
Email: jg.nijhuis@mumc.nl

Nold, Christopher J.
97 Brentwood Drive
Glastonbury, CT 06033
Telephone: (860) 972-2884
Email: christopher.nold@hhchealth.org

Norman, Jane E.
University of Edinburgh
MRC Centre for Reproductive Health
The Queens Medical Research Institute
47 Little France Crescent
Edinburgh, EH16 4TJ
United Kingdom
Telephone: 0-131-242-6623
Email: jane.norman@ed.ac.uk

Norwitz, Errol R.
Tufts University
Dept. of Ob/Gyn
800 Washington Street
Boston, MA 02111
Telephone: (617) 636-2382
Email: enorwitz@tuftsmedicalcenter.org

Nothnick, Warren B.
University of Kansas Medical Center
Molecular & Integrative Physiology
3901 Rainbow Blvd
3095 HLSIC
Kansas City, KS 66160
Telephone: (913) 588-6277
Email: wnothnic@kumc.edu

Ober, Carole
University of Chicago
Dept. of Human Genetics
920 E. 58th Street
Room 425
Chicago, IL 60637
Telephone: (773) 834-0735
Email: c-ober@genetics.uchicago.edu

O'Brien, William F.
MFM of SW Florida
8270 College Pkwy
205
Ft. Myers, FL 33919
Telephone: (239) 333-3826
Email: wfobrien@earthlink.net

Odunsi, Kunle
Roswell Park Cancer Institute
Dept. of Gyn/Oncology
Elm & Carlton Streets
Buffalo, NY 14263
Telephone: (716) 845-8376
Email: kunle.odunsi@roswellpark.org

Oehninger, Sergio C.
Jones Institute - EVMS
Dept. of Ob/Gyn
601 Colley Ave.
Norfolk, VA 23507
Telephone: (757) 446-7119
Email: oehninsc@evms.edu

Okamura, Kunihiro
Tohoku Kosai Hospital
Dept. of Ob/Gyn
2-3-11, Kokubuncho
Aoba-ku
Sendai, 980-0803
Japan
Telephone: 81-22-227-2211
Email: okamura@tohokukosai.com

Oktay, Kutluk H.
New York Medical College/Innovation
Fertility
Dept. of Ob/Gyn
Munger Pavillion Room 617
Rm. B05
Valhalla, NY 10595
Telephone: (914) 594-3435
Email: koktay@fertilitypreservation.org

Olive, David L.
Wisconsin Fertility Institute
3416 Deming Way
Middleton, WI 53562
Telephone: (608) 824-0075
Email: lapskyboy@aol.com

Olson, David M.
University of Alberta
Dept. of Ob/Gyn
220 HMRC
Edmonton, AB T6G 2S2
Canada
Telephone: (780) 492-8559
Email: david.olson@ualberta.ca

Ory, Steven J.
Florida International University
Dept. of Ob/Gyn
IVF Florida Reproductive Assoc
2960 North State Rd. 7, Ste. 300
Margate, FL 33063
Telephone: (954) 247-6247
Email: sjory@msn.com

Osol, George J.
University of Vermont College of
Medicine
Dept. of Ob/Gyn
C-217A, Given Bldg.
Health Science Complex
Burlington, VT 05405-0068
Telephone: (802) 656-1203
Email: george.osol@uvm.edu

Osteen, Kevin G.
Vanderbilt University Medical Center
Dept. of Ob/Gyn
B-1100 Medical Center North
Women's Reproductive Health
Research
Nashville, TN 37232-2519
Telephone: (615) 322-4196
Email: kevin.osteen@vanderbilt.edu

Osuga, Yutaka
The University of Tokyo
Obstetrics and Gynecology
7-3-1, Hongo, Bunkyo-ku
Tokyo, 113-8655
Japan
Telephone: 81-3-3815-5411
Email: yutakaos-tky@umin.ac.jp

O'Tierney-Ginn, Perrie Faye
MetroHealth Medical Center
2500 MetroHealth Drive
Cleveland, OH 44118
Telephone: 216-778-8983
Email: poginn@metrohealth.org

Padmanabhan, Vasantha
University of Michigan
7510 MSRB I
1150 West Medical Center Drive
Ann Arbor, MI 48109-5718
Telephone: (734) 647-0276
Email: Vasantha@umich.edu

Paidas, Michael J.
Yale University School of Medicine
333 Cedar St.
PO Box 208063
New Haven, CT 06460
Telephone: (203) 737-1982
Email: michael.paidas@yale.edu

Pancharatnam, Jeyasuria
Wayne State University
Dept. of Ob/Gyn, PRB (NICHD)
275 E Hancock St.
Room 338
Detroit, MI 48201
Telephone: (313) 577-2153
Email: suria@med.wayne.edu

Parast, Mana M.
University of California San Diego
Dept. of Pathology
9500 Gilman Dr, MC 0695
La Jolla, CA 92093
Telephone: (858) 534-8631
Email: mparast@ucsd.edu

Park, Chan-Wook
Seoul National University College of Medicine
Obstetrics and Gynecology
101 Daehak-ro, Jongno-gu
Seoul, 110-744
Korea
Telephone: 82-2-10-5350-9192
Email: csparkmd@hanmail.net

Parry, Samuel
University of Pennsylvania
Dept. of Ob/Gyn
2000 Ravdin Courtyard Building
3400 Spruce Street
Philadelphia, PA 19104-4283
Telephone: (215) 662-6913
Email: parry@mail.med.upenn.edu

Patel, Nima R.
Christiana Care Health System
4755 Ogletown Stanton Rd.
Suite 1905
Newark, DE 19718
Telephone: (302) 733-6610
Email: npatel@christianacare.org

Patrelli, Tito Silvio
University of Parma
Dept. of Mother & Child Health - Ob/Gyn
Viale F. Rodolfi, 37
Vicenza, 34100
Italy
Telephone: 00-393-392-81-7381
Email: titosilvio.patrelli@gmail.com

Pauli, Samuel A.
IVF New England / Boston IVF
1 Forbes Road
Lexington, MA 02421
Telephone: (800) 858-4832
Email: sapauli@yahoo.com

Pavone, Mary Ellen
1844 N. Sedgwick St Apt A
Chicago, IL 60614
Telephone: (312) 695-7269
Email: mepavone@yahoo.com

Pearce, William J.
Loma Linda University
Dept of Perinatal Biology
11234 Anderson Street
Loma Linda, CA 92350
Telephone: (951) 315-0243
Email: wpearce@llu.edu

Peebles, Donald M.
University College London
Institute for Women's Health
74 Huntley Street
London, WC1E 6AU
United Kingdom
Telephone: 44-20-7679-0834
Email: d.peebles@ucl.ac.uk

Pejovic, Tanja
Oregon Health & Science University
Dept. of Ob/Gyn
3181 SW Sam Jackson Park Rd.
L466
Portland, OR 97239
Telephone: (503) 494-3107
Email: pejovict@ohsu.edu

Pellicer, Antonio
University of Valencia
Instituto Valenciano de Infertilidad
Plaza Policia Local, 3
Valencia, 46015
Spain
Telephone: 34-96-305-0900
Email: pellicer124@gmail.com

Pennell, Craig E.
University of Western Australia
School of Women's & Infants Health
35 Stirling Highway
M550
Crawley, 6009
Australia
Telephone: 61-8-9340-1326
Email: craig.pennell@uwa.edu.au

Pennington, Kathleen A.
Baylor College of Medicine
1102 Bates Avenue
FC. 1870
Houston, TX 77030
Telephone: (832) 824-0402
Email: kapennin@bcm.edu

Pepe, Gerald J.
EVMS
Physiological Sciences
700 W. Olney Road
Norfolk, VA 23507
Telephone: (757) 446-5616
Email: pepegj@evms.edu

Perez, Maria Claudia
Takeda Pharmaceuticals
Medical Affairs
519 Washington Avenue
Wilmette, IL 60091
Telephone: (224)-554-2897
Email: maria.perez@takeda.com

Peterson, C. Matthew
University of Utah HSC
Dept. of Ob/Gyn
30 North 1900 East
2B200
Salt Lake City, UT 84132-2209
Telephone: (801) 587-8303
Email: c.matthew.peterson@hsc.utah.edu

Petraglia, Felice
University of Siena
Dept. of Molecular and Develop. Medicine
S. Maria Alle Scotte - Viale Bracci
Via Di Citta,46
Siena, 53100
Italy
Telephone: 39-0577-586-601
Email: felice.petraglia@unisi.it

Phillippe, Mark
Massachusetts General Hospital
Dept. of Obstetrics & Gynecology
55 Fruit Street
Founders Bldg, Rm 5-520
Boston, MA 02114
Telephone: (617) 724-1217
Email: MPhillippe@MGH.harvard.edu

Phipps, Maureen G.
Warren Alpert Medical School of Brown University
Departments of Ob/Gyn & Epidemiology
Women & Infants Hospital
101 Dudley Street
Providence, RI 02905
Telephone: (401) 274-1122 x:41575
Email: mphipps@wihri.org

Piper, Jeanna M.
18034 Red Rocks Drive
Germantown, MD 20874
Telephone: (240) 292-4798
Email: piperj@niaid.nih.gov

Pisarska, Margareta D.
Cedars Sinai Medical Center
Dept. of Ob/Gyn
8635 W. 3rd Street
Suite 160W
Los Angeles, CA 90048
Telephone: (310) 423-5763
Email: pisarskam@cshs.org

Platt, Lawrence D.
1505 Glenville
Los Angeles, CA 90035
Telephone: (323) 857-1952
Email: ldplatt@gmail.com

Polotsky, Alex J.
University of Colorado Denver
Dept. of Reproductive Endocrinology
12631 East 17th Avenue, Mail Stop B-198
Aurora, CO 80045
Telephone: (303) 724-2001
Email: alex.polotsky@ucdenver.edu

Popovici, Roxana M.
Center for Gynecologic Endocrinology and Reproductive Medicine
Bayerstr. 3
Munich, 80335
Germany
Telephone: 49-89-45221780
Email: roxana.popovici@kiiz.de

Poston, Lucilla
King's College London
Division of Women's Health
St. Thomas Hospital, Westminster Bridge
10th Floor, North Wing
London, SE1 7EH
United Kingdom
Telephone: 44-20-7188-3639
Email: lucilla.poston@kcl.ac.uk

Powell, Theresa
University of Colorado Anschutz Medical Campus
12700 East 19th Avenue, P15-3100A
Mail Stop 8613
Aurora, CO 80045
Telephone: (303) 724-2016
Email: theresa.powell@ucdenver.edu

Powers, Robert W.
University of Pittsburgh
Dept. of Ob/Gyn
204 Craft Ave
A311
Pittsburgh, PA 15213
Telephone: (412) 641-6005
Email: powersrw@upmc.edu

Pressman, Eva K.
University of Rochester
Dept. of Ob/Gyn
Strong Memorial Hospital
601 Elmwood Avenue, Box 668
Rochester, NY 14642
Telephone: (585) 275-5201
Email: eva_pressman@urmc.rochester.edu

Price, Thomas M.
Duke University Medical Center
Dept. of Ob/Gyn
Div of Reproductive Endocrinology
5704 Fayetteville Rd
Durham, NC 27713
Telephone: (919) 572-4673
Email: price067@mc.duke.edu

Qiang, Wenan
1680 Young Drive
Libertyville, IL 60048
Telephone: (847) 467-7382
Email: w-qiang@northwestern.edu

Qiao, Chong
China Medical University
Department of Obstetrics and Gynecology
No. 36, Sanhao Street, Heping District
Shenyang, 110004
Peoples Republic of China
Telephone: +86-18940251859
Email: qiaochong2002@hotmail.com

Quirk, J. Gerald
Stony Brook University SOM
Dept. of Ob/Gyn & Repro. Med.
UMC, HSC, T9-060
Stony Brook, NY 11794-8091
Telephone: (631) 444-3987
Email:

Racicot, Karen
Michigan State University
333 Bostwick Avenue NE
Phase 2, 4018
Grand Rapids, MI 49503
Telephone: (616) 234-0986
Email: karen.racicot@hc.msu.edu

Raha, Sandeep
McMaster University
Dept. of Pediatrics
1280 Main Street West
HSC-3N11j
Hamilton, ON L8S 4K1
Canada
Telephone: (905) 521-2100
Email: rahas@mcmaster.ca

Rajakumar, Augustine
Emory University School of Medicine
Gynecology & Obstetrics
101 WoodruffCircle
4329 WMB
Atlanta, GA 30322
Telephone:
Email: arajaku@emory.edu

Rajkovic, Aleksandar
Magee Women's Research
204 Craft Ave.
Pittsburgh, PA 15213
Telephone: (412) 641-7531
Email: rajkovic@upmc.edu

Ramadoss, Jay
Texas A&M University
Physiology and Pharmacology
4466 TAMU
College Station, TX 77843-4466
Telephone: (979) 458-3280
Email: jramadoss@cvm.tamu.edu

Ramin, Kirk D.
University of Minnesota
Dept. of Ob/Gyn
606 24th Ave., S.
Suite 401
Minneapolis, MN 55454
Telephone: (612) 301-3414
Email: ramin003@umn.edu

Rana, Sarosh
University of Chicago
Department of Obstetrics and Gynecology
5841 S. Maryland Avenue
MC 2050
Chicago, IL 60637
Telephone: (773) 702-9866
Email: saroshrana@gmail.com

Randolph, John F.
University of Michigan
Dept. of Ob/Gyn
1500 East Medical Center Dr.
Ann Arbor, MI 48109-0617
Telephone: (734) 936-7401
Email: jfrandol@med.umich.edu

Rao, C.V.
Florida International Univ.
Cell Biology, Molecular & Human Genetics
Herbert Wertheim COM, 11200 S.W. 8th St
Modesto A.Maidque Campus, GL495C
Miami, FL 33199
Telephone: (305) 348-0659
Email: crao@fiu.edu

Rapkin, Andrea J.
UCLA Medical Center
Dept. of Ob/Gyn
10833 LeConte Ave.
27-139 CHS
Los Angeles, CA 90095-1740
Telephone: (310) 825-6963
Email: arapkin@mednet.ucla.edu

Rappolee, Daniel A.
Wayne State University Medical School
Dept. of Ob/Gyn
275 East Hancock Street
Detroit, MI 48201
Telephone: (313) 577-1228
Email: drappole@gmail.com

Rauk, Phillip N.
University of Minnesota
Dept. of Ob/Gyn
MMC 395
420 Delaware Street, S.E.
Minneapolis, MN 55455
Telephone: (612) 301-3414
Email: raukx004@umn.edu

Reece, E. Albert
University of Maryland SOM
655 W. Baltimore St.
Room 14029
Baltimore, MD 21201-1559
Telephone: (410) 706-7410
Email: deanmed@som.umaryland.edu

Reed, Kathryn L.
University of Arizona
Dept. of Ob/Gyn
Arizona Health Science Center
1501 N. Campbell Ave.
Tucson, AZ 85724
Telephone: (520) 626-6174
Email: kreed@u.arizona.edu

Reed, Susan D.
University of Washington
FHCRC 1100 Fariview Ave N
Seattle, WA 98104-2499
Telephone: (206) 667-6509
Email: reeds@uw.edu

Reese, Jeff
Vanderbilt University Med Center
Dept. of Pediatrics
1135 MRB IV Bldg.
2215 B Garland Ave.
Nashville, TN 37232
Telephone: (615) 322-3476
Email: jeff.reese@vanderbilt.edu

Reinheimer, Torsten M.
Ferring Pharmaceuticals A/S
Non-Clinical Development
Kay Fiskers Plads 11
Copenhagen, DK-2300
Denmark
Telephone: 45-28-78-7452
Email: trr@ferring.com

Reis, Fernando M.
University of Minas Gerais
Dept. of Ob/Gyn
Av. Alfredo Balena, 110
9o Andar
Belo Horizonte, 30130-100
Brazil
Telephone: (55-31) 3409-9845
Email: fmreis@ufmg.br

Reiter, Jill L.
Indiana University SOM
Dept. of Ob/Gyn
975 W Walnut St.
IB 356
Indianapolis, IN 46202
Telephone: (317) 278-8052
Email: jireiter@iupui.edu

Repke, John T.
Penn State University
Dept. of Ob/Gyn
M.S. Hershey Medical Center
500 University Dr., MC:H103
Hershey, PA 17033-0850
Telephone: (717) 531-8629
Email: jrepke@psu.edu

Reynolds, Lawrence Paul
North Dakota State University, Center for Nutrition & Pregnancy
Center for Nutrition and Pregnancy
Hultz Hall, NDSU Dept. 7630
PO Box 6050
Fargo, ND 58108-6050
Telephone: (701) 231-7646
Email: larry.reynolds@ndsu.edu

Rice, Laurel W.
University of Wisconsin-Madison
Dept. of Ob/Gyn
McConnell Hall, 4th Floor
1010 Mound Street
Madison, WI 53715
Telephone: (608) 417-4213
Email: lwrice@wisc.edu

Richardson, Bryan S.
University of Western Ontario
Dept. of Ob/Gyn
LHSC Victoria Hospital Room E2-620G
800 Commisioner`s Road E
London, ON N6A 5W9
Canada
Telephone: (519) 646-6106
Email: brichar1@uwo.ca

Rinaudo, Paolo Francesco
UCSF
Dept. of Ob/Gyn
513 Parnassus Ave.
San Francisco, CA 94143
Telephone: (415) 353-7475
Email: rinaudop@obgyn.ucsf.edu

Roberts, Claire T.
University of Adelaide
Robinson Research Institute
Adelaide, SA 5005
Australia
Telephone: 61-8-831-33118
Email: claire.roberts@adelaide.edu.au

Roberts, James M.
Magee Women's Research Institute
University of Pittsburgh
Dept. of Ob/Gyn
204 Craft Avenue, Suite A311-B
Pittsburgh, PA 15213-3180
Telephone: (412) 641-1427
Email: jroberts@mwri.magee.edu

Roberts, Victoria HJ
Oregon National Primate Res. Ctr.
Div of Diabetes, Obesity & Metabolism
505 NW 185th Ave.
Beaverton, OR 97006
Telephone: (503) 690-5288
Email: robertsv@ohsu.edu

Robertson, Sarah Anne
The University of Adelaide
Dept. of Paediatrics & Repro. Health
Medical School, Frome Road
Adelaide, SA 5005
Australia
Telephone: 61-8-831-34094
Email: sarah.robertson@adelaide.edu.au

Robins, Jared
Northwestern University Feinberg School of Medicine
676 N. St. Clair
Suite #1845
Chicago, IL 60611
Telephone: (312) 926-8244
Email: jared.robins@northwestern.edu

Robinson, Randal D.
University of Texas HSC-San Antonio
Dept. of Ob/Gyn
Mail Code 7836
7703 Floyd Curl Drive
San Antonio, TX 78229
Telephone: (210) 567-4924
Email: robinsonr3@uthscsa.edu

Rogers, Peter A.w.
University of Melbourne
Royal Women's Hospital/Dept. of Ob/Gyn
Flemington Road
Parkville, VIC 3052
Australia
Telephone: 61-3-834-53722
Email: parogers@unimelb.edu.au

Roh, Cheong-Rae
Samsung Medical Center
Dept. of Ob/Gyn
81 Ilwon-Ro
Gangnam-Gu
Seoul, 135-710
Korea
Telephone: 82-2-3410-3516
Email: crroh@skku.edu

Romero, Roberto
Perinatology Research Branch of NICHD/NIH
Perinatology Research Branch
3990 John R, 4 Brush South
Detroit, MI 48201
Telephone: (313) 993-2700
Email: prbchiefstaff@med.wayne.edu

Rosenn, Barak M.
523 Harbor Place
West New York, NJ 07093
Telephone: (212) 523-6266
Email: brosenn@chpnet.org

Rosenwaks, Zev
Cornell University, Weill Medical College
Ronald O. Perelman & Claudia Cohen Center for Repro. Medicine & Infertility
1305 York Ave., 7th Floor
New York, NY 10021
Telephone: (646) 962-3745
Email: zrosenw@med.cornell.edu

Ross, Michael G.
Geffen School of Medicine at UCLA
Dept. of Ob/Gyn
1000 W. Carson Street, RB3, Box 467
Torrance, CA 90502
Telephone: (310) 781-3628
Email: mikeross@ucla.edu

Rozance, Paul J.
University of Colorado School of Medicine
13243 E. 23rd. Ave. F441
Aurora, CO 80045
Telephone: (303) 724-1149
Email: paul.rozance@ucdenver.edu

Rueda, Bo R.
MGH_Harvard Medical School
Dept. of Ob/Gyn
55 Fruit Street, THR 9
THR 901
Boston, MA 02114
Telephone: (617) 724-2825
Email: brueda@MGH.Harvard.edu

Saade, George R.
UTMB
Dept. of OB/Gyn
301 University Blvd.
3.400 JSA
Galveston, TX 77555-0587
Telephone: (409) 747-0482
Email: gsaade@utmb.edu

Sadovsky, Yoel
Magee-Womens Research Inst.
University of Pittsburgh Dept of OBGYN
204 Craft Avenue
Pittsburgh, PA 15213
Telephone: (412) 641-2675
Email: ysadovsky@mwri.magee.edu

Saed, Ghassan M.
Wayne State University
Dept. of Ob/Gyn
275 East Hancock Street
Detroit, MI 48201
Telephone: (313) 577-5433
Email: gsaed@med.wayne.edu

Salafia, Carolyn Margaret
Placental Analytics, LLC
187 Overlook
Circle
New Rochelle, NY 10804
Telephone: (914)834-3764
Email: carolyn.salafia@gmail.com

Salamat, Sharon M.
Perinatal Research & Consulting
12545 SW 68th Court
Pinecrest, FL 33156
Telephone: (954) 447-2704
Email: ssalamat@bellsouth.net

Salih, Sana M.
West Virginia University
Dept. of Ob/Gyn
PO Box 9186
1322 Pineview Drive
Morgantown, WV 26505
Telephone: (608) 442 1328
Email: sanasalih5@gmail.com

Sameshima, Hiroshi
University of Miyazaki
Dept. of Ob/Gyn
Center for Perinatal Medicine
5200 Kihara, Kiyotake
Miyazaki, 889-1692
Japan
Telephone: 81-985-85-0988
Email: hsameshima@med.miyazaki-u.ac.jp

Sanfilippo, Joseph S.
Magee Women's Hospital
Dept. of Ob/Gyn & REI
300 Halket Street
Room 2309
Pittsburgh, PA 15213-3180
Telephone: (412) 641-1204
Email: jsanfilippo@mail.magee.edu

Santin, Alessandro D.
Yale University SOM
Dept. of Ob/Gyn
333 Cedar Street
PO Box 208063, LSOG 305
New Haven, CT 06520
Telephone: (203) 737-4450
Email: alessandro.santin@yale.edu

Santolaya-Forgas, Joaquin
Jersey Shore University Medical Center
Perinatal Institute
Medical Arts Building. Suite 204.
1944 Route 33
Neptune, NJ 07753
Telephone: (732) 776-4755
Email: jsantolaya@meridianhealth.com

Santoro, Nanette F.
University of Colorado
Dept. of Ob/Gyn
12631 East 17th Avenue, Mailstop B-198
Academic Office. 1, Rm. 4004
Aurora, CO 80045
Telephone: (303) 724-2041
Email: nanette.santoro@ucdenver.edu

Sasa, Hidenori
National Defense Medical College
Dept. of Ob/Gyn
3-2 Namiki
Tokorozawa, 359-8513
Japan
Telephone: 81-4-2995-1687
Email: hsasa@ndmc.ac.jp

Sauer, Mark V.
Columbia University
Dept. of Ob/Gyn
College of Physicians and Surgeons
622 West 168th Street, PH16-69
New York, NY 10032-3784
Telephone: (212) 305-9175
Email: mvs9@columbia.edu

Saunders, Philippa T.
University of Edinburgh
Centre for Inflammation Research
Queen's Medical Research Institute
Edinburgh, EH164TJ
United Kingdom
Telephone: 0-13-124-246-388
Email: p.saunders@ed.ac.uk

Sayegh, Raja A.
Boston University SOM
Dept. of Ob/Gyn
720 Harrison Ave.
DOB Suite 1105
Boston, MA 02118-2526
Telephone: (617) 638-7851
Email: raja.sayegh@bmc.org

Schenken, Robert S.
UTHSC-San Antonio
Dept. of Ob/Gyn
7703 Floyd Curl Drive, MSC 7836
San Antonio, TX 78229-3901
Telephone: (210) 567-4950
Email: schenken@uthscsa.edu

Schiff, Isaac
Massachusetts General Hospital
Dept. of Ob/Gyn
55 Fruit Street
Boston, MA 02114
Telephone: (617) 726-3001
Email: ischiff@partners.org

Schlaff, William D.
Sidney Kimmel Medical College,
Thomas Jefferson University
Dept. of Ob/Gyn
833 Chestnut Street
Mezzanine Level
Philadelphia, PA 19107
Telephone: (215) 955-5577
Email: william.schlaff@jefferson.edu

Schmella, Mandy J.
University of Pittsburgh School of Nursing
440 Victoria Building
3500 Victoria Street
Pittsburgh, PA 15261
Telephone: (717) 250-1875
Email: mjb111@pitt.edu

Schoeberlein, Andreina
University of Bern & University Women's Hospital Bern
Laboratory for Prenatal Medicine
Inselspital
KKL P302
Bern, 3010
Switzerland
Telephone: +41316328517
Email: andreina.schoeberlein@dkf.unibe.ch

Schulz, Laura C.
University of Missouri
Dept of Ob-Gyn & Women's Health
NW509 Health Sciences Center
1 Hospital Drive
Columbia, MO 65212
Telephone: (573) 884-1408
Email: schulzl@missouri.edu

Schust, Danny J.
Univ. of Missouri-Columbia SOM
Dept. of Ob/Gyn & Women's Health
500 N. Keene St
Suite 203
Columbia, MO 65201
Telephone: (573) 817-3114
Email: schustd@health.missouri.edu

Schwartz, Peter E.
Yale SOM
Dept. of Ob/Gyn
333 Cedar Street, Room FMB 328
PO Box 208063
New Haven, CT 06520-8063
Telephone: (203) 785-4014
Email: peter.schwartz@yale.edu

Sciscione, Anthony C.
Delaware Center for Maternal and Fetal Medicine of Christiana Care
1 Centurian Drive
Suite 312
Newark, DE 19713
Telephone: (302) 319-5680
Email: asciscione@christianacare.org

Scott, Richard T.
Reproductive Medicine Associates
140 Allen Road
Basking Ridge, NJ 07920
Telephone: (973) 656-2831
Email: nancyn@rmanj.com

Segars, James H.
Johns Hopkins University School of Medicine
Division of Reproductive Sciences
720 Rutland Avenue
Room 624, Ross
Baltimore, MD 21205
Telephone: (410) 614-2000
Email: jsegars2@jhmi.edu

Seifer, David B.
3601 SW River Pkwy
Suite 2010
Portland, OR 97239
Telephone: (718) 283-8600
Email: dseifer@comcast.net

Seli, Emre
Yale SOM
Dept. of Ob/Gyn
310 Cedar Street, P.O. Box 208063
LSOG 304B
New Haven, CT 06520-8063
Telephone: (203) 785-7873
Email: emre.seli@yale.edu

Session, Donna R.
Vanderbilt University
3042 Flagstone Dr
Franklin, TN 37069
Telephone: (404) 556-9434
Email: Drsession@comcast.net

Severi, Filiberto Maria
University of Siena
Dept. of Peds., Ob. & Repro. Med.
Viale Bracci
Siena, 53100
Italy
Telephone: 39-0577586515
Email: filiberto.severi@unisi.it

Sfakianaki, Anna Katerina
Yale University School of Medicine
Dept. of Ob/Gyn
333 Cedar St.
PO Box 208063
New Haven, CT 06520-8063
Telephone: (203) 785-2671
Email: anna.sfakianaki@yale.edu

Shah, Dinesh M.
University of Wisconsin-Madison
Meriter Hospital/McConnell Hall [4th Fl]
Dept. of Ob/Gyn, Div. of MFM
1010 Mound St
Madison, WI 53715
Telephone: (608) 417-6099
Email: dmshah@wisc.edu

Shalev, Eliezer
Technion, Israel
Faculty of Medicine
1 Efron St
Haifa, 31096
Israel
Telephone: 972-4-8295200
Email: shaleve@technion.ac.il

Shibata, Eiji
Univ. of Occupational and Environmental Hlth.
Maternal & Child HC
Japan Environmental & Children's Study
1-1 Iseigaoka, Yahatanishi-ku
Kitakyushu, 807-8555
Japan
Telephone: 81-0-93-284-5180
Email: age-s@med.uoeh-u.ac.jp

Shifren, Jan L.
Massachusetts General Hospital
Vincent Ob/Gyn Service
55 Fruit Street
YAW 10A
Boston, MA 02114
Telephone: (617) 726-8868
Email: jshifren@partners.org

Shoupe, Donna
16534 Las Casas Place
Pacific Palisades, CA 90272
Telephone: (323) 226-3351
Email: shoupe@usc.edu

Shulman, Lee P.
4134 Rutgers Lane
Northbrook, IL 60062
Telephone: (312) 472-4683
Email: lshulman@nm.org

Sibley, Colin P.
University of Manchester
Maternal & Fetal Health Research Group
St. Mary's Hospital
Oxford Road
Manchester, M13 9WL
United Kingdom
Telephone: 44-161-276-6484
Email: colin.sibley@manchester.ac.uk

Siler-Khodr, Theresa M.
Center for Investigation of Cell Regulation & Replication
7614 Louis Pasteur, Ste 320
San Antonio, TX 78229
Telephone: (210) 615-8249
Email: Cicrr4@aol.com

Silver, Richard K.
NorthShore University HealthSystem
Dept. of Ob/Gyn
2650 Ridge Ave.
Suite 1507
Evanston, IL 60201
Telephone: (847) 570-2521
Email: rsilver@northshore.org

Silver, Robert M.
University of Utah
Dept. of Ob/Gyn
30 N. 1900 E. SOM 2B200
Salt Lake City, UT 84132
Telephone: (801) 581-8425
Email: bob.silver@hsc.utah.edu

Simhan, Hyagriv N.
Magee Women's Hospital
Dept. of Ob/Gyn
300 Halket Street
Room 2228
Pittsburgh, PA 15213
Telephone: (412) 641-4874
Email: hsimhan@mail.magee.edu

Simon, Carlos
Igenomix; Valencia University; INCLIVA; Stanford University
Igenomix
Narcis Monturiol Estarriol, 11 B
Edificio Europark, Parque Tecnologico Paterna (Valencia), 46980
Spain
Telephone: 34-96-390-5310
Email: carlos.simon@igenomix.com

Simon, Melissa Andrea
Northwestern University SOM
Dept. of Ob/Gyn
633 N. St Clair
Suite 1800
Chicago, IL 60611
Telephone: (312) 503-0808
Email: Simonmelissa@yahoo.com

Simpson, Joe Leigh
March of Dimes Foundation
1275 Mamaroneck Avenue
White Plains, NY 10605
Telephone: (914) 997-4555
Email: jsimpson@marchofdimes.org

Singer, Tomer
North Shore LIJ Health System
Dept. of Ob/Gyn
Lenox Hill Hospital
150 East 71st Street
New York, NY 10021
Telephone: (212) 324-2229
Email: tsinger@nshs.edu

Sites, Cynthia K.
Baystate Medical Center, Tufts University School of Medicine
Dept. of Ob/Gyn
759 Chestnut Street, S1683
Springfield, MA 01199
Telephone: (413) 794-5608
Email: cynthia.sites@baystatehealth.org

Skaznik-Wikiel, Malgorzata E.
University of Colorado School of Medicine
Department of Obstetrics and Gynecology
12631 E 17th Avenue, AO-1
Mail Stop B198-3
Aurora, CO 80045
Telephone: 303-724-2014
Email: malgorzata.skaznik-wikiel@ucdenver.edu

Slater, Donna M.
Calgary University
Dept. of Physiology & Pharmacology
277 Heritage Medical Research Bldg.
Rm. 280/ 282A, 3330 Hospital Dr. NW.
Calgary, AB T2N 4N1
Canada
Telephone: (403) 210-7660
Email: dmslater@ucalgary.ca

Slayden, Ov Daniel
Oregon Health & Sciences University
Div. Reproductive & Dvlp Sciences
Oregon National Primate Research Center
505 NW 185th Ave.
Beaverton, OR 97006
Telephone: (503) 609-5320
Email: slaydeno@ohsu.edu

Smith, Gordon C.S.
University of Cambridge
Dept. of Ob/Gyn
The Rosie Hospital
Robinson Way, Box 223
Cambridge, CB2 0SW
United Kingdom
Telephone: 44-0-1223-336871
Email: paoandghod@medschl.cam.ac.uk

Smith, Graeme N.
Queen's University
Dept. of Ob/Gyn
Kingston Hospital, 76 Stuart St.
Kingston, ON K7L2V7
Canada
Telephone: (613) 548-2405
Email: gns@queensu.ca

Smith, Roger
University of Newcastle
Mothers & Babies Research Centre
HMRI-MBRC Level 3East HMRI
University Drive Callaghan
Newcastle, NSW 2310
Australia
Telephone: 61-499771492
Email: roger.smith@newcastle.edu.au

Smith, Yolanda R.
University of Michigan Health System
L4000 UH-South
1500 E. Medical Center Dr.
Ann Arbor, MI 48109
Telephone: (732) 232-9033
Email: ysmith@med.umich.edu

Smulian, John C.
Lehigh Valley Health Network
Dept. of Ob/Gyn
3900 Hamilton Blvd
Suite 201
Allentown, PA 18103
Telephone: (484) 664-7521
Email: john.smulian@lvhn.org

Socol, Michael L.
Northwestern University Feinberg SOM
Dept. of Ob/Gyn & MFM
250 E. Superior St.
Suite 5-2182
Chicago, IL 60611
Telephone: (312) 472-4685
Email: msocol@nmh.org

Sood, Anil K.
UT MD Anderson Cancer Ctr.
Dept. of Ob/Gyn & Reproductive Medicine
1155 Herman P. Pressler
Unit 1362
Houston, TX 77030
Telephone: (713) 745-5266
Email: asood@mdanderson.org

Spaanderman, Marc E.
Maastricht University MC
Dept. of Ob/Gyn
PO Box 5800
Maastricht, 6202 AZ
Netherlands
Telephone: 03-143-387-4764
Email: marc.spaanderman@mumc.nl

Spencer, Jessica B.
Emory University SOM
Emory Reproductive Center
550 Peachtree Street
Suite 1800
Atlanta, GA 30308
Telephone: (310) 508-0005
Email: jbspenc@emory.edu

Spencer, Thomas E.
University of Missouri
Division of Animal Sciences
S158A ASRC
920 East Campus Drive
Columbia, MO 65211-5300
Telephone: (573) 882-3467
Email: spencerte@missouri.edu

Stanczyk, Frank Z.
USC Keck SOM
Dept. of Ob/Gyn
Livingston Research Building
1321 North Mission Road
Los Angeles, CA 90033
Telephone: (323) 226-3220
Email: fstanczyk@att.net

Stanic, Aleksandar
University of Wisconsin-Madison
Dept. of Ob/Gyn
Division of Reproductive Sciences
202 S Park Street, Atrium B Meriter Hosp
Madison, WI 53715
Telephone: (608) 417-4229
Email: stanickostic@wisc.edu

Steegers, Eric A.P.
Erasmus University MC
Dept. of Obstetrics & Prenatal Medicine
University Medical Centre Rotterdam
PO Box 2040
Rotterdam, 3000 CA
Netherlands
Telephone: 31-10-7036886
Email: e.a.p.steegers@erasmusmc.nl

Stephenson, Mary D.
University of Illinois at Chicago
OB/GYN
Reproductive Endocrinology & Infertility
820 South Wood Street, MC 808
Chicago, IL 60612
Telephone: (312) 996-7006
Email: msteph@uic.edu

Stewart, Elizabeth A.
Mayo Clinic and Mayo SOM
Dept. of Ob/Gyn
Charlton 3A
200 First Street SW
Rochester, MN 55905
Telephone: (507) 266-3845
Email: stewart.elizabeth@mayo.edu

Stock, Sarah J.E.
University of Edinburgh
MRC Centre for Reproductive Health
Queen's Medical Research Institute
Little France
Edinburgh, EH16 4TJ
United Kingdom
Telephone: +44-131-242-6449
Email: sarah.stock@ed.ac.uk

Stone, Joanne
Mount Sinai Medical Center
Dept. of Ob/Gyn
5 East 98th Street
Box 1171
New York, NY 10029
Telephone: (212) 241-0535
Email: joanne.stone@mssm.edu

Stonestreet, Barbara S.
Women & Infants Hospital of RI
Dept. of Pediatrics
101 Dudley Street
Providence, RI 02905
Telephone: (401) 274-1122 ext 47429
Email: Bstonestreet@wihri.org

Stratton, Pamela
11824 Farmland Dr
Rockville, MD 20852
Telephone: (301) 496-9079
Email: strattop@mail.nih.gov

Straughen, Jennifer K.
Henry Ford Health System
Department of Public Health Sciences
1 Ford Place
Detroit, MI 48202
Telephone: 1-313-874-3764
Email: jstraug1@hfhs.org

Strauss, Jerome F.
Virginia Commonwealth University
VCU School of Medicine
1201 East Marshall Street
4th Floor, Suite 4-100
Richmond, VA 23298
Telephone: (804) 828-9788
Email: jerome.strauss@vcuhealth.org

Strickler, Ronald C.
44 Colonial Road
Grosse Pointe Shores, MI 48236
Telephone: (248) 637-4050
Email: rstrick1@hfhs.org

Stuebe, Alison Mann
University of North Carolina at Chapel Hill
3010 Old Clinic Bldg.
CB# 7516
Chapel Hill, NC 27599-7516
Telephone: (919) 966-1601
Email: astuebe@med.unc.edu

Styer, Aaron K.
Massachusetts General Hospital/ Harvard Medical School
Dept. of Ob/Gyn
55 Fruit Street, Yaw 10A
Boston, MA 02114
Telephone: (617) 726-6942
Email: astyer@partners.org

Su, Emily J.
University of Colorado Denver
12700 E. 19th Avenue, MS8613
Aurora, CO 80045
Telephone: (303) 724-9227
Email: emily.su@ucdenver.edu

Sugawara, Junichi
Tohoku Medical Megabank Organization, Tohoku University
Feto-Maternal Medical Science
2-1, Seiryocho
Aobaku
Sendai, 980-8573
Japan
Telephone: 81-22-273-6283
Email: jsugawara@med.tohoku.ac.jp

Sugimura, Motoi
Hamamatsu University SOM
Dept. of Ob,Gyn and FM
1-20-1 Handayama
Hamamatsu, 431-3192
Japan
Telephone: 81-53-435-2309
Email: msugimu@juntendo.ac.jp

Surbek, Daniel V.
University of Bern
Dept. of Ob/Gyn
University Women's Hospital
Effingerstr, 102
Bern, 3010
Switzerland
Telephone: +41-79-239-21-91
Email: daniel.surbek@insel.ch

Swamy, Geeta K.
Duke University
Dept. of Ob/Gyn
DUMC Box 3967
Durham, NC 27710
Telephone: (919) 681-5220 or (919) 6
Email: swamy002@mc.duke.edu

Tanaka, Mamoru
Keio University SOM
Dept of Ob-Gyn
Shinanomachi 35
Shinjuku-ku
Tokyo, 160-8582
Japan
Telephone: 81-3-3353-1211
Email: mtanaka@keio.jp

Tarlatzis, Basil C.
School of Medicine, Aristotle University of Thessaloniki
9 Agias Sofias Street
Thessaloniki, 54623
Greece
Telephone: 30-2310-991508
Email: basil.tarlatzis@gmail.com

Tayade, Chandrakant
Queen's University
Botterell Hall
Room 916
Kingston, ON K7L 3N6
Canada
Telephone: (613) 533-6354
Email: tayadec@queensu.ca

Taylor, Anthony Henry
University of Leicester
Medical Education
Room 2.56 Centre for Medicne
Leicester, LE2 7RH
United Kingdom
Telephone: 44-116 373 6209
Email: superdoc.at@gmail.com

Taylor, Hugh S.
Yale University SOM
Dept. of Ob/Gyn
333 Cedar Street
P.O. Box 208063
New Haven, CT 06520-8063
Telephone: (203) 785-4001
Email: hugh.taylor@yale.edu

Taylor, Robert N.
Wake Forest SOM
Dept. of Ob/Gyn
1 Medical Center Blvd.
Winston-Salem, NC 27157-1066
Telephone: (336) 716-5451
Email: rtaylor@wakehealth.edu

Teixeira, Jose
Michigan State University
Dept. of Ob/Gyn & Repro. Biology
333 Bostwick Ave. NE
Room 4018A
Grand Rapids, MI 49503
Telephone: (616) 234-0976
Email: jose.teixeira@hc.msu.edu

Thaete, Larry G.
NorthShore University HealthSystem
Dept. of Ob/Gyn
2650 Ridge Avenue
Walgreen #1507
Evanston, IL 60201
Telephone: (847) 570-2372
Email: lthaete@northshore.org

Thomas, Michael A.
University of Cincinnati
Dept. of Ob/Gyn
2123 Auburn Avenue
Suite A44
Cincinnati, OH 45219
Telephone: (513) 584-0739
Email: michael.thomas@uc.edu

Thompson, Loren P.
University of Maryland SOM
Dept. of Ob/Gyn & Repro. Sci.
655 W. Baltimore Street
(BRB 11-029)
Baltimore, MD 21201
Telephone: (410) 706-4422
Email: lthompson1@umm.edu

Thornburg, Kent L.
Oregon Health & Science University
Heart Research Center
3030 SW Moody Ave
Mailcode: MDYMI
Portland, OR 97239
Telephone: (503) 494-4238
Email: thornbur@ohsu.edu

Thornburg, Loralei L.
University of Rochester
Dept. of Ob/Gyn
601 Elmwood Ave.
Box 668
Rochester, NY 14642
Telephone: (585) 275-7480
Email: loralei_thornburg@urmc.rochester.edu

Thung, Stephen F.
Ohio State University
Dept. of Ob/Gyn
395 West 12th Street, 5th Floor
Columbus, OH 43210
Telephone: (614) 293-4929
Email: stephen.thung@osumc.edu

Tilly, Jonathan L.
Northeastern University
Department of Biology
134 Mugar Life Sciences Building
360 Huntington Avenue
Boston, MA 02115
Telephone: (617) 373-2260
Email: j.tilly@northeastern.edu

Timms, Kathy L.
University of Missouri-Columbia
Dept. of Ob/Gyn & Women's Health
Div of Reproductive & Perinatal Research
1 Hospital Dr., NW510 HSC Dc051.00
Columbia, MO 65212
Telephone: (573) 882-1725
Email: timmsk@health.missouri.edu

Tomoda, Shoji
3-16-12 Mozu-Umemachi, Kita-ku
Sakai, 591-8032
Japan
Telephone: 81-72-250-9235
Email: shoji-kun1028@zeus.eonet.ne.jp

Tong, Stephen
University of Melbourne
Dept. of Ob/Gyn
Level 4, 163 Studley Road
Mercy Hospital for Women
Heidelberg, VIC 3084
Australia
Telephone: 61-384-58-4377
Email: stong@unimelb.edu.au

Tribe, Rachel M.
King's College London
Div. of Women's Health
10th Flr NW, St Thomas's Hospital Campus
Westminster Bridge Road
London, SE1 7EH
United Kingdom
Telephone: 00-44-207-188-3635
Email: rachel.tribe@kcl.ac.uk

Tschugguel, Walter
Medical University of Vienna
Nibelungengasse 1-3/2/4A
Vienna, A-1010
Austria
Telephone: 4314040029150
Email: walter.tschugguel@meduniwien.ac.at

Tsibris, John C. M.
University of South Florida
Dept. of Ob/Gyn
12901 Bruce B. Downs Blvd.
MDC 18
Tampa, FL 33612
Telephone: (813) 974-7025
Email: jtsibris@health.usf.edu

Tskitishvili, Ekaterine
Faculty of Medicine, University of Liege
Dept. of Ob/Gyn
Pathology Tower 4 (B23), Sart-Tilman
Lab of Tumor & Development Biology
Liege, B-4000
Belgium
Telephone: 32-4-366-2569
Email: ekaterinet@hotmail.com

Udagawa, Jun
Shiga University of Medical Science
Division of Anatomy and Cell Biology
Dept. of Anatomy
Seta Tsukinowa-cho
Otsu, 520 2192
Japan
Telephone: 81-77-548-2135
Email: udagawa@belle.shiga-med.ac.jp

Udoff, Laurence
Genetics & IVF Institute
3015 Williams Drive
#300
Fairfax, VA 22031
Telephone: (703) 289-1795
Email: ludoff@givf.com

Umans, Jason G.
MedStar Health Research Institute
6525 Belcrest Rd, Ste 700
Hyattsville, MD 20782
Telephone: (301) 560-2959
Email: jason.umans@gmail.com

Valenzuela, Guillermo J.
Valley Ob-Gyn
Dept. of Ob/Gyn
PO Box 1762
Colton, CA 92324
Telephone: (909) 580-3470
Email: valenzuelag@armc.sbcounty.gov

Van Den Veyver, Ignatia B.
Baylor College of Medicine
Dept. of Ob/Gyn
Duncan Neurological Research Institute
1250 Moursund Street, N1025.14
Houston, TX 77030
Telephone: 832-824-8125
Email: iveyver@bcm.edu

Van Lith, Jan M.
LUMC
Dept. of Obstetrics and Fetal Medicine
PO Box 9600
Leiden, 2300 RC
Netherlands
Telephone: 31-6-8104-64477
Email: j.m.m.van_lith@lumc.nl

Van Voorhis, Bradley J.
University of Iowa Hospitals & Clinics
Dept of OB/GYN
200 Hawkins Drive, 31335 PFP
Iowa City, IA 52242-1080
Telephone: (319) 356-4536
Email: brad-van-voorhis@uiowa.edu

Vargas, Vladimir E.
University of South Florida
12901 Bruce B. Downs Blvd.
Tampa, FL 33612
Telephone: (405) 702-2649
Email: vevargas@health.usf.edu

Varner, Michael W.
University of Utah HSC
Dept. of Ob/Gyn
30 N 1900 East 2B200 SOM
Salt Lake City, UT 84132
Telephone: (801) 581-8425
Email: michael.varner@hsc.utah.edu

Velez Edwards, Digna R.
Vanderbilt University
Dept. of Ob/Gyn
2525 West End Avenue
Suite 600 6th Floor
Nashville, TN 37203
Telephone: (615) 322-1288
Email: digna.r.velez.edwards@vanderbilt.edu

Vickers, Mark H.
University of Auckland
Liggins Institute
85 Park Road
Grafton
Auckland, 1142
New Zealand
Telephone: 64-9-923-6687
Email: m.vickers@auckland.ac.nz

Vilella, Felipe
Valencia University; INCLIVA
Narcís Monturiol Estarriol Nº11
Parcela B Edificio Europark
Parque Tecnológico de Paterna
Paterna (Valencia), 46980
Spain
Telephone: +34963905310
Email: felipe.vilella@igenomix.com

Vintzileos, Anthony M.
14 Tappanwood Drive
Locust Valley, NY 11560
Telephone: (516) 663-8657
Email: avintzileos@winthrop.org

Vollenhoven, Beverley J.
Monash University
Dept. of Ob/Gyn
246 Clayton Road
Level 5, Monash Medical Centre
Clayton, VIC 3168
Australia
Telephone: 61-3-9544-6688
Email: beverley.vollenhoven@med.monash.edu.au

Vriens, Joris
KU Leuven
Herestraat 49 Box 611
Leuven, 3000
Belgium
Telephone: (321) 632-7279
Email: joris.Vriens@med.kuleuven.be

Walker, James
University of Leeds
Dept. of Ob/Gyn
12 Shire Oak Road
Leeds, LS6 2DE
United Kingdom
Telephone: 44-113-278-9599
Email: j.j.walker@leeds.ac.uk

Wallace, Euan M.
Monash University
Dept. of Ob/Gyn
The Ritchie Centre, Monash University
Monash Medical Centre, 246 Clayton Road
Clayton, VIC 3168
Australia
Telephone: 61-39-594-5145
Email: euan.wallace@monash.edu

Walsh, Scott W.
Virginia Commonwealth University
Dept. of Ob/Gyn
PO Box 980034
Richmond, VA 23298-0034
Telephone: (804) 828-8468
Email: scott.walsh@vcuhealth.org

Wang, Yuping
LSUHSC-S
Dept. of Ob/Gyn
1501 Kings Highway
PO Box 33932
Shreveport, LA 71130
Telephone: (318) 675-5379
Email: ywang1@lsuhsc.edu

Ward, Kenneth
Lucina Foundation
2749 E. Parley's Way
Suite 210
Salt Lake City, UT 84109
Telephone: (801) 487-6000
Email: ken.ward.hi@mac.com

Warren, Michelle P.
Columbia University
Dept. of Ob/Gyn
622 West 168th Street
PH 16
New York, NY 10032
Telephone: (212) 305-8723
Email: mpw1@cumc.columbia.edu

Warren, Wendy B.
New Jersey Perinatal Associates, LLC.
94 Old Short Hills Rd.
East Wing Siute 402
Livingston, NJ 07039
Telephone: (973) 322-5657
Email: wwarren@njperinatal.com

Wax, Joseph R.
MMC
Dept. of Ob/Gyn, Div. Of MFM
Ob-Gyn Associates
887 Congress Street, Suite 200
Portland, ME 04102
Telephone: (207) 771-5549
Email: joerwax@gmail.com

Webb, R. Clinton
Augusta University
Dept. of Physiology
1120 Fifteenth Street
Augusta, GA 30912-3000
Telephone: (706) 721-7742
Email: cwebb@augusta.edu

Wegienka, Ganesa
Henry Ford Health System
Dept. of Public Health Sciences
1 Ford Place, 3E
Detroit, MI 48202
Telephone: (313) 874-3566
Email: gwegien1@hfhs.org

Weiner, Carl Philip
University of Kansas SOM
Dept. of Ob/Gyn
3901 Rainbow Blvd., MS 2028
MS 2028
Kansas City, KS 66160-7316
Telephone: (913) 588-6250
Email: cweiner@kumc.edu

Weissgerber, Tracey L.
Mayo Clinic
Division of Nephrology and Hypertension
200 First Street SW
Rochester, MN 55905
Telephone: 507-266-2844
Email: weissgerber.tracey@mayo.edu

Werner, Erika F.
Brown University
Women & Infants Hospital
MFM Division
101 Dudley Street
Providence, RI 02905
Telephone: (401) 274-1122
Email: erika_werner@brown.edu

Whirledge, Shannon D.
Yale University
333 Cedar St
New Haven, CT 06520
Telephone: (203) 785-7255
Email: shannon.whirledge@yale.edu

White, Wendy
Mayo Clinic
Dept. of Ob/Gyn, MFM
200 First Street SW
Rochester, MN 55905
Telephone: (507) 284-5145
Email: white.wendy@mayo.edu

Wild, Robert A.
University of Oklahoma HSC
Dept. of Ob/Gyn
920 S.L. Young Blvd.
WP 2410
Oklahoma City, OK 73104
Telephone: (405) 271-1075
Email: robert-wild@ouhsc.edu

Williams, Carmen J.
NIH/NIEHS
RDBL
PO Box 12233
MD E4-05
Research Triangle Park, NC 27709
Telephone: (919) 541-2158
Email: williamsc5@niehs.nih.gov

Williams, R. Stan
University of Florida
Dept. of Ob/Gyn
PO Box 100294
1600 SW Archer Road, M-302
Gainesville, FL 32610-0294
Telephone: (352) 265-0111
Email: rwilliam@ufl.edu

Wing, Deborah A.
University of California-Irvine Med. Ctr.
Dept. of Ob/Gyn
101 The City Drive, South
Bldg. 56, Suite 800
Orange, CA 92868
Telephone: (714) 456-5967
Email: dwing@uci.edu

Winger, Quinton
Colorado State University
Department of Biomedical Sciences
3107 Rampart Road
Fort Collins, CO 80523-1683
Telephone: (970) 491-7702
Email: quinton.winger@colostate.edu

Winn, Hung N.
University of Missouri-Columbia SOM
Dept. of Ob/Gyn & Women's Health
500 Keene Street
Suite 405
Columbia, MO 65201
Telephone: (573) 817-3306
Email: winnh@health.missouri.edu

Winn, Virginia D.
Stanford University School of Medicine
H303
300 Pasteur Dr., Boswell A364 MC5317
300 Pasteur Drive, Stanford, CA
Stanford, CA 94305-5317
Telephone: (650) 575-7871
Email: vwinn@stanford.edu

Witkin, Steven S.
Weill Cornell Medicine
Dept. of Ob/Gyn
525 East 68th Street.
Box 35
New York, NY 10065
Telephone: (212) 746-3165
Email: switkin@med.cornell.edu

Wolff, Erin Foran
Celmatix
14 Wall St
Suite 16D
New York, NY 10005
Telephone: (301) 402-6080
Email: e.wolff@celmatix.com

Wood, Charles E.
University of Florida
Dept. of Physiology & Functional Genomic
1345 Center Drive/ Room M552
PO Box 100274
Gainesville, FL 32610
Telephone: (352) 294-5064
Email: woodc@ufl.edu

Word, Ruth Ann A.
UT Southwestern Medical Center
5323 Harry Hines
F2.304A
Dallas, TX 75390
Telephone: (214) 648-9593
Email: ruth.word@utsouthwestern.edu

Wray, Susan
University of Liverpool
Dept. of Cellular & Molecular Physiology
Centre for Women's Health Research, Liverpool Women's Hospital, Crown Street
Liverpool, L8 7SS
United Kingdom
Telephone: 44-151-794-5306
Email: S.Wray@liverpool.ac.uk

Wu, Jie
The First Affiliated Hospital of Nanjing Medical University
368 Jiangdong North Road
Nanjing, 210036
Peoples Republic of China
Telephone: +8613905183607
Email: jie.wuyale@gmail.com

Xenakis, Elly
Univ. of Texas HSC at San Antonio
Dept. of Ob/Gyn
7703 Floyd Curl Drive
MSC 7836
San Antonio, TX 78229
Telephone: (210) 567-5009
Email: xenakis@uthscsa.edu

Xiao, Daliao
Loma Linda University
Center for Perinatal Biology
11234 Anderson Street
Loma Linda, CA 92350
Telephone: (909) 558-4325
Email: dxiao@llu.edu

Xue, Qing
First Hospital of Beijing University
No 1, Xi An Men Street
Xi Cheng District
Beijing, 100034
Peoples Republic of China
Telephone: 86-13601038626
Email: 13601038626@163.com

Yagel, Simcha
Hadassah-Hebrew University Medical Center
Dept. of Ob/Gyn
Mt. Scopus
PO Box 24035
Jerusalem, 91240
Israel
Telephone: 972-2584-4111
Email: simcha.yagel@gmail.com

Yallampalli, Chandrasekhar
Baylor College of Medicine
1102 Bates Ave, Ste 1870
Houston, TX 77030
Telephone: (832)824 4188
Email: cyallamp@bcm.edu

Yamaleyeva, Liliya M.
Wake Forest University SOM
Hypertension & Vascular Research Center
Medical Center Blvd.
Winston-Salem, NC 27157
Telephone: (336) 716-2155
Email: lyamaley@wakehealth.edu

Yang, Peixin
University of Maryland SOM
655 W. Baltimore St.
BRB11-039
Baltimore, MD 21201
Telephone: (410) 706-8402
Email: pyang@fpi.umaryland.edu

Yang, Qiwei
Augusta University
1120 15th Street, CB-2915E
Augusta, GA 30912
Telephone: (224) 616-1516
Email: qyang@augusta.edu

Yankowitz, Jerome
University of South Florida
Dept. of Ob/Gyn
2 Tampa General Circle
Suite 6016
Tampa, FL 33606
Telephone: (813) 259-8514
Email: jyankowi@health.usf.edu

Yee, Lynn M.
Northwestern University Feinberg School of Medicine
250 E. Superior Street, #5-2191
Chicago, IL 60611
Telephone: (312) 472-0119
Email: lynn.yee@northwestern.edu

Yellon, Steven M.
Loma Linda University
Dept. of Basic Sciences, Div of Phys.
Center for Perinatal Biology
MRW A572 SOM
Loma Linda, CA 92350
Telephone: (909) 558-4325
Email: syellon@llu.edu

Yen, Chih-Feng
Chang Gung Memorial Hospital
Dept. of Ob/Gyn
5 Fu-Hsing Street, Kuei-Shan
Tao-yuan, 33305
Taiwan
Telephone: (886) 332-81200
Email: franklin.yen@gmail.com

Yoneyama, Yoshio
Tokyo Institute of Repro. Sci.
Dept. of Medical Research
3-5-20 Nishiaraisakaecho
Adachi-ku
Tokyo, 123-0843
Japan
Telephone: 03-3849-3333
Email: yoshi1wisdom@gmail.com

Yoshinaga, Koji
NIH
FIB ,NICHD, NIH
6710B Rockledge Dr. Rm 2353A
Bethesda, MD 20892-7002
Telephone: (301) 435-6992
Email: ky6a@nih.gov

Young, Steven L.
UNC at Chapel Hill
Dept. of Ob/Gyn
CB# 7570
4005 Old Clinic Bldg.
Chapel Hill, NC 27599-7570
Telephone: (919) 966-5483
Email: youngs@med.unc.edu

Yu, Bo
5101 25th Ave NE, Apt C137
Seattle, WA 10801
Telephone:
Email: boyumich2@gmail.com

Zacur, Howard A.
Johns Hopkins University
10751 Falls Road
Suite 280
Lutherville, MD 21093
Telephone: (410) 583-2761
Email: hzacur1@jhmi.edu

Zakar, Tamas
University of Newcastle
Mothers & Babies Res. Centre
Room 3404 HMRI, Lot 1, Kookaburra Circui
Hunter Medical Research Institute
New Lambton Hgts, NSW 2305
Australia
Telephone: (612)404-20358
Email: Tamas.Zakar@newcastle.edu.au

Zamah, Alberuni M.
Univeristy of Illinois at Chicago
820 S Wood Street, MC 808
CSN, Room 232B
Chicago, IL 60612
Telephone: (312) 355-0458
Email: mzamah@uic.edu

Zamudio, Stacy
Hackensack University MC
Dept. of Ob/Gyn
Division of MFM and Surgery
30 Prospect Ave., Suite 4-90G
Hackensack, NJ 07601
Telephone: (201) 996-5768
Email: szamudio@HackensackUMC.org

Zeitoun, Khaled M.
Jamaica Hospital
Dept. of Ob/Gyn
159 West 53rd Street
Apt #24-C
New York, NY 10019
Telephone: (917) 855-3382
Email: drkzeitoun@outlook.com

Zhang, Lubo
Loma Linda University
Center for Perinatal Biology
School of Medicine
Loma Linda, CA 92350
Telephone: (909) 558-4325
Email: lzhang@llu.edu

Zhao, Hui
Stanford University
Dept. of Pediatrics
300 Pasture Drive
Grant Bldg., S230
Stanford, CA 94305
Telephone: (650) 498-7246
Email: huizhao2@stanford.edu

Zheng, Jing
University of Wisconsin-Madison
Dept. of Ob/Gyn
PAB1, Meriter Hospital
202 S. Park Street
Madison, WI 53715
Telephone: (608) 417-6314
Email: jzheng@wisc.edu

Zinkhan, Erin
University of Utah
Dept. of Pediatrics/Neonatology
295 Chipeta Way
Salt Lake City, UT 84108
Telephone: (801) 581-7052
Email: Erin.Zinkhan@hsc.utah.edu

Zondervan, Krina T.
University of Oxford
Nuffield Dept of Obstetrics & Gynaecol
John Radcliffe Hospital
Oxford, OX3 9DU
United Kingdom
Telephone: 44-1865-287627
Email: krinaz@well.ox.ac.uk

Associate Members

Bok, Rachael
University of Colorado School of Medicine
Dept of OB-GYN
12700 E. 19th Avenue
Research Building 2, Room 3430E
Aurora, CO 80045
Telephone: (303) 724-6398
Email: rachael.bok@ucdenver.edu

Hickok, Durlin Edward
Sera Prognostics, Inc.
417 Erie Avenue
Seattle, WA 98122
Telephone: (801) 990-0530
Email: dhickok@gmail.com

McCarthy, Ronald T.
Washington University at St. Louis
425 S. Euclid Ave.
BJCIH 10124
St. Louis, MO 63110
Telephone: (314) 747-6665
Email: mccarthyr@wudosis.wustl.edu

Morton, Jude Sally
University of Alberta
Dept. of Obstetrics And Gynaecology
232 HMRC
Edmonton, AB T6G 2S2
Canada
Telephone: (780) 492-8562
Email: jude@ualberta.ca

Ogle, Amy
Private Practice
3726 Dupont St
San Diego, CA 92166
Telephone: (619) 823-6623
Email: aogle5@cox.net

Shynlova, Oksana
Mount Sinai Hospital
Lunenfeld-Tanenbaum Research Institute
25 Orde Street Room 6-1019
Toronto, ON M5T 3H7
Canada
Telephone: (416) 586-4800
Email: shynlova@lunenfeld.ca

Vyas, Vibhuti
University of Colorado
Dept. of OB/GYN
12700 E, 19th Ave.
Aurora, CO 80045
Telephone: (518) 772-8050
Email: vibhuti.vyas@ucdenver.edu

In-Training Members

Aghajanova, Lusine
UCSF
Dept. of OB/GYN & Repro. Sciences
499 Illinois Str
San Francisco, CA 94143
Telephone: (650) 353-1777
Email: aghajanova@yahoo.com

Allison, Beth J.
Hudson Institute
The Ritchie Centre
27-31 Wright Street
Clayton, VIC 3168
Australia
Telephone: +61418929920
Email: beth.allison@hudson.org.au

Amabebe, Emmanuel
University Of Sheffield
Oncology and Metabolism
Level 4 Jessop Wing
Tree Root Walk
Sheffield, S10 2SF
United Kingdom
Telephone: +447958813501
Email: eamabebe1@sheffield.ac.uk

Arenas-Hernandez, Marcia
Wayne State University
Dept. of Ob/Gyn
275 E. Hancock Street
Room 317
Detroit, MI 48201
Telephone: (313) 577-1828
Email: marenash@med.wayne.edu

Bachkangi, Panayoti
University of Leicester
Cancer Studies and Molecular Medicine
32 Mount Pleasant
Leicester, LE2 4UA
United Kingdom
Telephone: +447800964204
Email: pb130@leicester.ac.uk

Barnett, Scott
University of Nevada, Reno
Dept. of Pharmacology
1664 N. Virginia Street
CMM308 MS0573
Reno, NV 89557
Telephone: (775) 784-4120
Email: sdbarnett@medicine.nevada.edu

Belotte, Jimmy
Wayne State University
Dept. of Ob/Gyn
1965 Lone Pine Road
Bloomfield Township, MI 48302
Telephone: (321) 431-2933
Email: jbelotte@med.wayne.edu

Bressler, Leah H.
Northwestern University
250 East Superior St
Suite 2177
Chicago, IL 60611
Telephone: 912653901
Email: leah.hawkins@northwestern.edu

Care, Alison S.
University of Alberta
Dept. of Ob/Gyn
232 HMRC
87 Ave. - 112 St.
Edmonton, AB T6G 2S2
Canada
Telephone: (780) 492-8562
Email: care@ualberta.ca

Carr, David J.
114 East 39th Street
Apartment 3A
New York, NY 10016
Telephone: (657) 294-7647
Email: davidcarr@doctors.org.uk

Chavan, Niraj R.
3600 Winthrop Drive
Apt - 9205
Lexington, KY 40514
Telephone: (859) 323-6434
Email: niraj.chavan09@gmail.com

Chuecos, Marcel A.
6611 Patriot Pkwy
Midland, TX 79706
Telephone: (432) 703-5167
Email: marcel.chuecos@ttuhsc.edu

Cindrova-Davies, Tereza
University of Cambridge
Dept. of PDN
Centre for Trophoblast Research
Downing Street
Cambridge, CB2 3EG
United Kingdom
Telephone: 44-122-333-3862
Email: tc269@cam.ac.uk

Colon-Caraballo, Mariano
Urb. Jardines Del Caribe
Calle # 40 NN-2
Ponce, PR 00728-2630
Telephone: (787) 840-2575
Email: colonmariano@gmail.com

DeAngelis, Anthony M.
1401 Cypress Drive
Danbury, CT 06811
Telephone: (203) 739-7872
Email: anthony.deangelis@wchn.org

Evans, Jemma
The Hudson Institute of Medical Research
27-31 Wright Street
Clayton, VIC 3168
Australia
Telephone: +61395944319
Email: jemma.evans@hudson.org.au

Feldman, Chelsea H.
Duke University
5012 Kettle Creek Rd
Durham, NC 27705
Telephone: (201) 819-0802
Email: chf4@duke.edu

Gold, Nathan
62 Roxborough Lane
Thornhill, ON L4J 4S9
Canada
Telephone: (647) 829-6625
Email: ngold5@mathstat.yorku.ca

Grechukhina, Olga
Yale-New Haven Medical Center
333 Cedar Street
PO Box 208063
New Haven, CT 06520
Telephone: (203) 499-8193
Email: olga.grechukhina@yale.edu

Hakim, Julie CE
4310 Dunlavy St #449
Houston, TX 77006
Telephone: (713) 252-6522
Email: jhakim@bcm.edu

Hebert, Jessica Faith
Portland State University/Oregon Health & Science University
Dept. of Pathology
3181 SW Sam Jackson Park Rd.
Dock 4, RJH 1346 (L113)
Portland, OR 97239
Telephone: (503) 494-7957
Email: jehebert@pdx.edu

Herington, Jennifer
Vanderbilt University
Dept. of Pediatrics/Neonatology
2215 B Garland Avenue
1125 Light Hall
Nashville, TN 37232-0656
Telephone: (615) 322-9548
Email: jennifer.l.herington@vanderbilt.edu

Herrera-Garcia, Guadalupe
Rutgers Robert Wood Johnson Medical School
Division of Maternal Fetal Medicine
125 Paterson Street, CAB-2100
New Brunswick, NJ 08901-1977
Telephone: (732) 235-6632
Email: lupe.garcia@rutgers.edu

Horii, Mariko
University of California, San Diego
Dept. of Pathology
2880 Torrey Pines Scenic Drive
La Jolla, CA 92037
Telephone: (858) 534-8648
Email: mhorii@ucsd.edu

Irani, Mohamad
Weill Cornell Medicine
1305 York Avenue, 6th Floor
New York, NY 10021
Telephone: (347) 286-2167
Email: mohamad.irani@hotmail.com

James, Catherine P.
18 Chiltern Court
Avonley Road
London, SE14 5EZ
United Kingdom
Telephone: +44 20 7679 6036
Email: catherine.james@ucl.ac.uk

Jimenez, Patricia Tereese
UT Southwestern MC
Dept. of Ob/Gyn
5323 Harry Hines Blvd
Dallas, TX 75390
Telephone: (214) 648-6745
Email: ptj6305@yahoo.com

Kadam, Leena T.
Wayne State University
275 E Hancock
C.S. Mott Center
Detroit, MI 48201
Telephone: (313) 577-1474
Email: fc3643@wayne.edu

Kanninen, Tomi
Jamaica Hospital Medical Center
Dept. of Ob/Gyn
531 Main St. Apt 523
New York, NY 10044
Telephone: (646) 379-6983
Email: ttkanninen@gmail.com

Kelleher, Meredith A.
Oregon National Primate Research Center
Division of Reproductive & Developmental
505 NW 185th Ave, ONPRC 1125, MC L584
ONPRC, 1125, MC L584
Beaverton, OR 97006
Telephone: (971) 282-2641
Email: kellehem@ohsu.edu

Kim, Soon Ok
Eastern Virginia Medical School
700 W. Olney Road
Physiological Sciences
Norfolk, VA 23507
Telephone: (757) 510-5775
Email: kims@evms.edu

King, Jennifer Renae
University of Southern California
Dept. of Ob/Gyn
1200 N. State St. Inpatient Tower
Room C3F107
Los Angeles, CA 90033
Telephone: (323) 409-8848
Email: jennyrenaeking@gmail.com

Klenov, Violet
14 North Kingshighway
Apt 2B
St. Louis, MO 63108
Telephone: (314) 362-1016
Email: violet.klenov@gmail.com

Kohan-Ghadr, Hamid-Reza
Wayne State University
Wayne State University SoM
275 E. Hancock #295
Detroit, MI 48201
Telephone: (313) 577-1474
Email: hkohangh@med.wayne.edu

Kulandavelu, Shathiyah
1450 Brickell Bay Drive, Unit 1606
Miami, FL 33131
Telephone: (305) 972-2324
Email: shathiyahk@gmail.com

Laganà, Antonio Simone
Via Lia Diramazione Vico I, 15
Reggio Calabria, 89122
Italy
Telephone: 39-090-221-2183
Email: antlagana@unime.it

Lechuga, Thomas J.
University of California Irvine
Dept. of Ob/Gyn & Experimental Pathology
Perinatal Research Labs
Med Surge I, Bldg. 810, Rm. 140
Irvine, CA 92697
Telephone: (949) 824-2739
Email: tlechuga@uci.edu

Leimert, Kelycia B.
University of Alberta
Physiology
227 HMRC University of Alberta
Edmonton, AB T6G2S2
Canada
Telephone: (780) 492-0029
Email: kelycia@ualberta.ca

Li, Yan
UW-Madison
Dept. of Ob/Gyn
202 S Park PAB 1
Madison, WI 53715
Telephone: (608) 417-6314
Email: li99@wisc.edu

Lin, Ken
UT Southwestern Medical Center
5323 Harry Hines Blvd
J7.120, Green Center for
Reproductive Biology Sciences
Dallas, TX 75390-8511
Telephone: (203) 535-9415
Email: ken.lin@utsouthwestern.edu

Lindgren, Isa M.
Oregon Health & Science University
3303 SW Bond Avenue
245 SW Hooker Street
Portland, OR 97239
Telephone: (503) 494-5879
Email: lindgrei@ohsu.edu

Majali Martinez, Alejandro
Medical University of Graz
Dept of Obstetrics & Gynaecology
Auenbruggerplatz 14
Graz, 8036
Austria
Telephone: +43 31685-17841
Email: alejandro.majali-martinez@
medunigraz.at

Marshall, Sarah A.
University of Melbourne
U3, 33-35 Piera St
Brunswick East, 3057
Australia
Telephone: (041) 753-0140
Email: saraham@student.unimelb.edu.
au

Martin-Fairey, Carmel
Washington University
Campus Box 1137
St. Louis, MO
Telephone: (919) 673-7154
Email: C.A.Martin-Fairey@wustl.edu

Mas Perucho, Aymara
Igenomix
Parc Cientific. Universitat de Valencia
Agustín Escardino, 9, Edif 2
Paterna, 46980
Spain
Telephone: +34 963 90 53 04
Email: aymara.mas@igenomix.com

Maybin, Jacqueline
University of Edinburgh
MRC Centre for Reproductive Health
The Queen's Medical Research
Institute
47 Little France Crescent
Edinburgh, EH16 4TJ
United Kingdom
Telephone: 0044-131-242-2698
Email: jackie.maybin@ed.ac.uk

McDonald, Chloe R.
Harvard School of Public Health
Dept of Global Health and Population
1634 Tremont Street
Boston, MA 02120
Telephone: (617) 495-1000
Email: chloe.mcdonald@mail.utoronto.
ca

McGillick, Erin V.
Hudson Institute of Medical Research
The Ritchie Centre, Level 5 TRF
27-31 Wright Street
Clayton, VIC 3168
Australia
Telephone: +61 3 85722899
Email: erin.mcgillick@hudson.org.au

Modi, Bhavi P.
Virginia Commonwealth University
1101 E Marshall St, Sanger Hall
Room # 11-025
Richmond, VA 23298
Telephone: (804) 833-2553
Email: modibp@vcu.edu

Moraitis, Alexandros A.
University of Cambridge
Department of OB/GYN
The Rosie Hospital
Box 223, Robinson Way
Cambridge, CB2 0SW
United Kingdom
Telephone: +44 1223763100
Email: am2167@medschl.cam.ac.uk

Mutlu, Levent
33 Lynwood Place
New Haven, CT 06511
Telephone: (857) 472-0307
Email: levent.mutlu@yale.edu

Nallasamy, Shanmugasundaram
UT Southwestern Medical Center
5323 Harry Hines Blvd
F2.116
Dallas, TX 75390
Telephone: (217) 417-4243
Email: shanmugasundaram.
nallasamy@utsouthwestern.edu

O'Brien, Christine
504 Laurel Park Drive
Nashville, TN 37205
Telephone: (314)757-3157
Email: cobrie5@gmail.com

Okeigwe, Ijeoma
1919 S Michigan Ave #200
Chicago, IL 60616
Telephone: (312) 926-8244
Email: ijeoma.okeigwe@northwestern.
edu

Ornaghi, Sara
Via Brennero 25
Vimercate, 20871
Italy
Telephone: +39 3381693586
Email: sara.ornaghi@gmail.com

Oyston, Charlotte
University of Auckland
Liggins Institute
85 Park Road
Auckland, 1023
New Zealand
Telephone: 64-9-923-4616
Email: c.oyston@auckland.ac.nz

Petropoulos, Sophie
Karolinska Institutet
Karolinska Universitetssjukhuset
Kliniskt Forskningscentrum Novum
Stamcellsgruppen Plan 5
Stockholm, 14186
Sweden
Telephone: +46076853553
Email: sophie.petropoulos@gmail.com

Plazyo, Olesya
Wayne State University School of
Medicine
Physiology, Perinatology Research
Branch
3990 John R, 4 Brush North
Detroit, MI 48201
Telephone: (313) 577-4875
Email: oplazyo@med.wayne.edu

Plows, Jasmine
University of Auckland
Liggins Institute
85 Park Road
Auckland, 1142
New Zealand
Telephone: 64-9-923-4616
Email: jasmine.plows@auckland.ac.nz

Post Uiterweer, Emiel D.
University M.C. Utrecht
Utrecht, 10016
Netherlands
Telephone: (929) 841-6441 (Cell)
Email: e.d.postuiterweer@umcutrecht.nl

Prins, Jelmer
University MC Groningen
Obstetrics & Gynaecology
Postbus 30001
HP CB21
Groningen, 9700RB
Netherlands
Telephone: +31503613867
Email: j.r.prins@umcg.nl

Rabaglino, María B.
Juan Mateo Olmos 134
Cordoba, 5000
Argentina
Telephone: (354) 148-1196
Email: belenrabaglino@icloud.com

Rahmioglu, Nilufer
University of Oxford
Wellcome Trust Centre for Human Genetics
Roosevelt Drive
Oxford, OX3 7BN
United Kingdom
Telephone: +447515528252
Email: nilufer@well.ox.ac.uk

Sacha, Caitlin Redd
11 Atherton Road
Unit 2
Brookline, MA 02446
Telephone: (617) 732-7801
Email: caitlinsacha@gmail.com

Schutt, Amy
3630 Grennoch Street
Houston, TX 77025
Telephone: (806) 535-0573
Email: amy.schutt@bcm.edu

Seferovic, Maxim D.
Baylor College of Medicine
314C Cullen Building
1 Baylor
Houston, TX 77030
Telephone: (713) 798-4192
Email: seferovi@bcm.edu

Shangaris, Panicos
University College London
Institute for Women's Health
Flat 212, Grove End Gardens
Grove End Road
London, NW8 9LT
United Kingdom
Telephone: 44-772-557-8001
Email: p.shangaris@ucl.ac.uk

Sharshiner, Rita
Oregon Health & Science University
Dept of OBGYN
3181 SW Sam Jackson Park Road
Mail Code L-458
Portland, OR 97239
Telephone: (503) 494-2685
Email: sharshin@ohsu.edu

Shree, Raj
University of Washington Medical Center
Obstetrics, Gynecology, and Reproductive
1959 NE Pacific Street
Box 356460
Seattle, WA 98195
Telephone: (917) 903-1641
Email: shreer23@uw.edu

Sokalska, Anna
3601 MArket Street
Unit 1113
Philadelphia, PA 19104
Telephone: (530) 601-0712
Email: annasokalska@gmail.com

Soncin, Francesca
University of California San Diego
Dept. of Pathology
9500 Gilman Drive, #0695
La Jolla, CA 92093
Telephone: (858) 534-8648
Email: fsoncin@ucsd.edu

Spaans, Floortje
University of Alberta
OB/GYN
232 HMRC
Edmonton, AB T6G 2S2
Canada
Telephone: (780) 492-8562
Email: floortje@ualberta.ca

Springel, Edward H.
12813 Church Road
Richmond, VA
Telephone: (804) 828-7787
Email: edwspringel@gmail.com

Stefanski, Adrianne L.
3906 Jackson St
Denver, CO 80205
Telephone: (734) 770-8332
Email: adrianne.stefanski@ucdenver.edu

Steinberg, Marissa L.
30 E. Huron Street
Suite 3107
Chicago, IL 60611
Telephone: (516) 459-3426
Email: marissasteinberg@gmail.com

Strug, Michael
1173 4th St NW
Grand Rapids, MI 49504
Telephone: (609) 315-0756
Email: mrstrug@gmail.com

Suff, Natalie
Institute for Women's Health
86-96 Chenies Mews
University College London
London, Wc1e 6hx
United Kingdom
Telephone: 00447753450043
Email: natalie.suff.14@ucl.ac.uk

Sykes, Lynne
Imperial College
Du Cane Road
London, W12 0NN
United Kingdom
Telephone: 07-95-762-1454
Email: l.sykes@imperial.ac.uk

Tal, Reshef
Yale School of Medicine
Dept. of Ob/Gyn & Reproductive Sciences
333 Cedar Street
New Haven, CT 06510
Telephone: 203-7854005
Email: resheft@gmail.com

Thomas, Megan
26741 Midland Road
Bay Village, OH 44140
Telephone: (304) 360-1384
Email: meganthomas320@gmail.com

Tong, Mancy
The University of Auckland
Department of Obstetrics and Gynaecology
FMHS, The University of Auckland
85 Park Road
Grafton, Auckland, 1023
New Zealand
Telephone: 64221066783
Email: mancy.tong@auckland.ac.nz

Vazquez, Jessica
University of Wisconsin-Madison
Meriter Hospital/PAB1
202 S Park St
Madison, WI 53715
Telephone: (323) 627-8836
Email: jvazquez3@wisc.edu

Verstraeten, Barbara S.
University of Alberta
Dept. of Obstetrics and Gynaecology
220 HMRC
Edmonton, AB T6G 2S2
Canada
Telephone: (780) 492-0029
Email: verstrae@ualberta.ca

Villalon Landeros, Rosalina
University of Wisconsin-Madison
Dept of Ob-Gyn
202 South Park St.
Madison, WI 53715
Telephone: (608) 417-6314
Email: villalonland@wisc.edu

Wallingford, Mary C.
University of Washington
UW Bioengineering
3720 15TH AVE NE N333C
UW MAILBOX 355061
Seattle, WA 918950001
Telephone: 12062215818
Email: marycwallingford@gmail.com

Weinheimer, Claudia
University of Utah, Division of Neonatology
295 Chipeta Way
Salt Lake City, UT 84108
Telephone: (801) 581-7052
Email: claudia.weinheimer@hsc.utah.edu

Whitaker, Lucy HR
77/5 Dublin St
Edinburgh, EH3 6NS
United Kingdom
Telephone: (448) 665-1725
Email: lucy.whitaker@ed.ac.uk

Willcockson, Alexandra R.
UT Southwestern Medical Center
Dept. of Ob/Gyn
5323 Harry Hines Blvd.
Dallas, TX 75390
Telephone: (214) 648-2793
Email: alexandra.willcockson@utsouthwestern.edu

Wong, Senny
University of Nevada School of Medicine
Department of _Pharmacology
1664 N. Virginia Street
CMM L307 MS0573
Reno, NV 89557
Telephone: 775-682-6522
Email: sennyw@medicine.nevada.edu

Xiong, Yali
Temple University
Fels Institute
3307 N. Broad Street
Philadelphia, PA 19140
Telephone: (267) 809-2186
Email: ylxiong@temple.edu

Xu, Jie
LSU Health Science Center
1501 Kings Highway
Shreveport, LA 71103
Telephone: (318) 675-5379
Email: jxu4@lsuhsc.edu

Yano, Jacqueline C.
913 Southerly Rd. #309
Towson, MD 21204
Telephone: (858) 361-4404
Email: jyano3@jhmi.edu

Yu, Liang
Eastern Virginia Medical School
829 Botetourt Gdns
Norfolk, VA 23507
Telephone: (757) 446-5002
Email: yuliang2006@gmail.com

Yung, Hong Wa
University of Cambridge
Depts of Physiology, Dvlpt & Neurscience
Downing Street
Cambridge, CB2 3EG
United Kingdom
Telephone: 44-122-333-3862
Email: hwy20@hermes.cam.ac.uk

Zhou, Chi
University of Wisconsin-Madison
Dept of OB/GYN
PAB 1, Meriter Hospital
202 S Park St.
Madison, WI 53715
Telephone: (608) 698-8783
Email: czhou69@wisc.edu

Zou, Qingyun
University of Wisconsin-Madison
Dept. of Ob/Gyn
PAB1, Meriter Hospital
202 S Park Street
Madison, WI 53715
Telephone: (608) 417-4290
Email: qzou2@wisc.edu

Emeritus Members

Abdul-Karim, Raja W.
SUNY Upstate Medical University
Dept. of Ob/Gyn
750 East Adams Street
Syracuse, NY 13210
Telephone: (315) 470-7905
Email: lamannas@upstate.edu

Amesse, Lawrence S.
Florida Atlantic University
Fertility Florida
7837 Venture Center Way #5105
Boynton Beach Florida, FL 33437
Telephone: (561) 257-0816
Email: amesse@fertilityflorida.com

Ances, Isadore G.
Robert Wood Johnson SOM
Dept. of Ob/Gyn
Cooper University Hospital
3 Cooper Plaza, Suite 221
Camden, NJ 08103
Telephone: (609) 342-3006
Email: ances-isadore@cooperhealth.edu

Barker, Kenneth L.
SUNY Upstate Medical University-Syracuse
Dept. of Biochemistry & Ob/Gyn
1065 Applo Way
Zanesville, OH 43701
Telephone: (740) 454-2312
Email: barkerk@mac.com

Bhavnani, Bhagu R.
University of Toronto
Dept. of Ob/Gyn
St. Michael's Hospital
30 Bond St., Ste. 7-074, Bond
Toronto, ON M5B 1W8
Canada
Telephone: (416) 864-5089
Email: bhagu.bhavnani@utornonto.ca

Blackwell, Richard E.
University of Alabama
Dept. of Ob/Gyn
1700 6th Ave South
WIC 10390
Birmingham, AL 35294-7333
Telephone: (205) 934-6090
Email: rblackwe@uabmc.edu

Brace, Robert A.
OHSU School of Medicine
Dept. of Ob/Gyn
3181 SW Sam Jackson Park Road
Mail Code L-458
Portland, OR 97239-3098
Telephone: (503) 494-2135
Email: bracer@ohsu.edu

Brenner, Paul F.
University of Southern California
Dept. of Ob/Gyn
4434 Mariota Avenue
North Hollywood, CA 91602
Telephone: (818) 749-3963
Email: pbrenner@usc.edu

Brenner, Robert M.
ORPRC/ OHSU
Dept. of Repro. Sciences
505 NW 185th Avenue
Beaverton, OR 97006
Telephone: (503) 690-5331
Email: brennerrmb@comcast.net

Brinkman, Charles R.
UCLA School of Medicine
Obstetrics and Gynecology
2695 Patterson St
Unit 2 #281
Grand Junction, CO 81506
Telephone: 970-628-4154
Email: cbrinkman3@msn.com

Bryant-Greenwood, Gillian D.
University of Hawaii
Dept. of Developmental & Repro. Bio.
John A. Burns SOM
Biosciences Bldg., 651 Ilalo St.
Honolulu, HI 96813
Telephone: (808) 692-1470
Email: gbg@pbrc.hawaii.edu

Calder, Andrew Alexander
Simpson Ctr. for Repro. Health
Dept. of Ob/Gyn
Room S7127
51 Little Crescent
Edinburgh, Scotland EH16 4SA
United Kingdom
Telephone: 44-131-242-2694
Email: a.a.calder@ed.ac.uk

Castracane, V. Daniel
42 Southampton Parish Road
Landenberg, PA 19350
Telephone: (432) 703-5062
Email: daniel.castracane@ttuhsc.edu

Cederqvist, Lars L.
40 River Rd.
APT 14K
New York, NY 10044-1141
Telephone: (212) 935-4176
Email: lars_cederqvist@hotmail.com

Challis, John R.G.
The University of Western Australia
Dept. of Ob/Gyn, Physiology
3710 Southridge Place
West Vancouver, BC V7V 3H8
Canada
Telephone: (604) 922-7100
Email: john.challis@uwa.edu.au

Chang, R. Jeffrey
University of California San Diego SOM
Dept. of Repro. Medicine
9500 Gilman Drive, mc 0633
BSB 5046
La Jolla, CA 92093-0633
Telephone: (858) 534-8930
Email: rjchang@ucsd.edu

Chatterton, Robert T.
Northwestern University SOM
Dept. of Ob/Gyn
710 N. Fairbanks Ct.
Olson 8272
Chicago, IL 60611
Telephone: (312) 503-5272
Email: chat@northwestern.edu

Cleary, Robert E.
Indiana University SOM
Dept. of Ob/Gyn
7036 Dubonnet Court
Indianapolis, IN 46278
Telephone: (317) 872-4269
Email: robertecleary@yahoo.com

Cohen, Wayne R.
University of Arizona
Ob/Gyn
4841 N. Valley View Rd
Tucson, AZ 85718
Telephone: 520-505-4213
Email: waynercohen@me.com

Creasy, Robert K.
400 Sausalito Street
Corte Madera, CA 94925
Telephone: (415) 924-2898
Email: rkcreasy@pacbell.net

Cruikshank, Dwight P.
Medical College of Wisconsin
Dept. of Ob/Gyn
431 Century Oak Drive
Waukesha, WI 53188
Telephone: (262) 349-9622
Email: dcruikshank@wi.rr.com

Curet, Luis B.
University of New Mexico
Dept. of Ob/Gyn
PO Box 50519
Albequerque, NM 87181
Telephone: (505) 296-7068
Email: bcuret@unm.edu

Davison, John M.
Newcastle University
Institute of Cellular Medicine
Wm. Leech Bldg., 3rd Floor
Medical School
Newcastle Upon Tyne, NE2 4HH
United Kingdom
Telephone: 44-191-282-4132
Email: j.m.davison@ncl.ac.uk

De Haan, Jelte
Research Institute Grow
Dorpsstraat 50
6277 NE Slenaken
Slenaken, 6277NE
Netherlands
Telephone: 31-43-457-3566
Email: j.dehaan@maastrichtuniversity.nl

Delivoria-Papadopoulos, Maria
Drexel University College of Medicine
Neonatal-Perinatal Med., Hahnemann Hosp.
245 N. 15th Street, NCB, Room #7402
Mail Stop 1029
Philadelphia, PA 19102
Telephone: (215) 762-7515
Email: mdelivor@gmail.com

Devoe, Lawrence D.
Georgia Regents University School of Medicine
Dept. of Ob/Gyn
1120 15th Street
Augusta, GA 30912
Telephone: (706) 721-3556
Email: ldevoe@gru.edu

DiSaia, Philip J.
University of California-Irvine
Dept. of Ob/Gyn
101 The City Drive, Bldg 56, Rm 260
Orange, CA 92868-3298
Telephone: (714) 456-5220
Email: pjdisaia@uci.edu

Dubin, Norman H.
Union Memorial Hospital
201 East University Parkway
Baltimore, MD 21218
Telephone: (410) 554-2893
Email: norman.dubin@medstar.net

Fox, Harold E.
Johns Hopkins University
Dept. of Ob/Gyn
600 N. Wolfe Street
Phipps 264A
Baltimore, MD 21287-1228
Telephone: (410) 614-0178
Email: hfox@jhmi.edu

Gant, Norman F.
ABOG
3425 Lookout Court
Grapevine, TX 76051-6827
Telephone: (214) 871-1619
Email: ngant@abog.org

Garfield, Robert E.
Translational Genomics Research Institute
Dept. of Ob/Gyn
445 N. 5th Street
Phoenix, AZ 85004
Telephone: (602) 708-7617
Email: drrobertgarfield@gmail.com

Gibb, William
University of Ottawa
Dept. of Ob/Gyn, General Hospital
501 Smyth Road
Room 8420
Ottawa, ON K1H 8L6
Canada
Telephone: (613) 241-7181
Email: wgibb@uottawa.ca

Gibbs, Ronald S.
University of Colorado Denver SOM
Dept. of Ob/Gyn
12631 E 17th Ave.
M/S B198-5
Aurora, CO 80045
Telephone: (303) 724-2032
Email: ronald.gibbs@ucdenver.edu

Gilstrap, Larry C.
ABOG
2915 Vine Street
Dallas, TX 75204
Telephone: (214) 871-1619
Email: lgilstrap@abog.org

Goodlin, Robert C.
3276 Amethyst Dr.
Cameron Park, CA 95682-8509
Telephone: (530) 672-8700
Email: rgoodlin@cwnet.com

Greene, John W.
1969 Hart Road
Lexington, KY 40502
Telephone: (859) 268-1416
Email:

Hammond, Charles B.
Duke University Med. Ctr.
Dept. of Ob/Gyn
PO Box 3853
307 Baker House
Durham, NC 27710
Telephone: (919) 684-3008
Email: hammo005@mc.duke.edu

Haseltine, Florence P.
Society for Women's Health Research
2181 Jamieson Ave
Apt. 1606
Alexandria, VA 22314
Telephone: (703) 566-8390
Email: fhaseltine@aol.com

Helmerhorst, Frans M.
Leiden University Med. Ctr.
Dept. of Ob/Gyn & Repro. Med.
Albinusdreef 2, Postbus 9600
K6-25
Leiden, 2300RC
Netherlands
Telephone: 31-71-526-2845
Email: f.m.helmerhorst@lumc.nl

Hunt, Joan S.
8347 Somerset Drive
Prairie Village, KS 66207
Telephone: (913) 642-2070
Email: jshunt1134@aol.com

Huszar, Gabor B.
Yale University SOM
Dept. of Ob/Gyn
333 Cedar Street
New Haven, CT 06520-8063
Telephone: (203) 785-4010
Email: gabor.huszar@yale.edu

Jackson, Benjamin T.
11 October Lane
Weston, MA 2493
Telephone: (781) 899-1914
Email: jdavis@comcast.net

Jaffe, Robert B.
UCSF
Dept. of Ob/Gyn & Repro. Sciences
533 Parnassus Ave.
Room U266
San Francisco, CA 94143-0556
Telephone: (415) 476-6130
Email: jaffer@obgyn.ucsf.edu

Jewelewicz, Raphael
Columbia University
Dept. of Ob/Gyn
22 Church Street
Alpine, NJ 7620
Telephone: (201) 768-5770
Email: ronijewel@msn.com

Jimenez, Juan M.
7124 Hunters Ridge Dr.
Dallas, TX 75248
Telephone: (972) 385-9491
Email: jmjo1938@sbcglobal.net

Kohorn, Ernest I.
Yale University
Dept. of Gynecology
820 Oakwood Road
Orange, CT 06477
Telephone: (203) 795-3151
Email: ernest.kohorn@yale.edu

Langer, Oded
10334 North River Trail
Knoxville, TN 37922
Telephone: (212) 523-5750
Email: odlanger@gmail.com

Lasley, Bill L.
PO Box 1093
Inverness, CA 94937
Telephone: (530) 752-8506
Email: bllasley@ucdavis.edu

Leppert, Phyllis C.
Duke University SOM
Dept. of Ob/Gyn
DUMC 103206
Durham, NC 27710
Telephone: (919) 684-4213
Email: phyllis.leppert@duke.edu

Levitz, Mortimer
NYU Medical Center
Dept. of Ob/Gyn
333 East 41 Street
Apt. 4B
New York, NY 10017
Telephone: (212) 682-5577
Email: mortimer.levitz@nyumc.org

Lindheimer, Marshall D.
5807 S. Dorchester
Apt 5E
Chicago, IL 60637
Telephone: (773) 684-1049
Email: mlindhei@medicine.bsd.uchicago.edu

Mabie, Bill C.
Greenville Hospital System
Dept. of Ob/Gyn
UMG
890 West Faris Road, Ste. 470
Greenville, SC 29605
Telephone: (864) 455-5032
Email: bmabie@ghs.org

McDonough, Paul G.
Georgia Health Sciences University
Dept. of Ob/Gyn, Physiology & Peds
1120 15th Street
BBR-7514
Augusta, GA 30912-3360
Telephone: (706) 721-3832
Email: pmcdonou@gru.edu

Miodovnik, Menachem
1401 North Oak Street
Apt. 605
Arlington, VA 22209
Telephone:
Email: mmiodovnik@gmail.com

Moawad, Atef
4 Norman Court
Burr Ridge, IL 60527
Telephone:
Email: ferialmoawad@comcast.net

Monroe, Scott E.
57 Southgate Street
Atherton, CA 94027
Telephone: (650) 367-9850
Email: monroese@yahoo.com

Morrison, John C.
University of Mississippi Med. Ctr.
Dept. of Ob/Gyn & Peds.
2500 North State Street
Jackson, MS 39216
Telephone: (601) 984-5343
Email: JMorrison@umc.edu

Mueller-Heubach, Eberhard
Wake Forest University School of Medicine
Obstetrics and Gynecology
PO Box 1335
Clemmons, NC 27012
Telephone: (336) 766-1846
Email: emueller@wfubmc.edu

Naftolin, Frederick
New York University SOM
Dept. of Ob/Gyn
Tisch Hospital 528
550 First Ave.
New York, NY 10016
Telephone: (212) 263-2823
Email: frederick.naftolin@nyumc.org

Nagamani, Manubai
15134 Blossom Bay Dr.
Houston, TX 77059
Telephone: (281) 486-0805
Email: mnagaman@gmail.com

Niebyl, Jennifer R.
University of Iowa Hospitals & Clinics
Dept. of Ob/Gyn
200 Hawkins Drive
31147 PFP
Iowa City, IA 52242
Telephone: (319) 384-9247
Email: jennifer-niebyl@uiowa.edu

Novy, Miles J.
OHSU
3107 S.W. Nottingham Dr.
Portland, OR 97201
Telephone: (503) 224-6940
Email: novym@hevanet.com

Oh, William
Women and Infants' Hospital
Dept. of Pediatrics
101 Dudley Street
125
Providence, RI 02905
Telephone: (401) 274-1122 ext: 1432
Email: woh@wihri.org

Peeters, Louis L.
Maliesingel 12-B
Utrecht, 3581BC
Netherlands
Telephone:
Email: l.l.h.peeters@umcutrecht.nl

Rebar, Robert W.
4625 Dolly Ridge Road
Birmingham, AL 35243
Telephone: (205) 970-6500
Email: rrebar@gmail.com

Redman, Christopher W.
University of Oxford
Nuffield Dept. of Ob/Gyn
John Radcliffe Hospital
Headington
Oxford, OX3 9DU
United Kingdom
Telephone: 44-1865-221-009
Email: christopher.redman@obs-gyn.ox.ac.uk

Riddick, Daniel H.
240 Blackwater Ridge Lane
Glade Hill, VA 24092
Telephone: (802) 847-5112
Email: abbariddick@gmail.com

Rose, James C.
Wake Forest University SOM
Dept. of Ob/Gyn
Medical Center Blvd.
Winston-Salem, NC 27157-1066
Telephone: (336) 716-1025
Email: jimrose@wfubmc.edu

Rosenfeld, Charles Richard
UTSW Medical Center at Dallas
Dept. of Peds. & Ob/Gyn
5323 Harry Hines Blvd.
Dallas, TX 75390-9063
Telephone: (214) 648-3903
Email: charles.rosenfeld@utsouthwestern.edu

Rotmensch, Jacob
Rush University Medical Center
Section of Gyn Oncology, Dept. of Ob/Gyn
5732 S. Kenwood Ave.
Chicago, IL 60637
Telephone: (312) 942-6312
Email: jrotmen@aol.com

Roux, Jacques F.
PO Box 415
Wilson, WY 83014
Telephone: (307) 733-6916
Email: jfroux@bluewin.ch

Sabbagha, Rudy E.
Northwestern University
Dept. of Ob/Gyn
Ob-Gyn Ultrasound Center
680 North Lake Shore Drive
Chicago, IL 60611
Telephone: (312) 654-9100
Email: rsabbagha@comcast.net

Salamonsen, Lois A.
Hudson Institute of Medical Research
27-31 Wright Street
Clayton, VIC 3168
Australia
Telephone: 61-3-9594-4373
Email: lois.salamonsen@hudson.org.au

Sanborn, Barbara M.
Colorado State University
Dept. of Biomedical Sciences
Animal Reproduction & Biotechnology Lab
Campus Delivery 1683
Fort Collins, CO 80523-1683
Telephone: (970) 491-8253
Email: barbara.sanborn@colostate.edu

Schneider, Henning
University of Berne
Dept. of Ob/Gyn
Frauenklinik-Inselspital
Ahornweg 4
Kehrsatz, CH-3122
Switzerland
Telephone: 41-31-961-7430
Email: henning.schneider@hispeed.ch

Schroder, Hobe J.
Loma Linda University
Center for Perinatal Biology
Loma Linda, CA 92350
Telephone: (909) 558-4325
Email: hobe.schroeder@gmail.com

Schruefer, John J.
2892 Balmoral Drive
Rockville, MD 20850-3049
Telephone: (301) 762-5629
Email: jschruefer@aol.com

Schulman, Joseph D.
Genetics & IVF Institute
3015 Williams Drive
Suite 202
Fairfax, VA 22031
Telephone: (703) 698-3948
Email: crichard@givf.com

Sciarra, John J.
Northwestern University Medical School
Dept. of Ob/Gyn
65 Woodley Road
Winnetka, IL 60093-3747
Telephone: (847) 446-1429
Email: jsciarra@northwestern.edu

Seeds, John W.
Virginia Commonwealth University
Dept. of Ob/Gyn
PO Box 980034
Health Science Center
Richmond, VA 23298
Telephone: (804) 828-7877
Email: jseeds@hsc.vcu.edu

Sokol, Robert J.
Wayne State University SOM
Dept. of Ob/Gyn
C.S. Mott Center, Human Growth & Dvlpt
275 E. Hancock
Detroit, MI 48201
Telephone: (313) 577-1337
Email: rsokol@moose.med.wayne.edu

Sorokin, Yoram
Wayne State University
Dept. of Ob/Gyn
Hutzel Hospital 3990 John R Box # 163, 7
4707 St. Antoine
Detroit, MI 48201
Telephone: (313) 993-3456
Email: ysorokin@med.wayne.edu

Subramanian, Marappa G.
Wayne State University
Dept. of Ob/Gyn
Mott Center
275 East Hancock Ave
Detroit, MI 48201
Telephone: (313) 577-0502
Email: msubrama@med.wayne.edu

Talledo, O. Eduardo
817 Aumond Place West
Augusta, GA 30909
Telephone: (706) 721-2542
Email: cordoba@comcast.net

Teramo, Kari A.
Helsinki University Hospital
Dept. of Ob/Gyn
Haartmaninkatu 2
PO Box 140
Helsinki, FIN 00290
Finland
Telephone: 358-50-427 9519
Email: kari.teramo@hus.fi

Tho, Sandra P.
2119 Cumming Road
Augusta, Ga 30904
Telephone: (706) 731-9174
Email: stho2@comcast.net

Tredway, Donald R.
Tredway Consulting, LLC
6301 S 225th East Avenue
Broken Arrow, OK 74014
Telephone: (918) 355-7405
Email: drtreds@aol.com

Trudinger, Brian J.
University of Sydney at Westmead Hospital
PO Box 151
Beecroft, NSW 2119
Australia
Telephone: 61(0)2 94810303
Email: brian.trudinger@me.com

Tyson, John E.
C.A.R.E. Health Resources
RR#3
Fire #6136
Clifford, ON N0G 1M0
Canada
Telephone: (519) 338-3499
Email: jtcare@aol.com

Van Assche, Frans Andre
Univ Leuven
Faculty of Medicine
Capuciene Voer, 35
Blok J
Leuven, 3000
Belgium
Telephone: 32-16-33-74-10/ 32-16-25
Email: Andre.vanassche@med.kuleuven.be

Wallach, Edward E.
Johns Hopkins at Greenspring Station
Dept. of Gyn/Ob-Div of REI
10751 Falls Road
Suite 280
Lutherville, MD 21093-4689
Telephone: (410) 583-2751
Email: ewallach@jhmi.edu

Wallenburg, Henk C.S.
Erasmus University Rotterdam
Dept. of Ob/Gyn, Erasmus University Rott
Tysjesdyk 53
Rhoon, 3161 CW
Netherlands
Telephone: 0031-10-501-3303
Email: hcswallenburg@hotmail.com

Weiss, Gerson
New Jersey Med Sch-Rutgers
185 West End Ave
Apt 7M
New York, NY 10023
Telephone: (212) 600-0940
Email: weissge@njms.rutgers.edu

Wentz, Anne Colston
64 Crescent Point Road
Bozeman, MT 59715
Telephone:
Email: acwentz5@gmail.com

Wynn, Ralph M.
45 Christopher Street
6C
New York, NY 10014
Telephone: (212) 645-3339
Email:

Yeh, Sze-Ya
2011 Elkins Place
Arcadia, CA 91006
Telephone: (626) 510-9182
Email: nobumasa168@gmail.com

Young, Bruce K.
New York University SOM
Dept. of Ob/Gyn
530 First Avenue
#5G
New York, NY 10016
Telephone: (212) 263-6359
Email: bruce.young@nyumc.org

Young, Roger C.
PreTel, Inc
Dept. of Ob/Gyn
262 Meadowgrove LN
Memphis, TN 38120
Telephone: (802) 658-4959
Email: youngschwarzenberger@gmail.com

Honorary Members

Benirschke, Kurt
University of Calif.-San Diego
Dept. of Pathology
200 W. Arbor Drive
MC 8433
San Diego, CA 92103-8321
Telephone: (619) 543-2618
Email: kbenirsc@ucsd.edu

Carsten, Mary E.
UCLA Medical Center
Dept. of Ob/Gyn
1000 Veteran Avenue
A1-61, Rehab. Ctr.
Los Angeles, CA 90095-1789
Telephone: (310) 825-5995
Email: mcarsten@ucla.edu

Cohen, Jean
8 rue de Marignan
Paris, 75008
France
Telephone: 33-1-49-5308-56
Email:

Dancis, Joseph
NYU Medical Center
Dept. of Pediatrics
550 First Avenue
New York, NY 10016
Telephone: (212) 263-5643
Email:

Rudolph, Abraham M.
UCSF
Dept. of Pediatrics
513 Parnassus Ave.
Box 0544 U585W
San Francisco, CA 94143-0544
Telephone: (415) 476-9311
Email: rudolpha@sbcglobal.net

Seppala, Markku T.
University of Helsinki
Dept. of Obstetrics & Gynecology
Biomedicum Helsinki, 4th Fl.
Haartmaninkatu 8
Helsinki, 00029
Finland
Telephone: 358-40-756-4237
Email: marseppa@mappi.helsinki.fi

Zarate, Arturo
National University of Mexico, Instituto
Mexicano Seguro Social
Endocrine Res. Unit
Centro Medico Nacional
Hospital de Mexico, Agrarismo 208-601
Mexico City, 11800
Mexico
Telephone: 52-55-558-87521
Email: zaratre@att.net.mx

Author Index

Aagaard, Kjersti M F-049, S-175
Abati, S S-046
Abdi, Shahram T-062
Abdollah Shamshirsaz, Alireza O-024
Abdulhasan, Mohammed T-179, S-207
Aberdeen, Graham W O-131, S-100
Aboulhosn, Lara T-195
Abrahams, Vikki M T-107, T-141, T-193, S-173
Abusamaan, Mohammed S F-124
Abu-Soud, Husam M O-123, T-196, S-178, S-180
Acevedo, Jesus T-029
Ackerman IV, William E F-030, S-025
Adam, E T-065
Adam, Stefanie F-153
Adams, Nyssa R O-002
Adeli, Sharareh T-151, F-020
Adeoye, Olayemi O O-134
Agaku, Israel T S-067
Agamasu, Enyonam T-138
Agno, Julio O-046
Agus, Sami S-204
Ahmad, Shakil O-038
Ahmed, Asif O-038
Ahmed, Hauwa S-031
Ahn, SooHyn S-113
Ahn, Soo Hyun F-114, S-114
Ahrendsen, Jared T T-049
Aiken, CE O-128
Ainscough, Kate M O-091, F-054
Ainsworth, Alessandra J T-175, S-121
Aitken, John F-151
Aja, Adama O-026
Akama, Tomoya T-181
Akselrod, Dikla T-163
Alahari, Sruthi O-081
Alali, Zahraa O-019
Alam, Sheikh MK O-030
Alamoudi, Rana T-177, F-042
Alarab, May S-125
Albertsen, Hans F-120, F-197
Albino, Nicole R T-041
Albright, Benjamin F-109, S-108
Aldahaheri, Sarah S-180
Aldaheri, Sara S-178
Alderman III, Myles H O-129
Aldhaheri, Sarah R O-123
Alfirevic, Z O-043
Alharbi, Mona T-108
Al-Hendy, Ayman O-107, O-156, T-125, F-124, F-126, S-001
Ali, Alhousseini T-055
Ali, Mehboob O-158
Ali, Mohamed A F-126
Al-Ibraheemi, Zainab F-055, S-092
Aljunaidy, Mais M F-077
Al-Khan, Abdulla O-041, T-039
Alkhotani, Emad T-177
Allen, Ronald F-098
Allen, TK T-026
Allison, B T-078
Allison, BJ O-053, O-055, O-060, O-062, T-046, S-099
Alrahmani, Layan F-092
Alrais, Mesk T-037
Alsenani, Nawal F-042
Alshehri, Wael O-133
Alsina, Angel F-171
Altwerger, Gary O-102, F-109, S-107, S-108
Alvarado, Fernanda L F-152
Alvero, Ayesha B T-107
Amabebe, Emmanuel T-013, F-018, S-006
Amador, Elizabeth S-199
Amdur, Richard F-111, F-123
Ampey, Bryan C T-172
Amro, Farah H T-037
Anamthathmakula, Prashanth O-085, T-034
Anand, Sonia T-070
Ananth, Cande V T-027, T-056, T-059, F-067, F-148, S-056
Anchan, Raymond M F-211
Anderson, Corrie P S-054
Anderson, Matthew L O-070, S-033
Anderson, Nathan O-141
Anderson, Sarah F-040
Anderson, Stasia T-073
Anderson, William S-044
Andrews, V F-044
Anelli, GM S-046
Ang, Wei S-096
Angata, Kiyohiko T-181
Ankumah, Nana-Ama E T-037
Anspach Will, Erica O-150
Antolic, Andrew T-101, F-076
Anton, Lauren F-154, S-022
Antonia, Alex F-014
Antoniou, Mike O-064
Antony, Kathleen M F-049
Anttonen, Julia F-003
Anucha, Eberechi T-015
Anumba, Dilly OC T-013, T-062, F-018, F-099, S-006
Apa, Rosanna F-205
Aplin, John D O-146
Archer, David T-116
Arcuri, Felice F-184
Arenas-Hernandez, Marcia O-036, F-023
Arian, Sara S-088, S-090
Arif, Hattan O-157, T-100, S-097
Arita, Yuko T-157, F-156
Arlier, Sefa O-072, O-110, O-143, T-007, T-011, T-020, F-167
Arlin, Blood T-156
Arnau, Vicente T-185
Arndt, Thomas J F-022
Arnold, Chris C T-040
Aronoff, David M T-051
Arosh, Joe A O-015, F-140
Arroyo, Viviana T-081
Arteaga-Cortes, Lourdes T-071
Aschengrau, Ann T-089
Asemota, Obehi O-120
Atlass, Jacqueline T-064
Aurélie, Hennes F-186
Austin-Williams, S F-073
Avecilla, Alexa S-149
Avril, Norbert O-106
Avril, Stefanie O-106
Awadalla, Michael S T-055
Ayad, Martina T S-029
Aydin, Mehmet Serif S-204
Aye, Irving LMH O-139
Azodi, Masoud O-102, F-106, F-108, F-109, S-107, S-108
Baack, Michelle F-083
Baart, Esther B T-197
Bacon, Phoebe L S-036
Badger, Gary T-134, F-162, S-132
Badger, Gary J T-167
Baeurle, Stefan T-113
Bafligil, Cemsel T-120
Bafor, Enitome E O-142
Baibakov, Boris S-179
Baig-Ward, K Maravet T-073
Bajaj-Elliott, Mona O-003
Baker, Bernadette C O-079, S-153
Baker, Philip O-094
Baker, Tina O-029
Balaguer, Nuria O-045
Balakrishnan, Meena F-078, F-081, S-175
Balayan, Shaina T-110, T-210
Balili, Avenir T-183
Banadakoppa, Manu S-175
Banks, Nicole S-179
Banu, Sakhila K O-015, F-140
Bao, Junjie T-019, F-034
Bao, Xiuliang T-142
Barbour, Kelli T-066
Barila, Guillermo O T-012, T-104, F-015
Barker, Gillian F-052
Barker, Hannah F-074
Barnard, Annabeth O-007
Barnea, Eytan R O-010, S-112
Barnes, Randall B S-202
Barnett, Scott D S-034
Barr, Andrew L T-040
Barragan, Fatima O-016, T-210
Barry, Peter A O-005
Bartlett, Thad Q S-085
Bartnitzek, Christina O-086
Baschat, Ahmet F-143
Bastarache, Lisa A T-051
Bastos, Larissa B T-014
Basu, Jayasri T-138
Bateni, Zhoobin S-103
Bates, Keenan T-072, S-072
Bates, Wright F-182
Battarbee, Ashley N F-050, S-135
Baum, Stephanie F-183, S-183
Baumann, Marc U O-135
Bautista, Claudia J S-070
Bayasula, Bayasula T-189
Beachy, Dawn F-190
Beall, Marie H O-130
Beaman, Kenneth T-174
Beard, Sally O-037
Beaudry-Richard, Alexandra S-018, S-021
Beck, C O-053, O-055, T-046
Becker, Christian T-120, F-117, F-121

Publication Number Prefix Key

Oral Presentations
O-001 - 052 = **Thursday** Oral Presentations
O-053 - 124 = **Friday** Oral Presentations
O-125 - 160 = **Saturday** Oral Presentations

Poster Presentations
T-001 - 212 = **Thursday** Presentations
F-001 - 212 = **Friday** Presentations
S-001 - 211 = **Saturday** Presentations

Bedaiwy, Mohamed A T-140
Beer-Weisel, Ruthy F-043
Behr, Barry F-185
Behrendt, Nicholas T-099, S-093
Belarbi, Lydia S-018
Belfort, Michael A F-158, S-049, S-088, S-089, S-090, S-103
Bell, Aleeca F F-057
Bellone, Stefania O-102, F-108
Belville, Corinne F-031
Benac, Drew D S-044
Benadiva, Claudio A O-150
Ben Bashat, Dafna S-101
Benfield, Rebecca T-001
Bennett, Michael O-009
Bennett, Phillip R O-031, O-033, O-109, T-009, T-015, T-017, T-186, F-187, S-013, S-020, S-031
Ben-Shalom Tirosh, Neta T-163
Benshalom-Tirosh, Neta F-043
Ben-Sira, Liat S-101
Bentley, Rex S-011, S-012
Bento, Giovana F F-065
Berdahl, Danielle M O-039
Berg, Jonathan T-095
Berga, Sarah L F-116
Bergmann, Ulrich F-003
Bergstrom, Colin S-111
Berkowitz, Ross S O-103
Bernal, John F-079, F-085
Bernardi, Lia A S-202
Bernstein, Ira M T-134, T-167, T-170, F-162, F-165, S-132, S-168
Berry, Mary J T-086
Berryman, Kathryn F-089
Besser, Limor T-163, F-043
Betancourt, Ancizar O-024, S-049
Beusker, Patrick O-102
Bevilacqua, Estela O-145
Bhatt, Shweta J S-026
Bhatti, Gaurav S-145
Bi, Wei Guang F-062
Bianchi, Diana W S-086
Bidarimath, Mallikarjun F-114
Bidwell, Christopher F-098
Biel, Frances M T-042, T-088
Biggio, Joseph F-040
Biggs, Sarah S-203
Binder, Natalie K O-037
Bird, Ian M O-039, T-172, S-174
Birnbaum, Shifra F-085
Biron-Shental, Tal F-169
Bischoff, Sabine J F-096
Bishop, Alexa T-148
Bishop, Andrew C F-079
Black, Jon S-107
Black, Jonathan D O-102, F-106, F-108, F-109, S-108
Blackwell, Sean C T-037
Blanchon, Loic F-031
Bledsoe, Tiffaney O-077
Blesson, Chellakkan S F-081
Block-Abraham, Dana F-143
Bloise, Enrrico O-082, F-069
Bloise, Flavia F F-069
Blumenthal, Elizabeth A F-037, S-038
Blundell, Mike O-064
Bocca, Silvina F-204
Bocking, Alan S-015
Boeck, Lourdes S-087
Boehmer, Brit H T-083, F-084
Boeldt, Derek S O-039
Boggess, Kim T-095, F-068, F-070
Boggess, Kim A T-004
Bok, Rachael O-141
Bollati, V S-046
Bolnick, Alan T-179
Bolumar, David F-188
Bonazzoli, Elena O-102, F-108
Bone, L O-017
Boniface, J Jay T-004
Bonney, A F-028
Bonney, Elizabeth A O-011
Borders, A T-065
Borggreven, Nicole V O-004
Borowski, Kristi S F-092
Botting, KJ O-053, O-055, T-046, F-073, S-045
Boudreault, Amarilys O-140
Bou Nemer, Laurice F-180
Bousiéguez, Manuel T-106
Bowe, Sophie F-101
Boyce, Susan O-017, T-113, F-122
Boyle, Ashley K T-018
Braeuer, Nico F-122
Brahmbhatt, Himanshu O-037
Brain, K T-078
Brain, KL O-053, O-055, O-060, O-062, T-046, F-073, S-099
Brandt, Kathleen R S-122
Bräuer, N O-017
Braun, Joseph F-047
Breathnach, Fionnuala O-043, T-169, F-150, S-169
Brewer, A O-044, F-166, S-167
Brian, Mercer M T-028
Brien, Marie-Ève S-018
Brigham, Denise T-001
Britten, Joy O-066, F-125
Brock, Clifton O F-061, S-042, S-043
Broeckel, Rebecca O-100
Brohman, Brian S-130
Brooks, Doug O-136
Brosens, Jan J O-051, T-009, F-187, S-184
Brosnihan, K Bridget O-077
Brouwer, Jenny F-091
Brown, Amy G T-012, T-104, F-015, F-154, S-022
Brown, Laura D T-083, F-084
Brown, Lucia T-133
Brown, Richard G O-031, S-020
Brown, Stephen T-133
Brownbill, Paul O-146
Brugh, Victor F-204
Bruner-Tran, Kaylon L O-015
Bucher, Matthew S O-148
Buckley, Suzanne MK O-003, T-022
Buelna, Mabel S-077
Buhimschi, Catalin S O-035, T-178, F-089
Buhimschi, Irina A O-035, O-096, O-158, T-026, T-106, T-178, F-089
Bukiya, Anna T-092
Bukulmez, Orhan F-180
Bullard, Janine E S-036
Bulmer, Judith N S-185
Bulun, Serdar E O-013, O-065, O-069, S-123
Burd, Irina O-034, O-133, O-157
Burney, Richard O O-152, S-186
Burrows, Julie T-070
Burton, Graham J S-142, S-184
Buss, C T-065
But, Anna F-118
Butler, Trent T-030
Butler Tobah, Yvonne S F-092
Buxton, Iain LO S-034
Buyuk, Erkan O-120
Buza, Natalia O-102
Cabanillas, Sergio F-188
Cackovic, Michael F-089
Caesar, Gerialisa T-150
Cahill, Alison G T-097, F-058
Calabuig-Navarro, Virtu T-154, F-152
Calhoun, Byron C F-011
Callaway, Chris O-058
Camacho, Leticia O-059, F-098
Camm, EJ F-073
Campbell, Heather F-176
Campbell, Lisa L T-140
Campo, Hannes S-209
Canaday, Pam O-118, T-153
Caniggia, Isabella O-081
Cann, Leonie M S-185
Cantone, L S-046
Cantonwine, David T-047, S-130
Cao, Bin S-008
Cardellicchio, M S-046
Carlson, Laura S-091
Carmeliet, Peter O-048
Carpenter, J S-073
Carr, Bruce R T-184, F-180
Carr, David J S-040
Carranza, Leslie S-038
Carrascosa, JP F-110
Carrillo, Maira T-155
Carter, Sue F-057
Cartwright, Judith E T-148
Carty, N O-017
Carvajal, Jorge A F-146
Casalechi, Maíra T-203
Casanello, Paola T-081
Case, Patrick F-077
Cass, Darrell L S-103
Castellani, Roberta O-010
Castellví, Josep F-113
Castro, Laura N T-192
Castro-Rodriguez, Diana S-084
Castro-Rodríguez, Jose T-081
Catherino, William H O-066, F-125
Catov, Janet T-064
Cattaneo, Dario S-057

Publication Number Prefix Key

Oral Presentations
O-001 - 052 = **Thursday** Oral Presentations
O-053 - 124 = **Friday** Oral Presentations
O-125 - 160 = **Saturday** Oral Presentations

Poster Presentations
T-001 - 212 = **Thursday** Presentations
F-001 - 212 = **Friday** Presentations
S-001 - 211 = **Saturday** Presentations

Caughey, Aaron B S-051, S-065
Caughey, Melissa T-131
Cavallo, Inês K T-203
Cervelló, Irene S-209
Cetin, Irene F-063, F-066, S-046, S-052, S-057
Ch, R S-167
Cha, Hyun-Hwa T-149
Chaemsaithong, Piya T-003, F-035, S-005, S-145
Chai, Daniel S-115
Chaiworapongsa, Tinnakorn S-142
Chakraborty, Damayanti T-147
Chalak, Lina F F-019
Chambers, Chester S-064
Chamley, Lawrence W O-116, S-173
Chan, Denise CY S-013
Chan, Eng-Cheng T-030, F-033
Chan, Kenneth K T-067
Chandrasekaran, S F-173, S-161
Chang, Eileen I T-102, F-022
Chang, Hao T-121
Chang, Patricia T-131
Chapman, David T-013, S-006
Chaput, Dale F-171
Charles, Cassandra T-054, T-111
Charnock-Jones, D Stephen O-139, T-168, F-141, F-142, F-157, S-156, S-166
Charron, Maureen O-120
Chattergoon, Natasha N T-102
Chatterjee, Prodyot T-105
Chau, Cindy T T-067, T-069
Chaubey, Alka T-087
Chauhan, Madhu S-134
Chavan, Niraj R T-075
Chavarria, Melina O-049
Chavez, Maria T-132
Chelliah, Anushka M S-147, S-149
Chemtob, Sylvain O-140, T-016, S-018, S-021
Chen, Chie-Pein S-172
Chen, Dong-bao T-135, S-171
Chen, Jennifer C S-171
Chen, Jia F-048, S-047
Chen, Kang O-113, O-159
Chen, Man F-102, F-130
Chen, Qi O-116, T-162
Chen, Xi S-053
Chen, Xin S-188
Chen, Yii-Der Ida S-139
Cheng, Janice C T-040
Cheng, Yvonne W S-051, S-065
Chervenak, Frank S-088, S-090
Chettier, R O-044, F-166
Chettier, Rakesh F-120, F-197
Chi, Yueh-Yun F-129
Chin, Peck-Yin S-018
Chin-Smith, Evonne C F-002
Chiossi, Guiseppe F-178
Chiu, Vicki Y F-038
Chiu, Yi-Lin T-116
Cho, A Ra T-057
Cho, SiHyun T-182, F-112
Cho, Su Jin S-076
Choe, Gina O-087
Choi, Minji F-145
Choi, Suk-Joo T-149, F-145
Choi, Young Min F-207
Choi, Young Sik T-182, F-112
Cholia, Anand T-132
Cholia, Saloni T-132
Chollet, André S-002, S-031
Chorich, Lynn P T-087
Chotai, Pranit N T-058
Choudary, Ahsan F-079
Chougnet, Claire A O-074
Chow, Greg E S-186
Chowdhury, Dipanjan O-103
Christenson, Lane F-026
Chuang, Tsai-Der O-067
Chuecos, Marcel T-132, T-155
Chwalisz, Kristof T-116
Cidlowski, John A F-088
Cifuentes-Zúñiga, Francisca T-081
Cindrova-Davies, Tereza S-184
Clairefond, Gaël F-031
Clark, Alys R T-152
Clark, Erin AS O-006
Clark, Steven L F-158, S-088, S-089, S-090
Clarke, Geoffrey D T-079, S-079
Clarke, P T-169
Clem, Tim S-186
Clementi, Emilio F-066, S-057
Clevert, Djork-Arne T-112
Clifton, Vicki L S-083
Cocker, Alexander S-193
Codsi, Elisabeth F-092
Cody, F O-043
Coelho, Anne-Marie O-017, T-113, F-122
Cohen, Matthew S-183
Colgin, Lois O-100
Colgrave, Eliza M O-020
Collier, Eric S T-024, F-029
Collins, Clare E F-071
Collins, Frances O-101
Colombo, Anna F-066
Comins-Boo, Alejandra T-194
Commins, Scott F-068
Comstock, Jessica M T-038
Comuzzie, Anthony G F-085
Conca Dioguardi, Carola S-188
Condon, David S-151
Condon, Jennifer C O-073, O-085, T-034, F-035
Conesa, Ana T-185
Confino, Rafael O-153, T-207, F-208
Conlon, FG S-045
Connell, Kathleen A O-111
Conrad, Kirk P O-117, F-129
Constance, Elizabeth S-194
Constância, M F-141
Constantinof, Andrea O-082, O-125
Conway, Cassandra T-005
Cooke, Christy-Lynn M O-061, F-077
Cooke, Katherine M S-140
Cooper, Kylie T-134, S-132
Cooper, Sara F-182
Correa, Francisco S-077
Corti, Silvia F-063, F-066, S-057
Costantine, Maged F-178
Costello, Katherine T-119
Cotán, D F-110
Cotter, A O-043, T-169, S-169
Coughlin, Eric F-011
Cousin, Emma O-021
Cousins, Fiona L F-193
Cox, Jeris O-066, F-125
Cox, Laura A O-147, T-098, F-079, F-085, S-070, S-071
Cramer, Daniel W O-103
Crawford, Michael A S-148
Cremers, Thomas IFH T-173
Crescini, Claudio F-159
Crimmins, Sarah S-048
Crispi, Fatima F-170
Critchley, Hilary OD O-048, T-114, S-110, S-184
Cuckle, Howard O-008
Cui, Wei F-212
Culhane, J T-065
Culliton, M T-169
Cuneo, Bettina T-099
Cusumano, Andrew S-182
Dada, Maqbool S-064
Dae Kim, Jung O-087
Daftary, Gaurang S O-018, T-175, F-119
Dahal, Sudip T-027
Daher, Silvia F-013
Dai, Aihua S-210
Dai, Jing T-179, F-210, S-207
Dale, Maryjane F-121
Dalloul, Mudar T-054, T-111
D'Alton, Mary E T-056, T-059, F-067
Daly, S O-043, T-169, S-169
Dambaeva, Svetlana T-174
Damiani, Francesco F-184
Danilack, Valery A F-177
Danny, Schust T-143
Darbinian, Nune O-005, O-132, F-086
Darby, Jack O-136
Das, Ananya F-016, S-155
Das, Subhendu O-113
Dasgupta, Chiranjib F-102, F-130, S-069, S-128
da Silva, Márcia G T-002
DaSilva-Arnold, Sonia O-041, T-039
Davenport, A O-017
Davenport, Hailey F-098
David, Anna L O-064, F-074
Davidge, Sandra T O-056, O-061, O-114, F-077
Davidson, Christina S-089
Davidson, Donald O-029
Davidson, Sasha M S-061
Davies, Michael T-174
Davies, Norman P F-092
Davies-Tuck, Miranda T-139
Davis, Melissa O-059, F-098
Davisson, Robin L T-165
Dean, Jurrien S-179
DeAndrade, Samantha P F-177
Debiève, Frédéric F-155
DeCherney, Alan H O-151, T-199, T-200, F-201, S-177, S-198

Publication Number Prefix Key

Oral Presentations
O-001 - 052 = **Thursday** Oral Presentations
O-053 - 124 = **Friday** Oral Presentations
O-125 - 160 = **Saturday** Oral Presentations

Poster Presentations
T-001 - 212 = **Thursday** Presentations
F-001 - 212 = **Friday** Presentations
S-001 - 211 = **Saturday** Presentations

De Cicco, Simona F-205
De Clercq, Katrien O-052, T-187
De Coppi, Paolo O-064
DeFillppis, Victor O-100
de Goffau, Marcus F-157, S-156
de Haas, Sander F-131, F-132
Deihl, Tiffany E T-082
Dela Cruz, Cynthia T-203
Delaney, Meaghan A O-070
De Leo, Bianca T-114
de Lima, Moisés D T-002
Delpiano, Ana M F-146
Demasio, Kafui A S-061
DeMayo, Francesco J O-002, T-096, T-118, S-033
Demment, Margaret T-206
De Moor, Bart S-117
Deng, Jie O-063
Deng, Sheng T-121
Denny, Joshua C T-051
Denny, Kathryn F-111, F-123
Depoix, Christophe L F-155
Derks, JB S-045
Dermont, Sarah S-193
Derricott, Hayley T-159
Derzic, Karen T-064
Desai, Mina O-130, T-085, F-080
Desai, Neeraj F-061
Desai, Nina S-208
Deshmukh, Uma F-106
Desrosiers, Laurephile T-005
Detti, Laura T-161
DeVine, Ann F-154, S-022
Devine, Kate F-201, S-177
Devlin, Maureen J O-083
DeVore, Greggory S-098
de Vries, Jeanne HM F-196
De Vries, Raymond G S-157
de Windt, Leon S-165
Dhal, Sabita O-113
Dhana, Klodian T-205
D'Hooghe, Thomas S-115, S-116, S-117
Diamond, Michael P O-105, O-156, T-125, F-124
Diamond, Michael S O-098
Diana, Krüger S-191
Diano, Sabrina O-087
Dias, Julia A T-203
Díaz, Ana S-209
Diaz, Johana S-036
Diaz-Gimeno, Patricia O-115, T-185, T-188
di Bartolo, Ilenia F-063
Dick, Jr., Edward J T-098, F-085
Dickens, Brett T-075
Dicker, P O-043, T-169, S-169
Dickinson, Hayley T-139, S-102
Diehl, Jéssica M F-179
Dietz, Paul F-011
DiFeo, Analisa O-106
Di Florio, Christian F-205
Dildy, Gary S-088, S-089, S-090
Dildy, Gary A F-158
Dilworth, Mark R T-158, T-190
Dimelow, Emma F-099
Di Nicuolo, Fiorella O-010
Dioni, L S-046
Dirong, Dong O-160
Di Salvo, Ivana F-209
Di Simone, Nicoletta O-010
Dixon, Christopher L O-076, T-006, F-004, F-163, S-004
Do, Keith F-040
Do, Samantha S-037
Dodson, Blair T-080
Doe, Zhulanqiqige F-107
Dokter, Wim O-102
Dolhain, Radboud JEM F-091
Dolitsky, Shelley N O-151
Domínguez, Francisco O-047, O-115
Dong, Daoyin O-001
Dong, Qunfeng T-071
Dong, Xuesen T-031
Dong, Yafeng O-008
Dong, Yuanlin O-093, S-049, S-134
Dong, Yupeng F-104
Donoghue, Jacqueline S-185
Dopico, Alex T-092
Dopierala, Justyna T-168, F-141, F-142
Dorien, O S-117
Dorin, Julia O-029
Dorit, Paz T-163
Doss, Robert S-130
Douglas, Nataki C T-165
Doulias, Paschalis T O-009
Downey, P T-169
Drakakis, Peter T-180
Drehfal, Lindsey C S-023, S-024
Drewlo, Sascha T O-144
Driggers, Paul H T-124
Drongelen, Joris F-132
Drury, Andrea O-098
Drutz, Harold S-125
Druzin, Maurice S-037
Dube, Peter T-071
Ducsay, C O-062, T-078, S-099
Dude, Annie M T-090, S-050
Duffy, Jennifer T-069
Dukler, Doron S-003
Dulay, Antonette T O-035
Duleba, Antoni S-116
Duncan, Jose R T-058, T-092, T-161
Duncombe, Gregory T-048, F-153
Dunk, Caroline E O-082, T-171
Dunn, Randall O-108
Dunn-Fletcher, Caitlin E O-080
Durairaj, Ruban P O-051
Dvir, Maya S-101
Dye, Timothy DV T-206, F-090, F-200, S-068
Dyson, Matthew T O-013
Dyson, Rebecca M T-086
Eaton, Simon O-064
Ebeling, Peter R T-139
Eddershaw, Peter S-039
Eden, Robert D S-062
Edge, Melydia T-001
Edison, Arthur F-076, S-147, S-149
Edlow, Andrea G O-127, S-086
Edrada-Ebel, RuAngelie O-142
Edwards, Stacey L S-120
Edwards, Todd S-124
Ehret, A S-027
Ehrhardt, Jens S-191
Eidem, Haley R F-007
Eisenberg-Loebl, Iris O-088, T-117
Eke, Ahizechukwu C T-094, S-067
Eke, Uzoamaka A S-067
El Aalamat, Yousef S-117
El Andaloussi, Abdeljabar O-107, S-001
Elfeky, Omar T-048, F-153
ElHusseini, Heba F-126
Elias, Kevin M O-103
Ellery, Stacey T-139, S-102
Elmikawy, Reem F-043
Eloundou, Solange O-133
Elovitz, Michal A T-012, T-104, F-015, F-154, S-022
El-Sayed, Yasser S-037
Elshenawy, Summer O-009
Elston, Marlee F-072
England, Sarah F-133
Engmann, Lawrence O-150
Enquobahrie, Daniel T-050
Ensari, Tugba S-195
Entringer, S T-065
Eppes, Catherine S F-158
Erez, Offer T-163, F-035, F-043, S-003, S-142, S-145, S-146
Erfani, Hadi S-088, S-090
Erickson, Elise N T-042, T-088
Ernst, Linda S-160
Erwich, Jan J T-139
Esakky, Prabagaran O-098
Escalona-Vargas, Diana T-032
Esmail, Arwa T-148
Esnal Zufiaurre, Arantza M O-101, T-114
Espinoza, Cheyenna S-147
Espinoza, Jimmy O-024, S-103
Esplin, Sean F-045
Estes, Jacob O-104, T-108
Estrada, Sarah M O-034, F-149, S-136
Eswaran, Hari T-032
Euser, Anna G T-049
Evans, James P T-095
Evans, Janice P O-121
Evans, Mark I O-089, S-062
Evans, Shara M O-089, S-062
Ezashi, Toshihiko T-143, S-210
Ezra, Yossef T-068
Faas, Marijke M T-173
Failor, Courtney F-127
Fais, Maria F F-016
Falcone, Tommaso O-019
Falk, Marni J F-154
Fan, Yanhong F-191
Fang, Xin T-008, F-006
Faraci, Christine E T-191
Farber, Charles R S-139
Farine, Tali F-175
Farkash, Rivka S-055
Farladansky-Gershnabel, Sivan F-169
Fassbender, Amelie S-117
Fassett, Michael J O-099, F-038

Publication Number Prefix Key

Oral Presentations
O-001 - 052 = **Thursday** Oral Presentations
O-053 - 124 = **Friday** Oral Presentations
O-125 - 160 = **Saturday** Oral Presentations

Poster Presentations
T-001 - 212 = **Thursday** Presentations
F-001 - 212 = **Friday** Presentations
S-001 - 211 = **Saturday** Presentations

Faus, Amparo S-209
Fauser, Bart CJ T-205
Favero, C S-046
Fay, Justin T-126
Fazleabas, Asgerally T O-016, S-113, S-114
Fears, Fayola T-097
Feldman, Sarah F-024
Feltovich, Helen S-008, S-023, S-024
Fendler, Wojciech F O-103
Feng, Du T-001
Feng, Liping T-026, F-014
Ferchaud-Roucher, Veronique S-152
Fernandez, M S-027
Fernando, Shavi S-203
Ferreira, Teresa F-117
Figueroa, Jorge P T-077, S-078
Finneran, Matthew S-044
Fischer, Oliver M O-017, T-120
Fisher, Andrew R S-200
Fisher, Heather S-092
Fisher, Susan J O-115
Flannery, Clare A O-087, S-140
Fleischer, Kathrin F-192
Fleischer, Tracey C T-004
Fletcher, Nicole M O-105, F-124
Foca, Kimberly F-029
Foeller, Megan E S-037
Fong, Alex T-067, T-069
Fontes, Klaus N F-069
Forbes, Karen O-079, S-153
Ford, Maegan T-039
Ford, SG S-045
Ford, Stephen P O-057, T-053
Foreman, Kate T-095
Forsyth, Alexandra O-021
Fortin, Claude T-122
Fortner, Kim T-069
Fox, Angela C T-004
Fox, Karin O-024, S-088, S-090
Franch, Juliet D S-120
Franco, Oscar H T-205
Frank, Karen S-036
Frasch, MG F-093
Frew, Lorraine O-029
Frias, Antonio E O-100
Friedman, Alexander M T-056, T-059, F-067, S-056
Friez, Michael J T-087
Fritsch, Martin T-112
Froehlich, Rosemary J F-047
Froeling, Fleur EM T-166
Fry, Rebecca S-063
Fue, Misaki F-107
Fugarolas, Keri O-132
Fuhrmann, Ulrike O-086
Fujii, Tatsuya F-203
Fujii, Tomoyuki F-203
Fukuda, Michiko T-181
Fukushima, Akimune O-028
Fulp, Abigail S-011, S-012
Fung, Jenny N O-020, S-120
Funghi, Lucia F-184
Furusho, Hisako F-017
Gaccioli, F F-141, S-166
Gal, Hilah F-169
Galan, Henry T-099, F-025, S-093
Gallos, George T-027, F-005
Gallot, Denis F-031
Gammill, Hilary S O-021, O-044, F-166, F-173, S-161, S-167
Ganapathy, Thashma O-094
Gandhi, Kushal T-155
Ganguly, Esha O-061
Ganieva, Umida S-187
Gao, Haijun F-048, F-078, S-047
Gao, Xiang T-071
Gao, Xiao-Bing T-121
Gao, Yuan S-159
Garavaglia, Elisabetta O-097
Garcia, Maria D T-194
Garcia-Flores, Valeria F-023
Garcia-Grau, Iolanda O-050
Gardner, Lucy S-184
Garfield, Robert E T-019, T-025, T-043, F-034
Garovic, Vesna D F-092
Garrido-Gomez, Tamara O-115
Garrion, Etoi T-076
Garrison, Etoi S-094
Garzon, Diego T-122
Gaskell, Sarah M F-177
Gatford, Kathryn L S-074
Geerts, Lauren F-132
Gelinne, Aaron T-133
Gemkow, M O-017
Genbacev, Olga O-115
Geng, Tingting O-063
Georgia, Atella F-069
Georgiou, Ektoras X T-009
Georgopoulou, Aikaterini O-040
Geraghty, Dan E T-171
Geremaia, Cassie T-049
German, Nadezhda F-103
Gerow, Kenneth G F-085, S-085
Getahun, Darios O-099, T-157, F-038, F-156
Gezahegn, Beakal F-133
Gharanei, Seley O-051
Ghezzi, Silvia O-097
Ghnenis, Adel B T-053
Ghosh-Choudhury1, Triparna O-070
Ghossein-Doha, Chahinda T-166, F-131, F-132, S-165
Gibb, William O-082
Gibbins, Karen J T-038, F-068, F-070
Gibbons, William O-046, O-070, T-096, S-196, S-197
Gibson, Douglas A O-101, F-193
Gidiri, Muchabayiwa F O-096, T-106
Gilbert, Nicole S-126
Gill, Pavinder S-208
Gillan, Allison T-036, F-105, S-093
Gillespie, Siobhan T-062
Gilmandyar, Dzhamala S-068
Gilman-Sachs, Alice T-174
Gilmore, Kelly T-095
Gil-Moreno, Antonio F-113
Gilner, Jennifer B S-011, S-012
Gil-Sanchis, Claudia S-209
Ginsberg, Yuval F-074
Girard, Sylvie S-018
Giri, Ayush S-124
Girling, Jane E O-020, F-164, S-120
Girsen, Anna S-037
Gishto, Arsela S-208
Gissler, Mika F-118
Gissy, Kelly T-119
Giudice, Linda C T-110, T-210
Giussani, DA O-053, O-055, O-060, O-062, O-128, T-046, T-078, F-073, F-082, F-093, S-045, S-081, S-099
Glenn, Jeremy P T-098
Goedings, Peter O-102
Goetz, Laura G O-083, S-116
Goetzl, Laura O-005, O-132, F-086
Goldberger, Adina O-092
Goldman-Wohl, Debra O-088, T-117
Goldsmith, Laura T S-026
Goldstein, Jeffery A T-051
Gomes, Hannailly R F-069
Gomez, Luis T-161
Gomez-Lopez, Nardhy O-036, F-023, S-145, S-192
Gong, S F-141, S-166
Gong, Sung F-142
Gonik, Bernard S-180
Gonzalez, Samantha T-138
Gonzalez, Tania L S-139
González-Montfort, Marta O-045
Goodman, Jean R F-001, S-060
Gopalakrishnan, Kathirvel O-027, T-129
Gorasiya, Samir S-016
Gordon, Adrienne F-071
Gordon, Emily F-182
Gordon, Lavinia F-041
Gordon, Siamon T-120
Gormley, Matthew O-115
Gornbein, Jeffrey F-037
Gossling, Megan O-054, O-090
Goswami, Sumanta S-190
Goto, Maki T-189, S-187
Gotteland, Jean-Pierre S-002
Gould, Jeffrey B F-064
Grafe, Marjorie O-100
Graham, Ernest T-100, S-097
Grasso, Esteban O-032
Gratacos, Eduard F-170
Gray, Lisa S-054
Gray, Nicola T-140
Gray, Theora T-008
Grebennikova, Stephaniya F-086
Green, Katherine A T-199
Greenbaum, Shirley T-163, F-043, S-003
Greenberg, Meir S-058
Greenblatt, Ruth M T-110
Greenfield, Caryn O-088, T-117
Greenwood, Susan L S-153
Gregg, Anthony R S-147, S-149
Grigsby, Peta L O-100, S-102
Grindler, N S-150
Grisaru Granovsky, Sorina S-055

Publication Number Prefix Key

Oral Presentations
O-001 - 052 = **Thursday** Oral Presentations
O-053 - 124 = **Friday** Oral Presentations
O-125 - 160 = **Saturday** Oral Presentations

Poster Presentations
T-001 - 212 = **Thursday** Presentations
F-001 - 212 = **Friday** Presentations
S-001 - 211 = **Saturday** Presentations

Grobman, William A T-044, T-065, T-090, F-046, S-035, S-051, S-065
Groom, Katie F-041
Grummer, Mary A S-174
Gu, Yang T-176, T-209
Guan, Jun F-121
Guanzon, Dominic O-104, F-153
Guelfi, Kym J F-051
Guerrero, Quinton W S-024
Guess, Marsha K O-111
Guimarães da Silva, Márcia F-179
Gulersen, Moti F-183, S-183
Guller, Seth T-141
Gumina, Diane T-036, F-105, S-093, S-098
Günalan, Elif S-204
Gunatilake, Ravindu O-007
Guner, Joie Z O-070
Gunnala, Vinay T-201
Guo, Manman T-120
Guo, Wei O-057
Gupta, MB O-147
Gupta, Neha T-157
Gurewitsch Allen, Edith D S-064
Guzeloglu-Kayisli, Ozlem O-072, O-110, O-143, T-007, T-011, T-020, F-167, S-172
Gyamfi-Bannerman, Cynthia O-092, F-148, S-042, S-043, S-131
Gysler, Stefan M T-107, F-109, S-108
Haapalainen, Antti M F-003
Hackmon, Rinat T-171
Hadley, Emily E O-137, F-010, F-178
Haese, Nicole O-100
Haimov-Kochman, Ronit O-088, T-117
Hajjar, Nadia T-136, F-136
Halabi, Jacques O-098
Halder, Sunil K F-126
Hales, Barbara T-016
Hall, Nicole R T-060
Hall, Timothy J S-023, S-024
Hallahan, Terrence W O-089
Hallman, Mikko F-003
Hamamo, Eika F-060
Hameroff, Avi T-054
Hamilton, Karen F-129
Hammad, Ibrahim F-161
Hammes, Andrew T-049
Hammiche, Fatima T-197
Hamood, Abdul T-137
Hampton, Moss T-155
Han, Christina S T-193, S-173
Han, Guang O-130, T-085, F-080
Han, Limin S-129
Handal-Orefice, Roxane T-198
Hanita, Takushi O-012
Hankes, Amanda C T-172, S-174
Hankins, Gary O-027, T-160
Hanmer, Kaitlin T-047
Hannan, Natalie J O-037, T-140, F-041, F-164, S-109
Hanton, Fabienne S-020
Hanyaloglu, Aylin T-186, S-031
Hanyaloglu, Aylin C F-187
Hapangama, Dharani O-112
Harada, Miyuki F-203
Harada, Yuki S-127
Hardison, Rachel L T-020
Hardisty, Emily T-095, S-091
Harkema, Jack F-075
Härkki, Päivi F-118
Harman, Chris S-048
Harper, Lorie F-182
Harper, Teresa T-036
Harris, Sally S-091
Hart, Bethany F-026
Hart, Laura F-086
Hartmann, Katherine E O-095, S-124
Has, Phinnara F-047, F-177, S-162
Hasenbein, Kati S-118
Hashimoto, Chiaki F-107
Hassan, Sonia S O-036, T-003, F-023, F-035, S-005, S-142, S-145, S-146, S-192
Hastie, Roxanne S-109
Hawley, Nicola F-047
Hay, William W T-083, F-084
Haynes, Monique S-188
Hazes, Johanna MW F-091
Healy, Mae W O-151, F-201, S-198
Heazell, Alexander EP O-079, T-158, T-159, T-190, S-153
Hebert, Jessica F T-153, F-138
Heidari-Bateni, Zhoobin S-088, S-090
Heidari Kani, Minoo T-030, F-033
Heikinheimo, Oskari F-118
Heim, Kathleen R T-193
Heitman, Ryan J T-200
Heitmann, Ryan J O-152
Helbing, Willem A F-100
Held, Katharina T-187
Hellner, Karin F-121
Hemberger, Myriam S-184
Hemmings, Denise G S-164
Hennebold, Jon D O-100
Hennes, Aurélie T-187
Henriksen, Tore O-078
Henry, Amanda F-041
Henson, Jennifer T-174
Herbert, Bronwen R F-016, S-148
Herbert, Jessica F T-152
Herington, Jennifer F-032
Herrera, Christina A O-006, T-066
Herrero, María O-045, F-188
Herrmann, M O-017
Herry, CL F-093
Hershlag, Avner S-183
Herzog, Erik F-133
Hesley, Gina K S-121, S-122
Hess, S O-017
Hesson, Ashley T-094
Hester, Mark O-158
Heuerman, Anne C S-007
Hewett, Peter O-038
Hezelgrave, Natasha L F-002
Hickok, Durlin E T-004
Higgins, J O-043, T-169, S-169
Hildebrandt, Marisa O-123
Hill, Micah J T-199, T-200, F-201, S-198
Hilz, Kristina MT T-192, F-194, S-105
Hirani, Nik O-048
Hirata, Tetsuya F-203
Hirsch, Alec J O-100
Hirst, Jonathan J T-086
Hiyama, Satoshi S-127
Ho, Eric F-078
Ho, Shannon F-171
Hobbins, John T-036, F-105, S-093, S-098
Hoffman, Matthew F-045
Hohensee, Kylie S-072
Holden, Emily C F-198, S-026, S-205
Holdsworth-Carson, Sarah J O-020, S-120
Hollenbach, Stefanie J F-090, F-200
Hollenbeck, Megan A S-210
Holloman, Conisha M T-094, F-061
Homer, Hayden T-202
Hong, Richard F-037
Hooper, John O-104, T-108
Hopkins, Matthew R S-122
Horcajadas, JA F-110
Horne, Andrew W T-114, T-140
Horne, Rosemary S-203
Hornstein, Samuel F-211
Horvath, Tamas O-149
Hou, Xin O-140, T-016, S-018, S-021
Hou, Yue T-128
House, M F-005, S-027
Houshdaran, Sahar T-110, T-210
Howard, Mindie T-179
Howell, Nathan T-131
Hozawa, Atsushi O-028
Hsieh, Frances T-105
Hsu, ChienTing T-004
Hu, Fengling T-136, F-136
Hu, Huiping F-034
Hu, Jianzhong T-142
Hu, Min F-049
Hu, Xiang-Qun F-102, F-130, F-134, F-135, S-128, S-129
Hu, Zhiwei S-116
Huang, Chun-Yen S-172
Huang, Eunice Y T-058
Huang, Joseph F-184, S-172
Huang, Xiaohui F-102, F-130, F-134, F-135, S-069, S-128
Huang, Yingqun O-063
Huang, Yongmei T-056, S-056
Hubbard, Carol F-121
Huber, Hillary F O-126, S-085, S-095
Huber III, Warren J S-162
Hubinont, Corinne F-155
Huerter, Hanna T-061
Huffman, Elizabeth L O-080
Hufnagel, Demetra O-129, S-116
Hughes, Brenna S-162
Hughes, Francine T-076, S-094
Hui, Lisa T-063
Hui, Pei O-102, F-106

Publication Number Prefix Key

Oral Presentations
O-001 - 052 = **Thursday** Oral Presentations
O-053 - 124 = **Friday** Oral Presentations
O-125 - 160 = **Saturday** Oral Presentations

Poster Presentations
T-001 - 212 = **Thursday** Presentations
F-001 - 212 = **Friday** Presentations
S-001 - 211 = **Saturday** Presentations

Humphrys, Michael T-012
Hundt, Juliane O-014, F-115
Hung, Wei-Ting F-026
Hunt, HW F-173, S-161
Hunter, A S-169
Hunter Cohn, Karen S-199
Hurst, Bradley S T-195
Hurt, Kenneth J O-141
Hutchison, Mark R O-075
Hwang, Jae Ryoung T-149, F-145
Hyrien, Ollivier T-206
Hyun, Eirleen T-071
Ibañez-Chavez, Carlos A S-071, S-077, S-087
Idler, Jay T-055
Ieronimakis, Nicholas O-034, S-136
Ieronimakis, Nicholas M F-149
Iihara, Koji F-060
Ikeda, Hideyuki O-012
Ikeda, Tomoaki F-056, F-060
Ikhena, Deborah E O-069, F-208, S-123
Illsley, Nicholas P O-041, T-039
Imai, Kenji S-154
Imami, Nesrina F-016, S-193
Imbar, Tal O-088, T-117
Immediata, Valentina F-205
Imperio, Guinever E O-082, F-069
Imterat, Majdi F-043
Imtirat, Majdi T-163
Ingleby, Bernie T-040
Ingles, Judith O-073
Inglis, Steven R O-022, S-014, S-019
Ippolito, Giuseppe O-097
Iqbal, Anwar T-093
Irani, Mohamad T-201
Ireland, Kayla E S-138
Irizarry, Javier Perez F-106
Irwin, Juan C T-110, T-210
Ischiropolous, Harry O-009
Ishida, Chiharu S-187
Ishikawa, Gen S-059
Ismail, Nahed O-107, S-001
Itani, N O-053, O-055, O-060, T-046
Ito, Kiyoshi F-107
Ito, Takuya T-103
Ito, Yumiko S-154
Ivester, Thomas T-131
Iwanaga, Ritsuko O-111
Iwase, Akira T-189, S-187, S-189
Jablonski, K S-073
Jackson, Courtney O-074
Jackson, Laurence O-064
Jackson, Roy T-122
Jackson-Humbles, Daven F-075
Jaeger, Kathleen S-182
Jäger-Lansky, Agnes F-115
Jain, Joses A T-059, F-067
Jain, Sangeeta F-178
Jalkanen, Sirpa O-051
James, Jo L O-116
Jansson, Thomas O-054, O-078, O-090, O-141, O-147, S-150, S-152
Janzen, Carla F-037
Jaspers, Loes T-205
Javan, Mohsen O-082
Jayaram, Aswathi O-022, S-014, S-019
Jeelani, Roohi O-123, T-196, S-178, S-180
Jefferson, Kimberly K O-030
Jelin, Angie C S-036
Jena, Manoj O-113
Jenkins, Susan L O-126, S-085
Jensen, Todd S-009
Jeong, Jae-Wook O-002, T-118
Jeyasuria, Pancharatnam O-073, T-034, F-035
Jha, Swati T-062
Ji, Shuhan S-143
Jimenez, Jorge F-185
Jimenez, Patricia T T-184
Jin, Tianrong O-051
Jobe, Alan H O-074, S-039
Joerger-Messerli, Marianne S F-209, S-211
John, Liam V O-026, T-133
Johnson, Clark T T-041, S-036
Johnson, Jasmine D S-063
Johnson, Joshua O-111, F-191, S-188
Johnson, Mark R O-040, T-009, T-021, T-127, F-016, S-030, S-017, S-148, S-155, S-193
Johnson, MD F-141
Johnstone, Edward D O-146
Johnston-MacAnanny, Erika B F-116
Jones, Peter T-070
Jones, Rebecca L O-079, T-158, T-159, T-190, S-153
Jones, Sarah H O-095
Jones, Tiffanny L O-018, F-119
Joo, SK T-052
Joris, Vriens O-052, F-186
Joseph, Serene T-074
Joshi, Niyati T-085, F-080
Joss-Moore, Lisa F-083, S-073
Joyal, Jean-Sébastien S-018, S-021
Juhani, Asem F-124
Juhasz, Gabor S-142
Juhasz, Kata S-142
Julian, Colleen G T-049, S-133
Jun, JK T-052
Junaid, Toluwalope O O-146
Jung, Yun Ji S-170
Jungheim, Emily S-200
Junker, Anthony D T-024
Justice, Sheryl S T-020
Kabiri, Doron T-068
Kachko, Eric F-043
Kadam, Leena T O-144
Kahn, Daniel A F-037
Kahr, Maike K F-049
Kaitu'u-Lino, Tu'uhevaha J O-037, S-109
Kalberer, Meredith F-055, S-092
Kalish, Flora F-195
Kallapur, Suhas G O-012, O-074
Kallen, Amanda F-191
Kalmbach, Keri H S-199
Kamdar, Neil S-194
Kamiya, Chizuko F-056
Kan, Ozgur O-154
Kanaan, Sami B O-021
Kanayama, Naohiro T-181
Kane, Stefan C F-041
Kang, Byeong-Cheol F-189
Kang, Danyang T-128, F-160
Kannan, K S-150
Kanninen, Tomi T O-022, S-014, S-019
Kapaya, Habiba F-099
Kapidzic, Mirhan O-115
Karda, Rajvinder O-003, T-022
Karjalainen, Minna K F-003
Karvas, Rowan M T-143
Kasahara, Yukiyo S-187, S-189
Kaskar, Khalied O-122, S-196, S-197
Kato, Nao S-187
Katrien, De Clercq F-186
Katsuragi, Shinii F-060
Katsuragi, Shinji F-056
Kattah, Andrea G F-092
Katzman, Philip J T-093
Kavousi, Maryam T-205
Kawabata, Hanae S-059
Kaye, Leah A O-150
Kayisli, Umit A O-072, O-110, O-143, T-007, T-011, T-020, F-167, F-171, S-172
Kazanjian, Avedis A O-152
Ke, Jun S-069
Kechichian, Talar O-137, S-029
Keck, Matthias S-119
Keelan, Jeffrey A F-051
Keenan-Devlin, L T-065
Kekesi, Katalin S-142
Kelleher, Meredith A O-100, S-102
Keller, Patrick S-028
Kellert, Brian A O-035
Keller-Wood, Maureen T-074, T-101, F-022, F-076, F-137, S-147, S-149
Kelly, Amy O-059, F-098
Kelly, Angela S-194
Kemp, Matthew W O-012, S-039
Kendal-Wright, Claire E T-024, F-029
Kennaway, David J S-074
Kennedy, Stephen T-120
Kennelly, Maria A O-091, F-054
Keswani, Sundeep S-103
Kettle-Oestreich, Arin S-182
Khalaj, Kasra F-114, S-113, S-114
Khalil, Asma F-101, S-176
Khan, Amir F-150
Khan, Waheed S-193
Khan, Zaraq O-018
Khanjani, Shirin T-186, F-187
Khattaby, Ingy S-086
Khazaie, Khashayarsha T-175, F-119
Khorram, Omid O-067
Kidron, Dvora F-169
Kiessling, Ann A T-180
Kikkawa, Fumitaka T-189, S-154, S-187, S-189

Publication Number Prefix Key

Oral Presentations
O-001 - 052 = **Thursday** Oral Presentations
O-053 - 124 = **Friday** Oral Presentations
O-125 - 160 = **Saturday** Oral Presentations

Poster Presentations
T-001 - 212 = **Thursday** Presentations
F-001 - 212 = **Friday** Presentations
S-001 - 211 = **Saturday** Presentations

Kilburn, Brian O-144, T-179
Kim, BJ T-052
Kim, Bomi S-146
Kim, Bona S-015
Kim, Chong S-142
Kim, Chong Jai S-145, S-146
Kim, Dahlim O-134
Kim, GM T-052
Kim, Gyoung E O-070
Kim, Hae Soon S-076
Kim, Hoon F-207
Kim, Hyung-Goo T-087
Kim, Jeong Sook T-182
Kim, Jong-Hwa F-145
Kim, Jong Woon T-057
Kim, Joo-Yeon S-146
Kim, Jung-Sun S-146
Kim, KY T-065
Kim, Minkyung T-182
Kim, Seok Hyun F-207
Kim, SM T-052
Kim, Sung Hye T-186, S-031
Kim, SY T-052
Kim, Tae Hoon T-118
Kim, W T-052
Kim, Yeon Mee S-145, S-146
Kim, Yong Jin F-189
Kim, Yoo-na S-170
Kim, Yoon Ha T-057
Kim, Yoon Young F-189, F-207
Kim, Young-Han S-170
Kim, Young Ju F-012, S-076
Kimura, Yoshitaka T-103, F-104
Kindinger, Lindsay O-031, O-033
Kinhal, Vyjayanthi T-006, F-002, F-004, F-170, S-004
Kirby, Michael A S-007
Kirk, Michael T-157, F-156
Kirkwood, Phoebe M F-193
Kirschenman, Raven F-077
Kisanga, Edwina P F-088, S-181
Kishore, Annvarapu H O-138, T-029, T-045
Kitajewski, Jan T-027
Kiulia, Nicholas S-115
Kivai, Stan S-115
Klebanoff, Mark A T-178, F-089
Klein, Cheri T-116
Klein, Vivien F-072
Kliman, Harvey J S-195
Kline, Richard O-104, T-108
Klock, Susan C O-153, T-207, F-208
Kluck, George F-069
Kniss, Douglas A F-030, S-025
Knoepp, Leise T-005
Ko, Dennis F-014
Ko, Nga Ling O-026, T-133
Kobernik, Emily S-194
Koch, Markus O-017, O-068, T-113, F-122
Koeppel, Alexander F S-139
Koga, Kaori F-203
Kohan-Ghadr, Hamid-Reza O-144, S-178
Kohlmeier, Amanda S-201
Kojima, Kaname S-106
Kole, Martha B F-177
Kolesnikova, Lyubov I T-123
Kominiarek, MA T-065
Koncinsky, J S-073
Koning, Anton HJ O-004, S-052, S-144
Koning, Anton K S-082
Konishi, Haruhisa F-017, S-010
Koo, Bon-Kyoung S-184
Koo, JN T-052
Kopelman, Jerome S-048
Koppitz, Marcus F-122
Kordunsky, Ilya T-105
Kort, Jonathan T-204
Kostaki, Alisa F-087
Kostamo, Kathryne F-061
Koster, Maria PH O-004, T-197, F-100, F-196
Koster, Wendy P S-144
Kotani, Tomomi S-154
Koti, Madhuri F-114
Kraig, Ellen T-071
Krantz, David A O-089, S-058
Krause, Bernardo J T-081
Krebs, Kendall O-011
Kreklywich, Craig N O-100
Krikun, Graciela S-116
Kriseman, Maya O-046
Krishan, Vidya T-011
Krishnan, Tara I F-074
Krispin, Manuel S-142
Krizhanovsky, Valery F-169
Kroener, Lindsay S-139
Kroenke, Chris D O-100
Kroker, Anne S-118
Krueger, Paula S-162
Kruger, Jenny T-062
Krul-Poel, Yvonne HM F-100
Ku, Seung-Yup F-189, F-207
Kuchel, Timothy R S-074
Kudo, Yoshiki F-017, S-010
Kuessel, Lorenz O-014, S-118
Kuhn, Natalia F-085
Kujawa, Stacy A O-065, O-069, S-123
Kumar, Deepak O-072, T-023, T-028
Kumar, Gopal T-105
Kumar, Sathish O-027, O-084, T-129, T-160, F-206, S-158
Kuo, Anderson D T-079
Kuo, Anderson H O-126, S-079
Kuo, Jung-Wen O-106
Kuohung, Wendy T-198
Kupferminc, Michael F-036
Kure, Shigeo O-028
Kuriyama, Shinichi O-028
Kurosawa, Yasuhiro T-164
Kurtzberg, Joanne S-011
Küssel, Lorenz F-115
Kwak-Kim, Joanne T-174, T-194
Kwon, Eun Jin F-012, S-076
Kwon, Ja-Young S-170
Kwon, JE T-052
Kyama, Cleophas S-115
Kyathanahalli, Chandrashekara N F-035
Kyrgiou, Maria O-109
Laberge, Philippe Y T-122
Lager, Susanne F-157, S-156
Lai, Andrew O-104, T-048, F-153, F-170
Lai, Jonathan O-109
Lai, Pei F S-030
Laknaur, Archana F-126
Lal, Ann F-001, F-094, S-060
Lamb, Christine T-192, F-194, S-105
Lambden, Simon T-021
Lambertini, Luca T-142
Lamontagne, Alain T-122
Lampley, Charles T-174
Landgren, Rachel T-037
Landon, Mark B T-178
Lange, Kenneth F-079, F-085
Lanz, Rainer B O-002
Lanzone, Antonio F-205
Lappas, Martha F-052, F-153
Larkin, Jacob F-097
Larrea, Fernando S-087
Larsen, Kellie O-072, O-110, O-143, T-007, T-011, T-020, F-167
Larumbe, Eneko F-103
Laughlin-Tommaso, Shannon K S-121, S-122
Laureano, Daniela P T-085
Laven, Joop SE T-197, T-205, F-091, F-100, F-196
Lavery, Stuart F-187
Lavie, Anat S-101
Lawson, Angela K O-153, T-207, F-208, S-202
Layman, Lawrence C T-087
Lean, Samantha C T-158, T-159, T-190
Lechuga, Thomas J T-135, S-171
Lee, Amy M T-180
Lee, Andy S-035
Lee, Bora S-139
Lee, Byung Seok T-182, F-112
Lee, Han F-006
Lee, Jae Hoon T-182, F-112
Lee, JeHoon O-015
Lee, Joon Ho S-170
Lee, Men-Jean T-142
Lee, SM T-052
Lee, Timothy S-103
Lee, Yun S O-031, O-033, O-109, T-017, S-013, S-020
Lee, Yu Qi F-071
Lees, CC O-060
Lei, Jun O-133, O-157
Lei, Kaiyu T-009
Leimert, Kelycia B T-008
Leiper, James O-040, T-021, T-127, S-017
Lemmens, Stephanie MP S-157
Lentscher, Jessica S-186
Leo, Chen H F-164
Leon-Martinez, Daisy S-173
Leron, Elad S-003
Lesche, Ralf O-014, O-086, T-112, F-115, S-110, S-118
Lessey, Bruce A T-118, F-114, S-113
Levitan, Robert T-035
Lewis, Amanda S-126
Lewis, Anne O-100

Publication Number Prefix Key

Oral Presentations
O-001 - 052 = **Thursday** Oral Presentations
O-053 - 124 = **Friday** Oral Presentations
O-125 - 160 = **Saturday** Oral Presentations

Poster Presentations
T-001 - 212 = **Thursday** Presentations
F-001 - 212 = **Friday** Presentations
S-001 - 211 = **Saturday** Presentations

Lewis, David F T-176, T-209
Lewis, Holly O-033
Lewis, Terrence D S-177
Leyland, Nicholas T-122
Li, Bin F-107, S-106
Li, Cun O-126, T-071, T-079, T-084, T-098, T-155, F-079, F-085, F-103, S-079, S-084, S-085, S-095
Li, Dongmei F-090, F-200, S-068
Li, Hua F-144
Li, JunFei T-084
Li, Pin T-043
Li, Quanwen O-159, S-207
Li, Shaofu F-051
Li, Tian T-121
Li, Xiaobai T-111
Li, Xilong O-002, S-033
Li, Xinshan T-062
Li, Yan O-023, O-049
Li, Yi-Ju S-012
Li, Yinan T-031
Li, Yong S-069
Libardoni, Mark F-079
Liechty, Kenneth T-099
Liff, Ingrid F-020
Lim, Ratana F-052
Lima, Luiza C T-203
Limesand, Sean O-059, F-098
Lin, Mabelle T-152
Lin, Qiong O-086
Lindenthal, Bernhard O-086
Lindgren, Cecilia F-117
Lindgren, Isa T-102
Lindsay, Karen L O-091, F-054
Lindsay, Morgan E O-152
Linehan, Leslie T-071
Lingis, Melissa D F-129
Link, Daphna S-101
Liong, Stella F-052
Lipschuetz, Michal T-068
Lira-León, Gabriela S-077
Lister, Rolanda L T-076, S-094
Litkouhi, Babak O-102, F-108, F-109, S-107, S-108
Liu, Ai-Xia F-172
Liu, Hong S-074
Liu, Huishu T-019, T-025, T-043, F-034
Liu, Hung Ching F-189
Liu, Jing F-129
Liu, Kuo-Kang O-051
Liu, Lilly Y S-035
Liu, Ping T-126
Liu, Shanrun O-064
Liu, Shimeng O-065, O-069, S-123
Liu, Ya O-063
Liu, Yuan T-144
Liu, Yuanyuan T-019
Liu, Zheng O-100
Lizneva, Darya V T-123
Lluel, Philippe S-002
Lo, Jamie O O-100
Lobashevsky, Elena F-040
Lock, Mitchell O-136
Locke, Megan O-035
Locklear, Brent F-083
Lockstone, Helen F-117
Lockwood, Charles J O-072, O-110, O-143, T-007, T-011, T-020, F-167, S-116, S-172
Logan, A O-053
Lohner, James T-027
Lomas, Consuelo S-070, S-071
Longo, Sherri T-048, F-153
Lopes van Balen, Veronica A F-131, S-157
Lopez, Gladys E O-025, T-130
Lopez, Salvatore F-108
López-Pérez, Nuria S-209
Lorenzo, Isabel O-122
Lorenzon-Ojea, Aline R O-145
Louden, Erica D O-159
Louey, Samantha T-102
Loukogeorgakis, Stavros O-064
Loutradis, Dimitri T-180
Louwen, Frank T-061
Lowery, Curtis L T-032
Lu, Lingen S-108
Lu, Lingeng F-109
Lu, Xiaohong T-209
Lu, Zhong-wu T-121
Lubell, William D S-018
Lueth, Amir J T-004
Lui, Sylvia O-079
Lüscher, Benjamin P O-135
Lydon, John P O-002, T-096
Lye, Phetcharawan O-082
Lye, Stephen J O-071, O-082, T-031, T-171, F-175, S-015, S-096, S-125
Lyerly, Anne D T-095
Lynne, Sykes T-017
Lyons, Deirdre O-109
Ma, Qinyi S-069
Ma, Xioafang F-133
Ma, Yula T-142
Määttä, Tomi A F-003
MacAllister, Rhonda O-100
MacDiarmid, Jennifer O-037
MacDonald, Julie A O-155
MacDonald, Teresa T-063
Machet, F O-017
MacIntyre, David A O-031, O-033, O-109, T-015, T-017, S-013, S-020
Mackey, David S-096
Macones, George A T-097, F-058
MacPhee, Daniel J S-032
MacPherson, Heather O-029
Madaan, Ankush S-021
Maeder, Angela B F-057
Maeng, Yong-sun S-170
Magi, Reedik F-117
Magness, Ronald R O-025, O-042, T-130, T-172, F-172
Maguire, O T-169
Mahadevan, Sangeetha O-122
Mahalingaiah, Shruthi T-089
Maher, James T-132, T-137, F-103
Mahlman, Mari F-003
Maimillapalli, Ramanaiah O-160
Maiti, Kaushik F-151
Majidi Zolbin, Masoumeh T-212
Majidi-Zolbin, Masoumeh O-083
Mäkikallio, Kaarin F-003
Malach, Megan T-008
Maldonado, Maria C T-055
Malik, Minnie O-066, T-124, F-125
Malinger, Gustavo S-101
Malone, F O-043, T-169, S-169
Maloyan, Alina O-148
Mamillapalli, Ramanaiah O-083, T-121, T-212
Mandalà, Maurizio O-026
Mandò, Chiara F-063, S-046, S-057
Mansouri, Nisma F-042
Manuck, Tracy T-066
Manuel, Clarence T-010
Many, Ariel S-101
Manz, Joren S-164
Marana, Riccardo O-010
Marchesi, Julian R O-031, O-109
Marconi, Daniela S-112
Marek, Nicole O-118
Marek, Zygmunt S-191
Marfori, Cherie F-111, F-123
Margulies, Samantha L F-111, F-123, S-107
Marh, Joel F-072
Mari, Giancarlo T-092
Marianoglou, Maria S-020
Marinello, W T-026
Marini, Camilla O-135
Marin Sierra, Estefania T-016
Markowitz, Sanford T-045
Marshall, Sarah A F-164
Marshburn, Paul B T-195
Martin, A O-062, T-078, S-099
Martin, Laura F T-002
Martin, Nicole M S-140
Martinez, Diana M S-066
Martinez, Noelle G T-136, F-136
Martinez, Stacy T-155
Martinez Estrada, Fernando T-120
Martin-Fairey, Carmel F-133
Martirosyan, Diana O-132
Mary, Galo S-115
Mas, Aymara O-156
Masand, Ramya O-046
Maslovitz, Sharon F-095
Masserdotti, Alice O-102, F-108
Massmann, Angela G T-077, S-078
Mata-Greenwood, Eugenia T-156, S-095
Maternity Log Project Team S-127
Mathew, Pretty R F-081
Matsubara, Keiichi F-168, S-141
Matsubara, Yuko F-168, S-141
Matsuda, Tadashi O-012
Mattar, Rosiane F-013
Mattei, Larissa H O-127, S-086
Matthews, Kainalu F-072
Matthews, Michelle L T-195
Matthews, Stephen G O-082, O-125, T-035, F-069, F-087
Matzuk, Martin O-046
Maybin, Jackie S-110
Maybin, Jacqueline A O-048
Maymon, Eli T-003, S-005

Publication Number Prefix Key

Oral Presentations
O-001 - 052 = **Thursday** Oral Presentations
O-053 - 124 = **Friday** Oral Presentations
O-125 - 160 = **Saturday** Oral Presentations

Poster Presentations
T-001 - 212 = **Thursday** Presentations
F-001 - 212 = **Friday** Presentations
S-001 - 211 = **Saturday** Presentations

Mayo, Jonathan F-064, S-037
Mazza, E S-027
Mazzocco, Martina F-063
McAuliffe, Fionnuala M O-043, O-091, T-169, F-054, S-169
McBain, John S-185
McBride, Carole A T-134, T-167, T-170, F-162, F-165, S-132, S-168
McCarthy, Ronald F-133
McCreary, J Keiko F-008
McCullough, Laurence S-088, S-090
McElrath, Thomas F T-047, F-024, S-130
McFarlin, Barbara L F-057, F-059
McGill, Jocelyn F-080
McGillick, EV O-055
McGovern, Peter F-198, S-205
McGuirk, Emma R F-211
McKinnon, Brett S-112
McKnight, Robert O-058
McLane, Michael O-157
McLean, Mamie F-182
McLennan, Amelia S F-148, S-042
McParland, P O-043, T-169, S-169
McPherson, Jessica T-131
McQuesten, Jenna E O-011
McRae, Karalyn E S-163
Meakin, Ashley S-083
Méen, Murielle S-002
Meeuwis, Luc T-187
Meiri, Hamutal S-142
Memaj, Ira O-105, F-124
Mendelson, Carole R T-146, F-021
Menderes, Gulden O-102, F-108, F-109, S-107, S-108
Menke, Marie T-064
Menkiti, Ogechukwu O-132
Menon, Poorna R T-006
Menon, Ramkumar O-076, O-137, T-006, T-144, T-157, F-004, F-009, F-010, F-027, F-028, F-156, S-004, S-008, S-029
Merabova, Nana O-005, O-132, F-086
Mercer, Brian T-023
Merhi, Zaher O-120
Meritahti, M F-044
Merriam, Audrey A T-056, S-042, S-056
Merriam, Kathryn S T-195
Mesch, Stefanie T-120
Mesiano, Sam O-071, O-137, T-023, T-028
Messer, Angela T-008
Messer, William O-100
Metoki, Hirohito O-028, S-127
Metz, Christine T-105
Metz, Gerlinde AS F-008
Meuleman, Christel T-187, S-117
Meun, Cindy T-205
Mial, Tara N O-036, F-023
Michelsen, Trond M O-078
Mielke, Michelle M F-092
Mikhael, Sasha T-196
Mikhail, Magdy T-138
Miki, Yasuhiro F-107
Millar, Jess F-138
Miller, Derek S-192
Miller, Emily S T-044, F-046, S-160
Miller, G T-065
Miller, Jena F-143
Miller, Jessica E S-113
Miller, Kristin T-005
Miller, Lauren A T-033, F-090, F-200
Miller, Lisa A O-074
Miller, Russell S F-148, S-042
Miller, Tom T-080
Mimori, Takahiro S-127
Minato, Takahiro T-103
Minematsu, Kazuko F-060
Minium, Judi T-154
Miot, Hélio A T-002, F-065
Mir, Imran N F-019
Miranda, Jezid F-170
Miryala, Chandra S O-085, T-034
Mishra, Aruna T-138
Mishra, Jay O-027, O-084, T-160, F-206, S-158
Miskiewicz, Ewa I S-032
Misra, Biswapriya F-079
Mistry, Vikash F-002
Mitchell, Murray D T-003, F-139, S-005, S-137
Mitra, Anita O-109
Mitsukura, Yasue S-104
Mittal, Priya O-124
Miwa, Koichiro F-056
Miyamoto, Susumu F-060
Miyauchi, Mutsumi F-017, S-010
Miyoshi, Hiroshi F-017, S-010
Miyoshi, Takekazu F-056, F-060
Mniarji, Victor T-054
Moaddab, Amirhossein F-158, S-088, S-089, S-090
Mobley, Yuvon T-174
Moço, Natália P T-002
Moffett, Ashley S-184
Mogami, Haruta O-138, T-029
Mogos, Mulubrhan F F-059
Mohamed Rasheed, Zahirrah Begam T-015, T-017
Mohd Nasri, Noor T-127
Mohseni, Zenab S-165
Moisiadis, Vasilis G O-125, F-087
Moldenhauer, Lachlan M O-075
Moley, Kelle H O-098, S-182
Mone, F O-043, T-169, S-169
Monga, Manju T-060
Monsanto, Stephany P F-013, S-113
Monsivais, Diana O-046
Monsivais, Luis F-178
Montalbano, Alina P F-021
Monteiro, Victoria RS F-069
Montgomery, Grant W O-020, S-120
Monthé-Drèze, Carmen F-053, F-068, F-070
Moon, Jong Ho T-057
Moon, Kimberly S-177
Moore, John J O-072, T-023, T-028
Moore, Lorna G T-049, S-133
Moore, Robert M O-072, T-023, T-028
Mor, Gil O-032, T-107, T-141
Moraitis, Alex O-139
Moran, Carmel O-029
Moravek, Molly S-194
Moravek, Molly B O-153, T-207
More, Amar O-084, T-160, F-206, S-158
Moreci, Rebecca O-085
Morelli, Sara S S-205
Moreno, Inmaculada O-045, O-050, F-188
Morgan, Nicole Y O-151
Morgan, Terry K O-100, O-118, T-004, T-152, T-153, F-138, S-111
Moriarty, John M F-037
Moridi, Irene T-212
Morita, Mayu O-118, T-153
Morley, Christopher T-206
Morris, Andrew F-117
Morris, Erin A T-167, T-170, F-165, S-168
Morris, Robert T O-105, S-178
Morrison, Janna O-043, O-055, O-136, T-169, S-169
Morse, Abraham T-043
Morshedi, Mahmood F-204
Morton, Jude S O-061, O-114, F-077
Mossayebi, Elaheh O-130, T-085, F-080
Motawea, Hanaa O-035
Mourad, Mirella S-131
Mouratidis, Alexandros F-087
Moustafa, Sarah S-181
Mrkaic, Ana S-075
Mudaliar, Nithya T-137
Mueller, Martin O-010, F-209, S-112, S-211
Mueller, Michael S-112
Muglia, Lisa M O-080
Muglia, Louis J O-080
Muhammad Imran, Siti Aminah F-212
Muhn, Peter O-086
Muka, Taulant T-205
Mukundan, Banupriya S-028
Mulcahy, C O-043, T-169, S-169
Mulder, Eva G T-166
Mulders, Annemarie G S-144
Mulla, Melissa J T-107, S-173
Müller, Jörg O-068, S-110
Mullin, Christine S-183
Muneyyirci-Delale, Ozgul T-054, T-111
Muralimanoharan, Sribalasubashini T-146
Murase, Tomohiko T-189, S-187, S-189
Murji, Ally T-122
Murphy, Aisling F-037
Murphy, MP O-053, S-081
Murray, Alison O-048, S-110

Publication Number Prefix Key

Oral Presentations
O-001 - 052 = **Thursday** Oral Presentations
O-053 - 124 = **Friday** Oral Presentations
O-125 - 160 = **Saturday** Oral Presentations

Poster Presentations
T-001 - 212 = **Thursday** Presentations
F-001 - 212 = **Friday** Presentations
S-001 - 211 = **Saturday** Presentations

Murtha, Amy F-014, S-011, S-012
Murtha, AP T-026
Murthi, Padma T-139
Mushi, Juliet S-016
Musk, Gabrielle C O-012
Musul, Biran S-190
Muto, Masanaga T-147
Muzic Jr, Raymond F O-106
Muzzio, Damián O T-192, F-194, S-105, S-191
Mwenda, Jason S-115
Myatt, Leslie O-148, S-138
Myers, D O-062, T-078, S-099
Myers, K F-005, S-027
Myers, Kristin T-027
Mysorekar, Indira S-008
Nabli, Henda T-119
Nacharaju, Vijaya T-054
Nadeau-Vallée, Mathieu O-140, T-016, S-018, S-021
Nadeem, Lubna O-071
Nagai, Takashi S-187
Nagamatsu, Takeshi F-203
Nagasaki, Masao S-106, S-127
Nagatsuka, Kazuyuki F-060
Nagel, J O-017
Nagel, Jens T-113
Nakai, Akihito S-059
Nakamura, Tomohiro O-028
Nakamura, Tomoko T-189, S-187
Nakanishi, Natsuki S-187
Nakanishi, Norifumi F-056
Nakano, Tomoko S-154
Nakaya, Naoki O-028
Nandu, Tulip S-028
Napolitano, Peter G O-034, F-149, S-136
Narwani, Kavita O-130, T-085, F-080
Nasirzadeh, Yasmin F-114
Nasri, Noor Mohd T-021, S-017
Natenzon, Anna O-041
Nathanielsz, Peter W O-057, O-126, T-053, T-071, T-079, T-084, T-098, T-155, F-079, F-085, F-096, F-103, S-070, S-071, S-077, S-079, S-084, S-085, S-087, S-095
Navarro, Roser F-185
Nayak, Neha O-113
Nayak, Nihar R O-113
Neagoe, I O-017
Neddleman, Daniel O-149
Neistadt, Barbara T-049
Neki, Reiko F-056, F-060
Nelen, Willianne LDM F-192
Nelson, Jay A O-100
Nelson, JL O-021
Ness, Amen S-037
Network, Polaris Data S-199
Neuber, Evelyn I O-150
Newnham, John P O-012, F-051
Newton, Edward T-001
Ng, Juki T-116
Ng, Nicholas F-211
Ng, Sinnie O-121
Nguyen, Nicole A T-135
Nguyen, Phuoc Xuan S-187
Nguyen-Ngo, Caitlyn F-052
Nhan-Chang, CL S-027
Nick, Harry F-190
Nicol, Moira S-110
Nicolaides, Kypros O-008
Nieman, Lynnette O-066, F-125
Nii, Masafumi F-060
Niikura, Hitoshi T-109
Nijland, Mark J T-071, F-079, F-085
Nistor, Marius F-096
Niu, Y O-053, O-055, O-060, T-046, F-093, S-045, S-081
Noda-Nicolau, Nathália M T-014
Nold, Christopher S-009
Norman, Jane E T-018
Normand, C O-043
Norwitz, ER T-052
Nothnick, Warren B O-019
Novak, Christopher T-100, S-097
Novielli, C S-046
Nowell, Cameron S-185
Nubbemeyer, Reinhard O-086
Nugent, William H O-030
Nulsen, John C O-150
Núñez Castro, Laura F F-194, S-105
Nuzzo, AM O-128
Nwabuobi, Chinedu O-072, O-143
Nyachieo, Atunga S-115, S-116
Oakley, Robert H F-088
Obendorf, Maik O-014, T-120, F-115, S-118
O'Brien, Christine F-032
O'Brien, John M T-075
Obwegeser, Reinhard F-115
Ochi, Daisuke S-127
Odhiambo, John F O-057, T-053
Odibo, Antony O-143, F-167
Oehninger, Sergio F-204
Ogo, Takeshi F-056
Oh, IH T-052
Oh, Soo-young T-149, F-145
Ohlmeier, Steffen F-003
Ojaniemi, Marja F-003
Okeigwe, I F-181, F-199
Oktay, Kutluk O-154, S-190
Okuka, Maja T-130, F-171
Okuzumi, Eri S-104
Olczak, Pola O-121
Oliver, Emily A T-178, F-089
Olivier, Michael F-079
Olson, David M T-008, F-006, F-008, S-018
Olson-Chen, Courtney F-200, S-068
Olutoye, Olutoyin A S-103
Olutoye, Oluyinka O S-103
O'Mahony, J O-043
Omolo, Erik S-115
Ona, Katherine O-115
O'Neill, Kathleen S-151
Ono, Erika F-013
Oostingh, Eline C F-196
Oppermann, Udo T-120
Oppliger, Byron F-209, S-211
Orgeig, S O-055
Ortiga-Carvalho, Tania M O-082, F-069
Osman, Abu T-175
Osol, George J O-026, T-133
Osteen, Kevin G O-015
Osuga, Yutaka F-203
Osuka, Satoko T-189, S-187, S-189
O'Sullivan, Elizabeth J O-091, F-054
O'Sullivan, Kelly F-164
O'Tierney-Ginn, Perrie T-154, F-152
Overdijkink, Sanne B T-197
Owen, Carter M O-121
Ozanne, SE O-128
Padbury, James S-162
Paddon, Kevin F-121
Padilla, Pablo O-115
Padmanabhan, Vasantha S-080
Pagani, Isabel O-097
Paidas, Michael O-063
Paiva, Premila O-020, S-185
Pal, Lubna S-195
Palarczyk, Jennifer J T-098
Palatnik, Anna T-044, S-035
Paley, Martyn F-018
Palliser, Hannah K T-086
Palma, Carlos O-104, T-006, F-002, F-004, F-170, S-004
Palmeri, Mark L S-023
Pan, Zhaoxing F-025
Pancharatnam, Jeyasuria O-085
Pandit, Ashwini P O-022, S-014, S-019
Panelli, Danielle M F-024
Panina-Bordignon, Paola O-097
Papapetrou, Ashley S-205
Papp, Zoltan S-142
Paquette, Alison G T-050
Parasar, Parveen F-211
Parikh, Pavan F-092
Parikh, Toral P F-201
Parisi, Francesca S-052, S-082
Park, Chang G F-057
Park, CW T-052
Park, Eun Ae S-076
Park, Haemin S-133
Park, Ji Hyun T-182, F-112
Park, Joo Hyun T-182, F-112
Park, JS T-052
Park, Juyoung F-145
Park, Mi Hye F-012
Park, Solji O-151
Park, Soo Yeon F-012
Park, Yejin S-170
Parkhill, Julian F-157, S-156
Parkins, Christopher J O-100
Parks, W Tony T-064
Parmeley, Lauren T-150
Parry, Laura J F-164
Parry, Samuel O-009
Paruchuri, Yasaswi F-097
Pasalodos, Omar T-179
Passarelli, Rachel F-106, F-109, S-108
Patel, Bansari F-116
Patel, Bansari A T-135
Patel, Kinari O-005
Patel, Priya F-061
Patel, Sonali T-099
Patil, Avinash O-007
Patterson, Amanda O-016
Pattinelli, Francesca O-102
Pattison, Scott O-037

Publication Number Prefix Key

Oral Presentations
O-001 - 052 = **Thursday** Oral Presentations
O-053 - 124 = **Friday** Oral Presentations
O-125 - 160 = **Saturday** Oral Presentations

Poster Presentations
T-001 - 212 = **Thursday** Presentations
F-001 - 212 = **Friday** Presentations
S-001 - 211 = **Saturday** Presentations

Paul, Jonathan W T-030, F-033
Paules, Cristina F-170
Pavlovic, Zoran F-061
Pavone, MaryEllen G O-153, T-207, F-208
Pavone, ME F-181, F-199
Peaceman, Alan M F-202, S-041
Peacock, Sharon J F-157, S-156
Pearce, William J O-134
Pearson, Kevin J T-075
Peavey, Mary T-096
Peebles, Donald O-003, T-022
Peek, Ron F-192
Pei, Bo O-113
Peiris, Hassendrini N T-003, F-139, S-005, S-137
Pellicer, Antonio T-185, T-188, S-209
Peltier, Morgan R O-099, T-157, F-038, F-156
Peña, Melanie T-106
Pendeloski, Karen F-013
Penfield-Cyr, Annie F-053
Pennell, Craig E T-040, S-096
Pennington, Kathleen F-128
Penova-Veselinovic, Blagica T-040
Peppelman, Malou F-192
Perales, Alfredo O-115
Pereira, Bruno F-031
Pereira, Leonardo T-042, T-088
Pereira, Leonardo M T-004
Pereira, Maria T T-203
Peress, Danielle A F-202, S-041
Perez, M F-005
Pérez, Silvia O-047
Perley, Lauren E S-140
Perry, Helen F-101, S-176
Personeri, Carlo F-066
Peter, Inga T-142
Peter, Schwartz S-108
Peters, Michaele F-122
Peters, Olaf T-113
Peterse, Daniëlle S-117
Petersen, John W F-129
Peterson, Logan S-186
Peterson, Nichole S-163
Peterson, Scott F-041
Petraglia, Felice F-184
Pettinella, Francesca F-108
Phillippe, Mark T-151, F-020
Phillips, III, John A T-087
Piao, Longzhu S-172
Pileri, Paola F-063, F-066, S-057
Pilgrim, Justin D T-200
Pinnaduwage, Lakmini T-171
Pino, Daniella T-132
Pinter, Mary T-036, F-105, S-093, S-098
Pinto, Silvia O-052
Pisarska, Margareta D S-139
Pitruzzello, Mary C T-107
Plows, Jasmine O-094
Podrabsky, Jason F-138
Pogliani, Laura S-057
Pohl, Oliver S-002, S-031
Polettini, Jossimara T-002
Poli, Guido O-097
Politch, Joseph T-198
Pollack, Rebecca S-044
Pollack, Rebecca E T-075
Polotsky, Alex J O-119, S-150
Polpitiya, Ashoka D T-004
Polsky, Joshua T-122
Polyak, Erzsebet F-154
Ponelle-Chachuat, Flora F-031
Porat, Natalie F-055, S-092
Porrello, Enzo O-136
Posner, Bruce T-045
Post Uiterweer, Emiel D O-117
Pothos, Emmanuel N O-127
Potter, Julie A T-107, T-193
Powell, Bradford T-095
Powell, Cindy T-095
Powell, Joseph E S-120
Powell, Theresa L O-054, O-078, O-090, O-141, O-147, S-150, S-152
Powers, Barbara F-039
Pradhan, Bhola S O-113
Pratt, Morgan T-206
Prearo Moço, Natália F-179
Presicce, Pietro O-074
Pressman, Eva T-033
Pressman, Matthew F-156
Price, Nathan T-050
Price, Nicole T-054
Pringle, Kirsty T-070, F-071
Pritchard, Melissa T-198
Prusinski, Lauren T-125
Pruski, Pamela O-033
Pruss, Diana T-117
Prussa, Jessica S-066
Pukkala, Eero F-118
Pundir, Sheetal S-018, S-021
Puppala, Sobha T-098
Puryear, Lucy J T-060
Puscheck, Elizabeth E O-159, T-179, F-210, S-207
Puttabyatappa, Muraly S-080
Qadri, Farnoosh O-123
Qian, Xueya T-043
Qiao, Chong T-128, F-160, S-159
Qin, Chunrong F-191
Qin, Wenmin T-194
Qin, Ying S-187
Quak, Stephanie F-052
Quake, Steven F-185
Quiniou, Christiane O-140, T-016, S-018, S-021
Quinn, Amy R T-098
Quiñonero, Alicia O-047, O-115
Quon, Anita O-056
Rabaglino, Maria B O-117, F-137
Rabban, Joseph T-210
Racicot, Karen F-075
Radford, Caitlin C O-087, S-140
Rae, Kym M T-070, F-071
Rafaeli-Yehudai, Tal F-043
Raghavan, Meera O-151
Raghavan, Rahul F-138
Raghuraman, Nandini F-058
Rahmioglu, Nilufer F-117, F-121
Rajendiran, K S-150
Rajkovic, Aleksandar O-124
Raju, Suraparaju T-155
Rakers, Florian F-096
Rämet, Mika F-003
Ramhorst, Rosanna O-032
Ramin, Susan M T-060, S-088, S-090
Ramon, Daniel O-050
Ramos, Bruna A F-065
Rampersad, Roxane T-097
Randolph, John S-194
Randolph, Todd L T-004
Rantakari, Pia O-051
Rao, Rashmi F-037
Rappolee, Daniel A O-159, T-179, F-210, S-207
Ratner, Elena O-102, F-106, F-108, F-109, S-107, S-108
Ravel, Jacques T-012
Raymond, Kyle F-039
Raz, Yael F-036
Razavy, Haide F-072
Ready, Joseph T-045
Reddy, Vikrant F-185
Reece, E Albert S-053
Reed, Beverly G T-184
Reed, Luckey C F-149, S-136
Reed, Sarah T-003, F-139, S-005, S-137
Reeder, Callie T-069
Reese, Jeff F-032
Reeves, Shane F-105
Refaeli-Yehudai, Tal T-163
Reginatto, Mila W F-069
Reijnders, Igna F S-144
Reinhart, Ursula S-211
Reis, Adelina M T-203
Reis, Fernando M O-082, T-203
Remohí, Jose T-185
Ren, Jun O-057
Reyes, Laura M O-056
Reyes-Castro, Luis A S-070, S-071, S-077, S-087
Reynolds, Clare O-094
Reynolds, Corey T-096
Reynolds, Leryn J T-075
Reynolds, Steven F-018
Reznik, Sandra E T-010, S-016
Rhoton, Alice F-190
Rhoton-Vlasak, Alice F-129
Ria, Francesco O-010
Riaposova, Lucia S-031
Ribeiro de Andrade Ramos, Bruna F-179
Rice, Gregory E O-104, T-048, T-108, T-202, F-002, F-153
Rice, Kenner C O-075
Rich, Stephen S S-139
Richards, Elaine T-074, T-101
Richardson, Lauren O-076, F-010, F-027, F-028
Richter, Kevin F-201
Riley, Joan K S-200
Rimon, Eli F-036
Rinaldi, Sara F O-029, T-018
Rinaldo, Denise E F-159
Rincon, Mercedes O-011
Rini, Christine T-095
Rittenschober-Böhm, Judith O-012
Rivera, Carlos S-021
Rivera, Christine C S-066
Rivera, Gabbrielle C S-066
Rivera, Ivelisse T-206
Rivera-Alsina, Manuel E S-066

Publication Number Prefix Key

Oral Presentations
O-001 - 052 = **Thursday** Oral Presentations
O-053 - 124 = **Friday** Oral Presentations
O-125 - 160 = **Saturday** Oral Presentations

Poster Presentations
T-001 - 212 = **Thursday** Presentations
F-001 - 212 = **Friday** Presentations
S-001 - 211 = **Saturday** Presentations

Robert, Welch T-055
Roberts, JM O-044, F-166, S-167
Roberts, R Michael T-143
Roberts, Victoria H O-100
Robertson, Sarah A O-075, S-018
Robins, Jared F-181, F-199, S-201
Robinson, Alice T-063
Robinson, Shannon S-063
Robuck, Michael F-032
Rocha, Clarissa R O-145
Rochelson, Burton T-105, S-058
Rodel, Rachel T-099
Rodriguez, Michelle F-022
Rodríguez-González, Guadalupe L O-057, F-096, S-070, S-087
Rodriguez Riesco, Laura G F-025
Rogers, Peter AW O-020, S-120, S-185
Roh, Cheong-Rae T-149, F-145
Rokas, Antonis F-007
Roldan, Francisco J S-077
Romagnoli, Graziela G F-179
Romano, Megan F-047
Rombauts, Luk S-203
Romero, Hedy O-071
Romero, Robert J T-003, S-005
Romero, Roberto O-036, F-023, F-035, S-142, S-145, S-146, S-192
Romney, Amie F-138
Romualdi, Daniela F-205
Rood, Kara M O-096, T-178, F-089
Rosado-Mendez, Ivan M S-023, S-024
Rosario, Fredrick J O-054, O-090, O-147
Rose, Carl H F-092
Roselaers, Yvonne CM S-157
Rosenblatt, Kevin S-130
Rosenfeld, Charles R F-019
Rosenn, Barak F-055, S-075, S-092
Rosenwaks, Zev T-201
Ross, Michael G O-130, T-085, F-080
Rossi, Adriano G T-018
Rossi, Carlo A F-074
Rossi, Gabriele S-112
Rostkowski, Amanda F-106
Rotgeri, Andrea O-017, F-122
Rotshenker-Olshinka, Keren S-055
Rotter, Jerome I S-139
Rottmann, A O-017
Rousian, Melek S-052, S-082
Rouzaire, Marion F-031
Rouzi, Abdulrahim Ali T-177, F-042
Rowan, Edward G O-142
Rowe, Melissa S-040
Rozance, Paul J T-083, F-084
Rozzah, Rayyan F-042
Rubin, Jessica O-108, S-196, S-197
Rubio, Alicia O-097
Rueda, Cesar M O-074
Rugarn, Olaf F-039
Rugino, Angela F-001
Ruiz-Alonso, María T-188
Rush, Demaratta F-190
Russell, Mckenzie F S-032
Rutherford, Thomas J F-106
Rutledge, Emily C T-060
Ryan, Thomas O-064
Saadalla, Abdulrahman M F-119
Saade, George R O-137, T-004, F-010, S-029
Saar, Tal T-117
Saavalainen, Liisu F-118
Sacher, Frank S-119
Sachs, Alice G T-194
Saed, Ghassan M O-105, F-124
Saed, Mohammed G O-105
Safrai, Myriam T-068
Sahabi, Sadia S-061
Sahin Ersoy, Gulcin T-212
Sahly, Nora F-042
Said, Joanne F-041
Saif, Zarqa S-083
Saigusa, Daisuke T-164
Saiki, Mie F-092
Saito, Masatoshi O-012, T-164
Saito, Sakae T-109, S-106
Sakkas, Denny O-149
Sakurada, Shoko T-109
Salafia, Carolyn M T-138
Salazar Garcia, Maria D T-174
Saleh, Farrah O-087
Salemi, Jason L F-059
Salihu, Hamisu H F-059
Salmi, Marko O-051
Salminen, Annamari F-003
Salomon, Carlos O-104, T-006, T-048, T-108, T-202, F-002, F-004, F-009, F-153, F-170, S-004
Salsano, Stefania O-047
Salstrom, Jan T-001
Samueloff, Arnon S-055
Sanchez, Tim O-149
Sánchez-Alcázar, JA F-110
Sánchez-Martín, P F-110
Sanders, Barry T-122
Sands, LeeAnna T-156
Sangar, Vineet T-050
Sangi-Haghpeykar, Haleh S-088, S-090
Santamaria, Xavier F-113
Santillan, Donna A F-174
Santillan, Mark K F-174
Santin, Alessandro D O-102, F-106, F-108, F-109, S-107, S-108
Santistevan, Anthony S-199
Sanz Cortes, Magdalena S-103
Sapin, Vincent F-031
Sargent, Ian L O-114
Sassine, AnnieBelle J S-148
Sathappan, Varsha O-122
Sato, Brittany L T-024
Sato, Naoaki T-103
Sato, Shinichi O-012
Sato, Toru F-060
Saunders, Philippa TK O-048, O-101, T-018, T-114, F-193
Sbarra, Michael T-039
Sbracia, Marco T-183, S-112
Scambia, Giovanni O-010
Scarinci, Elisa F-205
Scarpellini, Fabio T-183, S-112
Schabel, Matthias C O-100
Schamme, David P T-118
Schatz, Frederick O-072, O-110, O-143, T-007, T-011, T-020, F-167, S-172
Scheaffer, Suzanne O-098
Scheepers, Hubertina CJ S-157
Schenken, Robert F-127
Schenone, Mauro H T-058
Scherjon, Sicco A T-173
Schermerhorn, Sophia MV T-199
Schiffner, René F-096
Schifrin, Barry S S-062
Schlabritz-Loutsevitch, Natalia T-132, T-137, F-103
Schleedoorn, Myra J F-192
Schmidt, Manfred O-064
Schmidt, Martin F-096
Schmitz, Arndt F-115, S-118
Schmoll, Maria O-007
Schneider, Philipp S-211
Schoeberlein, Andreina F-209, S-211
Scholz-Romero, Katherin O-104, F-153
Schreiner, Pamela S-124
Schuitemaker, Joost HN T-173
Schulte, Maureen M S-182, S-200
Schulz, Laura C T-072, T-150, T-143, S-072
Schur, EA F-173, S-161
Schust, Danny J S-210
Schutt, Amy F-081
Schwartz, D S-150
Schwartz, Peter E O-102, F-106, F-108, F-109, S-107
Schwenkel, George F-023
Scott, Regan L T-147
Scroggins, Sabrina M F-174
Sebastián-León, Patricia T-185, T-188
Sebold, Dara F-011
Secrist, Emily K T-119
Seeho, Sean F-041
Seeraj, Valmiki T-138
Seffens, Angelina M T-165
Segal, Mark S F-129
Segars, James H O-121, T-073, T-124, T-200
Seiler, Kristian S-194
Seli, Emre O-149
Seligman, Neil S T-093, S-054
Semerci, Nihan O-072, O-110, O-143, T-007, T-011, T-020, F-167, S-172
Sen, Sarbattama F-053, F-068, F-070, F-150
Senoy, Chandra C F-119
Senthamaraikannan, Paranthaman O-074
Seo, Seok Kyo T-182, F-112
Seong, Won Joon T-077, S-078
Seravalli, Viola F-143
Sfakianaki, Anna T-094

Publication Number Prefix Key

Oral Presentations
O-001 - 052 = **Thursday** Oral Presentations
O-053 - 124 = **Friday** Oral Presentations
O-125 - 160 = **Saturday** Oral Presentations

Poster Presentations
T-001 - 212 = **Thursday** Presentations
F-001 - 212 = **Friday** Presentations
S-001 - 211 = **Saturday** Presentations

Shacklett, Barbara L T-110
Shade, Robert E F-085
Shaeib, Faten T-196
Shah, Amin O-056
Shah, Dinesh M O-039
Shah, Meera S T-208, F-185
Shaikh, Shafiq O-160
Shakib, Julie O-006
Shamir, Alexandra T-179
Shamshirsaz, Alireza A F-158, S-088, S-089, S-090, S-103
Shamshirsaz, Amir S-088, S-089, S-090
Shang, Catherine T-120
Shangaris, Panicos O-064
Shannon, Allison S-048
Shapiro, Alice J F-198
Sharalaya, Zarina T-131
Sharkey, David J S-018
Sharma, Shayna O-104
Sharma, Surendra S-162
Sharpe-Timms, Kathy L T-119
Shaw, CJ F-082
Shaw, CS O-060
Shaw, Gary M F-064, S-037
Shaw, Julia C T-086
Shawber, Carrie J T-165
Sheehan, Elaine S-176
Sheetz, Michael T-027
Sheffield, Jeanne S-067
Sheller, Samantha O-137
Shen, Wei-Bin O-001
Shen, Yuanyuan O-063
Shennan, Andrew H F-002
Shenoy, Chandra C O-018, T-175
Shi, Haolin F-180
Shi, Shao-Qing T-019, T-025, F-034
Shibata, Toshiaki T-181
Shibuya, Yusuke T-109, S-106
Shimizu, Ken S-187
Shin, Jung Ho F-112
Shin, S T-052
Shin Sim, Myung S-038
Shiu, Li-Yen S-172
Shlabritz-Loutsevitch, Natalia T-155
Shoemaker, Mary K T-060
Sholohov, Leonid F T-123
Shook, Lydia L O-096, T-106
Shree, R O-044, F-166, S-167
Shree, Raj O-021
Shreiber, Letizia S-055
Shynlova, Oksana O-071, F-175, S-015, S-125
Sibai, Baha M T-037
Siddiq, Zainab T-059, F-067
Siegel, Eric R T-032
Sierra, Luz-Jeannette T-012, F-015, S-022
Silasi, Dan-Arin O-102, F-106, F-108, F-109, S-107, S-108
Silasi, Michelle O-032, S-140
Silpanisong, Jinjutha O-134
Silva, Angela O-050
Silva, Márcia G T-014, F-065
Silva, Nathalia L F-069
Silva-Palacios, Alejandro S-077
Silver, Robert O-006, T-066
Simhan, Hyagriv N T-065, T-082
Simmilion, Cedric S-112
Simmons, Rebecca A O-009, S-151
Simon, Bailey L O-148
Simón, Carlos O-045, O-047, O-050, O-115, T-185, T-188, F-185, F-188, S-209
Simon, Eva O-014, F-115, S-118
Simon, Melissa A T-136, F-136
Simon-Freeman, Rebecca T-067
Simons, Benjamin D S-184
Simsek, Suat F-100
Sinaii, Ninet T-111
Singer, Tomer F-183, S-183
Singh, Aalem O-144
Singh, Natasha F-016, S-148
Singh, Sukhbir S T-122, F-114
Singh, Vineeta T-188
Sinkey, Rachel O-072, T-007, F-171
Sison, Christia Angela M O-013
Sisti, Giovanni O-022, S-019
Sivakumar, Kirthiram K F-140
Sivarajasingam, Sivatharjini P F-016
Siver, Robert M T-038
Skariah, Annie M T-174, T-194
Skaznik-Wikiel, Malgorzata E O-119
Skeffington, KL O-053, O-055, T-046, S-045, S-081
Skinner, Debra T-095
Skobowiat, Cezary T-155
Skornick-Rapaport, Avital F-095
Slaggle, Anna K T-058
Slater, Donna T-031
Sligman, Neil T-033
Sliskovic, Inga T-196
Smeester, Lisa S-063
Smid, Marcela C F-053, F-068, F-070
Smith, Ann O-031, O-109
Smith, Arianna L F-075
Smith, Gordon CS O-139, T-168, F-141, F-142, F-157, S-156, S-166
Smith, Graeme N S-163
Smith, Jessica O-100
Smith, Kristin N O-153, T-207
Smith, Patricia O-100
Smith, Roger T-030, F-033, F-151
Smith-McCune, Karen T-110
Snowden, Jonathan M T-042, T-088
Soares, Michael J T-147
Sommer, Anette O-068
Son, Moeun T-044
Sones, Jennifer L T-165
Song, Hong F-147
Soni, Shelly S-058
Soo, Jia Yin O-136
Sooranna, Gavin R S-148
Sooranna, Suren R T-009, S-148, S-155
Sorensen, Tanya K T-050
Soto-Carrasco, Gustavo T-081
Sovio, Ulla F-141, F-142, S-166
Spaanderman, Marc EA T-166, F-131, F-132, S-157, S-165
Spaans, Floor O-114
Spandorfer, Steven D T-201
Speck, Sarah F-133
Spinelli, Marialuigia F-209
Spiroski, AM O-128, F-082, S-081
Spooner, Kiara K F-059
Sprawka, Nicole F-094
Sqapi, Maria H T-035
Stadtmauer, Laurel F-204
Stafford, Graham F-018
Stanic, Aleksandar K O-023
Stanic-Kostic, Aleksandar O-049
Stanley, Joanna O-094
Stanley, Jone A F-140
Stanton, A T-169
Stavsky, Moshe T-163
Stawiski, Konrad O-103
Steegers, Eric A S-052, S-082, S-144
Steegers-Theunissen, Régine PM O-004, T-197, F-100, F-196, S-052, S-082, S-144
Steffens, Nathan O-059
Steinmeyer, Andreas O-017, T-113, F-122
Stephens, Katie J T-158
Stephenson, Megan L F-039
Stern, Catharyn S-185
Stern, Victoria T-013, F-018, S-006
SternAscher, Conrad T-027
Stetson, Bethany T O-035
Stevens, Stanley F-171
Stevenson, David K F-064, F-195
Stewart, Elizabeth A S-121, S-122
Stock, Owen F-041
Stock, Sarah J O-029
Stojanovic, Ivana S-075
Stone, Julie S-009
Stone, Peter R O-116
Stratton, Pamela T-111
Strauss, III, Jerome F O-030
Streblow, Daniel N O-100
Strohbach, Angelina M T-136, F-136
Strug, Michael R O-016
Stuart, Tami S-151
Stuckey, Daniel O-064
Stuebe, Alison F-070
Su, Emily J S-143
Su, Kuan-Hao O-106
Su, Ren-Wei O-016
Su, Szu-Chi T-073
Suárez-Salvador, Elena F-113
Subramaniam, Sindhu O-064
Suff, Natalie O-003, T-022
Sugawara, Junichi O-028, T-164, S-127
Sugihara, Kazuhiro T-181
Sugiyama, Takashi F-168, S-141

Publication Number Prefix Key

Oral Presentations
O-001 - 052 = **Thursday** Oral Presentations
O-053 - 124 = **Friday** Oral Presentations
O-125 - 160 = **Saturday** Oral Presentations

Poster Presentations
T-001 - 212 = **Thursday** Presentations
F-001 - 212 = **Friday** Presentations
S-001 - 211 = **Saturday** Presentations

Suh, Chang Suk F-207
Suharwardy, Sanaa H T-208
Sullivan, Megan E T-087
Sullivan, Ryan T-092
Sultana, Zakia F-151
Summerfield, Taryn L F-030, S-025
Sun, Tianyanxin S-139
Sun, Yao O-077
Sundermann, Alexandra C O-095
Sung, Ji-Hee F-145
Sung, Juliana F-001
Sung, Nayoung T-174
Surbek, Daniel V O-010, O-135, F-209, S-211
Suter, Melissa A F-049
Sutherland, MR F-073
Suturina, Larisa V T-123
Suzuki, Takashi F-107
Swanson, Kate F-046
Swenson, Helen P F-190
Swindle, Delaney C O-119
Sykes, Lynne T-015, S-013
Syngelaki, Argyro O-008
Tabak, Selcuk F-167
Taglauer, Elizabeth F-150
Tagliaferri, Valeria F-205
Takagi, Kiyoshi F-107
Takagi, Yaemi F-056
Takata, Takashi F-017, S-010
Takats, Zoltan O-033
Takeshita, Toshiyuki S-059
Takhar, Harpreet S F-038
Takikawa, Sachiko T-189, S-187
Tal, Reshef O-160
Talar, Kechichian T-006, F-004, S-004
Talati, Ajay J T-058
Talton, Omonseigho T-072, S-072
Talus, Ponjeli T-054
Tan, Bee K O-051
Tanabe, Osamu S-127
Tanaka, Hiroaki F-060
Tanaka, Kayo F-060
Tanaka, Sota F-107
Tanchico, Daren F-081
Tang, Zhonghua T-141
Tangney, Mark O-003, T-022
Tannetta, Dionne S O-114
Tapelband, Julia S-007
Tarantal, Alice F O-005
Tarca, Adi L F-035, S-142
Tare, Marianne F-164
Tarry-Adkins, JL O-128
Taska, David F-098
Tate, Danielle T-092
Tayade, Chandrakant F-013, F-114, S-113, S-114
Taylor, Brandie S-029
Taylor, Dyese F-055, S-092
Taylor, Hugh S O-063, O-083, O-087, O-129, O-160, T-087, T-121, T-212, F-113, S-116
Taylor, Robert N O-137, F-116, S-181
Teal, Nicole T-007
Teal, S S-150
Teh, Wan Tinn S-185
Tellam, Ross O-136
Telugu, Bhanu P F-147
Temming, Lorene A T-097
Tempest, Nicola O-112
Templin, Megan T-195
Teoh, TG S-013
Teraoka, Yuko F-017, S-010
Terebesi, Ildiko O-086
Terlezky, Sveta S-055
Terzidou, Vasso T-186, F-044, S-031
Teulings, NEWD S-045
Thagard, Andrew O-034
Thakur, Mili O-123, T-196, S-178, S-180
Than, Nandor S-142
Theilen, Lauren F-045
Theofanakis, Charalampos T-180
Theriot, Sarah T-032
Thiel, John A T-122
Thilaganathan, Basky F-101, S-176
Thomas, Ann M T-047, F-024
Thomas, Kesha F-061
Thomas, S F-044
Thomas, Voets O-052
Thompson, Loren P O-131, F-147, S-100
Thomson, Adrian J O-029, T-018
Thornberg, Loralei F-200
Thornburg, Kent L T-102
Thornburg, Loralei L F-090, S-054
Thornton, Kimberley O-120
Thrasher, Adrian O-064
Tian, Yuchen S-210
Tiitinen, Aila F-118
Tillman, Alex O-151
Tilly, Jonathan L O-155, T-191, T-211
Timmers, Marco O-102
Titus, Shiny S-190
Tivari, Samir S-075
Tobiasz, Ana T-092, T-161
Toedling, Joern S-118
Tokunaga, Hideki T-109, S-106
Tolar, Jakub F-026
Tolcher, Mary C F-158
Tong, Mancy O-116
Tong, Stephen O-037, T-063, T-140, F-041, S-109
Too, Gloria S-131
Torloni, Maria R F-010
Torstenson, Eric S O-095
Tortelli, Brett T-126
Toth, Thomas L T-180
Towers, Craig V T-069
Toyoda, Kazunori F-060
Trainá, Evelyn F-013
Treviño, Lindsey S O-156
Tribe, Rachel M F-002, S-030
Triplett, Eric W F-022
Trivedi, Jayshil J S-029
Tropea, Anna F-205
Truman, Alisha M T-211
Truong, Tracy S-012
Tsai, Pai-Jong S F-152
Tsai, Stephanie S-200
Tsibris, John C F-171
Tsigas, E O-044, F-166, S-167
Tsuchiya, Naho O-028
Tsuda, Hiroyuki S-154
Tsunemoto, Yoshiki S-127
Tsur, Abraham F-064
Tulina, Natalia M T-104
Tully, E O-043, T-169, S-169
Tully, Elizabeth F-150
Tunc, Mustafa O-106
Turan, Ozhan S-048
Turan, Shifa O-131, S-100
Turco, Margherita Y S-184
Turkistani, Moayad T-177
Turner, Stephen D S-139
Tursun, Ablat T-084
Tuuli, Methodius G T-097, F-058
Tyagi, Tanya S-125
Tyrell, E O-043
Uauy, Ricardo T-081
Uchikura, Yuka F-168, S-141
Ulisse, Adele O-097
University of Melbourne S-109
Unkel, Ronald S-192
Urabe, Satoshi F-017, S-010
Uretsky, Aubrey T-122
Urrabaz-Garza, Rheanna O-137, T-006, F-004, S-004, S-008, S-029
Urschitz, Johann F-072
Usadi, Rebecca S T-195
Usoltseva, Elena S-206
Usuda, Haruo O-012, S-039
Utama, Budi O-122
Vadillo-Ortega, Felipe O-036
Valbuena, Diana O-050, T-188
Valdes, Cecilia O-070, O-108, T-096
Valdes, Gloria L F-146
Vallvé-Juanico, Júlia F-113
Van De Bunt, Martijn F-117
Van den Eynde, Charlotte O-052
Van den Veyver, Ignatia O-122
Vander Haar, Emilie O-092
van der Lee, Miranda O-102
Vanderlinden, L S-150
VanDerslice, Jim F-161
van der Walt, Nicola F-128
Van De Ven, Cosmas S-194
Van Dijk, Matthijs R O-004
van Drongelen, Joris F-131
van Duijn, Linette F-100
van Gansewinkel, Tessa AG F-131
Vanhie, Arne S-115, S-117
van Kuijk, Sander MJ F-131
van Pampus, Mariëlle G T-173
Varcoe, Tamara J S-074
Vargas, G F-027
Vargas, Lilia S-071
Vargas, Maria V F-111, F-123
Vargas, Vladimir E O-025, T-130
Varner, Michael W O-006, T-066, F-161, S-073
Vaswani, Kanchan T-003, F-139, S-005, S-137
Vaughan, Lisa E F-092, S-121
Vaughan, Owen R O-054, F-074
Vazquez, Jessica O-023, O-049
Veerapaneni, Chharitha F-023
Vega, Claudia C S-087
Veglia, Manuela O-010
Velez Edwards, Digna R O-095, S-124

Publication Number Prefix Key

Oral Presentations
O-001 - 052 = **Thursday** Oral Presentations
O-053 - 124 = **Friday** Oral Presentations
O-125 - 160 = **Saturday** Oral Presentations

Poster Presentations
T-001 - 212 = **Thursday** Presentations
F-001 - 212 = **Friday** Presentations
S-001 - 211 = **Saturday** Presentations

Vella, Anthony S-009
Ventolini, Gary T-137, T-155, F-103
Verstraelen, Hans F-008
Verstraeten, Barbara SE F-008
Vicenzi, Elisa O-097
Vickers, Mark O-094
Viganò, Caterina F-066
Vilchez, Gustavo S-147
Vilella, Felipe O-045, O-050, F-185, F-188
Villalon-Landeros, Rosalina O-025, O-042, T-130
Villancio-Wolter, Maria O-151
Villazana-Kretzer, Diana S-136
Vilos, Angelos T-122
Vilos, George T-122
Vincent, Catherine F-057
Vink, Joy T-027, F-005, S-027
Visser, Jenny A F-091
Vitonis, Allison O-103
Voets, Thomas T-187
Vohra, Nidhi S-058
Voigt, Isabel T-061
Vonderheid, Susan C F-057
Vora, Neeta L T-095, S-063, S-091
Vriens, Joris T-187
Vyas, Vibhuti O-141
Wada-Hiraike, Osamu F-203
Waddington, Simon N O-003, T-022
Wade, Katrina O-104, T-108
Wadhwa, P T-065
Waelkens, Etienne S-117
Wagata, Maiko O-028, T-164, S-127
Wagenfeld, Andrea O-068, S-110
Wahi, Gita T-070
Wahid, Hanan H O-075
Wainstock, Tamar S-003
Walejko, Jacquelyn F-076, S-147, S-149
Wales, N F-044
Walker, Cheryl Lyn O-156
Walker, David W T-139, S-102
Walker, Susan P T-063, F-041
Wallace, Euan M T-139, S-203
Walsh, Scott W O-030
Walter, Daryl T-113, F-122
Walton, Robert B F-149, S-136
Wan, Jiayi T-162
Wander, Pandora L T-050
Wang, Ange T-204
Wang, Ann A S-160
Wang, Carol A T-040, S-096
Wang, Erica S-139
Wang, Hailan F-160
Wang, Haimei F-083
Wang, Keqing O-038
Wang, Lei S-069
Wang, Lele T-025, T-043, F-034
Wang, Luying F-127
Wang, Michelle T-142
Wang, Qiurong O-057
Wang, Qiushi T-128
Wang, Rui-Fang F-172
Wang, Tianren O-149
Wang, Tianyuan S-033
Wang, Wanxin F-185
Wang, Wei O-064
Wang, Xiang-Zhen F-144
Wang, Xiaojie O-100
Wang, Xiaoqiu O-002
Wang, Xinye O-124
Wang, Ya-Xin T-144, T-145
Wang, Yu O-148
Wang, Yuping T-176, T-209
Wapner, R F-005, S-027
Wapner, Ron T-027
Ward, K O-044, F-166, S-167
Ward, Kenneth T-091, F-120, F-197
Washington, Chantel I T-124
Washington, Sonya L O-030
Watanabe, Shimpei O-012
Watanabe, Yoh T-109
Waters, Brenda L T-167
Waters, Thaddeus P S-060
Weaver, Amy L F-092, S-121
Weber, Miriam T-206
Weck, Karen T-095
Wei, Shu Qin F-062
Weiner, Carl O-008
Weinheimer, Claudia F-083
Weitzenkamp, David W T-049
Wellons, Melissa S-124
Wen, Tony F-178
Wenzl, Rene O-014, F-115, S-118
Werner, Erika F F-047, F-177
Wernimont, Sarah A F-174
Wesolowski, Stephanie R O-090, T-083, F-084
West, Camilla T-186, F-187
Westervelt, AR F-005, S-027
Weston, Christopher O-051
Westphal, Lynn M T-204, T-208
Wheeler, Karen C O-113
Whicker, Margaret F-109, S-108
Whirledge, Shannon D F-088, S-181
Whitaker, Lucy S-110
White, Anthony F-074
White, Gary T-132, T-137
White, Melanie K T-040, S-096
White, Scott W T-040, S-096
White, Wendy M F-092
Whitehead, Clare L F-041
Whitehead, William E S-103
Whitley, Guy S T-148
Wiggins, Adrienne F-040
Wilkerson, Matthew O-066
Willaims, Lacey S T-087
Willemsen, Sten P O-004, S-052, S-082
Williams, Alistair RW O-101
Williams, James M O-134
Williams, Michelle T-050
Williams, R Stan F-129
Williams III, John S-139
Williamson, D T-065
Wilson, Kirsten O-029
Wing, Deborah A F-039
Winter, Michael T-089
Wissler, Richard S-054
Witkin, Steven S O-022, S-014, S-019
Witte, Elizabeth F-075
Wolff, Erin F O-151, S-199
Wolfson, Gabriel S-133
Won, Kyoung S-151
Wong, Ronald J F-195
Wong, Serena O-102
Wood, Charles E F-022, F-137
Woodard, Terri S-196
Woods, Dori C O-155, T-191, T-211
Woods, James T-206
Woodward, Eleanor O-012
Word, Ruth A O-138, T-029, T-045, T-184, F-180, S-028
Wright, Jason D T-056, T-059, F-067, S-056
Wu, Catherine S-061
Wu, Dan O-133
Wu, San-Pin O-002, S-033
Wu, Wei-Bin T-145
Wuebbolt, Danielle F-150
Wu Healyt, Mae S-177
Wun, Alfred O-108
Xiao, Daliao T-156, F-102, F-134, F-135, S-069, S-128
Xie, Li O-157
Xie, Ning T-031
Xin, Hong S-143
Xiong, Yajing T-038
Xu, Jie T-176
Xu, Xinjing T-165
Xu, Yi S-142, S-145, S-192
Xu, Yue-Ying T-145
Xue, Chang O-127
Xue, Xiangying T-105
Yaba Uçar, Aylin S-204
Yaegashi, Nobuo O-028, T-103, T-109, T-164, F-104, F-107, S-106, S-127
Yagel, Simcha O-088, T-117
Yallampalli, Chandra O-024, O-093, F-048, F-078, F-081, S-047, S-049, S-134, S-175
Yallampalli, Uma F-081, S-134
Yamada, Hidekazu T-109
Yamaleyeva, Liliya M O-077
Yamamura, Yasuko F-026
Yamashita, Riu S-127
Yamauchi, Takafumi S-127
Yang, I S-150
Yang, Peixin O-001, S-053
Yang, Penghua S-053
Yang, Qiaoni T-128
Yang, Qiwei O-156, T-125
Yang, Shanshan S-084
Yang, Shumei S-128
Yang, Xiaohua O-106
Yang, Ying T-143
Yang, Yu F-210
Yang, Yueqin T-080
Yang-Hartwich, Yang O-032
Yasuda, Jun T-109, S-106
Yauger, Belinda J S-177
Yazdani, Anusch T-202
Ye, Aihua T-019
Ye, Louie S-109
Yeaton-Massey, Amanda S-037
Yee, Lynn M T-136, F-050, F-136, F-202, S-035, S-041, S-050, S-051, S-065, S-135

Publication Number Prefix Key

Oral Presentations
O-001 - 052 = **Thursday** Oral Presentations
O-053 - 124 = **Friday** Oral Presentations
O-125 - 160 = **Saturday** Oral Presentations

Poster Presentations
T-001 - 212 = **Thursday** Presentations
F-001 - 212 = **Friday** Presentations
S-001 - 211 = **Saturday** Presentations

Yellon, Steven M S-007
Yildirim, Ecem S-204
Yilmaz, Bayram S-204
Yin, Ophelia O-121
Yin, Ping E O-065, O-069, S-123
Yin, Yongxiang T-162
Yoganathan, Sabesan S-016
Yogev, Yariv F-036
Yohannes, Elizabeth H O-152
Yoo, Jung-Yoon T-118
Yoon, Bo Hyun S-145
Yoon, Da Hee S-170
Yoon, Young-Ran S-145, S-146
Yoshimatsu, Jun F-056, F-060
You, Young Ah F-012, S-076
Young, Roger T-033
Young, Roger C F-033
Young, Steven L T-118, F-114, S-113
Yu, Baifeng O-058, T-080
Yu, Jie F-116
Yu, Victoria X T-027, F-148
Yulia, Angela T-009, F-044
Yun, Bo Hyon T-182
Yun, Bo Hyun F-112
Yun, Lee S T-015
Yurttas Beim, Piraye S-199
Zaki, Mary N F-039
Zambrano, Elena S-070, S-071, S-077, S-087
Zammataro, Luca O-102, F-108
Zamudio, Stacy O-041, T-039
Zarate, Miguel A F-022
Zaretsky, Michael T-099, F-025, S-098
Zarutskie, Paul S-197
Zazueta, Cecilia S-077
Zeng, Ke T-162
Zeuner, Rachel O-127, S-086
Zhang, Honghai S-171
Zhang, Hong-hai T-135
Zhang, Hui-Juan T-144, T-145
Zhang, J F-181, F-199
Zhang, Jiangyang O-133
Zhang, Jianhong T-171
Zhang, Jie T-077, S-078
Zhang, John X S-201, S-202
Zhang, Lubo T-156, F-102, F-130, F-134, F-135, S-069, S-128, S-129
Zhang, Min T-019
Zhang, Weijuan T-025
Zhang, Xijun O-066
Zhang, Zhen S-130
Zhao, Guomao O-035
Zhao, Hongxi O-157
Zhao, Hui F-195
Zhao, Jiu-Ru T-144, T-145
Zhao, Lisa O-158
Zhao, Min T-162
Zhao, Yangu S-179
Zhao, Ying-Jie F-144
Zheng, Jing O-025, O-042, T-130, F-144, F-172
Zheng, Ye O-018, T-175, F-119
Zheng, Zheng T-025
Zhong, Guangming F-127
Zhou, Bin T-076, S-094
Zhou, Chi O-042, F-144, F-172
Zhou, Helen O-008
Zhou, Jie S-210
Zhu, Chaoqun O-057
Zhu, Liyong O-063
Zilioli, Anna F-159
Zinkhan, Erin K O-058, T-080
Zöllner, Julia T-021, T-127, S-017
Zollner, Thomas M O-014, O-017, O-068, O-086, T-112, T-113, T-120, F-115, F-122, S-110, S-118, S-119
Zolton, Jessica R T-199, S-198
Zondervan, Krina T-120, F-117, F-121
Zong, Lu O-157
Zork, Noelia S-131
Zou, Qing-Yun F-144, F-172
Zuk, Jeannie F-025
Zygmunt, Marek T-192, F-194, S-105

Publication Number Prefix Key

Oral Presentations
O-001 - 052 = **Thursday** Oral Presentations
O-053 - 124 = **Friday** Oral Presentations
O-125 - 160 = **Saturday** Oral Presentations

Poster Presentations
T-001 - 212 = **Thursday** Presentations
F-001 - 212 = **Friday** Presentations
S-001 - 211 = **Saturday** Presentations

Subject Index

A

Andrology, Testis Biology O-085, O-098, S-205
Angiogenesis, Endothelial Dysfunction O-038, O-039, O-040, O-042, O-114, O-116, T-171, T-172, T-173, F-171, F-172, S-170, S-171

B

Basic Parturition, Prematurity O-071, O-072, O-073, T-001, T-002, T-003, T-004, T-005, T-006, T-007, T-008, F-001, F-002, F-003, F-004, F-005, F-006, F-007, F-008, F-009, S-001, S-002, S-003, S-004, S-005, S-006, S-007, S-008
Brain O-132, O-134, T-103, T-104, T-105, F-104, F-105, S-101, S-102, S-103

C

Cancer Biology O-101, O-102, O-104, O-105, O-106, T-107, T-108, F-107, F-108, S-105, S-106
Cardiometabolic O-057, O-058, T-076, T-077, T-078, T-079, T-080, T-081, F-076, F-077, F-078, F-079, F-080, F-081, F-082, S-075, S-076, S-077, S-078, S-079, S-080, S-081
Clinical T-109, F-109, S-107, S-108
Clinical Diagnosis, Outcomes O-115, O-118, T-177, T-178, F-177, F-178, S-176
Clinical Parturition, Prematurity O-007, O-008, O-009, O-010, T-041, T-042, T-043, T-044, T-045, T-046, F-042, F-043, F-044, F-045, F-046, S-040, S-041, S-042, S-043, S-044, S-045
Clinical Perinatology O-012, T-035, T-036, T-037, T-038, T-039, T-040, F-036, F-037, F-038, F-039, F-040, F-041, S-035, S-036, S-037, S-038, S-039
Contraception O-110

D

Developmental Programming O-053, O-054, O-055, O-056, T-070, T-071, T-072, T-073, T-074, T-075, F-071, F-072, F-073, F-074, F-075, S-069, S-070, S-071, S-072, S-073, S-074

E

Embryonic Stem Cells, IPS O-159, T-211, F-211, S-210
Endometriosis, Adenomyosis O-013, O-014, O-015, O-016, O-017, O-018, O-019, O-020, T-111, T-112, T-113, T-114, T-116, T-117, T-118, T-119, T-120, T-121, F-112, F-113, F-114, F-115, F-116, F-117, F-118, F-119, F-120, F-121, F-122, S-111, S-112, S-113, S-114, S-115, S-116, S-117, S-118, S-119, S-120
Epidemiology O-095, O-099, T-088, T-089, T-090, T-091, F-089, F-090, F-091, F-092, S-088, S-089, S-090

F

Fertility Preservation O-151, O-153, O-154, T-207, T-208, F-208, S-207
Fetus O-059, O-062, O-133, T-092, F-093
Fibroids O-065, O-066, O-067, O-068, O-069, O-070, O-124, O-156, T-122, T-123, T-124, T-125, F-123, F-124, F-125, F-126, S-121, S-122, S-123, S-124

G

Gametogenesis, Fertilization, Development O-121, O-122, T-180, T-181, F-181, F-182, S-178, S-179, S-180
Genetics, Teratology, Prenatal Diagnosis O-001, O-064, T-093, T-094, T-095, F-094, F-095, S-091, S-092, S-093
Global Health O-096, T-106, S-104
Growth O-126, O-130, T-082, T-083, T-084, F-083, F-084, S-082, S-083
Growth and Metabolism O-063, O-135, T-096, T-097, T-098, F-096, F-097, F-098, S-094, S-095, S-096
Growth, Metabolism, Transport O-077, O-078, O-079, O-148, T-149, T-150, T-151, T-152, T-153, T-154, F-148, F-149, F-150, F-151, F-152, F-153, F-154, S-147, S-148, S-149, S-150, S-151, S-152, S-153
Gynecologic Oncology O-103, F-106
Gynecology O-107, O-112, T-110, F-110, F-111, S-109, S-110

H

Hormones, Growth Factors O-080, T-009, T-155, T-156, F-155, S-154
Hypoxia, Cardiovascular Function O-061, O-131, O-136, T-099, T-100, T-101, T-102, F-099, F-100, F-101, F-102, S-097, S-098, S-099, S-100

I

Immune, Cytokines O-113, T-174, T-175, T-176, F-173, F-174, F-175, F-176, S-172, S-173, S-174, S-175
Immune Function O-049, T-192, T-193, T-194, F-193, F-194, F-195, S-191, S-192, S-193
Immune Function, Microbiome O-022, O-023, T-137
Implantation, Endometrium O-002, O-045, O-046, O-047, O-048, O-050, O-051, O-052, T-182, T-183, T-184, T-185, T-186, T-187, T-188, F-183, F-184, F-185, F-186, F-187, F-188, S-181, S-182, S-183, S-184, S-185, S-186
Infection, Cytokines, Microbiome O-082, T-157, T-158, F-156, F-157, S-155, S-156
Infection, Microbiome O-097, O-109, T-126, T-127, F-127, S-126
Infectious Disease O-005, O-006, O-011, T-067, T-068, T-069, F-068, F-069, F-070, S-066, S-067, S-068

Publication Number Prefix Key

Oral Presentations
O-001 - 052 = **Thursday** Oral Presentations
O-053 - 124 = **Friday** Oral Presentations
O-125 - 160 = **Saturday** Oral Presentations

Poster Presentations
T-001 - 212 = **Thursday** Presentations
F-001 - 212 = **Friday** Presentations
S-001 - 211 = **Saturday** Presentations

Infertility, ART O-108, O-149, O-150, O-152, T-197, T-198, T-199, T-200, T-201, T-202, T-203, T-204, F-198, F-199, F-200, F-201, F-202, F-203, F-204, S-196, S-197, S-198, S-199, S-200, S-201, S-202, S-203
Inflammation, Infection, Microbiome O-003, O-029, O-030, O-031, O-032, O-033, O-034, O-035, O-036, O-074, O-075, O-100, T-010, T-011, T-012, T-013, T-014, T-015, T-016, T-017, T-018, T-019, T-020, T-021, T-022, F-010, F-011, F-012, F-013, F-014, F-015, F-016, F-017, F-018, F-019, F-020, F-021, F-022, F-023, S-009, S-010, S-011, S-012, S-013, S-014, S-015, S-016, S-017, S-018, S-019, S-020, S-021, S-022
Invasion, Angiogenesis, Trophoblast O-081, O-143, T-143, T-144, T-145, T-146, T-147, T-148, F-143, F-144, F-145, F-146, F-147, S-141, S-142, S-143, S-144, S-145, S-146

M

Maternal Biology, Health O-021, T-128, T-129, F-128, S-127
Maternal Nutrition, Obesity, Diabetes O-004, O-090, O-091, O-093, O-094, T-047, T-048, T-049, T-050, T-051, T-052, T-053, F-047, F-048, F-049, F-050, F-051, F-052, F-053, F-054, S-046, S-047, S-048, S-049, S-050, S-051, S-052, S-053
Maternal Physiology O-024, O-025, O-026, O-027, T-130, T-131, T-132, T-133, T-134, T-135, F-129, F-130, F-131, F-132, F-133, F-134, F-135, S-128, S-129, S-130, S-131, S-132, S-133, S-134
Membranes, Cervix O-076, O-137, O-138, T-023, T-024, T-025, T-026, T-027, T-028, T-029, F-024, F-025, F-026, F-027, F-028, F-029, F-030, F-031, S-023, S-024, S-025, S-026, S-027, S-028, S-029
Menopause O-086, T-206, F-207, S-206
Myometrial Biology, Contraction O-139, O-140, O-141, O-142, T-030, T-031, T-032, T-033, T-034, F-032, F-033, F-034, F-035, S-030, S-031, S-032, S-033, S-034

N

Neuroendocrinology, Endocrinology O-060, F-103
Neurologic Behavioral O-125, O-127, T-085, T-086, F-085, F-086, F-087, S-084, S-085, S-086

O

Ovarian Biology, Reproductive Aging O-119, O-120, T-189, T-190, T-191, F-189, F-190, F-191, F-192, S-187, S-188, S-189, S-190
Ovarian Stem Cells O-155

P

Placenta O-144, O-145, O-146, O-147, T-138, T-139, T-140, T-141, T-142, F-137, F-138, F-139, F-140, F-141, F-142, S-136, S-137, S-138, S-139, S-140
Placental Stem Cells T-209, F-210
Polycystic Ovary Syndrome O-084, O-088, T-205, F-205, F-206, S-204
Population Health T-159, T-160, F-158, F-159, S-157, S-158
Post Pregnancy Physiology, Health O-028, T-136, F-136, S-135
Preeclampsia, Related Disorders O-037, O-041, O-043, O-044, O-117, T-161, T-162, T-163, T-164, T-165, T-166, T-167, T-168, T-169, T-170, F-160, F-161, F-162, F-163, F-164, F-165, F-166, F-167, F-168, F-169, F-170, S-159, S-160, S-161, S-162, S-163, S-164, S-165, S-166, S-167, S-168, S-169

R

Regenerative Medicine T-212, F-212, S-211
Reproductive Biology O-123, T-179, F-179, F-180, S-177
Reproductive Endocrinology, Infertility O-083, O-087, T-195, T-196, F-196, F-197, S-194, S-195
Reproductive Function O-128, O-129, T-087, F-088, S-087
Risk Factors, Outcomes, Mortality O-089, O-092, T-054, T-055, T-056, T-057, T-058, T-059, T-060, T-061, T-062, T-063, T-064, T-065, T-066, F-055, F-056, F-057, F-058, F-059, F-060, F-061, F-062, F-063, F-064, F-065, F-066, F-067, S-054, S-055, S-056, S-057, S-058, S-059, S-060, S-061, S-062, S-063, S-064, S-065

S

Stem Cells O-157, O-158, F-209, S-208

U

Urogynecology, Pelvic Floor O-111, S-125
Uterine Stem Cells O-160, T-210, S-209

Publication Number Prefix Key

Oral Presentations
O-001 - 052 = **Thursday** Oral Presentations
O-053 - 124 = **Friday** Oral Presentations
O-125 - 160 = **Saturday** Oral Presentations

Poster Presentations
T-001 - 212 = **Thursday** Presentations
F-001 - 212 = **Friday** Presentations
S-001 - 211 = **Saturday** Presentations

The SRI would like to thank the following companies for their support of the 2017 SRI Annual Scientific Meeting

AbbVie
Bayer AG
Burroughs Wellcome Fund
Giorgio Pardi Foundation
March of Dimes
Pfizer Pharmaceuticals

FUTURE SRI ANNUAL SCIENTIFIC MEETINGS

2018
March 7 – 10, 2018, San Diego, CA, USA

2019
March 13 – 16, 2019, Paris, France

2020
March 11 – 14, 2020, Vancouver, Canada

555 East Wells Street
Suite 1100
Milwaukee, WI 53202

Anne Krolikowski	+1 (414) 918-9888	akrolikowski@sri-online.org
Leah Miller	+1 (414) 918-9888	lmiller@sri-online.org
Nicole Dahms	+1 (414) 918-9888	ndahms@sri-online.org
Morgan Derby	+1 (414) 918-9888	mderby@sri-online.org

Fax: +1 (414) 276-3349
Web Site: www.sri-online.org