The Division of Pediatric Genetics and Metabolism, under the direction of Ralph DeBerardinis, M.D., Ph.D., is responsible for the evaluation, diagnosis and treatment of children with genetic disorders, including birth defects, malformation syndromes, genetically-defined developmental delays, and inborn errors of metabolism. Approximately one in four admissions to tertiary care pediatric hospitals results from conditions with a genetic basis. Although many genetic conditions are rare, there are hundreds of these diseases and they collectively account for a disproportionate amount of illness and death in children. Furthermore, identifying the genetic basis of rare conditions often leads to specific treatments that dramatically improve the health of the patient.

There are three major components to the Division's mission: Patient Care, Research, and Education.

Ralph DeBerardinis, M.D., Ph.D.
Division Chief

Patient Care

With a large and growing team of physicians, genetic counselors, nurse practitioners, dieticians, and social workers, we are a major regional resource for children and families with genetic diseases. Our team evaluates more than 250 patients each month with known or suspected genetic diseases. Particular strengths of our clinical program include:

- We have the largest regional practice specializing in the diagnosis and treatment of children with inborn errors of metabolism.
- We have several clinics specializing in malformation syndromes and genetic forms of developmental delay.
- We are experts in the use and interpretation of advanced genetic diagnostics, including tests involving next-generation sequencing.
- We are the only clinic in Dallas that accepts referrals from the Texas Department of Health's newborn screening program for biochemical disorders.
- We have the largest regional multidisciplinary clinic to evaluate and follow children with Down syndrome.
- We are initiating new clinics specializing in relatively common disorders such as 22q11.2 deletion syndrome and skeletal dysplasias.
- We provide 24/7 coverage for our patients, with a M.D. Medical Geneticist on call at all times.

Research

Our clinical team is unique in that it is fully synchronized with a state-of-the-art research program in the Children's Medical Center Research Institute (CRI), a joint venture between UT Southwestern and Children's Health. The Genetic and Metabolic Disease Program (GMDP) within the CRI is comprised of a team of scientists dedicated to identifying new genetic diseases and developing new ways to treat children with genetic disorders. We use advanced technologies to evaluate each patient's genetic and metabolic individuality. State-of-the-art laboratory-based approaches in cellular and molecular biology are then used to understand the precise consequences of the DNA mutations identified in our patients. Our research team is funded through federal, state, and private grant support. Specific research goals within the GMDP include efforts to:

- Discover new genetic causes of childhood diseases.
- Understand the genetic basis of metabolic diversity and its relationship to health and disease in children.
- Develop new diagnostic methods to detect genetic diseases in patients.
- Develop imaging techniques to monitor metabolic states non-invasively in patients.
- Establish clinical trials to assess the effect of new treatments.

- Construct new disease models using genetically-modified mice, and use these models to test the effect of experimental therapies.
- Use a multidisciplinary approach (chart review, public health databases) to identify and characterize novel malformations syndromes.

Education

We are a vital part of UT Southwestern Medical Center's mission to train medical students, residents, fellows, and allied health professionals in pediatrics, genetics, and metabolism. We teach medical students and pediatric residents throughout their training, manage an accredited residency program to train the next generation of physicians in Medical Genetics, co-direct a fellowship program in Laboratory Genetics and Genomics, and provide continuing medical education in genetics and metabolism to the Dallas-Fort Worth medical community.

Faculty

The Division has five full-time faculty members, all with special interests in the diagnosis and management of a variety of genetic conditions such as inborn errors of metabolism, lysosomal storage disorders, Down syndrome, Marfan syndrome, craniofacial malformation syndromes, incontinentia pigmenti, osteogenesis imperfecta, and other disorders of skeletal development.

Honors / Awards

Best Pediatric Specialists, *D Magazine*

- Ralph DeBerardinis
- Garrett Gotway
- Angela Scheuerle
- Luis Umaña

Texas Super Doctor, Texas Monthly

- Angela Scheuerle

Ralph DeBerardinis

- Edith and Peter O'Donnell Award in Medicine, The Academy of Medicine, Engineering and Science of Texas (TAMEST)
- UT Southwestern Post-doctoral Mentoring Award

Invited Lectures

Ralph DeBerardinis (selected lectures)

- Sick Kids Hospital, Toronto, Canada, January, 2019
  - "Metabolic Dysfunction and Human Diseases"
- Keystone Symposia Cancer Metastasis: The Role of Metabolism, Immunity and the Microenvironment, Florence, Italy, March, 2019
  - "Metabolic Enablers of Cancer Progression"
- Nature Conference on Cellular Metabolism, Xiamen, China, April, 2019
  - "Metabolic Perturbations and Human Disease"

- Fusion Conference, Puerto Vallarta, Mexico, June, 2019
  - "Metabolic Anomalies and Tissue Dysfunction in Humans"
- CIG Symposium, Lausanne, Switzerland, May, 2019
  - "Understanding Metabolic Phenotypes in Human Tumors"
- Keystone Symposia Conference | Tumor Metabolism, Keystone, CO, February, 2019
  - "Metabolic Perturbations and Human Disease"
- 2nd Nature MSKCC Conference "The Tumor Cell Plasticity, Progression and Therapy," New York, NY, March, 2019
  - "Metabolic Complexity in Cancer Cells and Tumors"
- AACR Annual Meeting, Atlanta, GA, April, 2019
  - "Analyzing Tumor Metabolism in Patients"
- Department of Laboratory Medicine and Pathology Grand Rounds Seminar, Minneapolis, MN, April, 2019
  - Metabolic heterogeneity and liabilities in cancer"
- ASPHO Conference, New Orleans, LA, May, 2019
  - "Metabolic Reprogramming in Human Tumors in Vivo"
- NYAS Cancer Metabolism and Signaling, New York, NY, May, 2019
  - "Metabolic Dysregulation and Human Disease Phenotypes "
- CSHL Mechanisms of Metabolic Signaling, Cold Spring Harbor, NY, May, 2019
  - "Mitochondria and Cancer Metabolism"
- Van Andel Symposium, Grand Rapids, MI, June, 2019
  - "Metabolic Dysfunction in Human Diseases"
- Human and Mammalian Genetics and Genomics: The 60th McKusick Short Course, Bar Harbor, ME, July, 2019
  - "Metabolomics and Human Disease"
- University Lecture Series, UT Southwestern, January, 2019
  - "Metabolic Dysfunction and Human Disease Phenotypes"
- American Thoracic Society Conference, Dallas, TX, May, 2019
  - "Metabolic Heterogeneity and Liabilities in Lung Cancer"
- 50th Commemorative International Symposium of The Princess Takamatsu Cancer Research Fund, Tokyo, Japan, November, 2019
  - "Metabolic Phenotypes and Cancer Progression"

Garrett Gotway

- Department of Pediatrics, Multidisciplinary Case Conference, January, 2019
  - "CblC and Texas Newborn Screening"
- Department of Pediatrics, Multidisciplinary Case Conference, March, 2019
  - "Menkes Disease"
- McDermott Center Clinical Genetics Grand Rounds, April, 2019
  - "Neurologic Phenotype in a Patient with Biallelic Variants in POU4F1"
- Pediatric Grand Rounds, UT Southwestern, March, 2019
  - "Normal Human Genetic Variation and Clinical Genetic Testing"
- Pediatric Research Retreat, UT Southwestern, June, 2019
  - "Reanalysis of Results from Clinical Genetic Testing"

- Ethics Grand Rounds, UT Southwestern, January, 2019
  - "Genomic Sequencing of Newborns: Bowl of Cherries or Can of Worms?"
- Department of Pediatrics, Multidisciplinary Case Conference, May, 2019
  - "Acute Intermittent Porphyria"
- Webinar, December 2019
  - Is it Safe? Safety Surveillance through the Antiretroviral Pregnancy Registry
- Neonatology Morbidity and Mortality Conference, Baylor University Medical Center, Dallas Texas, December 2019
  - Presentation and commentary about genetic testing results.

Conference Presentations

2019 AAAAI Annual Meeting, San Francisco, California, February 2019

Namazy JA, Blais L, Andrews EB, **Scheuerle AE,** Cabana MD, Thorp JM, Umetsu DT, Veith JH, Sun D, Kaufman DG, Covington DL, Sun D, Mukhopadhyay, S, Fogel RB, Lopez-Leon S, Spain V. Poster Presentation. The Xolair Pregnancy Registry (EXPECT): Perinatal outcomes among pregnant asthmatics treated with omalizumab (Xolair) compared against those of a cohort of moderate to severe asthmatics.

2019 International Workshop on HIV &Women Seattle, WA, March 2019

Albano JD, Vannappagari V, **Scheuerle A**, Watts H, Thorne C, Ng Leslie, Urdaneta VV, Mofenson LM. Platform Presentation, "Insti Exposure and Neural-Tube Defects: Data from Antiretroviral Pregnancy Registry"

American College of Medical Genetics, Seattle, Washington, April 2019

Gotway G, Guptha S. Poster Presentation, "A Novel Cranial Nerve Phenotype in a Patient with a Homozygous Frameshift Variant in NRP2"

59th Teratology Society Annual Meeting, San Diego, CA, June 2019

Scheuerle AE, Mofenson L, Vannappagari V, Beckerman KP, Betman H, Santanello N, Short WR, Thorne C, Vinas V, Albano JD.
Invited Presentation, "Management of Neural Tube Defect Signals in the Antiretroviral Pregnancy Registry: Efavirenz vs. Dolutegravir"

Hoyt AT, Ramadhani T, Shumate CJ, Canfield MA, Le M, **Scheuerle AE**, and the National Birth Defects Prevention Study.
Poster Presentation, "Acculturation and Selected Birth Defects among Non-Hispanic Blacks in a Population-Based Case-Control Study"

11th International Pediatric HIV Workshop, 10th International AIDS Society Conference, Mexico City, Mexico, July 2019

Mofenson LM, Vannappagari V, **Scheuerle AE**, et al. on behalf of the APR Steering Committee.
Platform Presentation, "Periconceptional Antiretroviral Exposure and Central Nervous System & Neural Tube Defects – Data from the Antiretroviral Pregnancy Registry"

David W Smith Workshop on Malformations and Morphogenesis, Snow Bird, Utah, August 2019

Gotway GK, Thomas JM, **Scheuerle AE**. Biallelic mutations in *POU4F1* in a patient with ocular and cochlear abnormalities, developmental delay, and apnea.

International Clearinghouse for Birth Defects Surveillance and Research Annual Meeting. Bratislava, Slovak Republic, September 2019

Benjamin RH, Yu X, Navarro Sanchez ML, et al, **Scheuerle AE**, et al.
Poster Presentation, "A Novel Software Platform for Assessing Patterns of Multiple Congenital Anomalies"

American Society of Human Genetics, Houston, Texas, October 2019

Navarro Sanchez ML, Benjamin RH, Chen H, Mitchell LE, Langlois PH, Canfield MA, Swartz MD, **Scheuerle AE**, Scott DA, Northrup H, Schaaf CP, Ray JW, McLean SD, Lupo PJ, Agopian AJ. Poster Presentation. CODA: A computational approach for prioritizing potentially syndromic patterns of birth defects involving cleft lip and/or palate. American Society of Human Genetics Annual Meeting. Houston, Texas. October 15-19, 2019.

Benjamin RH, Yu X, Navarro Sanchez ML, Chen H, Mitchell LE, Langlois PH, Canfield MA, Swartz MD, **Scheuerle AE**, Scott DA, Northrup H, Schaaf CP, Ray JW, McLean SD, Lupo PJ, Agopian AJ. Platform Presentation CODA: A platform for assessing patterns of multiple congenital anomalies.

Society for Inherited Metabolic Disorders, Bellevue, WA, April 2019

Gotway G, et al.
Poster Presentation, "A New Report of Lipoyltransferase-1 Deficiency with Functional Assessment"

National Birth Defect Prevention Network (virtual meeting), May 2019

Scheuerle AE.
"Review of Genetic Testing" (recorded April 16, 2019) with live Q&A on May 8, 2019

Education and Training

The Division of Pediatric Genetics and Metabolism is committed to providing quality medical education for medical students, residents, and fellows.

Medical Student Education

Genetics is an essential component of all facets of medicine, and the Division of Pediatric Genetics and Metabolism is proud to take a major role in the education of medical students and other trainees within the UT Southwestern system.

First-Year Medical Students

We are highly involved in the first year medical school curriculum, including:

- Tissues Course: protein and amino acid metabolism, hyperammonemia and urea cycle defects, defects in amino acid metabolism (PKU, MSUD, etc.), purine and pyrimidine metabolism, and treatment of inborn errors of metabolism

Third-Year Medical Students

Third-year medical students participate in pediatrics rotations involving:

- Case studies in clinical genetics
- Genetics clinic outpatient rotations
- Clinical genetics consultations

Fourth-Year Medical Students

We offer an elective in clinical genetics to fourth-year medical students involving outpatient genetics clinics and inpatient genetics consultations.

Medical Genetics Interest Group

We provide mentorship to UT Southwestern medical students considering a career in Medical Genetics. This highly successful interest group meets periodically to discuss new developments in clinical and research-based genetics. We seek to provide an environment to educate students about career opportunities in this exciting and rapidly expanding area of pediatrics.

Resident Education

We play a major role in the education of residents at UT Southwestern. Some of our activities include:

Medical Genetics Residency Program

The Department of Pediatrics, through the Division of Pediatric Genetics and Metabolism, is the sponsoring clinical department for our ACGME certified training program in Medical Genetics. Medical Genetics is a specialty of its own, rather than being a subspecialty of Pediatrics, Internal Medicine, or Obstetrics/Gynecology. The training program

encompasses many clinical departments at UT Southwestern, including Pediatrics, Internal Medicine, Obstetrics/Gynecology (prenatal diagnosis), Neurology and Pathology (Clinical Molecular Genetics, Cytogenetics, and Biochemical Genetics), among others. The program is directed by Garrett Gotway, M.D., Ph.D., a board certified pediatrician and medical geneticist. Given its interdepartmental nature, the residency is managed through the McDermott Center for Human Growth and Development, the Human Genetics Center of UT Southwestern. Learn more about the Medical Genetics program.

Pediatrics

The Division provides didactic teaching for the pediatric residents, including but not limited to:

- Clinical dysmorphology
- Teratology
- Cause and evaluation of birth defects
- Common chromosome anomalies
- Newborn screening
- Acute metabolic disorders
- Genetic storage disorders

We provide direct teaching for the residents in the regular departmental clinical conferences, as well as part of our inpatient consultation service.

Finally, there is a Clinical Genetics elective available for second- and third-year pediatric residents. The residents see outpatients in our clinics and inpatients for consultation services under the supervision of one of the members of the Division faculty. We encourage the residents to participate in clinical research projects if they are interested.

Other Specialties

Trainees in other departments also spend time in our clinics. Residents in Neurology, Pathology, and other specialties may receive some of their training through our Division.

Graduate Student Education

We teach a variety of courses to students pursuing Ph.Ds. and post-doctoral training, including seminars on:

- Human genetics and genomics
- Mendelian genetic diseases
- The use of metabolic tracers and metabolomics in the evaluation of human diseases
- Cancer metabolism
- Regulation of metabolic pathways in health and disease
- Informatic analysis of high-content genomic and metabolomic data sets

Residents

Training in genetics crosses departmental lines and is considered a residency rather than a fellowship. The Department of Pediatrics is the sponsoring clinical department, and the residency is managed through the McDermott Center for Human Growth and Development, the Genetics Center at UT Southwestern.

Research Activities

The Division has been involved in clinical research projects involving clinical trials of new therapies, as well as multicenter studies in clinical and molecular genetics. We have been involved in translational research, helping to make a bridge between the basic science researchers in molecular genetics and the patients. Our large and varied patient population gives us the ability to conduct clinical studies in several areas.

The laboratory of Dr. DeBerardinis is interested in understanding the metabolic activities that support cell growth and proliferation in normal cells and in cancer. In order to produce daughter cells, which occur with each round of the cell cycle, cells need to double their biomass (proteins, lipids, and nucleic acids). This is a tremendous challenge requiring energy, building blocks, and the coordination of a large number of metabolic pathways. Dr. DeBerardinis is exploring the idea that these metabolic activities are orchestrated by growth factor-stimulated signal transduction pathways, which direct cells to take up abundant nutrients and allocate them into the proper metabolic pathways. He wants to understand how signal transduction impacts metabolic fluxes during physiologic states of cell proliferation (e.g., embryogenesis, wound healing, activation of the immune system) and during pathological states (e.g., cancer).

To do this, the DeBerardinis Lab uses a combination of techniques in molecular biology, cell biology, and biochemistry, coupled with metabolic flux analysis using mass spectrometry and nuclear magnetic resonance, and animal models of metabolism and cancer. Current projects include developing imaging probes to identify abnormal metabolic activities in tumors and in children with metabolic diseases and using metabolomics and genomics to identify new disease genes.

Dr. Gotway is participating in a new endeavor at the McDermott Center for Human Growth and Development to enhance the discovery of new gene – disease associations in patients with novel clinical presentations. The Human Gene Discovery Laboratory will analyze whole exome and genome data from patients with unknown clinical syndromes to identify variants in novel genes that will expand our knowledge and understanding of human genetics.

Dr. Scheuerle is a co-investigator on Dr. A.J. Agopian's study out of the University of Texas School of Public Health entitled A Multidisciplinary Approach for Identifying and Characterizing Novel Congenital Malformation Syndromes (NIH 1R01HD093660-01A1). This study uses a combination of Texas Department of State Health Services Birth Defects Registry data and chart review with the goal of identifying previously unrecognized malformation associations. Additionally, this study links birth defects with other health databases, such as cancer, to evaluate potential associations.

Dr. Scheuerle additionally has ongoing research in the natural history of Incontinentia Pigmenti. This is a survey generating study that has the current goal of elucidating the adult phenotype.

Clinical Activities

We accept referrals from all pediatricians and children's hospitals in the Dallas/Fort Worth metroplex, as well as from more distant areas within and beyond Texas. The Division's clinical activities at Children's Medical Center are focused in the following areas:

Metabolic Disease Clinics

The Metabolic Diseases Clinic provides evaluation and testing for children with known or suspected inborn errors of metabolism (IEMs). IEMs are a family of hundreds of rare diseases caused by mutations in the genes that allow the body to produce energy and grow. We are a regional center of excellence in these diseases, establishing the diagnosis in affected children, counseling and educating their families about these conditions, and optimizing therapy tailored to the needs of each child. Blood, urine, enzyme, and DNA analyses are performed for diagnosis. Patients with a confirmed diagnosis are then provided with nutritional evaluation, genetic counseling and psychosocial assessment as well as long-term care.

The Metabolic Disease Clinic is closely associated with the Newborn Screening Clinic. We are a major referral center for the Texas Newborn Screening Program. This statewide program seeks to identify newborn babies with any of 30 different treatable diseases, many of which are genetic/metabolic in nature. A large fraction of the approximately 400,000 babies born in Texas each year are evaluated through our Division. When a baby in North Texas is found to have a metabolic abnormality on the newborn screen, the family is referred to our team for definitive diagnosis, treatment, and long-term care if necessary. Through the Texas Newborn Screening Program, more than 75 children with genetic metabolic diseases are identified each year, and the coordinated care of these children by the Metabolic Disease Clinic at Children's significantly improves their development and survival. Efforts in newborn screening are led by Dr. Luis Umaña.

A dedicated clinic is also provided for teenagers with IEMs transitioning into adult medicine. This clinic at Children's is staffed by Dr. Markey McNutt, who is board certified in both Medical Genetics and Internal Medicine, and follows these patients after age 18 at a clinic in the Aston Center.

Genetics/Dysmorphology Clinic

Children with conditions involving birth defects, developmental delay or mental retardation, or other known or suspected genetic disorders receive evaluation and testing in the Genetics/Dysmorphology Clinic. Chromosomal and DNA analysis for diagnosis of genetic disease is provided, as well as psychosocial assessment, counseling, and comprehensive case management with referral to medical specialists, community resources, and support groups. Family history analysis and risk counseling to discuss reproductive options also are available through a team of board-certified genetic counselors. As of August, 2016, this clinic is now available at the Children's Specialty Center at THR Presbyterian in addition to the Children's Health Dallas campus.

Down Syndrome Clinic

Faculty and staff with the Down Syndrome Clinic have more than 50 collective years of experience in caring for children with Down Syndrome and provide comprehensive treatment for children and their families, including medical management, genetic counseling, physical, speech and motor development evaluation and recommendations, psychosocial support, screening and referral for behavioral and psychiatric problems, and referral to community agencies for educational intervention or therapies. New patients are seen at the Children's Health Dallas campus with follow up available both there and at the Legacy campus.

Interdivisional and Interdepartmental Collaborations

The genetic basis of many human diseases, and the broad utility of genetic testing across numerous subspecialties of Pediatrics and Internal Medicine, make the consultative services of our physicians essential to the clinical and academic missions of UT Southwestern.

Dr. Scheuerle is a key contributor to the Children's Craniofacial program, participating in weekly care conferences involving Plastic Surgery, Dentistry, Otolaryngology, Medical Genetics, Psychology, and various ancillary services such as speech therapy and social work. Dr. Scheuerle sees adult patients as referred from both UTSW and community obstetricians and maternal fetal medicine specialists in the THR Presbyterian clinic. These are coordinated through the Children's FETAL program. She also has joined the Stillbirth Committee, an organ of the Obstetrics & Gynecology department that reviews all the Parkland Hospital stillbirths.

Beginning in summer 2019, under the direction of Dr. James Seaward in Plastic Surgery, a multidisciplinary group was formed for care and management of patients with 22q11.2 deletion syndrome. A large number (>250) of these patients already exist in the Children's Health system, receiving care in disparate clinics: Genetics, Plastic Surgery, Immunology, Endocrinology, Cardiology, Developmental/Behavioral Pediatrics, Psychology, Otolaryngology and Complex Care. The ultimate goal has been to provide care and treatment in a single location. Through 2019 this was a "virtual" clinic with monthly meetings to review patients. As of January 8, 2020, a brick-and-mortar clinic is being held in the Plastic Surgery space on the 6th floor of the Ambulatory Services Center. Because Genetics evaluations and counseling are time intensive, all patients will be seen separately in the Genetics clinic once prior to follow-up in the 22q11.2 deletion clinic.

Current Grant Support

Ralph DeBerardinis

Grantor: National Institutes of Health/National Cancer Institute – R35
Title of Project: Metabolic Regulators of Tumor Cell Growth and Progression
Role: Principal Investigator
Dates: 09/2017 – 08/2024

Grantor: Howard Hughes Medical Institute
Title of Project: HHMI Investigator Program
Role: Principal Investigator
Dates: 09/2018 – 08/2025

Grantor: Cancer Prevention and Research Institute of Texas – Independent Research Award
Title of Project: Carbamoyl Phosphate Synthase-1: A New Metabolic Liability in Non-small Cell Lung Cancers
Role: Principal Investigator
Dates: 03/2016 – 02/2019

Grantor: The Robert A. Welch Foundation – Research Award
Title of Project: Compartmentation of Pro-survival Metabolic Activities in the Cancer Cell Peroxisome
Role: Principal Investigator
Dates: 06/2016 – 05/2019

Grantor: NIH – Emory University Subcontract
Title of Project: Signaling and Targeting of 6-Phosphogluconate Dehydrogenase in Human Cancers
Role: Principal Investigator of Metabolomics, sub-contract (PI-Chen)
Dates: 04/2014 –02/2019

Grantor: NIH – Project 3 (1 P50 CA196516-01A1)
Title of Project: UTSW SPORE in Kidney Cancer
Role: Principal Investigator of Metabolomics Project (Overall PI: James Brugarolas)
Dates: 08/2016 –07/2021

Grantor: NIH R21 CA220090-01A1 (NIH)
Title of Project: Metabolic Profiling in Pediatric Fusion Positive Sarcoma
Role: Co-investigator
Dates: 03/2018 – 02/2019

Grantor: Cancer Prevention and Research Institute of Texas – IIRA
Title of Project: Mechanisms of Melanoma Metastasis
Role: Co-investigator (Overall PI: Sean Morrison)
Dates: 12/2016 – 11/2019

Grantor: Cancer Prevention and Research Institute of Texas – MD Anderson Subcontract
Title of Project: Exploiting Molecular and Metabolic Dependencies to Optimize Personalized Therapeutic Approaches for Melanomas
Role: Co-Investigator (Overall PI: Michael Davies)
Dates: 03/2016 – 02/2019

Grantor: NIH R01 CA174786 02
Title of Project: Signaling and Targeting of 6-Phosphogluconate Dehydrogenase in Human Cancer
Role: PI of Metabolomics Sub-contract (Overall PI: Jing Chen)
Dates: 04/2014 – 02/2019

Grantor: CPRIT RP180778
Title of Project: Metabolic Enablers of Melanoma Progression
Role: PI of Project 3 and Metabolism Core (Overall PI: Sean Morrison)
Dates: 08/2018 – 08/2022

Grantor: Lawrence Steinberg Endowment
Title of Project: Joel B. Steinberg, M.D. Chair in Pediatrics
Role: Principal Investigator
Dates: 12/2018 – Ongoing

Grantor: Robert L. Moody, Sr. Faculty Scholar Endowment
Title of Project: Moody Faculty Scholar
Role: Principal Investigator
Dates: 10/2018 – Ongoing

Grantor: Once Upon a Time Foundation
Title of Project: Discovering and Treating Genetic Metabolic Diseases in Children
Role: Principal Investigator
Dates: 03/2016 – 02/2020

Angela Scheuerle

Grantor: National Institutes of Health/National Institute of Child Health and Human Development (R01)
Title of Project: A Multidisciplinary approach for identifying and characterizing novel congenital malformation syndromes
Role: Co-Investigator
Dates: 9/2018 – 9/2023

Peer-Reviewed Publications

1. Aljeaid D, **Lombardo RC**, Witte DP, Hopkin RJ. A novel pathogenic variant in OFD1 results in X-linked Joubert syndrome with orofaciodigital features and pituitary aplasia. *Am J Med Genet A*. 2019 Jun;179(6):1010-1014. PMID: 30895720

2. Benjamin RH, Yu X, Navarro Sanchez ML, Chen H, Mitchell LE, Langlois PH, Canfield MA, Swartz MD, **Scheuerle AE**, et al. Co-occurring defect analysis: A platform for analyzing birth defect co-occurrence in registries. *Birth Defects Res*. 2019 Nov 1;111(18):1356-1364. PMID: 31313535

3. Cai L, Luo D, Yao B, Yang DM, Lin S, Girard L, **DeBerardinis RJ**, Minna JD, Xie Y, Xiao G. Systematic Analysis of Gene Expression in Lung Adenocarcinoma and Squamous Cell Carcinoma with a Case Study of *FAM83A* and *FAM83B*. *Cancers (Basel).* 2019 Jun 25;11(6). PMID: 31242643

4. Chalishazar MD, Wait SJ, Huang F, et al, **DeBerardinis RJ**, Oliver TG.MYC-Driven Small-Cell Lung Cancer is Metabolically Distinct and Vulnerable to Arginine Depletion. *Clin Cancer Res.* 2019 Aug 15;25(16):5107-5121. PMID: 31164374

5. Chen PH, Cai L, Huffman K, et al, **DeBerardinis RJ**. Metabolic Diversity in Human Non-Small Cell Lung Cancer Cells. *Mol Cell.* 2019 Dec 5;76(5):838-851.e5. PMID: 31564558

6. Cooper EE, Szumlas GA, **Lombardo RC**, Real FJ. A Jittery Newborn With an Abnormal Newborn Screen. *Clin Pediatr (Phila).* 2019 Oct;58(11-12):1354-1356. PMID: 31402696

7. DeVorkin L, Pavey N, Carleton G, et al, **DeBerardinis RJ**, Lum JJ. Autophagy Regulation of Metabolism Is Required for $CD8_+$ T Cell Anti-tumor Immunity. *Cell Rep.* 2019 Apr 9;27(2):502-513.e5. PMID: 30970253

8. Faubert B, **DeBerardinis RJ**, Minna JD. AIF: an acquired metabolic liability in lung cancer. *Cell Res.* 2019 Aug;29(8):607-608. PMID: 31267018

9. Fischer GM, Jalali A, Kircher DA, et al, **DeBerardinis RJ**, Marszalek JR, Zhang J, Holmen SL, Tetzlaff MT, Davies MA. Molecular Profiling Reveals Unique Immune and Metabolic Features of Melanoma Brain Metastases. *Cancer Discov.* 2019 May;9(5):628-645. PMID: 30787016

10. Galan-Cobo A, Sitthideatphaiboon P, Qu X, et al, **DeBerardinis RJ**, Minna JD, Heymach JV. LKB1 and KEAP1/NRF2 Pathways Cooperatively Promote Metabolic Reprogramming with Enhanced Glutamine Dependence in *KRAS*-Mutant Lung Adenocarcinoma. *Cancer Res.* 2019 Jul 1;79(13):3251-3267. PMID: 31040157

11. Gao X, Zhao L, Liu S, et al, **DeBerardinis R**, et al. y-6-Phosphogluconolactone, a Byproduct of the Oxidative Pentose Phosphate Pathway, Contributes to AMPK Activation through Inhibition of PP2A. *Mol Cell.* 2019 Dec 19;76(6):857-871.e9. PMID: 31586547

12. Gu Z, Liu Y, Cai F, et al, **DeBerardinis RJ**, Xu J. Loss of EZH2 Reprograms BCAA Metabolism to Drive Leukemic Transformation. *Cancer Discov*. 2019 Sep;9(9):1228-1247. PMID: 31189531

13. Gupta A, Dsouza NR, Zarate YA, **Lombardo R**, et al. Genetic variants in DGAT1 cause diverse clinical presentations of malnutrition through a specific molecular mechanism. *Eur J Med Genet*. 2019 Nov 25:103817. PMID: 31778854

14. Guptha S, Shumate C, **Scheuerle AE**. Likelihood of meeting defined VATER/VACTERL phenotype in infants with esophageal atresia with or without tracheoesophageal fistula. *Am J Med Genet A*. 2019 Nov;179(11):2202-2206. PMID: 31436871

15. Hao YH, Lafita-Navarro MC, Zacharias L, et al, **DeBerardinis RJ**, Conacci-Sorrell M. Induction of LEF1 by MYC activates the WNT pathway and maintains cell proliferation. *Cell Commun Signal.* 2019 Oct 17;17(1):129. PMID: 31623618

16. Hoyt AT, Shumate CJ, Canfield MA, Le M, Ramadhani T, **Scheuerle AE**; National Birth Defects Prevention Study. Selected acculturation factors and birth defects in the National Birth Defects Prevention Study, 1997-2011. *Birth Defects Res*. 2019 Jun 1;111(10):598-612. PMID: 31021057

17. Hsieh MH, Choe JH, Gadhvi J, et al, **DeBerardinis RJ**, Kim TH, Kim JW. p63 and SOX2 Dictate Glucose Reliance and Metabolic Vulnerabilities in Squamous Cell Carcinomas. *Cell Rep*. 2019 Aug 13;28(7):1860-1878.e9. PMID: 31412252

18. Kim J, **DeBerardinis RJ**. Mechanisms and Implications of Metabolic Heterogeneity in Cancer. *Cell Metab.* 2019 Sep 3;30(3):434-446. PMID: 31484055

19. Kim J, Hu Z, Cai L, et al, **DeBerardinis RJ**. Author Correction: CPS1 maintains pyrimidine pools and DNA synthesis in KRAS/LKB1-mutant lung cancer cells. *Nature*. 2019 May;569(7756):E4. PMID: 31043737

20. Kofuji S, Hirayama A, Eberhardt AO, et al, **DeBerardinis RJ**, et al. IMP dehydrogenase-2 drives aberrant nucleolar activity and promotes tumorigenesis in glioblastoma. *Nat Cell Biol.* 2019 Aug;21(8):1003-1014. PMID: 31371825

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