Virtual Research Week

February 22 – 26, 2021

Presented by the Office of Research

Digital Event Catalog

Welcome!

The Office of Research warmly welcomes you to Virtual Research Week. Whether you are joining us remotely in February, or if you are just browsing the Catalog to learn more about MCW research, we are pleased to be able to share the work of our outstanding faculty, staff, and student scientists.

COVID-19 has prevented us from hosting our annual in-person Research Day event, but it has not stopped science and discovery at MCW. On behalf of the institution, the Office of Research sends its regards to the hard-working investigative teams who have prevailed and thrived in spite of the pandemic.

Thank you to everyone who has contributed to the event—we look forward to sharing, collaborating, and meeting again soon.

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Specialty Programs, Cores, and Shared Resources

Schedule of Events

Monday, February 22

Noon – 1:00 p.m. View Session	**Resource Sessions:** • Quantitative Health Sciences (Dr. Pippa Simpson & Jody Barbeau) • Echocardiography Core Lab (Megan Schoessling) • Center for International Blood & Marrow Transplant Research (Dr. Larisa Broglie) • Center for Microbiome Research (Dr. Mary Holtz) • All of Us Research Program (Dr. Jeff Whittle)
1:00 p.m. – 2:00 p.m. View Session Presenter Feedback Form	**Live Poster Sessions:** Community Studies, Population Sciences, and Education 1. Dr. Robert Treat presents "Medical Student Metacognition: The Predictive Personality Facets of Conscientiousness and Emotional Stability" 2. Nathan Staidl presents "Wisconsin Views on Addiction and Mental Health" 3. Sara Kohlbeck presents "A Qualitative Analysis of Suicide among Farmers in Wisconsin" 4. Jazzmyne Adams presents "Defying the Inequitable Odds: OTO Clinomics" 5. Dr. Michael Nagy presents "Student pharmacist preference and perceptions of synchronous versus asynchronous virtual learning" 6. Brian Conway, Meghan Conroy, and Ji Won Kim present "Heart Disease, Advanced Age, Minority Race, and Hispanic Ethnicity Predict Mortality in COVID-19 Patients" *Moderated by Dr. Julia Dickson-Gomez*

Tuesday, February 23

11:00 a.m. – Noon View Session Presenter Feedback Form	**Live Poster Sessions:** Translational Research 1. Jenica Abrudan presents "Methylome analyses - an update" 2. Dr. Michael Zimmermann presents "Structural Bioinformatics Enhances Mechanistic Interpretation of Human Genomic Variation: Demonstration Through Analysis of 935 Distinct RAS-Family Mutations" 3. Qian Nie presents "Quality control and annotation of variants in Whole Exome and Genome sequencing" 4. Thomas Luo presents "Predicting the Seizure Onset Zone from Interictal ECoG Data using Machine Learning" 5. Lida Zeighami presents "SARS-CoV-2 genomic data analysis: from sequencing to clade identification" 6. Haidy Nasief presents "Feasibility of precise oncologic profiling of chemoradiation therapy for pancreatic cancer in early stages during treatment incorporating delta-radiomics and clinical biomarkers" *Moderated by Dr. Frank Pintar*
1:00 p.m. – 2:00 p.m. View Session	**Focused Talks** 1. Dr. Cecilia Hillard presents "CBD Benefits-Real or Imagined?" 2. Dr. Mingyu Liang presents "Molecular Systems Medicine - An Emerging Discipline"

Wednesday, February 24

1:00 p.m. – 3:00 p.m.

View Session

Presenter Feedback Form

Live Poster Sessions

Basic Science Research

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2. Dr. Angela Mathison presents "A Focus on the Transcriptome, Assays providing an Innovative Dissection of the Cell Biology"
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4. Dr. Jesus Ferre-Fernandez presents "Deletion of conserved non-coding elements downstream of foxc1a in zebrafish affects its expression and produces ocular phenotype"
5. Mahima Vedi presents "Introducing Multi-Ontology Enrichment Tool (MOET): a web-based enrichment tool at the Rat Genome Database"
6. Michael Tschannen presents "Advancing Precision Medicine with Basic and Translational Research Tools, Services, and Assays at GSPMC"
7. Thiago Milech De Assuncao presents "Functional Validation of the Kras G12D variant associated with RASophaties and Cancer"
8. Dr. Andrey Sorokin presents "Small molecule drug SHetA2 restores renal microvascular responses in hypertension-induced nephropathy"
9. Lindsey McAlarnen presents "Investigating social vulnerability among patients participating in gynecologic oncology virtual visits during the COVID-19 pandemic"
10. Kaitlyn Sonnentag presents "Emergency Department Utilization"
11. Dr. Ankan Gupta presents "Quantifying Deciliation as Prognosis of Cerebrovascular Health"

Moderated by Dr. Allen Cowley

Thursday, February 25

2:00 p.m. – 3:00 p.m.

View Session

Resource Sessions:

- Drug Discovery Center (Dr. Ranjit Verma)
- Human Induced Pluripotent Stem Cell (iPSC) Program (Dr. Gracious Ross)
- Cancer Center Redox Biology Shared Resource (Dr. Jacek Zielonka)
- Mass Spectrometry for Small Molecules (Dr. Mike Thomas)

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1:00 p.m. – 2:00 p.m.

View Session

Presenter Feedback Form

Live Poster Sessions:

Clinical Research

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2. Lauren Hipp presents "NO ASSOCIATION BETWEEN NON-ALCOHOLIC STEATOHEPATITIS OR ADVANCED FIBROSIS AND IBD CLINICAL REMISSION AT ONE AND FIVE YEARS"
3. Sonya Dave presents "Racial and Gender Disparities Exist in Influenza Vaccination Rates Among Patients with Inflammatory Bowel Disease"
4. Linda Reis presents "Dominant variants in PRR12 result in unilateral or bilateral complex microphthalmia"
5. Laura Grogan presents "Impact of patient safety bundle on timely treatment of severe hypertension in obstetric patients"
6. Dr. Bhavna Bhasin presents "Acute Kidney Injury in hospitalized patients with COVID-19 and seasonal influenza: A comparative analysis"

Moderated by Dr. Prakash Laud

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VRW Abstracts

A few notes regarding the abstracts:

- Abstracts were submitted by MCW students, staff, postdoctoral and clinical fellows, residents, and faculty
- Researchers were invited to submit optional materials, including a graphic of their poster and a recording of their presentation. These are indicated with buttons at the bottom of the abstract as "Ancillary Materials"

- Some researchers will present their abstracts live virtually during Virtual Research Week. These sessions will be recorded and added to the Catalog.

Category	Allergy, Immunity & Infectious Disease, #1
Primary Author	Jue Zhang
Title	Na/K-ATPase Is a Negative Regulator of LPS-Induced Macrophage Activation
Introduction	Recent studies indicate that the Na/K-ATPase (NKA) is a novel regulator of innate immunity. Nevertheless, its role in bacterial lipopolysaccharide (LPS)-induced innate immune responses remains unclear. In this study, we aim to investigate how NKA regulates LPS signaling and innate immunity.
Methods	Using murine peritoneal macrophages isolated from genetically modified mice, we tested MAPK signaling including JNK and p38MAPK and NF-κB signaling, with western blot and RNA sequencing in WT and NKA α1 deficient macrophages after LPS treatment. Nuclear translocation of NF-κB was tested with immunostaining and western blot. Moreover, we tested pro-inflammatory cytokine production such as IL-1B, IL-6, MCP-1 and TNF-A with ELISA. We further checked cellular ROS production with a fluorescent redox probe and mitochondrial ROS with MitoNeoD in different groups. For in vivo study, LPS and antioxidant N-acetylcysteine (NAC) was injected in WT and NKA α1 heterogonous mice, survival rate was observed and cytokines in plasma was tested.
Results	We showed that macrophages partially deficient in NKA α1 were hypersensitive to LPS. 100 ng/ml LPS triggered a higher extent and prolonged MAPK signaling including JNK and p38MAPK. Moreover, activation and nuclear translocation of NF-κB, the downstream effector of LPS signaling, was augmented and pro-inflammatory cytokine production such as IL-1B, IL-6, MCP-1 and TNF-A was significantly enhanced. Furthermore, intraperitoneal injection of LPS inducing septic shock in mice resulted in higher plasma pro-inflammatory cytokine levels and lower survival rate in NKA α1 heterozygous null mice. Mechanistically, we demonstrated that NKA A1 negatively regulated LPS-induced reactive oxygen species (ROS) production through NADPH oxidase 2. Reduction in NKA α1 resulted in higher ROS induction by LPS stimulation, which contributes to prolonged NF-κB activation as well as enhanced cytokine production. In addition, the antioxidant NAC partially blocked the production of pro-inflammatory cytokine and nuclear translocation of NF-κB in NKA α1 deficient macrophages. NAC treatment also improved the survival rate and protected against LPS induced septic shock in wild type and NKA α1 heterozygous null mice.
Conclusions	The NKA is a novel negative regulator of LPS-mediated innate immunity by regulating ROS production in macrophages.
Ancillary Materials	VIEW MY POSTER WATCH MY PRESENTATION

Category	Allergy, Immunity & Infectious Disease, #2
Primary Author	Kevin Jennings
Secondary Authors	Rajrupa Chakraborty, Christopher Kristich, Nita Salzman
Title	Ceftriaxone-mediated macrophage depletion: A novel mechanism for Enterococcus dissemination?
Introduction	Enterococcus spp. are gram-positive commensals found in the mammalian gastrointestinal tract. Enterococcus are resistant to broad-spectrum cephalosporins and treatment with these antibiotics drives expansion of intestinal Enterococcus populations and can lead to systemic Enterococcus infection. We have developed an experimental mouse model that recapitulates Enterococcus dissemination in response to ceftriaxone administration. We sought to use this model to study the intestinal immune response during ceftriaxone-induced Enterococcus dissemination.
Methods	Mice were colonized by suspending EF in drinking water for 2 weeks. Antibiotics or saline were injected intraperitoneally once daily for 5 days. Intestinal EF abundance was tracked by plating fecal contents on selective agar to enumerate EF colony forming units. Changes in immune cell populations were identified by flow cytometry and live cells were sorted using fluorescence-activated cell sorting (FACS). J774 peritoneal macrophage cell lines were used for in vitro assays. Mice devoid of all Enterococcus species (Enterococcus-free mice) were housed in a gnotobiotic facility and regularly monitored for contamination.
Results	Ceftriaxone treatment resulted in the reduction of intestinal macrophages in conventional and Enterococcus-free mice, irrespective of EF colonization. Treatment with a combination of streptomycin and bacitracin did not alter intestinal macrophage populations. Ceftriaxone inhibited normal expansion of J774 macrophage cultures at 2.5 mg/mL. FACS-purified intestinal macrophages obtained from ceftriaxone treated mice were more likely to harbor intracellular EF than macrophages from saline treated mice. J774 macrophages infected with EF effectively killed approximately 99% of intracellular EF after 24 hours.
Conclusions	These data indicate that ceftriaxone treatment depletes intestinal macrophage populations and that this depletion may have profound effects on the control of disseminating Enterococcus. The observation that intestinal macrophage depletion is not a general feature of antibiotics, nor reliant on the presence of commensal Enterococcus suggests that macrophage depletion is a unique consequence of ceftriaxone administration. This previously undescribed phenomenon has broad clinical implications, especially regarding the prevention and management of gut-associated infections.
Ancillary Materials	VIEW MY POSTER

Category	Allergy, Immunity & Infectious Disease, #3
Primary Author	Kemi Adeyanju, PhD
Secondary Authors	Lawrence G. Lum, MD and Jeffrey A. Medin, PhD
Title	Evaluation of novel human recombinant antibodies against PD1
Introduction	A key part of the adaptive immune system is Programmed cell death 1 (PD1), an inhibitory immune checkpoint protein that binds to Programmed death ligand 1 (PDL1) to suppress T cell activation and proliferation. PD1/PDL1 ligation on naïve T cells promotes phosphatase and tensin homolog (PTEN) expression, a component of the PI3K-AKT signaling pathway, and limits downstream AKT activation, resulting in Treg formation. Alternatively, PD1/PDL1 binding on activated T cells attenuates the P13K/AKT signaling cascade, reducing their immunoreactivity. Tumor cells commonly use the PD1/PDL1 engagement to downregulate anti-tumor immune responses. Thus, blocking the PD1/PDL1 interaction by way of an antibody can improve T cell-associated immune responses in the tumor microenvironment, making antagonist antibodies against PD1 an important target for cancer treatment. Conversely, previous studies in our laboratory have shown that the ligation between PD1 and PDL1 on human Th1 (T helper 1) cells results in the generation of functional, Foxp3+ regulatory T cells (Tregs). Therefore, agonist antibodies against PD1 may be applicable for the generation of Tregs for treatment of autoimmune diseases such as Type 1 Diabetes, inflammatory bowel disease and graft-versus-host-disease (GVHD). Here, a naïve human single-chain variable fragment (scFv) phage display library was used to generate human antibodies against PD1.
Methods	Antibody phage display was used to select for scFv antibody fragments against the extracellular, immunoglobulin variable (IgV) domain of PD1. The scFv fragments were screened via Enzyme immunoassay (ELISA) and DNA sequencing and different clones were ultimately subcloned into a vector allowing for the expression of the scFv fragments as dimeric scFv-Fc fusion molecules. The anti-PD1 scFv-Fc clones (anti-PD1-Fc) were produced in mammalian cells and subsequently characterized for binding specificity to PD1 using ELISA and flow cytometry. The anti-PD1-Fc clones were also assessed for applicability by evaluating the downstream signaling pattern induced after incubation of the anti-PD1-Fc molecules with a human B lymphocyte cell line that constitutively expresses PD1. This was carried out by immunoblotting for phosphorylated proteins in the PI3K/AKT pathway such as phosphorylated PTEN (pPTEN).
Results	Five anti-PD1-Fc clones were selected by phage display from a naïve human scFv phage library. All five clones demonstrated binding to PD1 via ELISA, but only clones 7.2 and 17.1 were shown to bind to extracellular PD1 via flow cytometry. Immunoblot data showed that both 7.2 and 17.1 clones increased expression of phospho-PTEN (pPTEN) in a concentration-dependent manner.
Conclusions	The recombinant anti-PD1-Fc antibody clones 7.2 and 17.1 promote signaling via the PI3K-AKT pathway, suggesting both clones are agonist antibodies.

Category	Allergy, Immunity & Infectious Disease, #4
Primary Author	Cameron G. Gmehlin, B.A.
Secondary Authors	Frida Rivera, MD; Jorge A. Ramos-Casteneda PhD; Lilliana E. Pezzin, PhD; Edmund H. Duthie, MD; L. Silvia Munoz-Price, MD, PhD
Title	Coronavirus in Wisconsin Nursing Homes: A Longitudinal Analysis of the First 10 Months of the Pandemic
Introduction	The COVID-19 pandemic has disproportionately affected nursing home (NH) residents, and emerging evidence suggests quality, location, resident demographics, and staffing levels may be related to COVID-19 incidence within facilities. We describe the distribution of COVID-19 cases in Wisconsin from January 2020 to October 2020, the effect of rural vs urban location of NHs on COVID-19 incidence, and temporal changes in COVID-19 incidence.
Methods	We constructed a database from publicly available Center for Medicaid and Medicare Services' data. Variables obtained included total beds, ownership type, average census, five-star ratings (overall, quality, health, staffing, and nurse staffing categories), number of COVID-19 cases, location, resident Medicaid/Medicare share, area deprivation index, and social vulnerability index. NHs were divided into tertiles based on COVID-19 cases for descriptive analysis (zero cases, 1-7 seven cases, >7 cases). Demographic and clinical variables were reported as frequencies, mean (standard deviation) or median (interquartile range). We compared groups using Pearson Chi-square test and Kruskal-Wallis test. COVID-19 incidence rates were calculated by dividing the number of COVID-19 cases by monthly occupied bed-days, then multiplying the result by 10,000.
Results	From January 1, 2020 to November 1, 2020, a total of 3,133 COVID-19 confirmed cases were reported in 248 (70.5%) NHs. Urban location ($p=0.027$), overall five-star rating ($p=0.035$), number of beds ($p<0.001$), and average count of residents per day ($p<0.001$) were associated with a greater number of COVID-19 cases. Temporal analysis showed that the highest incidence rates of COVID-19 in NHs were observed from January to May and in October (11.36 and 30.33 cases per 10,000 occupied-bed days) 2020. Urban nursing homes experienced higher COVID-19 incidence rates until September, when incidence rates among rural facilities surged (Figure 1, panel A). In the first half of the year, NHs with lower quality scores (1-3 stars) had a higher COVID-19 incidence rate, however in August this trend reversed and facilities with higher quality scores (4-5 stars) showed the highest incidence rates (Figure 1, panel B).
Conclusions	Higher COVID-19 incidence rates during the first 5 months of the pandemic were observed in larger facilities with lower five-star rating, and those located in urban settings. By the end of the year, NHs in rural areas and those with higher quality ratings had higher incidence rates of the disease.
Acknowledgements	Funding Source: Advancing a Healthier Wisconsin Endowment (AHW)
Ancillary Materials	VIEW CORRESPONDING FIGURES

Category	Cancer, #5
Primary Author	Paul Beinhoff
Secondary Authors	Marja Nevalainen, MD, PhD
Title	Jak2-Stat5: A New Approach in Treating Anti-Androgen Resistant Prostate Cancer
Introduction	Androgen deprivation therapy is a therapeutic standard in treating prostate cancer (PC). However, there are well documented resistance mechanisms that affect the majority of diagnosed patients, regarded as castrate-resistant prostate cancer (CRPC). Resistance is highly likely through AR mutations, variant splicing, and enzymatic upregulation. Therefore, there is great need for a novel mechanistic approach in treating CRPC. Jak2/Stat5 is upregulated in PC, and inhibition of this pathway leads to apoptosis, decreased proliferation, and hindered viability. Using already available Jak2/Stat5 inhibitors is thus a highly relevant means of potential therapy.
Methods	A literature review was conducted to identify Jak2 inhibitors that pose potential for our purposes in CRPC. The sources used were scientific publications, clinical trial results, the FDA, and evidence provided by sponsoring pharmaceutical corporations. Two experiments were conducted in vitro and in parallel to determine the effects of Fedratinib, a Jak2 inhibitor, on CWR22-Rv1 PC cell lines. In experiment #1, cells were treated for 4 days at a therapeutic dose (.6µM) and evaluated for Stat5 phosphorylation status via immunoprecipitation (IP) and western blotting (WB). In experiment #2, cells were treated for 4 days (.6µM) and evaluated for cell viability via crystal violet staining.
Results	Overall, 35 drugs with Jak2 inhibitory activity have been included in this review. There are 14 Jak2 inhibitors that have been investigated for use in solid tumors, 5 of which have already been FDA approved. Fedratinib, a selective Jak2 inhibitor, holds efficacy at its therapeutic dose (.6µM) in CWR22Rv1 cells as indicated by a decrease in Stat5 phosphorylation and cell viability.
Conclusions	Off-label usage of currently approved and investigated Jak2/ Stat5 inhibitors is highly applicable in treating anti-androgen resistant CRPC from available in vitro, in vivo, and clinical studies. Fedratinib revealed efficacy in vitro as determined by inhibited Stat5 phosphorylation in correlation with decreased PC cell viability.
Ancillary Materials	VIEW MY POSTER WATCH MY PRESENTATION

Category	Cancer, #6
Primary Author	Alexander Hall
Secondary Authors	Sarah White, MD, MS Lisa Baumann Kreuziger, MD, MS William Rilling, MD
Title	Incidence and risk factors for venous thromboembolic disease in patients with hepatic malignancy undergoing liver-directed therapy
Introduction	Patients with hepatic malignancy have an increased incidence of venous thromboembolic disease (VTE). This risk is further increased with surgical resection, and hepatectomy patients receive prophylactic anticoagulation peri-procedurally. As liver-directed therapy (LDT) becomes increasingly utilized, understanding VTE incidence and prevalence could help provide the necessary information to develop anticoagulation protocols following LDT. The purpose of this study was to identify the incidence of VTE in patients who have undergone LDT and define independent risk factors for developing VTE following LDT.
Methods	A single institution (Froedtert Health, Milwaukee, WI) retrospective chart review was conducted to evaluate patients who underwent LDT and had VTE between 6/1/2010 and 8/1/2019. Independent risk factors that were collected included patient demographics, diagnosis, type of LDT, extent of malignancy, ECOG status, comorbidities, and laboratory values. Risk factors were compared between patients that had VTE following LDT and patients that did not develop VTE.
Results	967 patients underwent either TARE or TACE. 65 (6.7%) patients had a VTE event following LDT. 24 (2.5%) of these VTE events were within 90 days of LDT, and 8 (0.8%) were within 30 days. The following risk factors were independently associated with developing VTE following LDT: TARE (compared to TACE, OR 2.64, p=0.021), other surgery within 1 year prior to LDT (OR 2.21, p=0.032), and presence of extrahepatic disease (OR 3.89, p=0.001). Cholangiocarcinoma (OR 3.5, p=0.075) and metastatic cancer (OR 5.04, p=0.00004), when compared to HCC, were also found to be associated with VTE. The following factors were found to be protective for VTE following LDT: African American race (OR 0.36, p=0.025), chronic anticoagulation (OR 0.52, p=0.091), cirrhosis (OR 0.416, p=0.015), and increased INR (OR 0.05, p=0.032).
Conclusions	The risk for VTE is multifactorial, with factors contributing to increased risk and others a decreased risk. A multifactorial model can be developed to categorize patients by risk for VTE, and prophylactic anticoagulation can be considered for individuals at high risk for VTE.
Ancillary Materials	VIEW MY POSTER

Category	Cancer, #7
Primary Author	El-Sayed H. Ibrahim, PhD
Secondary Authors	Abdul Kareem Parchur, Gayatri Sharma, Jaidip M. Jagtap, Christopher Hansen, Venkateswara Rao Gogineni, Peter S. LaViolette, Michael J. Flister, Sarah B. White, Amit Joshi
Title	MRI relaxometry for tracking nanoparticle mediated ablation therapy of colorectal cancer liver metastasis
Introduction	Surgical intervention is only possible in less than one third of colorectal liver metastases cases. Chemotherapy and hyperthermia ablation are the only other clinically available treatment options. In this respect, detecting accurate tumor location during the therapeutic procedures is essential to effective treatment. In this study, we explore the value of Relaxometry for identifying the tumor response to theragnostic nanoparticles (TNPs)mediated photothermal therapy (PTT)and distinguishing it from normal surrounding tissues.
Methods	Au nanorods resonant at 830nm were synthesized, and encapsulated with Gd2O3:Yb/Er shell and PEGylated, resulting in formation of sub-100 nm TNPs. Three WAG/RijCmcrrats implanted with colorectal cancer liver metastasis (CLRM)tumors were scanned on 9.4T MRI scanner. TNPs (0.5 mL, 1013 NP/mL) were locally injected into the liver via hepatic portal vein. The rats were imaged to determine MRI R2* relaxometry immediately after TNPs injection, followed by 3-minute laser ablation (~700 mW/cm2), and at 10 days post procedure. R2* relaxometry was assessed using a gradient-echo T2* mapping sequence to acquire axial and coronal stacks of 6-12 images covering the liver. Nine echoes were acquired with echo times ranging from 4ms to 48ms in 5.5ms increments. R2* was measured for each pixel as 1000/T2*, and the results were used to generate R2* maps.
Results	The TNPs' R1 =1.1 × 108mM−1s−1and R2 =4.8 × 108mM−1s−1. The CLRM tumor R2* =25.2±0.6 s-1in post-PTT rats, which is ~5 times higher than normal liver R2* relaxivity (5.9±0.6 s-1). The tumor R2* relaxivity decreased to 15.3±0.9 s-1at 10-days post therapy, which is ~3 times higher than normal value in the liver (5.9±0.6 s-1). The results showed significant difference between R2* values in tumor and normal tissues at the two imaging timepoints.
Conclusions	In conclusion, inclusion of MRI contrast in gold nanoparticles with plasmon resonance in near-infrared optical region can play a significant role in precise image-guided PTT by accurately tracking the tumor boundaries, which enables high-efficiency PTT by delivering a sufficient amount of light to the tumor.
Reference 1	Parchur et al, ACS Nano; 12:6597-6611
Reference 2	Wahidiyat et al, Hematology; 22: 501-507
Reference 3	Garbowskiet al, J Carduiovasc Magn Reson; 16:40
Ancillary Materials	VIEW MY POSTER

Category	Cancer, #8
Primary Author	Matthew Scheidt, MD
Secondary Authors	Osmani Deochand, Sarah White, MD, MS, FSIR, William Rilling, MD, Eric Hohenwalter, MD and Amanda Smolock, MD, PhD
Title	Transarterial Chemoembolization with Conventional Dual Drug versus Cisplatin Triple Drug Therapy: A Comparison of Outcomes
Introduction	The purpose of this study was to evaluate outcomes of transarterial chemoembolization (TACE) performed with standard dual drug therapy versus triple drug therapy for the treatment of hepatic malignancy.
Methods	This was an IRB-approved retrospective study of all TACE procedures performed between 7/1/2019 and 6/30/2020. A total of 110 TACE procedures were reviewed for patient and tumoral characteristics as well as procedural details. Clinical, laboratory, and imaging outcomes were recorded at one-month follow-up. Post procedure toxicities were recorded according to CTCEA classification.
Results	Over a 1-year period, 110 TACE cases were performed in 76 patients (62 males, average age 65 Â± 9.5 years). Of these, 94 were performed for HCC, 15 for mNET, and 1 for cholangiocarcinoma with a total of 93 cases done in the presence of cirrhosis. 63 of 110 cases were performed with two chemotherapy agents of doxorubicin and mitomycin (“double regimen TACE”) while 47 of 110 were done with triple drug therapy of doxorubicin, mitomycin, and cisplatin (“triple regimen TACE”). 57/63 (90.5%) double regimen TACE procedures and 28/47(59.6%) triple regimen TACE procedures were performed in a superselective manner. There were no significant changes in pre- and post- procedure bilirubin and creatinine values with either treatment regimen. The most common adverse event was post-embolization syndrome, accounting for about 50% of all reported adverse events in patients treated with either chemotherapy regimen. The total number of remaining adverse events was similar between the TACE groups (20/63 double regimen TACE and 15/47 triple regimen TACE). There was no statistically significant difference in the rate of biliary complications in the double regimen TACE group (4/63, 6.3%) compared to the triple regimen TACE group (2/47, 4.2%). Similarly, the rate of recorded acute kidney injury was not different between groups (3/63 in the double regimen TACE group vs 5/47 in the triple regimen TACE group). There were no differences in treatment response at 1-month imaging.
Conclusions	The use of triple regimen TACE compared to double regimen TACE does not appear to be associated with any difference in treatment outcome or adverse event. Given the recent re-availability of cisplatin for TACE administration, these findings may help guide operators’ decisions on whether or not to use triple regimen therapy.
Reference 1	Clark, Timothy. “Complications of Hepatic Chemoembolization.” Seminars in Interventional Radiology, vol. 23, no. 2, 2006, pp. 119-125., doi:10.1055/s-2006-941442.
Reference 2	Dhamija, E., et al. “Biliary Complications of Arterial Chemoembolization of Hepatocellular Carcinoma.” Diagnostic and Interventional Imaging, vol. 96, no. 11, 2015, pp. 1169-1175., doi:10.1016/j.diii.2015.06.017.
Reference 3	Jeliazkova, Petia, et al. “Prognostic Factors in Hepatocellular Carcinoma Patients Undergoing Transarterial Chemoembolization and Radioembolization: A Retrospective Study.” European Journal of Gastroenterology & Hepatology, vol. 32, no. 8, 2019, pp. 1036-1041., doi:10.1097/meg.0000000000001625.
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Category	Cancer, #9
Primary Author	Lindsey A. McAlarnen, MD, MSc**
Secondary Authors	Rana Aliani, MD; Natasha Simske: Elizabeth E. Hopp, MD
Title	Investigating social vulnerability among patients participating in gynecologic oncology virtual visits during the COVID-19 pandemic
Introduction	The COVID-19 pandemic has rapidly transformed healthcare systems worldwide with a significant expansion in virtual health and telemedicine platforms and capabilities. Oncology patients are at risk for severe COVID-19 infection. These patients also require frequent medical care due to treatment plans, therapeutic toxicities, and necessary surveillance visits. Health equity and access to care contributes to differing cancer care outcomes and likely impacts the utilization of telemedicine. Here we describe the utilization of virtual visits by patients with gynecologic malignancies and assess social vulnerability of such patients.
Methods	Patients seen virtually through the gynecologic oncology clinic at Froedtert Cancer Center from March 1, 2020 to August 31, 2020 were obtained, and honest broker was utilized for patient demographic and geographic factors. Patients' addresses were used to determine each patient's home Federal Information Processing Standard (FIPS) code, which was matched to the census tract. The CDC's Social Vulnerability Index (SVI) was used to assign social vulnerability indices and ranks from 2018 to each patient and how that patient's census tract compared to others in Wisconsin and the United States. Clinical data was collected through chart review. Data was analyzed through simple statistics.
Results	Two hundred seventy-four patients had a virtual visit with a gynecology oncology provider in a six-month period during the COVID-19 pandemic. The mean tract summary ranking variable for all patients when compared to all census tracts in Wisconsin was 0.391 (range 0-0.997), where 0 indicates no vulnerability and 1 indicates the most vulnerability. The mean tract summary ranking variable for all patients when compared to all census tracts in the United States was 0.316 (range 0.0001-0.9856). The mean age of patients was 64.59 years (range 25-92 years). The majority of patients seen had ovarian cancer (140 patients), followed by uterine (118 patients), cervix (11 patients), and vulva/vaginal cancer, respectively (5 patients). Of the 274 patients participating in virtual visits, eighty-six percent were Caucasian (236 patients), 9.5% African American (26 patients), 3.3% other, all of which identified as Hispanic (9 patients), and 1.1% Asian (3 patients). When patients were compared to US vulnerability ranks, African Americans were the most vulnerable of our patients participating in virtual visits with a mean SVI rank of 0.637 (range 0.013-0.986) compared to Asian patients 0.577 (range 0.529-0.603), Hispanic patients 0.426 (range 0.020-0.955), and white patients 0.274 (range 0.0001-0.982) who were the least vulnerable.
Conclusions	Virtual visits were utilized by patients of all ages and sites of gynecologic malignancy. African American and Asian patients were more vulnerable than Hispanic and white patients in our population. Telemedicine is a useful platform for medical care across all ages and ethnic groups. Further research and outreach efforts are needed to ensure access to virtual visits are available for all cancer patients particularly during times when access to healthcare is limited such as the COVID-19 pandemic.
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Category	Cancer, #10
Primary Author	Guillermo Urrutia M.D.
Secondary Authors	Gwen Lomberk PhD
Title	Replication Stress Induces G9a-mediated H3K9Me2 Deposition at Replication Forks
Introduction	DNA replication is a tightly regulated process for faithful duplication of the genome during the cell cycle. When unscheduled events occur, such as aberrant origin firing or collision with the transcription machinery, replication fork progression is stalled, resulting in replication stress (RS), fork collapse and eventually DNA damage and cell death. Activated oncogenes, such as KRAS which is mutated in almost 95% of pancreatic cancers (PDAC), drive higher proliferation rates, and thus, trigger RS. RS induced by activated oncogenes has been implicated as an impactful, early event in tumorigenesis, which if not tolerated causes cell senescence or death. Mechanisms for bypassing the deleterious effects of oncogene-induced RS is key to tumor progression, yet remain poorly understood. Here, we investigated a novel function for the G9a histone methyltransferase (HMT), responsible for the Histone H3 lysine 9 di-methylation (H3K9Me2) mark, at replication forks during the response to RS in PDAC cells.
Methods	Subcellular fractionation followed by western blot was used to evaluate the expression and localization of G9a and H3K9Me2 on L3.6 PDAC cells. Association of H3K9Me2 to replication forks was assessed by FACS-based in situ protein interactions at replication forks assay (SIRF).
Results	Using western blot, we evaluated expression of the G9a-deposited H3K9Me2 mark in response to RS, using the RS inducer Aphidicolin (APH), which triggers RS through direct inhibition of DNA polymerases alpha and delta. We found an increase of this epigenomic mark, as well as total protein di-methylation, in a time-dependent manner after RS induction. Subcellular fractionation followed by western blot on APH-treated L3.6 PDAC cells revealed enhanced recruitment of RPA32 protein to chromatin, confirming activation of the RS response. In addition, chromatin-bound G9a and H3K9Me2 increased after induction of RS. To evaluate the deposition of H3K9Me2 at stalled replication forks, we performed flow cytometry-based in situ protein interactions at replication forks assay (SIRF). SIRF assays revealed an increase of the H3K9Me2 deposition on APH-stalled replication forks, while 24-hours pre-inhibition of G9a before APH treatment, using BRD4770, reverted H3K9Me2 deposition at replication forks, confirming the involvement of G9a and its product H3K9Me2 in response to acute RS.
Conclusions	Future studies will be focused on evaluating these location-specific epigenomic changes to determine their functional role in replication fork stability during the RS response and bypassing oncogene-induced RS. In summary, this data demonstrates that RS induction in PDAC cells elicits a G9a-mediated response, resulting in the deposition of the H3K9Me2 histone mark at replication forks. These findings reveal a potential new target for the development of novel combination strategies to sensitize PDAC cells to RS-inducing agents.
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Category	Cancer, #11
Primary Author	Thiago Milech De Assuncao**
Secondary Authors	Romica Kerketta, Angela J. Mathison, Elise Leverence, Guillermo Urrutia, Timothy Stodola, Marina Pasca di Magliano, Michael T. Zimmermann, Gwen Lomberk, and Raul Urrutia
Title	Functional Validation of the Kras G12D variant associated with RASophaties and Cancer
Introduction	Direct targeting of the KRAS gene has been clinically unsuccessful and the downstream impact that the constitutive activation of KRAS has on chromatin remains unknown KRASG12D is a genomic variant associated to the development of several RASopathies and is also mutated in many cancers, including pancreatic, colon, lung, liver, biliary, thyroid, and breast. Extensive functional validation for this important pathogenic variant has been primarily focused on understanding it signaling capabilities. However, how this mutation impacts the epigenome is poorly understood. Thus, here investigate the earliest changes at the transcriptomic and epigenomic levels that occur following activation of this oncogene.
Methods	RNA-seq, ChIP-Seq, Atac-Seq
Results	RNA-seq data indicated that following KRAS induction, genes involved in the regulation of epithelial to mesenchymal transition (EMT) and metabolic pathways were downregulated, while genes involved in KRAS signaling and cellular proliferation were upregulated. ChIP-seq revealed that KRAS activation was correlated with an increase in the deposition of histone marks associated with enhancers/super-enhancers (H3K27ac and H3K4me1), activated promoters (H3K4me3), and an increase in regions silenced by polycomb (H3K27me3). Integration of RNA-seq and ChIP-seq data demonstrated that up- or down-regulated genes also had corresponding alterations of the H3K27ac and H3K4me3 activating histone marks near their promoters. DNA methylation levels of several CpG islands were also altered following KRAS induction. Atac-seq revealed a global remodeling of accessible chromatin regions around gene transcription start sites.
Conclusions	Based on our results, exposure to oncogenic KRAS induced pancreatic cells to acquire a more epithelial-like phenotype with increased proliferation, which coincided with changes in the transcriptome, proteome and the epigenome. RRBS demonstrated that KRAS induction shifts the differentially methylated regions across the genome. Through genomic mapping of histone modifications, we observed a marked increase in active enhancers and super-enhancers, as measured by H3K27ac and H3K4me1 peaks, implicating histone acetyltransferases as downstream epigenetic modulators of the KRAS signaling pathway. These enzymes may therefore serve as potential drug therapy targets in future studies to disrupt KRAS mediated oncogenesis pathways and mitigate the progression of PDAC.

Category	Cancer, #12
Primary Author	Lishu He**
Secondary Authors	Gwen Lomberk, PhD
Title	Inhibition of PRMT5 Activates the ATR DNA Damage Response Pathway, Revealing a Potential Novel Combination Therapy for Pancreatic Cancer
Introduction	Pancreatic ductal adenocarcinoma (PDAC), the most common form of pancreatic malignancy, remains one of the most aggressive and lethal cancers. Like many cancers, PDAC cells often possess defects in DNA damage repair (DDR) pathways that are not observed in healthy cells, which can be exploited for therapeutic strategies. DNA is packaged into chromatin. Critical to the structure and function of chromatin are post-translational modifications of histones. For example, histone lysine methylation impacts various cellular processes, including DNA repair. Protein arginine methyltransferase 5 (PRMT5), a type II histone arginine methyltransferase, is involved in a variety of cancers and participates in transcription and DNA repair, among other functions. PRMT5 is associated with DDR via both non-homologous end joining and homologous recombination depending on specific molecular environments, but the mechanism by which PRMT5 expression in PDAC contributes to tumor progression and patient survival is not well understood. Here, we examined the effect of PRMT5 inhibition on PDAC cells in vitro, the impact of its inhibition on DDR pathways, and potential synergy of PRMT5 inhibition combined with inhibitors of key players in DDR signaling.
Methods	We used the Genotype-Tissue Expression Project and The Cancer Genome Atlas databases to analyze PRMT5 expression in PDAC and its clinical significance. Cellular and molecular assays were also performed, including cell proliferation, colony formation, flow cytometry-based cell cycle analysis, western blot, and quantitative real-time RT-PCR.
Results	Public databases revealed that PRMT5 is upregulated in PDAC tissues compared to matched normal controls, and its high expression associated with reduced overall survival of PDAC patients in Kaplan-Meier curves. Treatment of PDAC cells with the PRMT5 inhibitor, EPZ015938, resulted in a dose-dependent decrease of cell proliferation. Clonogenic survival assays demonstrated reduced PDAC colony formation upon PRMT5 inhibition. This inhibition of cell growth was congruent with aberrant cell cycle progression, as measured by flow cytometry-based cell cycle analysis. In protein lysates from PDAC cells treated with EPZ015938 followed by western blot, we found an increase in phosphorylation of Ataxia-telangiectasia and Rad3 related (ATR), a serine/threonine kinase and key responder to replication stress and DNA damage, compared to control treatments. This result suggests that inhibition of PRMT5 activates a DNA damage response in PDAC cells via ATR. Screening the expression of genes involved in various DDR pathways by quantitative real-time PCR, we found that EPZ015938 caused downregulation of ATM, a DNA damage sensor with common and divergent downstream effectors as ATR. Combined PRMT5 and ATR inhibition displayed a greater reduction in cell proliferation over control and single treatments, revealing a potential avenue for new combination strategies.
Conclusions	Future studies will focus on elucidating specific mechanisms through which PRMT5 inhibition facilitates expression of critical DDR markers and identifying novel combination strategies for potential clinical benefits in PDAC.
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Category	Cancer, #13
Primary Author	Pui Kei Wu, Ph.D**
Secondary Authors	Seung-Keun Hong, Ph.D., Research Associate, Department of Biochemistry. Jong-In Park, Ph.D., Professor of Biochemistry and Surgery
Title	Mortalin depletion induces MEK/ERK-dependent and ANT/CypD-mediated death in vemurafenib-resistant B-Raf(V600E) melanoma cells
Introduction	Activating mutations affecting B-Raf kinase domain, e.g., B-Raf(V600E,K,D), are the most frequently detected oncogenic alterations in cutaneous melanomas, making B-Raf and its effector pathway mitogen-activated protein kinase (MEK)/extracellular signal-regulated kinase (ERK) a key therapeutic target in these tumors. Although FDA-approved precision medicine drugs such as B-Raf or MEK1/2 inhibitors have advanced the therapy of BRAF-mutant melanomas, many tumors initially responsive to these drugs develop resistance, eventually causing patient casualty. Therefore, strategies to treat therapy-resistant BRAF-mutant tumors are required. We previously reported that deregulated MEK/ERK activity in tumor cells harboring BRAF or KRAS mutations can increase mitochondrial permeability but mortalin, a mitochondrial chaperone that is overexpressed and mislocalized in these tumors, counteracts this effect on mitochondrial permeability by limiting a physical interaction between adenine nucleotide translocase (ANT) and cyclophilin D (CypD) (Science Signaling, 2020; Oncogene, 2020). As such, mortalin depletion in these cells results in perturbed mitochondrial permeability and, consequently, tumor cell death. Based on this discovery, we have proposed that mortalin is a potential therapeutic target for BRAF- or KRAS-mutant tumors. In this study, we sought to determine whether mortalin depletion can suppress B-Raf inhibitor (BRAFi)-resistant melanoma cells via a similar mechanism.
Methods	Vemurafenib-resistant progenies of BRAF(V600E)-mutant melanoma A375 and Colo-829 and their parental cells were infected with lentiviral vectors expressing small hairpin RNA targeted to mortalin, ANT3, or CypD. Cell viability and death were determined by trypan blue exclusion assay and flow cytometry of cells stained with TO-PRO 3 or Annexin V. Mitochondrial membrane permeability was analyzed using calcein retention assay by MitoProbe Transition Pore Assay kit and flow cytometry. Protein expression levels were determined by immunoblotting. In vivo xenograft experiments were conducted by subcutaneously inoculating tumor cells into athymic nude (nu/nu) mice. Statistical significance was determined by two-tailed paired student's t-test, one-way ANOVA with Dunnett posttests, or two-way ANOVA with Bonferroni posttests using Prism.
Results	Mortalin depletion induced substantial cell viability loss via caspase-dependent apoptosis, in association with increased mitochondrial permeability in vemurafenib-resistant B-Raf(V600E) melanoma cells, similarly as it did in parental vemurafenib-naïve cells. Knockdown of ANT3 or CypD rescued this tumor cell viability loss and perturbed mitochondrial permeability, which suggest that ANT3 and CypD are required for mortalin depletion to induce cell death and to perturb mitochondrial permeability in these tumor cells. Noteworthy was that inhibitors of MEK1/2 or ERK1/2 substantially attenuated mortalin depletion-induced lethality and mitochondrial permeability perturbation in these cells, suggesting the requirement of MEK/ERK activity for mortalin depletion to induce death in BRAFi-resistant cells. We also observed that mortalin depletion can effectively suppress the xenografts of vemurafenib-resistant B-Raf(V600E) melanoma cells in athymic nude mice. Together, these findings suggest that mortalin has potential as a candidate therapeutic target for BRAFi-resistant BRAF-mutant tumors.
Conclusions	Our findings suggest that mortalin is an Achilles heel in BRAF-mutated melanomas, not only BRAFi-naïve but also BRAFi-resistant. Our data provide a rationale to consider mortalin inhibition as a therapeutic strategy to overcome the drug resistance. This study has been accepted for publication in Cancer Letters.
Acknowledgements	This study was supported by the NIH/National Cancer Institute grant R01CA138441 to Dr. Jong-In Park.
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Reference 2	Wu, P. K., Hong, S.-K., Starenki, D., Oshima, K., Shao, H., Gestwicki, J., Tsai, S., Park, J.-I., Mortalin/HSPA9 targeting selectively induces KRAS tumor cell death by perturbing mitochondrial membrane permeability. Oncogene, 2020. [PMID: 32291414]
Reference 3	Wu, P. K., Hong, S.-K., Park, J.-I., Mortalin depletion induces MEK/ERK-dependent and ANT/CypD-mediated death in vemurafenib-resistant B-RafV600E melanoma cells. Cancer Letters, 2021. 502, 25-33. [PMID: 33440231]
Ancillary Materials	VIEW MY POSTER

Category	Cardiovascular & Heart, #14
Primary Author	Vincent Renta
Secondary Authors	Rebekah Walker, PhD, Emma Garacci, MS, Aprill Dawson, PhD, MPH, Jennifer Campbell, PhD, MPH, Leonard Egede, MD, MS
Title	The Relationship between Social Capital and Hypertension in Two African Countries
Introduction	Africa has seen a shift in its burden of disease from infectious to non-communicable diseases (NCDs) coupled with the largest increase in chronic disease incidence worldwide.1,2 Hypertension and its related diseases are estimated to be responsible for over a third of total NCD deaths.3 Several positive behaviors and social determinants of health such as social capital have been linked to lower odds of NCD development. Previous studies have largely focused on interactions between social capital, health behaviors, and cognitive health. There is a lack of information on the association between social capital and NCDs in Africa and the degree to which, sociodemographic factors influence the relationship. We sought to examine the relationship between social capital and hypertension among adults in Ghana and South Africa.
Methods	9,800 adults were analyzed from the Study on Global Ageing and Adult Health Wave 1 individual data files for Ghana and South Africa. Outcomes were self-reported hypertension, measured hypertension (â‰¥140/90, systolic, and diastolic), and undiagnosed hypertension. The primary independent variable was social capital, dichotomized into low vs. medium/high levels. Preliminary analysis included descriptive statistics to understand sociodemographic differences between South Africa and Ghana. Interaction terms were tested between social capital and rural/urban residence status, with models stratified by rural/urban status if significant. Then unadjusted and adjusted linear and logistic models were run separately for South Africa and Ghana for each outcome.
Results	There was a significant difference in the prevalence of self-reported hypertension by the level of social capital in South Africa and Ghana ($p<0.001$). Ghana showed significant differences in measured hypertension and undiagnosed hypertension with individuals reporting low social capital having higher hypertension and more undiagnosed hypertension ($p<0.001$). After adjustment, those with low social capital in Ghana were more likely to have hypertension (OR=1.35, 95% CI=1.18;1.55), have 3.25 mmHg increase in systolic, 2.37 mmHg increase in diastolic and were more likely to have undiagnosed hypertension (OR=1.25, 95% CI=1.08;1.44). Finally, rural residents in Ghana with low social capital were more likely to have undiagnosed hypertension when compared to those with medium/high social capital (OR=1.44, 95% CI=1.19;1.78), while in urban areas the relationship was not significant.
Conclusions	This study found that the relationship between social capital and hypertension differed between South and West African countries. In West Africa, lower social capital is associated with higher likelihood of having hypertension. Secondly, we found that the relationship between social capital and undiagnosed hypertension differed by area of residence with limited relationship in urban areas. Further analysis of the relationship in other countries is needed and investigation into the pathway through which low social capital is associated with hypertension outcomes in Ghana but not in South Africa.
Acknowledgements	Renta effort supported by The Cullen Family Healthy Heart Research Fellowship and MCW Cardiovascular Center. Effort for all other authors partially supported by NIH/NIDDK (K24DK093699, R01DK118038, R01DK120861, PI: Egede), NIH/NIMHD (R01MD013826, PI: Egede/Walker), ADA (1-19-JDF-075, PI: Walker).
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Ancillary Materials	VIEW MY POSTER WATCH MY PRESENTATION

Category	Cardiovascular & Heart, #15
Primary Author	Nahee Park
Secondary Authors	Byung-IL Choi, MD
Title	Impact of BMI in predicting Atrial Fibrillation Trends and Recovery
Introduction	Atrial Fibrillation (AF) is defined as irregularly irregular heart rhythm that is associated with significant cardiovascular morbidities and mortalities. Previous studies show that obesity is associated with left atrial enlargement, AF, and cardiovascular death; however, an inverse relationship between obesity and a better cardiovascular prognosis has been long observed, known as the “obesity paradox.” This study will identify if there is a maximum threshold to the obesity paradox in which increased BMI will no longer provide a better AF prognosis, and identify variables that predict successful AF recovery. Whether patients are better able to maintain normal sinus rhythm (NSR) after cardioversion or ablation procedures, defined as successful rhythm control (SRC), will be compared to differences in BMI and atrial size.
Methods	One-hundred patients with AF was divided into 6 BMI categories from Group 1: < 18.5 kg/m2 to Group 6: > 40.0 kg/m2. Incidence of AF recovery post procedures was determined in each BMI category. Additional cardiac pathology anatomy and functional data was assessed with echocardiography.
Results	o Patients with successful rhythm control (SRC) had higher instances of severe LA enlargement than patients with failed rhythm control (P=.023), which contradicts with published data. Perhaps, subjective interpretation of “severe LA enlargement” may not be a good contraindication for cardioversion procedures. o Patients with SRC had larger BMI (33.60 kg/m2) compared to patients with failed rhythm control (FRC) (28.76 kg/m2) (P=.049), which supports the obesity paradox. However, obesity paradox presents with limitations as Group 6 exhibited worsening SRC. o A regression equation found that the variables gender, height, and LVPWd could predict the occurrence of SRC. This equation was 77% accurate in predicting SRC and 82% accurate in predicting FRC.
Conclusions	Physicians have used LA dimensions to identify whether a patient would be a good candidate to receive cardioversion procedures. However, our data displays patients with SRC having higher instances of severe LA enlargement than patients with FRC. Therefore, subjective interpretations of a patient having severe LA enlargement is a poor contraindication for cardioversion procedures. The obesity paradox phenomenon has been long observed in providing better cardiovascular prognosis in obese patients. While patients with SRC had higher BMI (P=0.49), further investigations measuring atrial size and SRC with individual BMI groups reveal the limitation of the Obesity Paradox. While not statistically significant, our data shows trends which suggest that BMI groups >40 kg/m2 show poor SRC. Therefore, there seems to be a maximum threshold to the “obesity paradox” since increasing BMI no longer yields favorable outcomes. This study developed an equation to provide a qualitative model in determining the likelihood of a patient with AF returning to NSR. Overall, this study provided a better understanding on the impacts of BMI in predicting AF trends and recovery.
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Category	Cardiovascular & Heart, #16
Primary Author	Boran Katunaric, MD
Secondary Authors	Mary E Schulz, Julie K Freed
Title	Investigation of S1P-induced Vasodilation in the Human Microvasculature
Introduction	The sphingolipid sphingosine-1-phosphate (S1P) has emerged as a regulator of microvascular tone in animals, however its role in the human microcirculation remains unknown. Pre-clinical studies suggest that S1P-induced activation of two endothelial-specific receptors, S1PR1 and S1PR3, elicits nitric-oxide (NO)-mediated vasodilation. As opposed to S1PR1, the S1PR3 pathway also activates NADPH oxidase (NOX) to produce reactive oxygen species (ROS). We therefore hypothesized that S1P induces vasodilation in the human microvasculature through activation of S1PR1 and S1PR3 in both a ROS-independent and ROS-dependent manner, respectively.
Methods	Human microvessels (100-200µm in diameter) were prepared for videomicroscopy. Following equilibration, arterioles were pre-constricted with endothelin-1 to 30-70% of their passive diameters. Luminal diameter was measured and recorded in regular intervals (1 min) in response to increasing concentrations of S1P (10-12 to 10-6 M) in the presence or absence of the S1PR1 receptor antagonist W146 (10-5 M), S1PR3 antagonist CAY10444 (10-5 M), nitric oxide synthase inhibitor Nω-nitro-L-arginine (L-NAME, 10-4 M), NO scavenger 2-4-carboxyphenyl-4,4,5,5-tetramethylimidazoline-1-oxyl-3-oxide (c-PTIO, 10-4 M), polyethylene glycol-catalase (peg-Cat, 500U/ml), NADPH oxidase inhibitor apocynin (3x10-4 M), NOX-2 inhibitor GSK2795039 (10-6 M) or the NOX-4 inhibitor GKT137831 (10−6 M).
Results	S1P induced vasodilation in a dose-responsive manner with a maximum dilation of 56.5%±4.9, n=12 (mean±SEM). Dilation was abolished during inhibition of S1PR1 (1.5%±5.2, n=4) and was reduced during inhibition of S1PR3 (19.7%±8.7, n=6). Both L-NAME and c-PTIO inhibited S1P-induced dilation (13.0%±7.5, n=4 and 11.2%±3.3, n=4, respectively). Interestingly, dilation was nearly completely inhibited by peg-Cat (11%±6.6, n=4), apocynin (12.5%±4.4, n=3) and the NOX-4 inhibitor (7.2%±3.1, n=4). Dilation was also partly reduced during inhibition of NOX-2 (25.6%±7.8, n=4).
Conclusions	These data suggest that S1P-induced dilation occurs through activation of S1PR1 and S1PR3 through formation of NO and NOX-4-generated H2O2. These translational studies highlight the inter-species variation observed in vascular signaling and provide insight into the mechanism by which S1P regulates microvascular resistance in humans.
Acknowledgements	We thank the surgeons and nurses at Froedtert Memorial Lutheran Hospital and the Ascension Healthcare Group for assistance in providing human tissue. This research was supported by National Institute of Health (NHLBI) K08 HL141562-02 (JKF).

Category	Cardiovascular & Heart, #17
Primary Author	Boran Katunaric, MD
Secondary Authors	Forrest J Stehula, Mary E Schulz, David D Gutterman, Julie K Freed
Title	Human Microvascular Reactivity In Vivo Using Incident Dark Field Videomicroscopy
Introduction	The microvasculature is increasingly recognized as a major contributor to many cardiovascular diseases including atherosclerosis and heart failure with preserved ejection fraction (HFpEF). Endothelial microvascular dysfunction, the inability to vasodilate to endothelial-dependent agonists, precedes the development of large artery disease. While microvascular (dys)function can be assessed using invasive techniques (e.g., cardiac catheterization) there are limited strategies in which to assess microvascular function in a non-invasive and cost-effective manner. Recent advances in hand-held vital microscopy allow for reliable direct imaging of the sublingual microcirculation at bedside. One of the latest advancements (Cytocam, Braedius Medical) utilizes state of the art incident dark field (IDF) technology to allow for quantification of total vascular density (TVD). We therefore hypothesized an increase in TVD in response to both an endothelial-dependent, and -independent vasodilator.
Methods	Cytocam-IDF was optimized to measure in vivo sublingual microvascular response to topical application of the endothelial-independent vasodilator nitroglycerin (NTG) (0.3mg) and the endothelial-dependent dilator acetylcholine (5.5 ·10-2 M). Five images were taken at baseline. Immediately following topical administration of acetylcholine, an additional 5 images were taken to compare TVD pre- and post-treatment. The area was washed and after 30 min of rest, a NTG tablet was administered sublingually and additional 5 images were obtained. Massey's microcirculation image quality score was applied, and TVD was measured using the De Backer score manual analysis by two separate investigators to account for interobserver variability, with consensus achieved.
Results	Both NTG (12.6 mm/mm2 ± 0.5, n=7 compared to baseline 9.9 mm/mm2 ± 0.42, n=7) (Mean±SEM) and acetylcholine (13.1 mm/mm2 ± 0.3, n=3 compared to baseline 10.4 mm/mm2 ± 0.5, n=3) increased TVD.
Conclusions	These data suggest that measurement of TVD in response to endothelium-specific pharmacological agonists may allow for assessment of the human systemic microvasculature in vivo. This is a promising strategy that may allow for early detection of endothelial microvascular dysfunction prior to the onset of large artery disease or heart failure.
Acknowledgements	This research was supported by National Institute of Health (NHLBI) K08 HL141562-02 (JKF).
Ancillary Materials	WATCH MY PRESENTATION

Category	Cardiovascular & Heart, #18
Primary Author	Andrey Sorokin, PhD**
Secondary Authors	Miller B., Benbrook, D., Imig, J.
Title	Small molecule drug SHetA2 restores renal microvascular responses in hypertension-induced nephropathy
Introduction	Microvascular reactivity of renal blood vessels is reduced in two major causes of end stage renal disease: hypertension-induced nephropathy (HN) and diabetic nephropathy. One of the highlights of vascular dysfunction in HN is the loss of autoregulation of blood resistance vessels. Using rat model of salt-sensitive (SS) HN we have previously shown that overexpression of adaptor protein p66Shc is implicated in the loss of microvascular reactivity during the progression of HN. In HN p66Shc is over-expressed in vascular smooth muscle cells of the walls of renal resistance arteries, including afferent arteriole. p66Shc knockout restores ability of afferent arteriole to contract in response to increased perfusion pressure and ATP and mitigates glomerular damage in SS rats on 1% salt diet. In this study we tested ability of a flexible heteroarotinoid called Sulfur Het A2 (SHetA2), known to inhibit p66Shc action, to restore renal microvascular responses in hypertensive rats.
Methods	At 6 weeks of age, rats were either given vehicle control or SHetA2 at 60mg/kg by oral gavage. Oral gavage was performed 3 times weekly every other day for a period of 18 weeks. Urine was collected from rats housed in metabolic cages for 1-2 hours, approximately 24 hours after last treatment after 6, 12 and 18 weeks of treatment. Vascular reactivity of renal afferent arterioles was measured using the juxtamedullary nephron technique approximately 24 hours after final treatment (18 weeks).
Results	Measurements of blood pressure confirmed that SHetA2 treatment did not prevent progression of hypertension caused by 1% salt diet. SHetA2 treatment resulted in statistically significant decrease of urinary protein excretion when compared to control-treated rats, indicating that SHetA2 preserves kidney function in hypertensive rats. Remarkably, SHetA2 restored renal microvascular responses in hypertensive rats, as detected by response of afferent arterioles either to increasing perfusion pressure or to ATP, known mediator of afferent arteriolar autoregulatory responses.
Conclusions	SHetA2 mitigated renal damage and restored renal microvascular reactivity in rat model of hypertension-induced nephropathy. Since compound SHetA2 demonstrates a reasonable pharmacokinetics and lack of mutagenicity, carcinogenicity and toxicity, it is a candidate for therapeutic intervention of p66Shc-mediated vascular diseases.
Acknowledgements	Supported by NIHR01 grant HL147976 to Sorokin

Category	Cardiovascular & Heart, #19
Primary Author	William Conley
Secondary Authors	Sai-Suma Samudrala, BS; Huan Ling Liang, MD; Mary Goetsch, MS; Min-Su Kim, PhD; Richard Willies, MD; Susan Foerster, MD; Michael E. Mitchell, MD; Aoy Tomita Mitchell, PhD.
Title	Elucidating the Genetic Etiology of a Familial Case of Supravalvar Aortic Stenosis and Peripheral Pulmonary Arterial Stenosis
Introduction	Supravalvar aortic stenosis (SVAS) is a congenital heart defect (CHD), accounting for 0.5% of CHD and 5% of congenital aortic stenosis cases. More than half of patients diagnosed with SVAS have accompanied peripheral pulmonary arterial stenosis (PPAS) and are at an increased risk of arrhythmias and sudden cardiac death. Patients with this arteriopathy typically present with heart murmurs, fatigue upon exertion, and syncope. In most cases, the obstructive lesion of SVAS is known to progress while that of PPAS resolves without intervention. Currently, treatments for this arteriopathy include surgical interventions such as patch repair or balloon angioplasty. Investigating the genetic etiology of a multigenerational familial case affected by SVAS and PPAS can help us elucidate the cause behind this CHD. Our study describes a family with five out of 11 family members having both SVAS and PPAS.
Methods	Clinical phenotyping was performed on each of the family members through chart review, including assessment of physical features, MRI, and echocardiography. Whole exome sequencing was performed on one unaffected and four affected family members. We filtered gene variants based on allele frequency < 0.2%, scaled CADD score > 25, and presence in affected or unaffected patients. Candidate variants were identified and will be further confirmed through Sanger sequencing.
Results	Exome sequencing analysis yielded a candidate list of four damaging coding variants: 1. SNIP1 (NM_024700.3:c.364C>T, scaled CADD score = 27.9) 2. SLC9A4 (NM_001011552.3:c.1289G>A, scaled CADD score = 34) 3. BSCL2 (NM_032667.6:c.1175G>A, scaled CADD score = 27.3) 4. TINAGL1 (NM_022164.2:c.122G>A, scaled CADD score = 27.2)
Conclusions	We will conduct Sanger sequencing on all family members to help us narrow down the genetic locus significantly associated in segregation with disease. The ability to genetically characterize this family may aid in future diagnosis and management of multiple family members. In addition, further literature review of filtered variants can help us understand how they may mechanistically contribute to SVAS and PPAS.
Ancillary Materials	VIEW MY POSTER WATCH MY PRESENTATION

Category	Genomics, Precision Medicine & Data Science, #20
Primary Author	Haidy G Nasief, PhD***
Secondary Authors	Cheng Zheng, William Hall, Susan Tsai, Beth Erickson, X. Allen Li
Title	Feasibility of precise oncologic profiling of chemoradiation therapy for pancreatic cancer in early stages during treatment incorporating delta-radiomics and clinical biomarkers
Introduction	Pancreatic cancer (PC) is a devastating malignancy and one of the leading causes of cancer death in the United States. Medical imaging is routinely used to monitor and/or predict treatment response for cancer treatment. Radiomics translates these medical images into quantitative data. Delta-radiomic features (DRF), assess the relative net change of radiomic features in longitudinal images which can offer abundant information to identify, quantify and potentially predict therapy-induced changes during chemoradiation therapy (CRT). Clinically for PC, carbohydrate antigen (CA19-9) and pancreatic intraepithelial neoplasia (PanIN) has been widely accepted as tumor biomarkers. Recently we showed that DRF, if combined with CA19-9, can predict early treatment response during CRT for PC. : In this study we aim to extend the work to include PanIN to the biomarker panel to investigate if treatment outcome and distant metastasis prediction for PC can be improved using K-nearest neighbor and principal component analysis (KNN-PCA) classifier to identify appropriate DRFs to be combined with clinical biomarkers, CA19-9 and PanIN and to examine the association of the combination with survival and distant metastasis prediction.
Methods	Daily non-contrast CTs acquired during routine CT-guided CRT from 26 PC patients, along with their CA19-9, PanIN, pathological results, and follow up data were analyzed. Radiomic features were extracted from pancreatic head on each daily CT and were used to calculate DRF between different days. Patients were divided into two groups based on their pathological responses. KNN-PCA based classifier was built to identify DRFs with highest explained variance that can be combined with CA19-9 and PanIN to result in improved treatment outcome prediction while reducing model complexity and avoiding overfitting. The time from the end of treatment until end point of death or distant metastasis was used to build survival model and distant metastasis-free survival (DMFS) models respectively. Patients not reaching the endpoint were censored at their last follow up. For DMFS, risk groups were defined based on metastasis-free disease (MFD) threshold with AUC >0.9 to predict distant metastasis within 5 year. Spearman correlation was performed to find significant DRF correlated to CA19-9 and PanIN. Kaplan Meier tests were used to assess association of DRF, CA19-9 and PanIN with DMFS and survival. A Cox univariate and multivariate analysis were performed to identify predictors and test the association of the combinations on survival and DMFS correlations.
Results	CA19-9 and PanIN are correlated to certain DRFs. The highest explained variance of DRFs with PCA was 0.96, an increase from 0.82 without using PCA. Incorporating CA19-9 and PanIN with the obtained DRFs increased AUC of the KNN-PCA classifier from 0.57 using single biomarker to 0.98 with 0.9 accuracy, indicating improved response predicting power. The pathology response can be predicted by the 2nd week during CRT using combined DRF-CA199-PanIN biomarkers, compared to 4th week if using CA19-9 alone. Such an earlier prediction would allow enough time to adapt treatment if necessary. MFD threshold of 2 years (AUC=0.92) can be used to identify high risk vs low risk groups for DMFS. The Kaplan Meier estimates indicated significant differences in DMFS between the two risk groups with log-rank p value< 0.0073.R). The metastasis predictive value increased from 0.57-0.66 using either PanIN or CA19-9 alone to 0.87 using DRF-PanIN-CA199 combination with 0.92 accuracy. The multivariate analysis showed that treatment related decrease in CA19-9 levels, low PanIN grade and DRFs were independent predictors of survival and DMFS. The hazard ratio was reduced from 0.73-0.9 using either CA19-9 or PanIN alone to 0.43, p=0.04 using DRF-CA199-PanIN combination.
Conclusions	KNN-PCA based classifier can identify appropriate DRF-PanIN-CA199 combinations to improve the predictions of pathology response, distant metastasis and survival for CRT of PDAC. with larger verification studies, this may develop into an invaluable tool for precise oncologic profiling in early stages during treatment.
Acknowledgements	Funding Source: Siemens Med.
Ancillary Materials	VIEW MY POSTER WATCH MY PRESENTATION

Category	Genomics, Precision Medicine & Data Science, #21
Primary Author	Qian (Sam) Nie**
Secondary Authors	Jenica Abrudan, Wendy Demos, Lida Zeighami, Stefano Rosati, Michael T Zimmermann
Title	Quality control and annotation of variants in Whole Exome and Genome sequencing
Introduction	The widespread use of Whole Genome Sequencing (WGS) and Whole Exome Sequencing (WES) for research discovery creates demand for efficient and effective workflows to support a diversity of applications including understanding mechanisms of human diseases and genetic predisposition. The basic output of a standard WGS/WES analysis is a variant call file (VCF). The VCF serves as a listing of coordinates where samples differ from a defined reference genome. All variants have standard information such as location, quality metrics, but additional data in the VCF usually relates to meaning of the variant and how it is distributed across a sample or cohort. Due to the size of WGS/WES, thousands to millions of variants can be called in each sample, necessitating scalable bioinformatic approaches.
Methods	We have developed a workflow and reporting infrastructure to efficiently bring together raw data processing and annotation to give meaning to variants found in WGS and WES based research initiatives. We have developed research specific WES and WGS workflows to compliment the long-standing clinical genomics services of the GSPMC. The underlying framework for the data processing utilizes the broadly used Genome Analysis Tool Kit (GATK)1 and implementation based on the Broad Institute best practices. We have also deployed a filtering method which can flag and filter out low quality variants in both variant and sample level. This method is customizable for single sample or cohort approaches. In order to support the flexibility in annotation resources required to drive research, we have also integrated BioR2 and SnpEff into our workflow to annotate genomic data with clinically relevant and domain-specific information, to enhance the scope of research and support discovery.
Results	We developed a standardized analysis workflow that processes raw sequence files and provides quality metrics, data visualizations, and knowledge-based annotations to facilitate the interpretation of experimental results. The workflow generates an interactive web-based report which provides at-a-glance insights to the sequencing quality, variant quality, impactful data summaries including the variant landscape, prioritization and classification. This workflow has been used to support multiple research programs and is being actively developed to empower further clinical and research opportunities.
Conclusions	We believe the systematic and comprehensive annotation of genomic data is required for extracting the most meaning out of each study. Therefore, we have built a robust end-to-end workflow that can be applied to a broad spectrum of research applications, increasing efficiency, standardization, and data interpretability. This process enables researchers to efficiently identify the most promising candidates in their study, develop hypotheses, and effectively reach to the next stage of their research endeavors.
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Reference 2	2. Kocher JP, Quest DJ, Duffy P, et al. The Biological Reference Repository (BioR): a rapid and flexible system for genomics annotation. Bioinformatics. 2014;30(13):1920-1922

Category	Genomics, Precision Medicine & Data Science, #22
Primary Author	Young-In Chi
Secondary Authors	Timothy J. Stodola, Thiago M. De Assuncao, Elise N. Levrence, Swarnendu Tripathi, Nikita R. Dsouza, Angela J. Mathison, Donald G. Basel, Brian F. Volkman, Brian C. Smith, Gwen Lomberk, Michael T. Zimmermann, and Raul Urrutia
Title	Molecular Mechanics and Dynamic Simulations of Kabuki Syndrome-Associated KDM6A Variants Reveal Putative Mechanisms of Dysfunction
Introduction	Kabuki syndrome is a genetic disorder that affects several body systems and presents with variations in symptoms and severity. The syndrome is named for a common phenotype of faces resembling stage makeup used in a Japanese traditional theatrical art named kabuki. The most frequent cause of this syndrome is mutations in the H3K4 family of histone methyltransferases (HMTs) while a smaller percentage results from genetic alterations affecting the histone demethylase, KDM6A. Because of the rare presentation of the latter form of the disease, little is known about how missense changes in the KDM6A protein sequence impact protein function.
Methods	In this study, we use molecular mechanic and molecular dynamic (MD) simulations to enhance the annotation and mechanistic interpretation of the potential impact of eleven KDM6A missense variants found in Kabuki syndrome patients. These measurements include global/local structure perturbation, binding and folding/stability energy calculation, pKa shift estimation, and all-atom 10 nanoseconds (ns) molecular dynamics (MD) simulations to complement the existing sequence- and structure-based analytical tools and further enhance the mutational impact predictions that are highly relevant to KDM6A-specific conformational change and molecular function.
Results	These variants (N910S, D980V, S1025G, C1153R, C1153Y, P1195L, L1200F, Q1212R, Q1248R, R1255W, and R1351Q) are predicted to be pathogenic, likely pathogenic or of uncertain significance by sequence-based analysis. Here, we demonstrate, for the first time, that although Kabuki syndrome missense variants are found outside the functionally critical regions, they could affect overall function by significantly disrupting global and local conformation (C1153R, C1153Y, P1195L, L1200F, Q1212R, Q1248R, R1255W and R1351Q), chemical environment (C1153R, C1153Y, P1195L, L1200F, Q1212R, Q1248R, R1255W and R1351Q), and/or molecular dynamics of the catalytic domain (all variants). In addition, our approaches predict that many mutations, in particular C1153R, could allosterically disrupt the key enzymatic interactions of KDM6A. These data reinforce the fact that Kabuki variants are loss-of-function mutations, and protein structure and dynamics are essential elements for protein's optimal function and normal physiology.
Conclusions	Our study demonstrates that the KDM6A Kabuki syndrome variants may impair histone demethylase function through various mechanisms that include altered protein integrity, local environment, molecular interactions and protein dynamics. Molecular dynamics simulations of the wild type and the variants are critical to gain a better understanding of molecular dysfunction. This type of comprehensive structure- and MD-based analyses should help develop improved impact scoring systems to interpret the damaging effects of variants in this protein and other related proteins as well as provide detailed mechanistic insight that is not currently predictable from sequence alone. The widespread adoption of these methods can provide better diagnosis, risk assessment, and clinical guidelines for the observed variants within the context of individualized medicine.
Ancillary Materials	VIEW MY POSTER

Category	Genomics, Precision Medicine & Data Science, #23
Primary Author	Michael T. Zimmermann**
Secondary Authors	Swarnendu Tripathi, Nikita R. Dsouza, Young-In Chi, Timothy Stodola, Raul Urrutia
Title	Structural Bioinformatics Enhances Mechanistic Interpretation of Human Genomic Variation: Demonstration Through Analysis of 935 Distinct RAS-Family Mutations
Introduction	Protein-coding genetic alterations are frequently observed in Clinical Genetics, but the high yield of variants of uncertain significance (VUS) remains a limitation in decision making. Clinical Genetics researchers and practitioners typically use genomic sequence-based predictive algorithms to help judge the likelihood of pathogenicity of VUS, but these scores rarely account for the effect of a variant on the encoded 3D protein molecule. RAS-family GTPases are cancer drivers, but only 54 variants, across all RAS-family members, fall within well-known hotspots. However, extensive sequencing has identified 881 non-hotspot variants for which significance remains to be investigated. Thus, RAS is an excellent family to test the added yield of 3D scores over genomic scores alone, for improving the interpretation of human genetic variation.
Methods	Here, we evaluate 935 missense variants from seven RAS genes, observed in cancer, RASopathies, and the healthy adult population. We characterized hotspot variants, previously studied experimentally, using 63 sequence- and 3D structure-based scores, chosen by their breadth of biophysical properties. Applying scores that display best correlation with experimental measures, we report new valuable mechanistic inferences for both hot-spot and non-hotspot variants.
Results	We demonstrate that 3D scores have little-to-no correlation with those based on DNA sequence, which are commonly used in Clinical Genetics, indicating that they contain unique information that is not present in genomics scores. Classic mutations that have known differences in disease incidence and biochemical function form clusters according to 3D structure scores, but not by genomics scores, further indicating that 3D scores offer more functionally relevant nuance. Further, we identified that certain structure-based feathers that, combined, indicate probability of local unfolding may discriminate among the effects of different classic mutations, in addition to VUS.
Conclusions	These new knowledge bear significant relevance for our understanding of RAS-family mutations. Further, it informs on the general challenge of how structural bioinformatics information can be used to enhance the interpretation of protein coding genetic variants identified by high-throughput sequencing.
Acknowledgements	This research was completed in part with computational resources and technical support provided by the Research Computing Center at the Medical College of Wisconsin. This work was supported by National Institutes of Health Grant R01 DK52913 (to R. U.), the Advancing a Healthier Wisconsin Endowment (R. U.) and an endowment from the Linda T. and John A. Mellowes Foundation (R. U.).
Reference 1	https://academic.oup.com/bioinformatics/advance-article/doi/10.1093/bioinformatics/btaa972/5998662
Ancillary Materials	VIEW MY POSTER

Category	Genomics, Precision Medicine & Data Science, #24
Primary Author	Elias DeVoe
Secondary Authors	Gavin R. Oliver, Roman Zenka, Patrick R. Blackburn, Margot A. Cousin, Nicole J. Boczek, Jean-Pierre A. Kocher, Raul Urrutia, Eric W. Klee, Michael T. Zimmermann
Title	P2T2: Protein Panoramic annoTation Tool Facilitates the Annotation and Interpretation of Protein Coding Variants
Introduction	The integration of genomic data with publicly available annotations and existing knowledge is a key component for understanding the potential functional effects of variants but is often an involved and manual process. A more efficient means of identifying existing knowledge about the functional impact of protein-coding variants discovered during genomic analysis is necessary. Additionally, methods that simplify and automate data integration will empower clinical genomics research.
Methods	Annotations were gathered from diverse resources and mapped to protein positions. We harmonized resources using canonical isoform sequences as a common mapping between genomic, transcript, protein sequence, and derived from protein structural data. A web application that provides an integrated view of the data and facilitates hypothesis generation was built.
Results	We present P2T2 for the annotation of proteins using extensive and diverse resources including experimentally validated and literature-mined variant-phenotype relationships, linear motifs, domains, and experimental 3D structures, along with multiple sequence alignments to associate information between the analogous residues of closely related proteins (termed paralog annotation analysis, PAA) in an interactive user interface. P2T2 presents these multiple annotation and data types in a unified view, facilitating the interpretation of coding variants and hypothesis generation. Additionally, it provides a REST API enabling data to be repurposed for other studies.
Conclusions	format, combining the information available from other tools into PAA across the human proteome. We believe the annotations aggregated in P2T2 and simplified interface will help researchers to interpret the effects of novel variants identified through next-generation sequencing.
Acknowledgements	This project is funded in part by the Advancing a Healthier Wisconsin Endowment at the Medical College of Wisconsin (R.U. and M.Z.), the Mayo Clinic Center for Individualized Medicine (E.K.), and by The Linda T. and John A. Mellowes Endowed Innovation and Discovery Fund and the Genomic Sciences and Precision Medicine Center of Medical College of Wisconsin (R.U.). This research was completed in part with computational resources and technical support provided by the Research Computing Center at the Medical College of Wisconsin. We thank the CTSI grant National Institutes of Health CTSA award, 2UL1TR001436, for resources, services, and facilities. We thank Curtis Younkin for programming expertise.
Ancillary Materials	VIEW MY POSTER WATCH MY PRESENTATION

Category	Genomics, Precision Medicine & Data Science, #25
Primary Author	Atefeh (Lida) Zeighami**
Secondary Authors	Stefano Rosati, Angela Mathison, Michael Tschannen, Honey Reddi, Rupa Udani, Kala Schilter, Michael T. Zimmermann, Raul Urrutia
Title	SARS-CoV-2 genomic data analysis: from sequencing to clade identification
Introduction	Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causal agent of COVID- 19, Initially were reported in mid-December 2019 in the Chinese city of Wuhan and continues to evolve. It spread across over 210 countries in <4 months, leading to>10 million confirmed cases and almost 500,000 reported deaths worldwide as of June 28, 2020. Thus, methods to rapidly and robustly assess viral pathogens is of high importance for academic medical centers. We broadly divide Covid-19 data analysis into two parts: Experimental and Computational. Experimental methods and their quality control (QC) are critical foundational steps. We developed a robust system for analyzing patient's genomic and experimental quality throughout our process. The experimental output is raw nucleotide sequences. Computational analyses begin from these data. There are different software and pipelines available from national and international consortia to analyze raw data and generate variant-Clade assignments, each with their own standards and points of access. As scientific inquiry is constantly evolving, robust yet flexible bioinformatics approaches are required to facilitate research.
Methods	To process COVID-19 Strain Typing data, we have built a workflow based on Whole Genome Sequencing (WGS) Pipeline. These custom WGS pipeline intake raw reads as input and output two different report formats. In this study, we have demonstrated how these data were generated and analyzed. We have analyzed the genomic sequence data of 11 samples which were prepared with different experimental protocols. We also downloaded 100 SARS-CoV-2 strains from Global Initiative on Sharing Avian Influenza Data (GISAID), and leveraged phylogenetic data derived from their analysis of all global virus data. Our 11 pilot samples' genomes were aligned using Multiple Sequence Alignment (MSA) method with reference NC_045512.2 SARS-CoV-2 Wuhan genome which was obtained from NCBI GenBank. Then Phylogenetic tree analyses have been performed on these genomes to discover strain types and characterizing identified mutations.
Results	We have designed a workflow to analyze Covid-19 patient raw sequences data and generate two reports, one comprehensive web-based research report to deliver the results of data analysis to investigators which includes summary of experiments/samples, sequencing metrics, quality assessment, Genome Coverage and Gene Average Depth of Coverage plots, Phylogenetic dendrograms, genomic variants within each sample, Variant-Clade identification table. An additional report is a one-page pdf summary, which will be developed into a clinical report and deliver a summary of Mutation-Clade identification for each sample.
Conclusions	We have Developed and Implemented a Robust and Thorough Covid-19 patient Data Analysis and Deliverable Report tool which can be used in research and clinical assay development.

Category	Genomics, Precision Medicine & Data Science, #26
Primary Author	Timothy J Stodola
Secondary Authors	Young-In Chi, Thiago De Assuncao, Elise N. Levrence, Swarnendu Tripathi, Nikita R. Dsouza, Angela Mathison, Brian Volkman, Brian Smith, Gwen Lomberk, Michael Zimmermann, and Raul Urrutia
Title	Computational Description of Key Molecular Properties and Dynamic Behavior of DOT1L and Partnering Complexes Involved in Leukemogenesis
Introduction	DOT1L is the only non-SET domain histone methyltransferase encoded in the human genome. The canonical function of this enzyme is to write H3K79 methylation marks on nucleosomes that are previously marked by ubiquitination in H2B. DOT1L has elicited significant attention in leukemia since DOT1L is recruited by the oncogenic family of AF fusion proteins. Many structures have been solved by both x-ray crystallography and NMR spectroscopy during the last decade, however the detailed dynamic behavior of DOT1L and its oncogenic complexes remain poorly understood.
Methods	We use molecular mechanic calculations and dynamic simulations to illuminate the time-dependent behavior of DOT1L, and DOT1L in complex with S-adenosyl methionine, histone H4, ubiquitin, AF10 and AF9.
Results	Structural analysis of DOT1L and SAM shows that there are four key residues with high frequency and energy-stabilizing interactions. There are 19 residues interacting with H4 and 13 residues interacting with ubiquitin in dynamics. Dynamic analysis of the DOT1L-AF10 heterodimer revealed five of the eight most stabilizing interactions were not predicted in the static structure. The tetramer of DOT1L-AF10 heterodimers demonstrates movements that displace the N-terminals, generating lateral displacement between 110 and 122 Ã… on ends connecting to the DOT1L enzymatic regions, while the C-terminal helixes are static. This provides insight in to how the DOT1L enzymatic region can move along nucleosomes. The dynamic DOT1L-AF9 interface includes 18 DOT1L residues.
Conclusions	These results are important to consider when describing the biochemical properties of DOT1L, under normal conditions and in disease as well as in the development of novel therapeutic agents. Disrupting these sites can prevent necessary DOT1L-SAM alignment, the formation of DOT1L-AF10 and DOT1L-AF9 complexes.

Category	Genomics, Precision Medicine & Data Science, #27
Primary Author	Jenica Abrudan**
Secondary Authors	Angela Mathison, Atefeh Zeighami, Michael Zimmermann
Title	Methylome analyses - an update
Introduction	Gene expression can be regulated at both genetic and epigenetic levels. Epigenetics is the study of inheritable phenotypic changes not encoded in the genome, such as by DNA methylation. The ability to characterize regulatory changes on a genome-wide level is critical for understanding disease mechanisms, possible treatment responses, and driving genomic research forward.
Methods	A critical first step is aligning sequence reads to a reference genome. As RRBS data sets consist of altered "C" positions that may cause errors during alignment (methyl-C is read as "T"), specialized aligners are used. For the mapping step we have decided on Bismark[1], a specialized aligner with high level of support in the community. The methylated CpG sites and the Differentially Methylated Regions (DMRs) have been identified using DMRfinder[2]. For the MethylChip data, we are using the popular Minfi[3] R package. Thus, our process leverages methods that are well established in the field, but presents the data, and data summaries, in a more easily accessible and understandable format.
Results	We have established a standardized methodology for summarizing genome-wide DNA methylation levels using two technologies: Reduced Representation Bisulfite Sequencing (RRBS) and are additionally processing methylation chip array data. We developed multiple analyses to identify differentially methylated regions from raw data (NGS sequences for RRBS and probe intensities for MethylChip) files and provide a set of data visualizations, statistical comparison and knowledge-based annotations to facilitate their interpretation. These pipelines are part of the GSPMC toolbox for methylome analysis and have been developed to be standardized, modular, efficient, and reproducible with multiple levels of data QC to ensure the highest quality data. Thus, our process is highly robust and can support genomic methylation research.
Conclusions	We have developed and will continue to improve, standardized methylome analysis workflows in order to provide efficient, robust, and thorough analysis service. Our existing process supports multiple lines of epigenetic research across the MCW and regional community
Reference 1	Krueger, F. and S.R. Andrews, Bismark: a flexible aligner and methylation caller for Bisulfite-Seq applications. Bioinformatics, 2011. 27(11): p. 1571-2
Reference 2	Gaspar, J.M. and R.P. Hart, DMRfinder: efficiently identifying differentially methylated regions from MethylC-seq data. BMC Bioinformatics, 2017. 18(1): p. 528.
Reference 3	1. Krueger, F. and S.R. Andrews, Bismark: a flexible aligner and methylation caller for Bisulfite-Seq applications. Bioinformatics, 2011. 27(11): p. 1571-2. 2. Gaspar, J.M. and R.P. Hart, DMRfinder: efficiently identifying differentially methylated regions from MethylC-seq data. BMC Bioinformatics, 2017. 18(1): p. 528. 3. Aryee, Martin J et al. Minfi: a flexible and comprehensive Bioconductor package for the analysis of Infinium DNA methylation microarrays. Bioinformatics (Oxford, England) vol. 30,10 (2014): 1363-9. doi:10.1093/bioinformatics/btu049

Category	Genomics, Precision Medicine & Data Science, #28
Primary Author	Valerie Wagner
Secondary Authors	Karen C Clark, Katie Holl, Thiago Milech De Assuncao, Derek Simonsen, M Velez-Bermudez, Kai Wang, Angela Mathison, Leah C. Solberg Woods, Hans Lehmler, Raul Urrutia, Anne E Kwitek
Title	Effects of Maternal Bisphenol F Exposure on Pituitary Gene Expression in Population-based Heterogeneous Stock Male Rats
Introduction	Bisphenol F (BPF) is marketed as a â€˜safe' substitute for bisphenol A (BPA), a risk factor for obesity and heart disease, in manufacturing polycarbonates and in common consumer products. BPF's environmental presence is growing rapidly and is detected in 66.5% of U.S. adults. Human biomonitoring studies implicate maternal exposure to BPA with altered lipid concentrations, glucose metabolism, and hypothalamic-pituitary-adrenal axis function. In rodents, maternal exposure to bisphenol A affects epigenetic modifications and the metabolic health of offspring. As a critical component of the endocrine system, the pituitary gland may participate in the mechanism underlying bisphenols' metabolic phenotypes. Traditional in vivo toxicity studies are performed in genetically undefined outbred rats or genetically homogeneous inbred mice, leading to conflicting results possibly due to GxE interactions. The N/NIH Heterogeneous Stock (HS) rats are outbred rats that better model the genetic diversity in humans yet are amenable to genetic study. Our overall hypothesis is that BPF exposure is a cardiometabolic disease risk factor based on underlying genetic susceptibility, which can be identified using the HS rat model. We previously demonstrated that five weeks of post-wean BPF exposure significantly impacts body growth and adiposity in male HS rats. The goal of this project was to determine if maternal BPF exposure also influences growth and adiposity in HS rats and how maternal BPF exposure impacts pituitary gene expression.
Methods	HS female breeders were randomly selected for exposure to either vehicle (0.1% Ethanol) or 1.125 mg/L BPF in 0.1% Ethanol in drinking water during gestation and lactation (~6 weeks total exposure time). One male from each litter was weaned at three weeks-of-age with no additional exposure. Weight and adiposity measures were obtained from weanlings until eight weeks-of-age. The pituitary gland was taken and Illumina stranded total RNA sequencing and data analysis was performed on the NovaSeq platform at the Genomic Science and Precision Medicine Center.
Results	Our study showed that maternal BPF exposure may impact specific fat depots, with male offspring showing a weak trend in increased gonadal white adipose tissue (GWAT) mass and a strong trend in increased perirenal white adipose tissue (PWAT) mass at eight weeks-of-age. There was no change in male offspring body composition as measured by nuclear magnetic resonance (NMR) at seven weeks-of-age. RNA sequencing of pituitary from maternally exposed vehicle and BPF male offspring identified 20 genes significantly downregulated in BPF males. Interestingly, these genes included the Nr4a subfamily of nuclear transcription factors (Nr4a1, Nr4a2, Nr4a3), which have epigenetic functions; Cartpt and Gpr88, which regulate feeding behavior and body composition; and Hmcsg1 and Idi1, which participate in cholesterol biosynthesis.
Conclusions	Our preliminary data suggest that maternal BPF exposure may increase adiposity through altered pituitary function. This work supports BPF exposure as a cardiometabolic disease risk factor and indicates that the HS rat will be a useful model for dissecting GxBPF interactions on metabolic health. Future work will interrogate in vitro effects of BPF on pituitary cell lines with special attention to the genes implicated here and will study if energy balance and cholesterol biosynthesis are impacted by BPF exposure in vivo.
Ancillary Materials	VIEW MY POSTER

Category	Hematology & Blood, #29
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Title	A Single Cell Cytokine Analysis of Bi-Specific anti-CD19, anti CD-20 CAR T-Cells Expanded in IL-2 Versus IL-7 and IL-15
Introduction	Bispecific lentiviral transduced anti-CD20, anti-CD19 (LV20.19) CAR T-cells may improve outcomes in relapsed, refractory (R/R) B-cell non-Hodgkin lymphoma (NHL) by limiting relapse from single antigen downregulation. We recently reported outcomes of a phase I trial of LV20.19 CAR T-cells expanded in IL-2 in R/R NHL & CLL (Shah et al. Nature Med. 2020). Preclinical models suggest that CAR T-cells expanded with IL-7 & IL-15 (IL-7+15) can improve in vivo persistence and increase the T-stem cell memory population. Therefore, we opened a Phase I/II trial of LV20.19 CAR T-cells expanded in IL-7+15 in R/R NHL (NCT04186520). We report single cell cytokine studies from final LV20.19 CAR T-cells expanded with IL-2 versus (vs) IL-7+15 using the Isoplexis proteomics device.
Methods	In both trials, 4-1BB/CD3ζ LV20.19 CAR T-cells were manufactured using the CliniMACS Prodigy device. While the first trial used IL-2 for CAR-T expansion, the ongoing trial uses IL-7+15. LV20.19 CAR T-cells were thawed, CD4 & CD8 cells sorted via immunomagnetic separation, and the subsets stimulated with CD19+ K562 cells. The stimulated cells were loaded onto single-cell, Adaptive Immune Isocode chips and read in an IsoLight instrument. The single cell production of 32 individual cytokines was determined and a polyfunctional strength index (PSI) generated for each product. Polyfunctionality (PFA) was defined as an individual cell generating ≥2 cytokines upon stimulation.
Results	11 pts in the IL-2 and 6 pts in the IL-7+15 cohort had adequate samples for analysis. Cytokine release syndrome (CRS) occurred in 83% (n=5, all grade 1) for the IL-7+15 cohort and 73% (n=8, grade 1-4) for the IL-2 cohort. The CAR-T single cell cytokine profile was dominated by effector cytokines independent of cell subset (CD4 vs CD8) or expansion conditions. The PSI of CD8 CAR T-cells was significantly higher for cells expanded in IL-7+15 vs IL-2 (p=0.016). Likewise, CD8 CAR T-cells expanded in IL-7+15 had a higher percentage of cells secreting ≥5 cytokines vs IL-2 (p=0.004). This correlated clinically with earlier median time to CRS—day 1 (1-2) with IL-7+15 vs day 2 (1-10) with IL-2. Overall, PFA was high in all cohorts with 47% of single cells secreting ≥2 cytokines.
Conclusions	CD8 LV20.19 CAR T-cells expanded in IL-7+15 have a higher PSI than cells expanded in IL-2, and PSI has previously been shown to correlate with treatment response (Rossi et al. Blood 2018). Moreover, CD8 cells expanded in IL-7+15 had a higher proportion of cells secreting â‰¥5 cytokines without increasing severity of CRS. The PFA of bispecific LV20.19 CAR T-cells was 47%, higher than a previously reported PFA of ~20-25% with single targeted CD19 CAR T-cells. These data suggest that expansion of bispecific CAR T-cells in IL-7+15 may improve polyfunctionality of CD8 cells potentially impacting clinical outcomes and toxicity profiles.
Ancillary Materials	VIEW MY POSTER

Category	Hematology & Blood, #30
Primary Author	Vasil Kukushliev
Secondary Authors	Roy Silverstein, MD
Title	Production of mature human megakaryocytes from induced pluripotent stem cells for study of CD36 redox-mediated platelet pro-thrombotic signaling
Introduction	Atherothrombosis is the most common cause of death from cardiovascular disease. After an atherosclerotic plaque rupture, platelet activation promotes thrombus formation and as a result may lead to heart attack or stroke due to vessel occlusion. The current redox-regulated platelet activation model involves CD36, a scavenger receptor that activates upon recognition of oxidized lipid motifs called oxPC_cd36 found on oxidized LDL (oxLDL) particles. oxLDL is an endogenous ligand that is highly produced under atherogenic conditions. Activated CD36 leads to subsequent activation of Src family kinases, Vav family guanine exchange factors, and MAP kinases, leading to cytoskeletal rearrangement and assembly of the reduced NADPH oxidase 2 (NOX2) complex. Activation of NOX2 increases levels of reactive oxygen species (ROS) such as superoxide radical and hydrogen peroxide. To study this system without the shortage limitations imposed by human donors, human induced pluripotent stem cells (iPSCs) were used to generate megakaryocytes (MKs) in a scalable manner using Matrigel, serum/feeder-free conditions. Readily available human MKs for experimentation would reduce the need for model organisms and allow for direct study of human processes. Furthermore, the iPS model also allows for genetic manipulation of platelets for mechanistic studies, which are otherwise not possible due to the lack of nuclei in human platelets.
Methods	MK quality was evaluated via flow cytometry, probing for expression of the surface markers CD36, CD41a, and CD42a. CD41 is a heterodimeric integral membrane protein receptor for fibrinogen and several other extracellular molecules. CD42a-d is a surface receptor complex for von Willebrand factor. Double positive CD41a/CD42a MKs correlate with successful iPS maturation toward MK lineage development.
Results	We were able to produce MKs that express CD36 at levels four-fold higher than generated MK controls. Further verification of CD36 expression was achieved by comparing expression to CD36 knockout MKs via CRISPR/Cas9 gene editing. Double positive CD41a/CD42a MKs were also generated, as two separate replicate experiments yielded 33% double positive and 41% double positive, respectively. Assessing for triple positive CD36/CD41a/CD42a cell populations yielded a population of under 5% triple positive generated MKs.
Conclusions	The low level of triple positive CD36/CD41a/CD42a cell populations is likely attributed to incomplete differentiation, as the CD36 surface marker is expressed after the CD41 and CD42 surface markers. Flow cytometry is limited to extracellular surface markers, therefore, further experimentation with the use of Western Blot could allow for more accurate tracking of all surface markers, even ones still in intracellular stores. In conclusion, we demonstrated the feasibility of using human iPSC for the study of the CD36 redox-regulated platelet activation model by expressing markers of MK differentiation (CD41a, CD42a) and CD36.
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Category	Hematology & Blood, #31
Primary Author	Hefei Liu
Secondary Authors	Grier Page, PhD; Robert Burns, PhD; and Alan E. Mast, MD, PhD
Title	Demographic, Clinical, and Biochemical Predictors of Pica in a Large Cohort of Blood Donors
Introduction	Pica is characterized as repeatedly eating or chewing of a non-nutritious substance including, but not limited to ice, clay and dirt, starch, raw pasta, chalk, coal, paint, or paper. Life-threatening conditions, such as gastrointestinal infections and lead poisoning, may occur depending on the substance consumed. The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition defines pica as an eating disorder, but with its strong link to iron deficiency, pica is also characterized as a hematological condition. Blood donation is associated with substantial iron loss. Blood donors often become iron deficient and are susceptible to pica, as well as restless legs syndrome (RLS), a condition characterized by an irresistible urge to move legs due to uncomfortable sensations such as tingling, crawling, burn, and pain. The National Heart, Lung, and Blood Institute sponsored REDS-III program prospectively enrolled 13,403 racially diverse blood donors in its RBC Omics study to investigate demographic, clinical, hematological, and biochemical factors associated with pica.
Methods	Demographic data, survey questions of pica behaviors and RLS, complete blood count (CBC), and ferritin were collected and analyzed using univariable and multivariable logistic regression analysis. Exclusion criteria were ferritin >800 ng/mL, body mass index (BMI) <17.5, and those with 9 or more donations in the 2 years prior to enrollment who were purposely oversampled for in RBC Omics. Pica was rigorously defined by questionnaire responses: 1) “Yes” to eating ice and, 2) Consumes “8 oz - 24 oz” or “more than 24 oz” of ice and, 3) At a frequency of “once a day” or “several times a day”. Alternatively, “yes” to eating non-ice substances regardless of amount and frequency was also characterized as pica.
Results	The analysis included 11,418 donors with 7,085 Caucasians, 1,573 African Americans, 1,596 Asians, and 1,164 Hispanics. Pica was present in 2.2% (250 out of 11,418) of the study subjects. Caucasian donors were more likely to have pica than Asian donors (Odds Ratio [OR], 0.41; p=0.002), but less likely when compared to African American (OR, 1.47; p=0.023) and Hispanic donors (OR, 1.61; p=0.009). Female donors (n=6,000) were more likely to have pica than males (n=5,418; OR, 1.84; p<0.001). The 31 to 40-year-old donors were less likely to have pica than 18 to 20-year-old (OR, 1.78; p=0.012) and 21 to 30-year-old donors (OR, 1.47; p=0.049). While not statistically different from 41 to 50-year-old (OR, 0.86; p=0.513) and 51 to 60-year-old donors (OR, 0.64; p=0.054), the 31 to 40-year-old donors were more likely to have pica than donors age 61 and up (OR, 0.53; p = 0.016). Normal/underweight donors (BMI 17.5 - 25) were more likely to have pica than overweight donors (BMI > 25 - 30) (OR, 0.68; p = 0.019), but not statistically different from obese donors (BMI > 30) (OR, 1.31; p = 0.067). Ferritin was negatively associated with pica (p<0.001). For donors with ferritin <12 ng/mL 4.1% (89/2155), 12-50 ng/mL 2.0% (101/5118), and >50 ng/mL 1.4% (60/4145) had pica. CBC values associated with low iron stores were also associated with pica: low hemoglobin (p<0.001), low hematocrit (p<0.001), low mean corpuscular volume (MCV) (p<0.001), and high red blood cell distribution width (RDW) (p<0.001). In multivariable analyses, RLS (OR, 1.99; 95% confidence interval, 1.16 - 3.21, p=0.008) and Asian race (OR, 0.31; 95% confidence interval, 0.15 - 0.57, p<0.001) emerged as two most powerful predictors of pica in our forward stepwise logistic regression model. Other significant demographic predictors of pica included hormone supplement use (p=0.006), smoking in the last 30 days (p=0.045), and nulligravida females (p=0.009).
Conclusions	Iron deficiency was confirmed as a strong predictor of pica. Consistently, demographic (female), clinical (RLS) and hematological (hemoglobin, MCV, RDW) parameters associated with iron deficiency were also associated with increased risk for pica. However, pica symptoms were also reported by donors with ferritin >50 ng/mL suggesting that non-iron related factors influence pica presentation as well. Pica has a significant prevalence in the blood donor population, and healthcare providers should consider non-iron related factors when diagnosing pica.

Category	Hematology & Blood, #32
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Title	Hospitalization, Case Fatality and Risk Factors in Individuals with Sickle Cell Disease and COVID-19 Infection
Introduction	Sickle cell disease (SCD) is an inherited hemoglobinopathy that can affect nearly every organ system. Individuals living with SCD are at high risk of developing serious infections which can further trigger disease related complications and attribute additional morbidity and mortality. In light of the evolving pandemic caused by SARS-CoV-2, the causative agent of COVID-19 disease, and the potential for future infectious disease epidemics, it is important to understand the impact that COVID-19 has on hospitalization rates and mortality in this medically vulnerable population. The objective of this study was to describe hospitalization and case fatality rates secondary to COVID-19 among individuals living with SCD in different age groups and compare these to the general population. Also, our aim was to identify factors associated with more severe COVID-19 illness and hospitalization in individuals with SCD.
Methods	The Medical College of Wisconsin established the international SECURE-SCD Registry to collect data on pediatric and adult COVID-19 infections in individuals living with SCD. Providers are instructed to report confirmed COVID-19 cases to the registry after sufficient time has passed to observe the disease course through resolution of acute illness and/or death. For each case, providers complete a short form that includes the following data: patient demographics, COVID-19 related hospitalization, COVID-19 severity/management strategies, if the patient died due to COVID, and other information about SCD complications. Data are de-identified and without protected health information to facilitate rapid and increased reporting. We calculated the hospitalization rate and case fatality rate for individuals with SCD by specific age group and contrasted it with the rates publicly available for the general Black population. We utilized data from California Department of Public Health for case fatality rate comparison in Blacks and data from COVID-NET for hospitalization rate comparison. We used indirect age adjustment to calculate standardized mortality ratios using COVID-19 data from California state as the reference population. We used multivariable models to estimate the independent effects of age, sex, genotype, SCD-related and non-related comorbidities grouped by organ systems on the outcomes of severe COVID-19 and hospitalization.
Results	As of October 12th 2020, 366 cases of COVID-19 in individuals with SCD were reported to the registry, 324 of them being from US. 41.5% of reported cases were patients 18 years and under. There were 16 deaths reported with overall mortality rate of 4.9%. Mortality rate in SCD patients was highest in the 50-64 years age group (17.6%) in contrast to mortality rate peak seen in the general population in patients older than 80 years. Young adult SCD patients aged 18-34 years had a case fatality rate of 2.6% and those aged 34-50 years had a rate of 11.9%. California Department of Public Health report case fatality rates for Blacks are less than 1% in both of these comparative age groups. Age-standardized mortality ratio shows that individuals with SCD are 6.2 times more likely to die due to COVID-19 infection compared to the general population. The overall hospitalization rate in individuals with SCD was 58.2% and 30.4% of reported hospitalized cases were children. Among hospitalized adults with SCD, stratification by age showed that 59.7% were aged 18-49, whereas only 29.5% of people 18-49 years in the general Black population were hospitalized. In multivariable models, previous acute care for pain (OR=4.6, 95% CI (2.0, 10.9), p=0.006), neurobehavioral disorders (OR=2.4, 95% CI (1.1, 6.8), p=0.03) and SCD-related heart and lung comorbidities (OR=4.2, 95%CI (1.6, 11.2), p=0.004) were associated with hospitalization in children with SCD, while previous acute care for pain was also associated with more severe COVID-19 course in children.
Conclusions	Our findings show that individuals with SCD who have COVID-19 infection have higher rates of death due to COVID-19 than the general Black population. Also, a large proportion of COVID hospitalization for the SCD population occurs among the younger age group. History of pain, SCD-related heart and lung comorbidities and neurobehavioral disorders are associated with COVID-19 hospitalization in children with SCD. Previous acute care for pain is also associated with more severe course of COVID-19 infection in children with SCD.
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Category	Kidney, Diabetes & Digestive, #33
Primary Author	Bhavna Bhasin, MD**
Secondary Authors	Vineet Veitla, Aprill Dawson, Zhuping Garacci, Daniel Sturgill, Mukoso N. Ozieh, Kevin R. Regner
Title	Acute Kidney Injury in hospitalized patients with COVID-19 and seasonal influenza: A comparative analysis
Introduction	Coronavirus disease 2019 (COVID-19) is often compared to seasonal influenza and the two diseases share similarities including the risk of systemic manifestations such as acute kidney injury (AKI). The aim of this study was to perform a comparative analysis of the prevalence, risk factors, and outcomes of AKI in hospitalized patients with COVID-19 or influenza.
Methods	Retrospective cohort study of hospitalized patients with COVID-19 (n=325) or seasonal influenza (n=433). AKI was defined by Kidney Disease: Improving Global Outcomes (KDIGO) criteria. Baseline characteristics and hospitalization data were collected, and multivariable analysis was performed to determine the independent predictors for AKI.
Results	AKI occurred in 32.6% of COVID-19 hospitalizations (COV-AKI) and 33.0% of influenza hospitalizations (Flu-AKI). After adjusting for age, gender, and comorbidity count, the risk of stage 3 AKI was significantly higher in the COVID-19 cohort (OR: 3.46; 95% CI 1.63, 7.37). Preexisting CKD was associated with a 6- to 7-fold increased likelihood for FLU-AKI and COV-AKI. African American race was associated with higher odds for COV-AKI and Flu-AKI and after adjustment comorbidities was an independent risk factor for AKI in the COVID-19 cohort.
Conclusions	AKI occurred in a relatively high proportion of patients in both cohorts. COVID-19 was associated with a higher risk for stage 3 AKI and poorer prognosis in comparison to seasonal influenza. Pre-existing comorbidities, especially CKD, were associated with a higher likelihood of developing AKI in both cohorts but more so for COVID-19. African American race was an independent risk factor for COV-AKI after adjusting for comorbidities. These findings may be useful in improving our understanding of the risk factors and prognosis of AKI in hospitalized COVID-19 patients.

Category	Kidney, Diabetes & Digestive, #34
Primary Author	Mir Zulqarnain, DO
Secondary Authors	Andres Yarur, MD
Title	Real-world effectiveness and safety of Ustekinumab in patients with ulcerative colitis: A multi-centre study
Introduction	Pivotal trials have shown that ustekinumab (UST) is effective in ulcerative colitis (UC). However, the population included on those trials do not always represent the cohort of patients treated in the “real world”. In this study, we aimed to describe the effectiveness and safety of UST in a “real world” cohort of patients with UC.
Methods	We performed a retrospective, multi-center cohort study and included patients with active UC starting UST. Variables collected included demographics, previous and current UC medications, disease activity (measured using partial and endoscopic Mayo score [PMS and EMS]) at 8 weeks, 6 months and end of follow-up. We also abstracted UST drug level and anti-UST antibodies (AUA), albumin and c-reactive protein levels. Primary outcomes were clinical response at week 8 defined as a reduction of 3 points in the PMS or PMS<2. Secondary outcomes were clinical remission defined as a PMS <2 and endoscopic remission defined as a MES â‰¤1, and the development of an adverse event (AE) attributed to UST.
Results	95 patients were included with a median age of 42 (IQR:32-57) and 53 (56%) were female. Median follow-up was 5 months (IQR:2.2-7.4). Only 4 (4.3%) were naïve to biologics or tofacitinib and 62 (66%) had previous exposure to at least 2 other biologics. The rates of response and remission at week 8 and 6 months are shown in Figure 1. No variables were found to be associated with response at week 8 (Figure 2). Those patients that responded at week 8 had higher median albumin levels vs those that did not but there were no differences in baseline CRP levels (median of 4.4 [IQR: 4.1-4.6] vs 4.1 g/dL [IQR:3.8-4.3], p=0.02 for albumin levels and 1mg/dL [IQR:0.6-2.8] vs 0.6 mg/dL [0.3-1.5], p=0.06 for CRP). Of the entire study group, 33 patients had follow-up endoscopic assessment. Of those, 7 (21.2%) had achieved endoscopic remission and 4 (12%) achieved histologic remission. Five patients underwent colectomy (5.3%). Median UST level was 4.1 mcg/ml (IQR:2.5-5.1) and no patients had detectable AUA. Only 6 patients (6.6%) presented with an AE (all minor that included, rash, headaches, arthralgias and infection).
Conclusions	In a population with refractory UC, UST was well tolerated and induce response and remission in a significant number of patients. The rate of response was lower in obese patients and those with pan-colitis but was not associated with previous exposure to biologics and/or tofacitinib. Larger studies with a longer follow-up are warranted.
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Category	Kidney, Diabetes & Digestive, #35
Primary Author	Shanna Cheng, MD
Secondary Authors	Elliot Yu, MD, Zhuping Garacci, MS, Angelika L. Erwin, MD, PhD, Thangam Venkatesan, MD
Title	Prevalence of Undiagnosed Acute Hepatic Porphyria in Cyclic Vomiting Syndrome
Introduction	Acute hepatic porphyria (AHP), a group of rare genetic disorders, presents with non-specific clinical symptoms: diffuse abdominal pain, nausea, and vomiting that can mimic cyclic vomiting syndrome (CVS). There is a lack of knowledge of the characteristics of symptoms in CVS that can overlap with AHP and the prevalence of undiagnosed AHP in these patients. The aim of this study was to characterize clinical features of CVS and determine the prevalence of AHP in this cohort via molecular analysis of the 4 AHP-associated genes HMBS, CPOX, PPOX, and ALAD.
Methods	We conducted a prospective study of patients diagnosed with CVS based on Rome IV criteria. Patients completed a detailed questionnaire about clinical symptoms. Patients were eligible for AHP genetic testing if they met the following criteria: Recurrent episodes of severe and diffuse abdominal pain with at least two of the following features—red/brownish urine, blistering skin lesions on sun-exposed areas, manifestations of dysfunction of the peripheral nervous system (PNS)(muscle weakness/aching, numbness, tingling), central nervous system (CNS) (confusion, anxiety, seizures, hallucinations) or the autonomic nervous system (ANS) (hyponatremia, tachycardia, hypertension, constipation, nausea/vomiting) around the time of abdominal pain. A family history of AHP or elevated urinary porphobilinogen (PBG)/aminolevulinic acid (ALA) levels were also criteria for genetic testing. Genetic testing for AHP was performed in eligible patients
Results	Of 188 respondents, mean age was 38.6$\pm$ 14 years, 146 (78%) were female and 165 (88%) were Caucasian. Most patients (79%) had abdominal pain >24 hours during a CVS episode. These patients also had other PNS, CNS, or ANS symptoms or red/brownish urine (Figure 1). Eligible patients were more likely to report numbness and or tingling (p=0.0146), fast or irregular heartbeat (p=0.0159), and hyponatremia (p=0.0259) with abdominal pain. Patients who experienced PNS (p=0.0018), CNS (p=<0.001), ANS (p=0.0035) manifestations or had red/brownish urine (p=0.001) were more likely to be hospitalized. Of 125 (66.5%) eligible patients, 66 completed genetic testing for AHP. None of the patients were found to carry pathogenic variants in the AHP genes. Variants of uncertain significance in the HMBS gene were identified in two patients, one of whom had normal urinary ALA and PBG concentrations. Biochemical porphyrin analysis for the other patient was not completed.
Conclusions	Most CVS patients have severe abdominal pain and other neurological symptoms in addition to nausea and vomiting. A significant overlap of symptoms with AHP was noted, but no cases of AHP were detected through genetic testing. Further testing in a larger sample will be needed to ascertain the true prevalence of undiagnosed AHP in CVS.
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Category	Kidney, Diabetes & Digestive, #36
Primary Author	Ryan J. Adam
Secondary Authors	Mark R. Paterson, Markus Bitzer, Alison J. Kriegel
Title	Plasminogen Activator Inhibitor 1 (PAI-1) as a Potential Mechanism Behind miR-146b-5p Sex-Differences in Chronic Kidney Disease Rats
Introduction	Approximately 15% of US adults have chronic kidney disease (CKD), and its progression is sex-dependent. Pre-menopausal women are widely considered protected from CKD by gonadal steroid hormones. The mechanisms behind this protection are not completely understood. Our 5/6 nephrectomy (5/6Nx) rat recapitulates hallmarks of human CKD and over ultimately renal failure. We previously found that knocking out microRNA 146b-5p (miR-146b) results in a profoundly sex-dependent phenotype in 5/6Nx rats. Male miR-146b-/- rats develop renal pathology similar to their WT counterparts. However, female miR-146b-/- rats experience markedly exacerbated renal pathology relative to WT, 5/6Nx, females as well as WT and miR-146b-/-, male, 5/6Nx rats. Exacerbated renal pathology includes highly elevated plasma creatinine, fibrosis, and more. These sex differences were abolished by removal of ovaries at the time of 5/6Nx surgery. These data suggest (1) that not only are the renoprotective effects of feminine gonadal hormones dependent upon the presence of miR-146b, but (2) in the presence of miR-146b, female gonadal steroids actually exacerbate CKD. The primary objective of research project is to identify a molecular mechanism behind these miR-146b dependent sex differences.
Methods	Molecular mechanisms are likely proteins that are associated with renal pathology, especially fibrosis, and whose expression is affected by miR-146b and female gonadal hormones. Predicted miR-146b targets, identified through online databases, were cross-referenced with direct miR-146b to mRNA interactions as identified by crosslinking and immunoprecipitation (CLIP) experiments.
Results	Plasminogen Activator Inhibitor 1 (PAI-1, aka SERPINE1) was identified from this list. PAI-1 has a predicted miR-146b target site in its coding domain sequence. PAI-1 is sensitive to both estrogen and progesterone, its basal renal expression is low in health, but highly elevated in a variety of pathological settings where it is considered pro-fibrotic through its regulation of MMPs. PAI-1 mRNA is highly elevated in untreated miR-146b-/- rat proximal tubular epithelial cells (NRK-52E) relative to WT controls (11.25 Â± 5.3 vs. 1.00 Â± 0.68, P<0.05). Conversely, WT NRK-52E cells treated with pre-miR-146b had significantly reduced PAI-1 mRNA expression (0.137 Â± 0.14 vs. 1.00 Â± 0.45, P<0.05). Transforming growth factor beta (TGFB) is elevated in our CKD rats and is known to contribute to renal pathology, especially fibrosis. Treatment of WT NRK-52E cells with doses of TGFB ranging from 1 ng/ml to 20 ng/ml all resulted in statistically significant increase of PAI-1 mRNA at all doses.
Conclusions	Collectively, these experimental observations suggest PAI-1 as a promising mechanistic candidate behind the sex-specific effects of miR-146b in CKD, and provide a rationale to pursue prospective PAI-1 animal and tissue experiments. Improved understanding of pre-menopausal reno-protection in females could potentially result in the identification of a mechanism that could be exploited to treat everyone with CKD.
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Category	Kidney, Diabetes & Digestive, #37
Primary Author	Lauren A. Hipp**
Secondary Authors	JP Esteban; Andres Yarur; Poonam Beniwal-Patel
Title	NO ASSOCIATION BETWEEN NON-ALCOHOLIC STEATOHEPATITIS OR ADVANCED FIBROSIS AND IBD CLINICAL REMISSION AT ONE AND FIVE YEARS
Introduction	Over the last decade, studies have found increased prevalence of non-alcoholic fatty liver disease (NAFLD) in patients with inflammatory bowel disease (IBD). Small studies suggest that more severe hepatic steatosis is associated with greater IBD endoscopic activity. Few patients with IBD experience worsening of advanced hepatic fibrosis using the validated NAFLD fibrosis score (NFS). However, there is incomplete evidence on whether non-alcoholic steatohepatitis (NASH) and fibrosis stage is associated with IBD disease course. We describe a cohort of IBD patients with concomitant NAFLD and describe IBD disease course one year and five years after NAFLD diagnosis.
Methods	This is a single-center retrospective study of IBD patients aged 18 years and above with concomitant NAFLD. Patients with a history of alcohol abuse and another chronic liver disease were excluded. Demographics, co-morbidities, IBD disease characteristics, lab, imaging and liver histologic data were reviewed at time of NAFLD diagnosis, then 1 and 5 years after. NFS was calculated at each time point. Advanced fibrosis was defined as stage 3/4 fibrosis in patients with biopsy, F3/4 in patients without biopsy but had Fibroscan, and NFS>0.676 in patients without biopsy or Fibroscan. Among patients with biopsy, NASH was defined as NAFLD Activity Score>5. IBD remission was defined as Harvey Bradshaw Index <5.
Results	There were 78 patients with IBD and NAFLD (63% male, 63% White, 9% Black). Average age at IBD diagnosis was 33.7+16.0 years and average age at NAFLD diagnosis was 50.4+14.8 years (94% of NAFLD diagnosed after IBD). Crohn's disease was more common than either ulcerative colitis or indeterminate colitis (69.2% vs 30.8%, p=0.0007). Only 48% were in IBD remission. Sixteen (20.3%) had advanced fibrosis using predefined histologic and non-invasive criteria. Thirty-eight (48.7%) had baseline liver biopsies, of whom 9 (23.7%) had NASH and 9 (23.7%) had stage 3/4 fibrosis. Histologic NASH or advanced fibrosis at baseline were not associated with IBD disease activity at years 1 and 5. Of 60 who had NFS at baseline and year 1, 85% did not have baseline advanced fibrosis and 4 (7.8%) patients had advanced fibrosis at year 1. Of 25 who had NFS at baseline and year 5, 92% did not have baseline advanced fibrosis and 2 (8.7%) patients had advanced fibrosis at year 5.
Conclusions	To our knowledge, this is the first study evaluating histologic NASH and hepatic fibrosis and IBD course. Histologic steatohepatitis and advanced fibrosis are not associated with IBD clinical remission at baseline, year 1, and year 5. On average, diagnoses of NAFLD were made 20 years after IBD diagnosis and 20-25% of NAFLD may have advanced fibrosis. Gastroenterologists should have heightened vigilance for NAFLD in IBD patients.
Ancillary Materials	VIEW MY POSTER

Category	Mental Health, Abuse & Addiction, #38
Primary Author	Nathan Staidl, MS3
Title	Wisconsin Views on Addiction and Mental Health
Introduction	Growing up in a very rural and conservative portion of Wisconsin, I found addiction and mental health were traditionally ignored. Therefore, I have often wondered if there is a correlation to certain social demographics and views on addiction.
Methods	Surveys were distributed via the Brown County Alcohol & Drug Coalition 4 Change, and collected using the online survey platform, Qualtrics. Data was interpreted to match answer patterns with self-proclaimed demographics.
Results	Approximately 88% of participants agree that addiction is a mental illness. Less than 50% believe that factors like education level and income contribute to addiction, while more than 50% believe family history and where the person grew up do contribute to addiction. Approximately 90% of participants do not believe addiction is the result of a character flaw or personal choice.
Conclusions	The majority of people who were surveyed do see alcohol and drug addiction as a mental illness. Some people still fail to recognize social factors such as education and income as high risk determinants of addiction. There appears to be no correlation between any one demographic and views on addiction, however small sample size and lack of diversity among participants may be contributing to false representations, as well as participants selecting "self-proclaimed" demographics which may be subjective. Other limitations may include selection bias due to the organizations I worked with giving access to participants who may have already been seeking to change views and policies on substance abuse.
Acknowledgements	I would like to thank the Brown County Alcohol & Drug Coalition 4 Change for their help in completing this research project. I would also like to thank the Medical College of Wisconsin - Green Bay staff for their tireless efforts to make every experience, clinical or otherwise, possible and unique.
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Ancillary Materials	VIEW MY POSTER

Category	Mental Health, Abuse & Addiction, #39
Primary Author	Sara Kohlbeck, MPH**
Secondary Authors	Katherine Quinn, PhD
Title	A Qualitative Analysis of Suicide among Farmers in Wisconsin
Introduction	Suicide is an increasing, yet preventable, public health concern - suicide rates in the United States are the highest they have been since the 1940's, after the Great Depression. In recent years, suicide research in the United States has focused on suicide in certain occupational groups. One CDC report demonstrated that certain occupation groups have higher rates of suicide, specifically mining, construction, agriculture, and transportation. Occupation, and specifically farming, may impact suicide risk through a number of pathways. Studies of suicide among farmers in Australia, for example, have found that stressors related to climate change, and its associated effects of crop damage and loss, can contribute to increased suicide. In the United States, there is a demonstrated need to address suicide among farmers and understand what contributes to suicide farmers in order to effectively prevent suicide among them.
Methods	The purpose of this qualitative study is to analyze narrative data from the WVDRS, using thematic analysis, in order to uncover circumstances that were present in the lives of farmers who died by suicide prior to their death.
Results	Four specific themes emerged from this analysis: stymied by physical health issues, grief from loss of relationships, prolific access to firearms in rural Wisconsin, and the burden of farming and the farm.
Conclusions	The findings in this study suggest that farmers who die by suicide experience certain unique life events and circumstances that lead to their eventual suicide. In addition, farmers who die by suicide have similar life experiences than non-farmers who die by suicide. These findings illustrate that while a focus on more "traditional" risk factors for suicide is important when considering farmer suicide, it is equally important to consider experiences that are unique to farming and farmers. With more focused suicide prevention efforts that build healthier and safer farming communities, there is hope of saving lives.

Category	Mental Health, Abuse & Addiction, #40
Primary Author	Esha Afreen, BS
Secondary Authors	Abigail Strong, MD/MPH; Jayla Watkins, BS; Anna Palatnik, MD; Rachel Harrison, MD
Title	Inpatient opioid consumption after cesarean delivery in patients with mood disorders
Introduction	Mood disorders, namely depression and anxiety, have been shown to modulate pain perception. How this effect impacts post-cesarean opioid consumption in the inpatient setting is not well-studied. Our objective was to examine the association between diagnosis of a mood disorder (MD) and inpatient opioid consumption after cesarean delivery (CD).
Methods	A retrospective cohort study of patients who delivered by CD between 2014 and 2019 was performed. Exposure was determined by maternal diagnosis of MD, defined as depression and/or anxiety. The primary outcome was inpatient opioid consumption after the first 24 hours postpartum, standardized to morphine milliequivalents per hour (MME/hr). Hourly, rather than total MME, was chosen as the primary outcome to standardize opioid consumption across patients with varying lengths of stay. Secondary outcomes included highest dose of oxycodone required and highest/lowest quartile of MME/hr consumption. Univariable and multivariable analyses were done to examine the associations between maternal MD and the primary and secondary outcomes, controlling for sociodemographic characteristics, clinical obstetric factors, and non-opioid analgesic intake postpartum.
Results	Of 1,620 eligible patients, 384 (23.7%) were identified as having MD. Patients with MD were more likely to be single, use tobacco, use illicit substances in pregnancy, undergo a tubal ligation, and have a hemorrhage at delivery. In univariable analysis, the rates of the primary outcome, MME/hr, were significantly higher among patients with MD compared to controls. After controlling for confounders, this finding did not persist. However, in regard to the secondary outcomes, patients with MD were more likely to require higher doses of oxycodone at a time, i.e. â‰¥10 mg vs. <10 mg (aOR 1.38, 95% CI 1.07-1.79). In addition, patients with MD were more likely to be in the highest quartile of MME/hr opioid consumption (aOR 1.75, 95% CI 1.34-2.29) and less likely to be in the lowest quartile (aOR 0.63, 95% CI 0.47-0.86).
Conclusions	Maternal diagnosis of MD was not associated with higher hourly consumption of MME during inpatient stay after CD. However, diagnosis of MD was associated with increased requirement of higher oxycodone doses. Mental health history should be taken into account to achieve effective postoperative pain management, while balancing risks of opioid exposure in postpartum women.
Ancillary Materials	VIEW MY POSTER WATCH MY PRESENTATION

Category	Mental Health, Abuse & Addiction, #41
Primary Author	Jessica Ohlrich, MPA
Secondary Authors	Julia Dickson-Gomez, PhD; Erika Christenson, MPH
Title	"Keeping people out of jail in regards to drugs is a collaborative effort": Public health and criminal justice collaboration in Milwaukee County Drug Treatment Courts.
Introduction	In light of the expanding prison population in the United States, most of which is due to drug related crimes, experts have increasingly called for more public-health oriented approaches to the opioid crisis. The National Association of Drug Court Professionals has released best practice standards for adult drug courts, many of which include ways to strengthen the relationship between the criminal justice system and public health sector.
Methods	We conducted in-depth, semi-structured interviews with Key Informants (KI) (e.g., District Attorney, Public Defender, Drug Court Judge, treatment coordinators, and treatment facilities) in Milwaukee County. We asked questions regarding: drug court organization and processes, the role each sector plays in the drug court, treatment availability, justice reinvestment, and effectiveness of the court. Responses related to public health and criminal justice cooperation and collaboration were analyzed collaboratively using inductive thematic content analysis. We also attended sessions of drug treatment court and drug court staffing meetings.
Results	KI agreed that Milwaukee county is unique in the degree that public health and criminal justice cooperate in the county's drug treatment court. KI also agreed that the current system is not equipped to handle comorbidity of opioid use disorders (OUD) and other mental health issues. Additionally, lack of resources in the community, waiting lists, limited capacity in the treatment court, and lack of adequate funding are barriers to further public health and criminal justice collaboration.
Conclusions	While the criminal justice system in Milwaukee county has made strides in collaborating with the public health sector, improvements can be made. Strengthening justice reinvestment in the community and treatment resources are necessary to further the success of the drug treatment court. A more individualized approach to drug treatment court can further the success of participants and ultimately help alleviate the impacts of the opioid crisis in Milwaukee.
Ancillary Materials	VIEW MY POSTER

Category	Neuroscience & Neurology, #42
Primary Author	Patrick D. Best
Secondary Authors	Jayme S. Nelson
Title	Assessing the Efficacy of Pre-Hospital Providers in Correctly Identifying Cerebrovascular Accident in De Pere and Ashwaubenon WI - A Retrospective Analysis
Introduction	CVA has long been a significant cause of morbidity and mortality in humans. Because of its insidious nature and acute presentation, it is a silent killer that places a large amount of financial and industrial burden on the healthcare system. There has been considerable work done in recent decades to improve the outcomes of CVA's via earlier identification and development of more effective therapeutics. The Los Angeles Motor Scale (LAMS) is a pre-hospital stroke scale developed for the purpose of earlier identification of CVA. Aurora BayCare Medical Center (ABMC) is the only Level 1 Comprehensive Stroke Center in the greater Green Bay area and is thus the standard destination for suspected CVA's.
Methods	This study sought to investigate the efficacy of the LAMS scale in identifying CVA's in the pre-hospital setting in De Pere and Ashwaubenon WI from 2016-2019 through the cross-referencing of de-identified patient records from the respective pre-hospital EMR's with those of ABMC.
Results	This study demonstrated an 80% sensitivity for CVA across both departments, in line with the 81% national average. Furthermore, our study demonstrated very similar efficacy of the LAMS tool in both De Pere and Ashwaubenon. The positive and negative predictive values of LAMS were 84.2% and 42.9%, respectively.
Conclusions	The results provide further support for both the efficacy and utility of the LAMS stroke scale in pre-hospital stroke identification.
Ancillary Materials	VIEW MY POSTER

Category	Neuroscience & Neurology, #43
Primary Author	Sophia G. Musacchio
Secondary Authors	Hershel Raff, John J. Leddy, Blair D. Johnson, Michael A. McCrea, Timothy B. Meier, & Lindsay D. Nelson
Title	Altered HPA and ANS Activity Post-Concussion: Characteristics and Clinical Correlations
Introduction	Concussion (uncomplicated mild traumatic brain injury) is highly prevalent and causes diverse symptoms that impair life function and quality. Alterations in the hypothalamic-pituitary-adrenal (HPA) axis and autonomic nervous system (ANS) stress systems may underlie concussion symptoms and recovery. We assessed the course and clinical correlates of two non-invasive markers of the HPA axis and ANS—salivary cortisol (sCORT) and alpha-amylase (sAA), respectively—in a prospectively enrolled sample of patients with concussion.
Methods	Twenty civilian concussed patients underwent cognitive (arithmetic) and exercise (Buffalo Concussion Treadmill Test) stressors in early-mid afternoon 1 week and 1 month post-concussion. Saliva was sampled 10x per exam. Natural log-transformed biomarker levels were evaluated for effects of Sample (1-10) and Visit (1-week, 1-month) and were correlated with concussion symptoms (Rivermead Post Concussion Symptom Questionnaire; RPQ).
Results	Baseline sCORT declined significantly from 1-week to 1-month post-concussion ($p < .001$). sAA showed more change in response to exercise at 1-month than 1-week post-injury, as evidenced by a greater sample effect across samples 6-10 at Visit B ($p<0.001$) as compared to Visit A ($p=0.026$). Having less change in sCORT from pre- to post-exercise at 1 week was associated with higher 1-month RPQ symptom burden ($r = -.68$, $p = 0.015$).
Conclusions	Lower cortisol at 1 month compared to 1 week post-concussion implies elevated HPA axis activity in acute concussion. More change in alpha amylase in response to exercise at 1 month post-concussion implies diminished ANS flexibility at 1 week. Lower HPA axis reactivity at 1 week was prognostic of higher symptom burden at 1 month. This study provides preliminary data supporting further study of these two stress systems jointly in concussion outcomes.
Ancillary Materials	WATCH MY PRESENTATION

Category	Neuroscience & Neurology, #44
Primary Author	Thomas Luo, BS**
Secondary Authors	Manoj Raghavan, MD, PhD
Title	Predicting the Seizure Onset Zone from Interictal ECoG Data using Machine Learning
Introduction	Epilepsy affects more than 65 million people globally. About a third of patients with epilepsy fail to achieve freedom from disabling seizures with pharmacologic therapy alone. For a subset of these patients, surgical ablation of the seizure onset zone (SOZ) in the brain is an effective treatment. Localization of the SOZ often requires multiday intracranial recordings of the electrocorticogram (ECoG) to capture seizures. While ictal (seizure) recordings remain the gold standard for localizing SOZs, interictal features—epileptic spike discharges, abnormally increased power at low-frequencies (0.5-4Hz delta, and 4-8Hz theta frequency bands), and bursts of pathological high frequency oscillations (HFOs) >80 Hz—have all been recognized as potential biomarkers of the epileptogenic cortex. More recently, cross-channel ECoG derived connectivity measures are actively being explored to identify SOZs. Alone, each of these individual features does not have sufficient sensitivity and specificity in predicting the SOZ. We hypothesize that a support vector machine can be trained using a set of interictal features extracted from ECoG signals to identify the signals arising in the SOZ with high sensitivity and specificity.
Methods	Archived multichannel interictal ECoG signals and SOZ determinations established by the clinical epilepsy team were retrieved for 10 patients (N=807). The ECoG data was preprocessed to eliminate noisy epochs using custom MATLAB scripts. The following ECoG features were extracted from all channels: epileptic spike-rates and mean-amplitudes; HFO-rates and mean-amplitudes; power spectral density in six frequency bands (delta, theta, alpha, beta, low-gamma, and high-gamma); node-strength and eigenvector centrality (EC) based on cross-channel signal envelope correlations (within each patient's data) in four bands (alpha, beta, low-gamma high-gamma); node-strength and eigenvector centrality (EC) based on cross-channel phase-locking value (PLV) for the same four bands. The known SOZ classification of 75% of channels was used to train each machine learning algorithm. The generalizability was evaluated by testing the SVM on the remaining 25% channels.
Results	Using the MATLAB machine learning toolbox, several classification algorithms including k-nearest neighbor, decision trees, regression, ensemble, shallow feed-forward neural networks, and SVM were applied to the ECoG feature data. An SVM using a Gaussian kernel had the highest AUROC of 0.93 captured ~90% of channels from the SOZ with a false positive rate of ~17%, using 15 features including: envelope-correlation node-strength (low, high gamma and EC (all four bands), PLV node-strength (alpha-band) and EC (alpha, low-gamma, high-gamma), and power spectral density (theta, alpha, beta, gamma).
Conclusions	Our results suggest that and spectral and connectivity-based features of ECoG signals likely carry more information relevant to identifying epileptogenic regions of the brain than traditional markers of epileptic cortex such as spike discharges or HFOs. Inclusion of more patients will improve the generalizability of the machine learning; Additional SOZ examples will increase the accuracy of more modern neural network models. Accurate interictal SOZ prediction could allow localization of surgical targets from brief intraoperative ECoG recordings, eliminating the need for multiday invasive recordings.

Category	Ophthalmology, #45
Primary Author	Linda M. Reis, MS, CGC**
Secondary Authors	Deborah Costakos, MD; Elena V Semina, PhD
Title	Dominant variants in PRR12 result in unilateral or bilateral complex microphthalmia
Introduction	Complex microphthalmia is characterized by small eyes with additional abnormalities that may include anterior segment dysgenesis. While many genes are known, a genetic cause is identified in only 4-30% of microphthalmia, with the lowest rate in unilateral cases.
Methods	Exome data was reviewed from 263 probands with microphthalmia and/or anterior segment dysgenesis.
Results	We identified four novel pathogenic loss-of-function alleles in PRR12 in families affected by complex microphthalmia and/or Peters anomaly, including two de novo, the first dominantly transmitted allele, as well as the first splicing variant. The ocular phenotypes were isolated with no additional systemic features observed in two unrelated families. Remarkably, ocular phenotypes were asymmetric in all individuals and unilateral (with structurally normal contralateral eye) in three. There are only three previously reported PRR12 variants identified in probands with intellectual disability, neuropsychiatric disorders, and iris anomalies. While some overlap with previously reported cases is seen, non-syndromic developmental ocular anomalies are a novel phenotype for this gene. Additional phenotypic expansions included short stature and normal development/cognition, each noted in two individuals in this cohort, as well as absence of neuropsychiatric disorders in all.
Conclusions	This study identifies new associations for PRR12 disruption in humans and presents a genetic diagnosis resulting in unilateral ocular phenotypes in a significant proportion of cases.
Acknowledgements	We are grateful to the patients and their families for participation in this study and to Samuel Thompson and Rebecca Fieseler for assistance with Sanger sequencing. This work was supported by NIH grants R21HD099701 and R01EY025718 as well as funds provided by the Children's Research Institute Foundation at Children's Wisconsin (EVS) and 1UL1RR031973 from the Clinical and Translational Science Award (CTSA) program.
Ancillary Materials	VIEW MY POSTER

Category	Ophthalmology, #46
Primary Author	Megan Yee
Secondary Authors	Militza Bonet Vazquez, Al Castro, Velinka Medic, Blanca Rodriguez, Judy E. Kim
Title	Analysis of Focus Group Results for Teleophthalmology to Improve Eye Health among Latinos(TIEHL)Study
Introduction	Compliance with annual dilated eye exams is low and telemedicine can be used as a solution. Using community-based approach, we established a teleophthalmology program at the United Community Center (UCC). We held focus groups (FG) to 1) ascertain the attitudes and knowledge of urban Latinos in Milwaukee about diabetic eye disease(DED)and telemedicine and 2) assess their response to teleophthalmology screenings at a community center facilitated by Spanish speaking staff.
Methods	Pre- and post- screening focus groups (FG) were held at United Community Center (UCC). FGs were in both English and Spanish to account for possible differences in acculturation levels and health beliefs. Participants also completed an Eye-Q test (National Eye Institute).
Results	The number of participants pre-screening was 7 for Spanish and 7 for English while the post-screening FGs were 6 for Spanish and 4 for English. Both FGs had a low understanding of DED based on the Eye-Q test (English FG scored 57% versus 41% for Spanish FG). Poor emphasis on preventative care was noted when asked about attitudes towards DED and seeking care. Most participants perceived convenience and efficiency as advantages of telemedicine, but loss of physician-patient relationship and insurance coverage as disadvantages. 100% of participants who underwent teleophthalmology screening at UCC responded positively, expressing preference for the location, trust in the staff, and comfort with speaking Spanish as factors that would encourage them to seek annual eye exams.
Conclusions	FG participants had positive experiences with teleophthalmology screenings done at UCC and listed various factors that broke down barriers to preventive eye screening. Unlike most teleophthalmology studies in the literature, our study is unique for assessing screenings done in a community center versus at clinics. High acceptance of this novel teleophthalmology approach may help improve compliance to annual screenings in the urban Latino communities.
Acknowledgements	United Community Center
Ancillary Materials	VIEW MY POSTER

Category	Ophthalmology, #47
Primary Author	Nathan Li
Secondary Authors	Kristina Ertel, Daniel Lipinski
Title	Development of Corneal Penetrating rAAV vectors for Topical Gene Delivery using Bioreversible Esterification
Introduction	Glaucoma is the leading cause of irreversible blindness worldwide, with open angle glaucoma (OAG) being most common in western populations. OAG is characterized by increased intraocular pressure (IOP) caused by an imbalance between aqueous humor production and outflow. A common pharmacological treatment for OAG is application of eye drops containing prostaglandin analogs in order to increase aqueous drainage and lower IOP. While effective, compliance with eye drops is poor, leading to the development of vision-threatening complications even in patients diagnosed early. Recombinant adeno associated viral vectors (rAAV) have been shown to be safe and effective at mediating gene transfer to ocular structures. However, gene transfer typically requires injection of rAAV vector into the eye, resulting in a transient spike in IOP and increased risk of surgical complications. Consequently, we aimed to develop a topical rAAV-based gene delivery technology that allows for effective gene transfer to cells of the cornea without having to perform an intraocular injection. The cornea presents a formidable barrier to gene transfer, with any vector applied to the surface being rapidly eluted in the tear film. We hypothesized that chemically modifying the rAAV capsid via esterification with 2-diazo-2-(p-methylphenyl)-N,N-dimethylacetamide (herein termed compound 1), followed by desiccation of the esterified vector onto a contact lens, would improve retention time and increase transgene delivery efficiency to the corneal endothelium.
Methods	Specific Aim 1: Evaluate transduction efficiency of rAAV2/2 after esterification reaction with compound 1 post desiccation. The infectivity of rAAV2/2 packaging a green fluorescent protein (GFP) reporter transgene driven by the ubiquitous small chicken beta actin (CBA) promotor was evaluated at each stage of the esterification reaction process to determine whether transduction efficiency was adversely affected. rAAV2/2 was incubated with each of the reaction buffers separately and in combination prior to being desiccated onto mouse-sized contact lenses or added directly to HEK293T cells in culture. The transduction efficiency of the desiccated and unbound (i.e. control) rAAV was subsequently compared by fluorescent microscopy and flow cytometry. Specific Aim 2: Evaluate in vivo transduction efficiency of esterified rAAV in C57Bl/6J mice. Two serotypes (rAAV2/2 and rAAV2/1) packaging a GFP transgene driven by a ubiquitous small CBA promotor were esterified using compound 1 and desiccated onto the inner surface of a custom fluoro-polymer contact lens. Lenses were subsequently applied to the corneal surface of anesthetized C57Bl/6j mice for 30 minutes. Expression of the GFP reporter gene in the cornea was assessed at 10 weeks post-application via non-invasive confocal scanning laser ophthalmoscopy (cSLO).
Results	Immunofluorescence imaging and flow cytometry performed on HEK293T cells three days post vector application revealed that the process of chemically esterifying the rAAV capsid does not significantly alter infectivity (63.8ï,±2.9% vs XX.X%, P=X.XX, students t-test). Application of esterified rAAV-coated contact lenses to the corneas of C57Bl/6j mice resulted in visible GFP expression by cSLO imaging by XX weeks. No adverse events were observed in any eyes; post-mortem histology is being performed to confirm cellular tropism.
Conclusions	We have successfully shown that the chemical reaction used to esterify the rAAV capsid does not significantly alter the transduction efficiencies of rAAV2/2. The observation of GFP expression in the corneas of C57Bl/6J mice following contact lens application indicates that topical delivery of esterified rAAV may be a safe and effective method by which to deliver therapeutic transgenes for the treatment of corneal disease.
Ancillary Materials	VIEW MY POSTER

Category	Ophthalmology, #48
Primary Author	Jenna E. Maurer, BA
Secondary Authors	Velinka Medic, MS; Joshua George, BA, MPH; Judy E. Kim, M.D.
Title	"Eyes on the Future:" Engaging a Future Generation of Latino Physicians and Scientists
Introduction	Latinos are considered an underrepresented group in science and medicine. Therefore, innovative methods are needed to increase Hispanic and Latino exposure, interest, and representation in these fields. A pipeline program called “Eyes on the Future” was created, and implementation and acceptance by the stakeholders was evaluated. It was believed that a program incorporating early exposure to medical science during education and mentoring by medical students may be effective.
Methods	8th grade students at St. Augustine Preparatory Academy in Milwaukee, which provides education to predominantly Latino students, participated in the project. Several activities led by MCW medical students were designed to engage the 8th grade students throughout the year, including an interactive presentation on the eye with an introduction to possible STEM careers, a collaborative eye dissection, and a visit to the STAR Center at MCW for clinical simulations. Students and teachers were asked to complete an anonymous evaluation upon culmination of the program.
Results	For the STAR Center visit, teachers selected 26/120 students who showed exceptional motivation and interest in the presentation and eye dissection. While the majority of students (63%) selected the STAR Center as their favorite event, the majority of students (81%) also indicated that they did not have a least favorite event. Overall, the number of students who demonstrated an interest in science/medicine before the program as compared to after increased from 40% to 73%. Both students and teachers expressed an overall satisfaction with the program, especially the hands-on components. Teachers reported high student engagement, which corresponded with comments from the students reflecting a joy in learning new things.
Conclusions	Creation and implementation of a pipeline program for mostly Latino middle school students was feasible, well-received, and may serve as a model that can be followed at other schools.
Ancillary Materials	WATCH MY PRESENTATION

Category	Pediatrics & Child Health, #49
Primary Author	Bryanna Buchman
Secondary Authors	Ruby Gupta, MD; Erwin Cabacungan, MD
Title	Effect of the COVID-19 pandemic on documentation of neonatal resuscitation in the delivery room.
Introduction	According to the American Academy of Pediatrics Neonatal Resuscitation Program, ensuring accurate documentation during resuscitation is important for clinical decision making and as a data source for quality improvement. A qualified team from the Children's Wisconsin (CW) neonatal intensive care unit (NICU) attends all high risk deliveries at Froedtert Hospital (FH). During the COVID-19 pandemic, the number of providers for these deliveries decreased in order to conserve personal protective equipment and maintain social distance. We hypothesize that the completeness of documentations and resuscitation outcomes are not affected by the limited number of providers attending high-risk deliveries. We aim to identify the lapses in neonatal resuscitation documentation during the COVID-19 pandemic.
Methods	This is a retrospective review of paper resuscitation forms for high-risk deliveries at FH over 13 weeks (02/02/20-05/02/20), exempted by the Medical College of Wisconsin and CW IRB. Variables collected included date of birth, time of delivery, number of providers present, and reason for attendance and disposition. Aspects of the delivery such as gestational age (GA), APGAR scores, physical exam, use of Continuous Positive Airway Pressure (CPAP) or Positive Pressure Ventilation (PPV), were recorded as being completely or incompletely documented. For analysis, we compared four groups: pre-COVID-19 (6 wks., 02/20/20-03/14/20) and during COVID-19 (7 wks., 03/15/20-05/02/20), and day shift (0701-1700) versus night shift (1701-0700). Kruskal-Wallis test was performed to compare the four groups.
Results	A total of 381 resuscitation forms were reviewed. There was no difference in the ratio of high-risk deliveries attended over total no. of deliveries for pre-COVID-19 (mean ï,± SD, 0.5 ï,± 0.07) versus during COVID-19 (0.46 ï,± 0.10), p = NS. However, the number of providers decreased by one (4 providers for pre-COVID-19 versus 3 providers during COVID-19, regardless of shift), p <0.001. We found a decrease in documentation during COVID-19. The mean CPAP documentation decreased by 22% during the dayshift [pre-COVID-19 (66.8%) versus during COVID-19 (44.8%)]; and decreased by 3% during the nightshift [pre-COVID-19 (51.7%) versus during COVID-19 (48.4%)]. Mean documentation of PPV of dayshift decreased by 13% [pre-COVID-19 (70.6%) versus during COVID-19 (57.9%)] and stayed the same at 42.1% on nightshift. In regards to GA and APGAR scores, there were no significant differences in the acuity of newborns resuscitated across all four groups.
Conclusions	During COVID-19, the decreased number of providers attending high-risk deliveries may have led to decreased documentation, particularly in dayshift. However, this decrease in providers and their documentation has not led to changes in resuscitation outcomes. Next steps include addressing the lack of complete documentation using quality improvement methodology by developing an electronic resuscitation form that facilitates real-time documentation. We speculate that improved documentation will help with the quality of resuscitations and may further lead to improved patient outcomes.
Ancillary Materials	VIEW MY POSTER

Category	Pediatrics & Child Health, #50
Primary Author	Sarah Yale, MD
Secondary Authors	Sarah C Bauer, MD, Alyssa Stephany, MD, Kelsey Porada MA, Tracey Liljestrom MD
Title	Addressing a safety gap for urgent issues post discharge: Implementation of a "safety set" for families
Introduction	The transition period from hospitalization to outpatient care can be high risk for pediatric patients. Our aim was to profile the use of a “safety net” for families through provision of specific inpatient provider contact information for urgent issues post-discharge.
Methods	In this prospective study, we implemented an updated after-visit summary (AVS) that directed families to call the hospital operator and specifically ask for the pediatric hospital medicine (PHM) attending on call if they were unable to reach their primary care provider (PCP) with an urgent post discharge concern. Education for nursing staff, operators and PHM providers was completed, and contact information automatically populated into the AVS. Information collected included the number of calls, topic, time spent, if family contacted the PCP first, and time of day. Descriptive statistics and Fisher’s exact test were used to summarize findings.
Results	Over a 13-month period, out of 5145 discharges, there were 47 post-discharge phone calls, averaging 3.6 calls per month. The average length of time spent on a call was 21 minutes. Of the calls, 30% of families had tried contacting their PCP first and 55% of calls occurred at night. Topics of calls included requesting advice about symptoms, timeline for re-evaluation, and assistance with medications.
Conclusions	This safety net provided families with real time problem solving for an urgent need post-discharge such as triaging patients symptoms at home, counseling on medication questions, information about timeline of illness recovery, and provision of additional resources.
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Category	Pediatrics & Child Health, #51
Primary Author	Megan Glait
Secondary Authors	Andrea Moyer, Kris Saudek, MD, Erwin Cabacungan, MD, Kelsey Ryan, MD
Title	ESC Drives Sustainable Change in Nursery NOWS Management
Introduction	Neonatal Opioid Withdrawal Syndrome (NOWS) is a growing epidemic across nurseries nationwide. Eat, Sleep, Console (ESC) management of NOWS is associated with reduced inpatient healthcare utilization for NOWS-affected infants. The objective of this study was to assess the sustainability of reduced healthcare utilization after ESC implementation.
Methods	A multidisciplinary team aimed to reduce patient length of stay (LOS) and morphine exposure by 30% in one year with ESC-based management of NOWS, and sustain change for two years after implementation (Figure 1). PDSA cycles were carried out across three nurseries within our hospital system (Figure 2). Process control charts tracked special cause variation and sustainability. Primary outcome measures were LOS and percent treated pharmacologically. Process measures included nursery site, medical specialty of the attending provider, and parental/volunteer presence for nonpharmacologic management. Balancing measures included polypharmaceutical treatment, transfers to a higher level of care, and 30-day readmission for NOWS. Infants at risk of NOWS were identified via systemwide retrospective database analysis. All infants at risk of NOWS and admitted to a non-NICU setting during their birth hospitalization from Jan 2016 to Sept 2020 within our hospital system were included. Infants were excluded if NOWS scores were not documented or if the infant was transferred to another institution.
Results	118 infants were managed with Modified Finnegan Neonatal Abstinence System Scoring (MFNASS) during PDSA0. 81 infants were managed with ESC methodology during PDSA1-3 (Figure 1). Process control charts demonstrated special cause variation in primary outcomes following ESC education and implementation, sustained for two years (Figure 3&4). Unexpected variation was detected April-June 2020, coinciding with increased community site admissions, increased management by specialties other than general pediatrics, reduced parental/volunteer presence, and increased polypharmaceutical management of NOWS. Other balancing measures did not increase over the study period.
Conclusions	ESC sustainably improved quality outcomes for NOWS-affected infants across diverse nursery settings for two years post implementation. Changes in hospital-based care due to the COVID-19 pandemic (starting late March 2020), among other factors, may have impacted the quality of care for NOWS-affected infants. Further process monitoring is needed to clarify this pattern and may inform future PDSA cycles.
Ancillary Materials	**WATCH MY PRESENTATION**

Category	Pediatrics & Child Health, #52
Primary Author	Ashin Mehta
Secondary Authors	Keri Hainsworth, Steven Weisman, Monica Gremillion, Johanna Michlig
Title	Adolescent with Chronic Pain during Covid-19 quarantine
Introduction	Pediatric chronic pain impairs quality of life and functioning. The Covid-19 pandemic and quarantine may exacerbate pain and undermine pain management. Understanding the immediate effects will inform intervention efforts in the short- and long-term.
Methods	We conducted a chart review of patients seen in the Children's Wisconsin Pain and Headache Center. This case report exemplifies the effects of the Covid-19 quarantine for this already at-risk patient population.
Results	In Dec 2019 a 17-year-old female patient presented to the pain clinic for vestibular migraine and functional neurological disorder. Her headaches occurred throughout the week and lasted several hours at a time. She had jaw pain and reduced vision and numbness on one side of her body. Symptoms began abruptly in September 2019, coincident with the start of her junior year of high school. Due to Covid-19, Wisconsin began an extended Safer-at-home quarantine period on March 24, 2020. By patient's report, the pain, Covid-restrictions and quarantine increased her stress, anxiety, and feelings of hopelessness ("Being quarantined makes it difficult to have things to look forward to"). During the quarantine, her jaw pain intensified to the point of slurring her speech and increased pain significantly impaired her overall functioning. Medications (e.g. acetaminophen, naproxen) did not alleviate symptoms, whereas acupuncture was most helpful for relieving headaches. Prior to the quarantine, the patient reported anxiety regarding her condition. However, mid-March the patient reported elevated levels of stress (8 out of 10, with 10 = extremely stressed) mostly correlated with pain and academic pressure. Her stress dropped from an 8 to a 1 out of 10 following the end of school but went back to 8 following the cancellation of the ACT. By August the patient reported she felt confident in her ability to manage stress and in the same session discussed how next year's schooling situation was stable. Physical activity was also beneficial for the patient's pain.
Conclusions	The quarantine intensified this patient's school-related anxiety and in turn, exacerbated her pain and physical symptoms. Once her schooling situation become more stable, the patient saw significant improvements in stress, mood, and overall functioning. While progress has been made in the development and distribution of COVID vaccines, it is likely much of the country will be in lockdown for the foreseeable future with continued disruption to primary schooling. As many pediatric patients are affected by academic stressors, it is critical to study the impact of the lockdown/pandemic to better prepare to care for future patients under similar circumstances. In addition, cases of patients affected by COVID-19 lockdowns may provide insight into the challenges facing chronic pain patients living in isolated or rural locations.
Reference 1	Jastrowski Mano KE. School anxiety in children and adolescents with chronic pain. Pain Res Manag. 2017;2017:8328174.
Reference 2	Anderson Khan K, Tran ST, Jastrowski Mano KE, et al. Predicting multiple facets of school functioning in pediatric chronic pain: examining

Category	Pediatrics & Child Health, #53
Primary Author	Jesus J. Ferre-Fernandez**
Secondary Authors	Sanaa Muheisen; Samuel Thompson; Ross F. Collery; Elena V. Semina
Title	Deletion of conserved non-coding elements downstream of foxc1a in zebrafish affects its expression and produces ocular phenotype
Introduction	FOXC1 is a transcription factor involved in heart, craniofacial and ocular development in vertebrates. Mutations in FOXC1, along with mutations in PITX2, cause Axenfeld-Rieger syndrome (ARS) and explain approximately half of the ARS cases. However, there is still a significant number of patients with an unknown genetic cause. Expression and activity of transcription factors involved in development are finely controlled by their regulatory elements that are often evolutionarily conserved. It has been shown that mutations in those regulatory elements could be also pathogenic. The goal of this project is to discover regulatory elements for FOXC1 using zebrafish as a vertebrate model and relate this information to human eye development and disease.
Methods	BLAST alignments involving regions surrounding human FOXC1 and two orthologous zebrafish genes foxc1a and foxc1b were carried out to identify conserved sequences. CRISPR-Cas9 was used to generate zebrafish lines carrying deletions for the identified conserved elements. The obtained lines were characterized by gross morphology examination, OCT and histology analysis. Expression of foxc1a and foxc1b genes and encoded proteins was assessed by RT-qPCR, in situ hybridization with RNAscope probes and immunohistochemistry.
Results	We identified 3 elements downstream of human FOXC1 and 1 element upstream of FOXC1 that were conserved in zebrafish foxc1a or in both foxc1a and foxc1b. The deletion of a 152kb intergenic region comprising all 3 downstream elements (ΔCED1-3) resulted in a downregulation of both the foxc1a transcript and protein in developing zebrafish embryos. Homozygous ΔCED1-3 larvae die at 1 month post fertilization and present with enlarged anterior chambers of the eye and a significant pericardial and other organs' edema. Deletion of an 82.7Kb region containing only 2 out of the 3 downstream conserved elements (ΔCED2-3) produced a similar but milder phenotype. Deletion of elements upstream either foxc1a (ΔCEU1a) and foxc1b (ΔCEU1b) did not produce a visible phenotype.
Conclusions	The identified downstream conserved elements are essential for normal foxc1a expression and their deletion results in a phenotype consistent with foxc1/FOXC1 deficiency in zebrafish and humans. Further studies of these regions in human patients is likely to explain additional ARS cases.

Category	Pediatrics & Child Health, #54
Primary Author	Chana Bushee BS
Secondary Authors	Scott Cohen, MD and Salil GInde, MD, Herma Heart Institute
Title	The Impact of a Formal Transition Program on Unplanned Hospitalizations in Adolescents and Young Adults with Congenital Heart Disease
Introduction	Currently, 90% of children living with congenital heart disease (CHD) survive into adulthood. Lack of a structured transfer process between pediatric and adult cardiology specialists can result in gaps of care that may result in higher rates of unplanned cardiac related hospitalizations (UCRH). Transition programs aide in patient education regarding health care needs and the importance of continued CHD specialized care. Our primary aim was to assess the impact of the Adult Congenital Heart Disease Transition program, established February 2016 at Children's Hospital of Wisconsin (CHW) Herma Heart Institute (HHI), on the number of UCRH of adolescents and young adults with congenital heart disease (CHD). Our secondary aim was to assess the impact of the Transition Program on the rate of transfer from a pediatric provider to an adult provider.
Methods	In February, 2016, a formal transition program was instituted at our institution, whereby all patients â‰¥ 16 years/old with CHD seen in the pediatric cardiology clinic met with an adult CHD nurse. A chart review was performed to determine the difference in cardiac-related hospitalizations in patients seen in the clinic before initiation of the transition program (2/1/2013-12/31/2015) compared with patients seen after at least 1 transition visit (2/1/2016-12/31/2018).
Results	350 CHD transition patients were compared with 303 control CHD patients seen before initiation of the transition program. There was no significant difference in age, gender, or race between the transition and control patients. The percentage of those with moderate/severe CHD complexity was also similar (80.6% vs. 80.2%, p=0.645). The rate of UCRH was significantly lower for patients that underwent at least 1 transition visit compared to the control patients (0.4%/yr vs. 1.9%/yr, p=0.008). When analyzing transition patients, there was a trend for a lower rate of unplanned cardiac-related hospitalizations after the first transition visit compared to before the first visit (0.4% vs. 3.3%, p=0.06). The rate of transfer from a pediatric to adult care provider was significantly higher in the transition patients compared to the control patients (47% vs. 38%, p=0.034).
Conclusions	A formal transition program for CHD patients seen in the pediatric cardiology clinic was associated with a lower rate of UCRH and an improved rate of transfer from pediatric to adult care providers. This study reinforces the importance of structured transition programs in patients prior to transfer to long-term adult CHD care.
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Category	Pediatrics & Child Health, #55
Primary Author	Diana Lerner, MD
Secondary Authors	Joel Friedlander, MD, Melodee Nugent, PhD, Pippa Simpson, PhD, Rachel Unteutsch, Bernadette Vitola, MD, MPH
Title	Effect of Cartoon Animation on Knowledge Retention and Anxiety in Parents and Pediatric Patients Undergoing Endoscopy, A Randomized Control Trial
Introduction	Objectives: The aim of this study is to evaluate the effectiveness of an animated video to prepare pediatric patients and their families for upper and lower endoscopy. We hypothesized that video exposure would decrease pre-procedure anxiety, increase comprehension about the procedure, and improve colonoscopy preparation quality.
Methods	Methods: An animated cartoon depicting a boy describing upper and lower endoscopy and bowel clean out instructions was developed by CI: designs Inc. with a script provided by Drs. Diana Lerner and Bernadette Vitola. The video was approved by the NASPGHAN endoscopy committee. Parents and children at least 8 years of age undergoing first-time, diagnostic upper or lower endoscopy under general anesthesia who were English-speaking were recruited at a large, tertiary referral pediatric hospital and randomized to standard consent process (N= 96) or standard consent plus video (N=100). At the time of enrollment, parents completed the State-Trait Anxiety Inventory (STAI) State and Trait forms to assess anxiety, the Rapid Estimate of Adult Literacy in Medicine short form to determine health literacy, and a knowledge comprehension questionnaire (Consent-20) to assess procedural knowledge. Children completed the STAI only. At the time of the procedure, parents completed the STAI Trait form, the Consent-20, and a satisfaction survey (Modified Group Health Association of America). Children completed the STAI Trait form and pain score. The quality of the colonoscopy prep was evaluated using the Ottawa scale by the endoscopist performing the procedure who was blinded to the group enrollment of the subject.
Results	Results: Parents in the video group had improved immediate (114.5 vs 110, p = 0.004) and delayed (113.5 vs 110, p = 0.019) procedural comprehension compared with the standard consent group (Table 1). Although there was no statistically significant difference between the groups in anxiety at either the time of enrollment or the time of the procedure, when assessing the difference in anxiety between the two time points, the parents in the video group had a significantly smaller increase in anxiety at the time of the procedure (0.5 vs 2, p = 0.036, Table 1). The Ottawa score was significantly lower in the video group indicating a better clean out (3 vs 5, p = 0.004, Table 1). There was no difference between the groups of parents regarding marital status, gender, type of insurance, or health literacy score. There were more parents aged 40-49 and fewer parents aged 50-59 in the video group (p=0.022).
Conclusions	Conclusion: Video animation education led to improved immediate and delayed procedural comprehension in parents and improved colonoscopy preparation in children. Anxiety increased from clinic to procedure time in parents without video education. There was no difference in anxiety in children, parent satisfaction, or pain scores between the groups (data not shown). Use of simple video education tools should be considered to improve procedural knowledge, improve cleanouts, & prevent increased anxiety in parents.
Reference 1	Rossi M, McClellan R, Chou L, Davis K. Informed consent for ankle fracture surgery: patient comprehension of verbal and videotaped information. Foot & ankle international. SAGE Publications; 2004;25(10):756-62.
Reference 2	Tait AR, Voepel-Lewis T, Malviya S. Do they understand? (part II): assent of children participating in clinical anesthesia and surgery research. Anesthesiology. 2003 Mar;98(3):609-14.
Reference 3	Kessels RPC. Patients' memory for medical information. JRSM. 2003.
Ancillary Materials	VIEW MY POSTER WATCH MY PRESENTATION

Category	Population Health, Disparities & Outcomes, #56
Primary Author	Benjamin Wrucke (M2)
Secondary Authors	Lauren Bauer, MD, MPH; Rebecca Bernstein, MD, MS
Title	Factors Associated with Tobacco use in Homeless Adults; A Mixed Methods Study
Introduction	Those who are homeless are four times more likely to smoke cigarettes than the general US population (Fazel et al., 2014). Previous studies have independently investigated quantitative factors associated with tobacco use in homeless adults (Arnsten et al., 2004; Baggett & Rigotti, 2010; Connor et al., 2002) and the personal experiences of homeless smokers (Okuyemi et al., 2006), but further investigation can link these two types of information. Students at the Medical College of Wisconsin have been conducting tobacco cessation educational sessions at a Milwaukee homeless shelter and service agency, and this mixed methods study investigates the interaction between quantitative factors and qualitative personal experiences associated with tobacco use in this population. The objectives of this study are to investigate factors associated with tobacco use and develop a theory for tobacco use and cessation in this population.
Methods	This study is organized into two phases. Phase I is a quantitative cross-sectional analysis of the agency's counseling clinic data bank. Phase II will be qualitative grounded theory research conducted via interviews with the agency's clients and staff and analysis of interview content. For phase I, clients of the counseling clinic completed assessments via counselor interview. Data was collected from 2014 to 2019. Logistic regression was then performed to determine predictors of smoking status.
Results	Phase I results show with significance that the odds of being a smoker decreased as education level increased. The odds of being a smoker was lower for those with state health insurance and greater for those with prior substance abuse treatment.
Conclusions	Smoking cessation programs could benefit from tailoring information to the education level of their audience; discussing health insurance, barriers to treatment, and affordable treatment options; and highlighting how smoking cessation could improve ability to quit other substances (Weinberger et al., 2017).
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Category	Population Health, Disparities & Outcomes, #57
Primary Author	Brian J. Conway**
Secondary Authors	Meghan Conroy, Ji Won Kim, David C. Brousseau
Title	Heart Disease, Advanced Age, Minority Race, and Hispanic Ethnicity Predict Mortality in COVID-19 Patients
Introduction	The number of confirmed cases and mortality rate of coronavirus disease-19 (COVID-19) remain high and continue to escalate. Additionally, there is some evidence certain comorbid conditions and patient demographics lead to worse outcomes following a COVID-19 diagnosis, but it is unclear how these variables contribute to mortality. The objective of this study was to determine whether the presence of comorbidities, like heart disease (HD) and obesity, as well as demographic factors are associated with an increased COVID-19 mortality rate in patients from the Froedtert Health System and Children's Hospital of Wisconsin.
Methods	Utilizing data from the Clinical Research Data Warehouse (CRDW) of the Clinical and Translational Science Institute (CTSI), we analyzed 8,810 patients diagnosed with COVID-19 from January 1st, 2020 to November 18th, 2020. We determined the association between HD, obesity, age group, sex, race, and ethnicity and mortality rate following COVID-19 diagnosis using a multivariate logistic regression.
Results	Increased patient mortality following COVID-19 infection was significantly associated with increased age, presence of heart disease, sex, race, and ethnicity. Through adjusted odds ratios (OR) and 95% confidence intervals (CI), we report heart disease (OR=2.85, CI= [2.11,8.83]), but not obesity (OR=1.04, CI= [0.53,3.10]), is a significant predictor of mortality in COVID-19 patients. We also demonstrate COVID-19 patients are more susceptible to death if they are age 45 or older, male, black, Asian, or Hispanic.
Conclusions	Since we show HD is a greater predictor of death than obesity in COVID-19 patients, we conclude that controlling for other comorbid conditions and patient demographics better characterizes patients' mortality risk factors. Further studies investigating multiple prevalent comorbid conditions as well as patient demographics would be a resource to clinicians in the early appropriate medical management of patients with COVID-19.

Category	Population Health, Disparities & Outcomes, #58
Primary Author	Jazzmyne A. Adams, MPH**
Secondary Authors	David R. Friedland MD PhD
Title	Defying the Inequitable Odds: OTO Clinomics
Introduction	Healthcare disparities originate from historically complex circumstances that perpetuate unequal distribution of social, political, economic, and environmental resources. For healthcare reform to address these inequities it is essential to identify barriers to care in all medical and surgical disciplines.
Methods	The Department of Otolaryngology and Communication Sciences developed OTO Clinomics, a department-wide initiative to improve clinical outcomes through comprehensive measurement of medical, social, and biological determinants of disease. This platform fosters the delivery of personalized care through standardized documentation and analysis of clinical care outcomes. More specifically, the platform employs machine learning and big data algorithms to interrogate the electronic medical record for defined determinants of health that impact an individual's care for specific otolaryngologic conditions.
Results	In the past year, we have utilized this platform to determine factors predicting access to healthcare interventions within our specialty. We now have a unique perspective of how patient geographic location, affects the rates of utilization for Otolaryngology care. We have identified the impact of income, insurance status, race, environment, and education level on receiving care for common and unique conditions within our specialty. For example, care for sinusitis is significantly impacted by the median income and college education rate of the patient's geographic residence. ZIP codes in the metropolitan area with the highest black populations had lower median income and education levels and correspondingly lower utilization rates for rhinology care. In contrast, Meniere's disease, an inner ear disorder, seems to be more prevalent in rural areas; more commonly affecting white, educated and higher income populations. Similar analyses have been performed for head and neck cancer, acoustic neuroma, otitis media, adult falls and dysphonia which have informed further studies to evaluate treatment pathways, outcomes and complication rates.
Conclusions	OTO Clinomics allows us to identify a more cohesive health profile of patients in order to provide the most precise clinical care. These data will help us to tailor interventions, develop outreach programs to vulnerable populations, and recognize barriers to care and compliance that may affect outcomes. In addition, we intend to leverage the comprehensive database of this platform as a foundation for collaborations with basic scientists to better understand biologic determinants of disease that affect clinical response and treatment. This will provide a clear path for expediting the translation of bench discovery to clinical practice. Through OTO Clinomics we aim to uphold our vision that every person deserves compassionate and quality healthcare personalized to their unique symptoms and biology.
Acknowledgements	A project funded through the Advancing a Healthier Wisconsin Endowment at the Medical College of Wisconsin

Category	Resources, Tools & Methods, #59
Primary Author	Kathryn E. K. Berlin, DO
Secondary Authors	Jeffrey A. Bispo, Briana Gruenewald, Angela F. Garza, Kathlyn E. Fletcher, MD
Title	Use of a Stoplight Communication Tool for Interprofessional Communication Correlated with a Decrease in Rapid Response Team Activations
Introduction	Effective communication is essential to optimizing patient safety. The inability to effectively communicate results in information being missed or misconstrued, especially when communicating between disciplines. Furthermore, the sheer volume of daily communications is daunting: a 2017 study found that residents were paged on average 22.4 times per day. It was our goal to have non-urgent communication occur during optimal times. Our aim was to reduce the number of interruptions both residents and nurses experienced during critical activities such as handoffs by use of our stoplight communication tool.
Methods	This QI project took place at the Clement J. Zablocki VA Medical Center (VAMC) in Milwaukee, WI during the 2019-2020 academic year on a 30-bed medical unit. Internal medicine residents and nurses on this unit were surveyed regarding communication and the information gained was used to design a “stoplight communication tool”. This tool was posted at all workstations and classified each hour of the day as red (highly critical, only emergent communication), yellow (high-traffic times, consider delaying communication), or green (go for collaboration). To evaluate intervention effectiveness, resident physician page logs obtained from our academic affiliate were analyzed using a one-way ANOVA. Communication directed to nursing was evaluated with a survey, as there was no objective way to track these communication. This survey was analyzed using two-sided t-tests. Finally, we evaluated the number of rapid response team (RRT) activations as a balancing measure. This project was reviewed by the VAMC’s IRB and met the criteria for exemption as a QI effort.
Results	The total number of average daily pages received by residents decreased during both yellow and red times. At baseline, there were 8.52 pages received during yellow times and 6.92 during red. This improved to 2.20 pages ($p<0.001$) during yellow times and 1.36 ($p<0.001$) during red. Nurses also reported decreased interruptions but the COVID-19 pandemic escalated during our second cycle: as such, nursing response to our second survey was too poor to analyze. RRT activations also decreased. During our baseline evaluation, there were 8 to 11 rapid responses on the unit for 158 to 201 discharges (average of 56.7% RRT utilizations). This decreased to 5 RRTs for 162 discharges (30.9% for Cycle 1) and further to 4 RRTs for 217 discharges (18.4% for Cycle 2).
Conclusions	Use of the stoplight communication tool reduced interruptions during key times for both residents and nurses. The rate of adjusted RRT activations on the unit decreased in a statistically significant manner. In conclusion, a stoplight communication tool can be utilized to reduce non-urgent communications between residents and nurses during busy times with a correlation in the decrease of RRT activations.
Acknowledgements	This material is based on support from the Office of Academic Affiliations and the Chief Resident in Quality and Safety program directed by the National Center for Patient Safety, Department of Veterans Affairs, and with resources and the use of facilities at Clement J. Zablocki VA Medical Center, Milwaukee, WI. The content is the responsibility of the authors alone and does not necessarily reflect the views or policies of the Department of Veterans Affairs or the United States Government.
Reference 1	Carlile N, Rhatigan JJ, Bates DW. Why do we still page each other? Examining the frequency, types and senders of pages in academic medical services. BMJ Quality & Safety. 2017;26(1):24-29.
Reference 2	Young JB, Baker AC, Boehmer JK, et al. Using NNAPPS (Nighttime Nurse and Physician Paging System) to Maximize Resident Call Efficiency within 2011 Accreditation Council for Graduate Medical Education (ACGME) work hour restrictions. J Surg Educ. 2012;69(6):819â€•825.
Reference 3	Utilization of the Rapid Response Team” from the Institute for Healthcare” Improvement. Accessed 06/09/2020
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Category	Resources, Tools & Methods, #60
Primary Author	Stephanie Dybul, MBA, RT
Secondary Authors	Michelle Back, RT, Jennifer Eklund, Beverly Gillespie, CPC, Kristin Kusnier, BS, CPC, RCC, Gary R. Seabrook, MD, Jon Mayer, MBA, CPME, William S. Rilling, MD, FSIR, Sean M. Tutton, MD, FSIR, Parag J. Patel, MD, MS, FSIR, Peter Rossi, MD, Robert A. Hieb, MD, FSIR
Title	Development of a Shared Productivity and Financial Model for Multidisciplinary Care
Introduction	Multidisciplinary approaches to patient care have been shown to improve patient outcomes. Within our current fee-for-service payment model, collaborative care is not incentivized for the majority of IR procedures, as only one physician can bill for the majority of shared services. The purpose of this study is to demonstrate that shared billing can allow reporting of productivity metrics and accurately capture shared work performed.
Methods	At our institution, we developed a model within our professional billing system to address concerns with shared procedures. Our coding staff apply "dummy modiers" to the shared CPT codes. These modiers have two purposes; to allow work relative value units (wRVUs) to be captured and divided equally between the two servicing providers for purposes of reporting physician productivity, and to allow for revenue to be identified and shared easily.
Results	In fiscal year 2019, 152 procedures (diagnostic and interventional) not eligible for a co-surgeon (-62) modier were performed in a collaborative nature between the divisions of Vascular/Interventional Radiology and Vascular and Endovascular Surgery. The "dummy modier" was used for these cases. The total wRVU collection for these procedures was 1753.2. Previously, all of these wRVUs would be attributed to a single division. With use of our modiers, each division was able to collect 876.6 wRVU from these shared procedures.
Conclusions	Strong interdisciplinary relationships are important for the survival of our specialty. To discourage internal competition and promote collaborative care, it is important to develop a model that can support the allocation of wRVUs and revenue amongst the physicians involved. With our model, each division can accurately capture the shared work performed.
Ancillary Materials	VIEW MY POSTER

Category	Resources, Tools & Methods, #61
Primary Author	Mike Tschannen**
Secondary Authors	Angela Mathison, Alyssa Jones, Honey Reddi, Raul Urrutia
Title	Advancing Precision Medicine with Basic and Translational Research Tools, Services, and Assays at GSPMC
Introduction	Multiple â€˜Omics techniques are being used to understand, prevent, detect, and treat diseases with precision. GSPMC is at the forefront of these innovative discoveries with our ability to pair cell and molecular biology techniques with NexGen sequencing. Integration and customization of NGS assays allows for mechanistic dissection of the initiation, establishment, and progression of diseases. At MCW, our goal is to allow the efficient translation of new technologies and applications to basic, translational, and clinical research, so as to address the unmet needs of patients and the research community. Here, we provide examples that highlight these activities.
Methods	GSPMC has established consultations for researchers to facilitate and ensure the focus is aligned and service products are appropriate to the hypotheses being asked. Working with investigators, we can initiate the experimental plan, customize and trouble shoot assay design, plan state-of-the-art library preparations and sequencing technologies, and prepare bioinformatic support for translating data to knowledge. By working in close collaboration with the molecular diagnostic laboratory, innovations can be methodically planned to enable translation to the clinic. All of these services are available to basic and translational researchers to ensure that Precision Medicine becomes a reality for all patients.
Results	The GSPMC has established a full spectrum work flow that include consultation and facilitation customizable per need from extraction-to-analysis sequencing services with troubleshooting and data bioinformatics support. GSPMC now extracts DNA and RNA from blood, formalin-fixed paraffin-embedded (FFPE), and fresh frozen cells or tissues. By understanding the input source material, the R&D team adjusts protocols to produce the most accurate and relevant data. Once extracted, GSPMC applies optimized methods to interrogate intact or degraded DNA through genome, exome and panel sequencing. GSPMC also provides dynamic snapshots of cellular activity at the molecular level through transcriptomic sequencing (RNAseq) and epigenomic sequencing offering reduced representation bisulfite (RRBS) and chromatin immunoprecipitation (ChIP) sequencing. Understanding and bringing knowledge to data concerning the molecular control on the cellular phenotype is supported through bioinformatic services and collaborations to analyze, interpret, and integrate these diverse data sources.
Conclusions	GSPMC’s vision is to innovate and drive cutting-edge technologies that will advance basic mechanistic understanding of disease etiology, pathophysiology, and potential therapeutics with the goal of increasing the knowledge base in translational, personalized medicine research. Using experience from a variety of projects, GSPMC will tailor assays, provide services and collaborate to address the current and future needs of researchers throughout MCW.

Category	Resources, Tools & Methods, #62
Primary Author	Angela Mathison**
Secondary Authors	Angela Mathison, Michael Tschannen, Alyssa Jones, Raul Urrutia
Title	A Focus on the Transcriptome, Assays providing an Innovative Dissection of the Cell Biology
Introduction	GSPMC strives to uncover biological knowledge from the large next generation sequencing data sets and establish innovative discoveries that have the potential to further the understanding of disease initiation, establishment, progression, and detection. We highlight here the focus and progression of transcriptional assays that can be utilized on translational and basic science research samples to uncover the mechanistic changes that result from a variety of diseases and treatments.
Methods	GSPMC continues to expand in capabilities and assay potentials for use with basic science research and always with an eye toward the translational practice of medicine. By expanding and continuing to troubleshoot tissue dissection and extraction, GSPMC now extracts DNA and RNA from blood, formalin-fixed paraffin-embedded (FFPE), and fresh frozen cells or tissues. By understanding and checking the quality of input source material, the R&D team adjusts protocols to produce the most accurate and relevant data. Through a variety of preparations, transcriptomic data can be obtained from a variety of tissues, that have been prepared and stored in a variety of manners, thus allowing researchers to continue asking questions and seeking molecular answers using rare and unique samples.
Results	GSPMC has established a full spectrum work flow that include consultation and facilitation customizable per need from extraction-to-analysis sequencing services with troubleshooting and data bioinformatics support. For transcriptomics, preparations can range from standard polyA selection, to low input template switching amplification, to selective degradation of highly abundant ribosomal RNA. As suits the needs of the investigator with consideration of the highly degraded nature of FFPE samples, RNA samples can be selectively amplified for full transcriptomic sequencing or panels of genes identified for capture and probe identification. Additionally, understanding the transcriptomics of individual cells in a mixed population of cells is the forefront of single cell transcriptomics and encompasses unique preparation methodologies. With all GSPMC services, bioinformatic support is available to collaborate, analyze, interpret, and integrate these diverse data sources.
Conclusions	GSPMC's vision is to innovate and drive cutting-edge technologies that will advance basic mechanistic understanding of disease etiology, pathophysiology, and potential therapeutics with the goal of increasing the knowledge base in translational, personalized medicine research. Using experience from a variety of projects, GSPMC will tailor assays, provide services and collaborate to address the current and future needs of researchers throughout MCW.

Category	Resources, Tools & Methods, #63
Primary Author	Mahima Vedi**
Secondary Authors	Jennifer R Smith, Harika S Nalabolu, Matthew J Hoffman, G Thomas Hayman, Shur-Jen Wang, Stanley JF Laulederkind, Mary L Kaldunski, Morgan Hill, Wendy Demos, Monika Tutaj, Jyothi Thota, Marek A Tutaj, Logan Lamers, Adam Gibson, Ketaki Thorat, Jeffrey L De Pons, Melinda R Dwinell, Anne E Kwitek
Title	Introducing Multi-Ontology Enrichment Tool (MOET): a web-based enrichment tool at the Rat Genome Database
Introduction	Gene set enrichment analysis is an approach for studying complex genomic and transcriptomic data by identifying common functional characteristics of genes based on their overrepresentation in a gene set. Most tools for enrichment analysis focus on gene, protein, and pathway annotations. The Rat Genome Database (RGD) has developed the Multi-Ontology Enrichment Tool (MOET, https://rgd.mcw.edu/rgdweb/enrichment/start.html) that generates a list of terms statistically overrepresented within the user's genes of interest leveraging multiple sets of ontology annotations. MOET provides functionality to analyze enrichment across five ontologies for all RGD species, including Rat, Mouse, Human, Bonobo, Squirrel, Dog, Pig, and Chinchilla.
Methods	MOET is available in the “Analysis Visualization” menu at the top of the RGD website, from individual RGD disease portal pages, and as one of the options in “RGD Tools” displayed wherever a list of genes is presented on the RGD website. After selecting a species and choosing an ontology, the user enters either a gene list using any of 11 identifier types or a genomic region of interest in MOET.
Results	The output includes a list of enriched terms from the specified ontology, and a graph of the number of genes annotated to each term with their corresponding p-values. The p-value displayed for each term is calculated using the Hypergeometric distribution. The output displays the p-value both with and without Bonferroni multiple test correction. In MOET, the toolbox icon at the top of the results page and “All Analysis Tools” link can be used to share the list of genes with other RGD analytical tools. The number of genes annotated to each term in the list gives one-click access to that sub-list of genes. The "Explore this Gene Set" link at the top of the popup automatically sends that sub-list back through MOET to do enrichment for that set of genes.
Conclusions	MOET’s improved features in comparison to other available ontology analysis tools are: (1) performs enrichment for Disease, Pathway, Phenotype, and ChEBI (Gene-chemical interactions) ontologies, in addition to GO; (2) freely accessible and intuitive, displays results with a few clicks in seconds; (3) seamless integration with the other RGD tools; (4) facilitates cross-species comparison and allows selection of different species to view their results on the same results page. Also, MOET leverages RGD's extensive corpus of functional annotations derived both from manual curation at RGD and imported/integrated from other databases such as Disease Ontology annotations from OMIM and ClinVar for Human, and Mammalian Phenotype annotations from Mouse Genome Informatics.
Ancillary Materials	VIEW MY POSTER WATCH MY PRESENTATION

Category	Surgery, #64
Primary Author	Brooke Olson, BS
Secondary Authors	Scott Van Valin, MD; Xue-Cheng Liu, MD, PhD
Title	Idiopathic Congenital Talipes Equinovarus in Wisconsin Newborns: Incidence and Associated Risk Factors
Introduction	Clubfoot, also known as idiopathic congenital talipes equinovarus (ICTE), is one of the most common pediatric deformities affecting 1 to 2 in every 1,000 live births. While an effective method of treatment has been established for this deformity, the etiology remains unknown. The objective of this study serves to provide the first analysis of incidence of clubfoot diagnoses over a defined period of time in the most populous region of Wisconsin. This study will also provide an analysis of certain risk factors associated with the diagnosis of clubfoot, comparing results to current published literature.
Methods	We performed a retrospective study on children treated for clubfoot at Children's Wisconsin from January 1, 2004 to December 31, 2018. Epic database was systemically searched for all clubfoot diagnoses encountered at Children's Wisconsin. Medical records of over 1,300 children were reviewed. To be eligible for inclusion in this study, patients were required to be born in Wisconsin. A total of 760 patients fit the required population criteria and were included in this study for review of risk factors. Risk factor data collected included date of birth, sex, zip code and county of birth, ethnicity/race, birth weight (kg), unilateral vs. bilateral, pre-term vs. term delivery, and family history (Y/N). Excel was used to graphically analyze the collected risk factor data. The incidence of clubfoot births was analyzed via a linear trend comparing the year to annual birth rate for the corresponding year. Incidence of clubfoot births was analyzed for each county in the southeastern region as well as the southeastern region as a whole.
Results	This study included a population of 760 clubfoot patients with the southeastern region of Wisconsin containing the largest patient population of 523 patients. Milwaukee was the county with the largest population of 269 patients. Linear trends of Milwaukee county and the southeastern region of Wisconsin showed a statistically significant increase in clubfoot births over the time period of 2004-2017 with P values <0.001. There were a total of 497 males (65%) and 263 females (35%). Laterality, birthweight, and term vs. pre-term birth data were insignificant. A majority of our population was Non-Hispanic/Latino (77%) and white (72%). A total of 414 patients (55%) had no family history of clubfoot, 130 patients (17%) had a positive family history of clubfoot, and 216 patients (28%) family history was unknown.
Conclusions	In this large study of children diagnosed with clubfoot, areas with high population showed a statistically significant increase in the number of children affected over time with a low evidence of family history. This study provides further insight into the possible etiology of clubfoot being related to an exogenous, environmental factor.
Ancillary Materials	VIEW MY POSTER

Category	Surgery, #65
Primary Author	Christina Feller BS, BA
Secondary Authors	Dr. Grant P. Sinson, MD
Title	Improving the Quality of Care surrounding Spinal Surgeries through DRG and Risk Model Analysis
Introduction	Documentation of care delivered to surgical patients is a universally important aspect of medicine. Clinical documentation of surgeries alters the coding accuracy and validity of Diagnosis Related Groups (DRGs) and comorbidity (CC) or major comorbidity (MCC). These factors are used to code a final Case Mix Index (CMIs) and Vizient quality metrics which in turn impacts physician profiling, medical center profiling, quality reporting, and revenue captured. Improvements in clinical documentation, specifically in spinal surgery, will lead to an increased CMI, improved quality metrics, and more accurate representation of hospital care.
Methods	Vizient software will be used to analyze DRGs, costs, LOSexp,, mortalityexp, and CMIs between physicians performing spinal surgeries at Froedtert Hospital (FH) as well as against other academic hospitals in Vizient's top 10 rank for quality. Chart reviews for all spinal procedures taken place in 2019 will be done to determine if there are additional variables missed by the documenting physician or coder. Based on any new variables found, quality variables will be re-calculated to compare to the original data pull. Within the spinal surgery service line, procedures are separated into one of five different DRGs (13, 146, 147, 148, 160, 171).
Results	FH performed 341 total spinal surgery cases from January 2019 to October 2019 with an average CMI of 3.683 and LOSexp of 4.48 days. 16 different surgeons performed these cases. Vizient ranked FH 12th overall (62.38%) in quality against other academic hospitals. Scores are based on 5 different domains: mortality, efficiency, safety, effectiveness, and patient centeredness. From chart reviews of spinal procedures performed in 2019, at least one new variable coding for mortality index and/or LOS was found in 28% of cases. An average of 1 new variable (0.868) was found coding for mortality and an average of 3 new variables were found coding for LOS. In one case, when these new variables were included in calculating expected LOS, the LOSexp increased by 4 days.
Conclusions	Inadequate documentation that includes specific variables encompassed within a DRG leads to misrepresentation of the quality of patient care being provided. In turn, this leads to a lower quality ranking. Physicians may not be aware of the specific variables coders are looking for and thus, may not document them properly while admitting a patient. With more information and a new Quality Improvement app, physicians will be better able to accurately document their patients and improve quality ranking scores overall for the hospital.
Ancillary Materials	VIEW MY POSTER WATCH MY PRESENTATION

Category	Surgery, #66
Primary Author	Nitesh Alluri
Secondary Authors	Caitlin Patten
Title	Associations Between Breast Infections and Future Core Needle Biopsy Rates
Introduction	Patients who are diagnosed with mastitis and breast abscesses will sometimes require an additional future core needle biopsy after the initial infection has resolved. Our retrospective study attempted to gauge the proportion of patients who received such a biopsy and the proportion of biopsies which showed malignant tissue.
Methods	The study primarily involved Epic chart data through Froedtert's database, and the review ran from 5/28/20 through 10/1/20. Out of an initial patient list of approximately 2,120 the final patient list that was relevant to our study came to 313, as male patients, those with a pre-existing history of breast history, granulomatous mastitis and duplicate results were all excluded. o Cumulative incidence curves were generated to characterize the time to biopsy and a gray's test was performed on those curves to assess for a difference between abscess and mastitis group. Kaplan-Meier survival plots were generated to assess the time to last follow-up or death and a Logrank test was done to assess for a difference between abscess and mastitis groups.
Results	91.7% of our patient sample did not receive a CNB and 92.6% of the CNBs which were performed did not show malignant tissue. 68% of the CNBs were performed on the same side of the breast as in the initial diagnosis. The time to biopsy at 125 months after initial diagnosis is much higher at 20.1% and 60.7% for abscess and mastitis respectively when looking at just the time the patient has an infection. If you consider the time they are non-infectious, their likelihood of biopsy is much lower at 6.23% and 24.6% for abscess and mastitis patients, respectively, at 125 months after the initial diagnosis.
Conclusions	Our study has indicated that when patients present with an abscess or mastitis, they are unlikely to receive a core needle biopsy in the future and the few who do are unlikely to show malignant pathology. Additionally, among the patients who will not need a CNB in the future, the majority will have their last follow-up related to the breast infection within 10 months of their initial presentation. Given that most patients in our had resolved infection quickly, their likelihood of biopsy even several years after initial diagnosis is relatively low. However, for patients who are experiencing long infection times with recurrent issues and complications, the likelihood of a biopsy in the future is significantly higher. There also appears to be a potential association between the side of the breast affected by the initial infection and the side which eventually receives a CNB, as the majority of the biopsies in this study supported such an association. Interestingly, this potential association seemed to be stronger for the abscess group than for the mastitis group, which could be an effect of the generally increased complications associated with an abscess.
Ancillary Materials	VIEW MY POSTER WATCH MY PRESENTATION

Category	Surgery, #67
Primary Author	Kent J Peterson
Secondary Authors	D. C. Eastwood, A. Szabo, K.Y. Hu, T. J. Ridolfi, K. A. Ludwig, and C. Y. Peterson
Title	Evaluation of the Rothman Index in Predicting 30-Day Readmission after Colon and Rectal Resections
Introduction	The patient, surgical team, and health system are all adversely impacted by inpatient readmissions, yet previous studies have shown they are challenging to predict. The Rothman Index (RI) is a health indicator score based on latest vitals, laboratory values, and nursing assessments that generates a real-time rating of the patient's condition. Although originally designed as an early alert system for inpatient adverse events, the RI has shown promising associations with readmissions in selected populations, such as orthopedics, neurosurgery, and critical care. This study aims to evaluate the utility of the RI in predicting readmissions following colorectal resections.
Methods	A single institution retrospective cohort study was performed. The electronic medical record was queried for patients having a colectomy or proctectomy between 7/1/2018 and 8/1/2020. Patient demographics, surgical factors, and post-operative measures were collected, including last RI, lowest RI, and a changing RI scores within 24 hours of discharge. Unplanned readmissions in 30 days were assessed. A prediction model was created using area under the receiver operating curves (AUC) and forward stepwise selection. Statistically and clinically significant covariates were carried into multivariable regression models to evaluate the association between RI and readmissions.
Results	Of the 427 included patients, 53 (12.4%) were readmitted within a mean of 11.6 days (+/- 9.2) from discharge. On univariate analysis, the readmitted cohort more often were older (56.8 vs 61.9 years, p=0.048), had longer length of stay (11.9 vs. 5.5 days, p<.001), had urgent/emergency surgery (24% vs. 9.3%, p=.001), and required intensive care unit stay (35.4% vs. 9.8%, p<.001). Last RI score alone had the best AUC (AUC=0.91). The statistical optimum RI for predicting readmission was 74, which is associated with a 13.7% risk of readmission, sensitivity of 83.3%, and specificity of 89.5%. Forward selection resulted in a model including Last RI and Decreasing RI, however Decreasing RI only slightly improved the Last RI model (AUC=0.92). After controlling for covariates in multivariate regression analysis, Last RI (odds ratio [OR] 0.76 [0.70-0.82], p<0.001) and Lowest RI (OR 0.96 [0.94-0.99], p=0.003) were both significantly associated with readmission, as well as a Decreasing RI (OR 16.83 [4.19-67.65], p<0.001) or Increasing RI (OR 0.32 [0.11-0.95], p=0.04) within 24 hours of discharge.
Conclusions	We found that Last RI at time of discharge is strongly associated with risk of readmission in 30 days, which is minimally improved by adding Decreasing RI (AUC=0.92). The RI score of 74 had the best prediction with a risk of readmission of 13.7%. The RI represents an intriguing and unique tool to assess readiness for discharge and risk of readmission. Further studies are needed to evaluate the validity and generalizability of this predictor.
Ancillary Materials	WATCH MY PRESENTATION

Category	Surgery, #68
Primary Author	Stephanie A. Armstrong
Secondary Authors	Burak Ozaydin, Walid Elshamy, and Mustafa K. Baskaya
Title	Outcomes of transcallosal microsurgical versus endoscopic third ventricular colloid cyst resections
Introduction	The interhemispheric and endoscopic approaches to colloid cyst resection are both established techniques, with the endoscopic approach becoming more popularized as a minimal invasive alternative. It remains to be determined which technique is more favorable by means of complications, recurrence rates, procedure-related morbidity and long-term outcome measures.
Methods	The authors performed a retrospective review of 33 patients who underwent a primary third ventricle colloid cyst resection between the years 2005-2018. Transcallosal and endoscopic approaches were used in 13 and 20 cases, respectively.
Results	In the total 33 reviewed cases (15 males, 17 females), the average patient age between microsurgical and endoscopic approaches were 38.1 and 36.3 years (p=0.38). Average follow-up was 48.7 days and 41 days (p=0.28). There was no significant difference in cyst sizes (12.0 vs 11.9, p=0.47), recurrence (9.1% vs 15.0%, p= 0.32), short term memory loss (8.3% and 26.3%, p=0.11), and postoperative bleeding (8.3% vs 15.8%, p=0.28). Readmission, recurrence, infection, and length of stay were not significant differences. The transcallosal approach did have a higher rate of gross total resection (91.7 vs 63.2%, p=0.04), along with a higher rate of postoperative seizures (18.1% vs 0%, p=0.02).
Conclusions	Colloid cyst resections using the transcallosal versus endoscopic approaches showed similar patient morbidity, mortality, recurrence, and complication rates. Further MR imaging analysis of gliosis and volume loss in the surgical trajectory between these approaches could further distinguish a favored method of colloid cyst resection.
Ancillary Materials	VIEW MY POSTER

Category	Surgery, #69
Primary Author	Stephanie Armstrong
Secondary Authors	Amgad S. Hanna
Title	Muscle anomalies in the wrist and associated compression syndromes
Introduction	Wrist muscle variation has been reported in association with compression syndromes and has been found incidentally during imaging, surgery, or cadaveric dissections. While often asymptomatic, patients with these muscles may present with symptoms of carpal or ulnar tunnel syndrome and require surgical intervention. Knowledge of muscular anomalies in the wrist can guide surgical dissection and resection.
Methods	The authors report on two cases of anomalous muscles of the wrist: 63-year-old patient redo carpal tunnel surgery with resection of a reverse palmaris longus and an accessory abductor digiti minimi (ADM) in an 89-year-old cadaveric dissection. A review of the volar wrist muscle variations reported in the literature was conducted.
Results	The reverse palmaris longus was tendinous until the distal third of the radius where a hypertrophied muscular belly laid on top of the median nerve. The cadaveric accessory ADM, originating from the antebrachial fascia, created the roof of Guyon's canal by the muscular portion of the accessory ADM wrapping around the distal portion of the flexor digitorum superficialis before crossing medial to the pisiform bone and inserting into the hypothenar eminence. Reported cases of other muscle variants included palmaris profundus, flexor digitorum superficialis indicis, lumbricals, flexor carpi radialis, flexor digiti minimi, opponens digiti minimi, an additional hypothenar muscle and flexor carpi ulnaris.
Conclusions	These volar wrist muscle anomalies may be associated with ulnar and median nerve compression and respective symptoms. While we report two cases of the most common muscle variations, the palmaris longus (reversed), and the abductor digiti minimi, several additional muscle variants have been appreciated in the volar wrist in the literature. In certain cases of compression syndrome and a concomitant aberrant muscle, resection may alleviate symptoms. Understanding these anomalies is important for diagnosis, treatment and surgical considerations. It also raises the question whether minimally-invasive techniques, like endoscopic-assisted carpal tunnel release, may miss such anomalies, and cause failure of improvement or recurrence of symptoms.
Ancillary Materials	VIEW MY POSTER

Category	Surgery, #70
Primary Author	Alexander Kerschner
Secondary Authors	David King, MD; Carole Vetter, MD
Title	Clinical Outcomes of Diffuse PVNS of the Knee Following Arthroscopic Complete Synovectomy +/- Posterior Open Resection
Introduction	Diffuse pigmented villonodular synovitis (DPVNS) is a disease characterized by the benign abnormal growth of the synovial membrane, causing swelling and inflammation of the joint. There is currently no gold standard in the treatment of DPVNS, and recurrence rates after treatment present a significant health challenge. This study seeks to compare the recurrence rates and functional outcomes of patients who have undergone two treatments: anterior arthroscopic synovectomy versus combined anterior arthroscopic synovectomy and posterior open synovectomy.
Methods	41 patients were identified with surgery to treat DPVNS in the knee between the years 2003-2018. Patients were grouped by their initial procedure type (anterior arthroscopic synovectomy or combined anterior arthroscopic and posterior open synovectomy) and tracked for follow up visits, MRIs, and additional procedures; additional knee functionality measures (Lysholm Scoring Scale) were collected by phone. Outcomes compared between the two groups include recurrence rates, Lysholm scores, and number of recurrences.
Results	24 patients (58.5%) had a recurrence [16 (57.1%) arthroscopic patients and 8 (61.5%) combined procedure patients]; half of these (n=12) had multiple recurrences. The difference between the recurrence rates was not statistically significant calculated using a chi square test (p=0.81). The mean Lysholm Score for the combined procedure patients (75.4) exceeded the mean score for the arthroscopic patients (68.1), but this difference is not statistically significant calculated by a two-sample t test (p=0.25). Patients with prior surgery to treat DPVNS or other knee pathology had higher rates of initial recurrence than those without a prior surgery [71.4% vs. 50.0% for combined, 75.0% vs. 50.0% for arthroscopic, 73.3% vs. 50.0% overall (p=0.32)].
Conclusions	This study provides no evidence that the combined anterior arthroscopic and posterior open procedure harms knee function more than an only arthroscopic procedure does. There is no statistical evidence that the recurrence rates differ between treatment methods. The recurrence rate is higher among patients with prior knee surgeries, but the difference is not statistically significant.
Acknowledgements	I would like to thank the Medical College of Wisconsin Department of Orthopaedic Surgery for helping establish and assist with this project.
Ancillary Materials	VIEW MY POSTER

Category	Surgery, #71
Primary Author	Audun Saterbak
Secondary Authors	Saurabh Mehta, MD; Dara Mickshl, PA; Steven Grindel, MD
Title	Impact of surgical technique on outcomes in reverse shoulder arthroplasty
Introduction	Reverse shoulder arthroplasty (RSA) is becoming more popular as an option for shoulder replacement but has come with the noted downside of scapular notching. Advancements in surgical technique and component design have been made to minimize scapular notching but our knowledge of their clinical effect on range of motion is limited to biomechanical and cadaveric studies. This study aims to investigate these effects, as well as the role of BMI, on patient ROM (forward flexion and internal rotation) in 2-year follow-up.
Methods	A retrospective chart review was conducted to investigate a population of patients who received RSA between 2009 and 2019 (N=300). Data was collected for internal rotation and forward flexion at pre-op, 6-month, 1-year, and 2-year timepoints. Data was analyzed using linear-mixed models to control for baseline function prior to surgery.
Results	Inferior glenosphere overhang had significant a significant difference in forward flexion in 2-year follow-up (P=0.01) but not internal rotation. Repair of the subscapularis during surgery was also observed to significantly improve forward flexion (P=0.04), but not internal rotation. Smaller sized glenospheres had a significant improvement in internal rotation (P=0.02) but not forward flexion. BMI, glenoid lateralization, and humeral retroversion had no significant differences with regards to forward flexion and internal rotation.
Conclusions	We were unable to verify the findings of previous biomechanical studies based on our patient population. Our data suggests that inferior glenosphere overhang may be the best operative technique to reduce scapular notching because of the added benefit of increasing range of motion. Smaller glenospheres and subscapularis repair will not lower the incidence of scapular notching but may be beneficial when attempting to maximize patient function. All other methods to prevent scapular notching were not observed to produce any significant improvement in range of motion.
Ancillary Materials	VIEW MY POSTER WATCH MY PRESENTATION

Category	Surgery, #72
Primary Author	Malek Ayoub
Secondary Authors	Carrie Y. Peterson; Emily Hetzel; Siddhartha Singh; Jon C Gould
Title	The Road Less Traveled - Is Hospital Distance from Home a Risk Factor for Post-Surgical Readmissions?
Introduction	Distance traveled for surgery from home is a potential risk for readmission. We hypothesized that patients are more likely to be readmitted within 30 days if they live more than 50 miles away from the index hospital.
Methods	A retrospective chart review using the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) data sets from 2017 to 2018 were used to identify patients who underwent one of 8 procedures at an academic medical center. Data was pulled from our local NSQIP database. Distance traveled from home was calculated based on zip code using the geodistance function in SAS statistical package version 9.4.
Results	A total of 1,722 patients were included. There were 113 (6.6%) readmissions. Patients were less likely to travel more than 50 miles for appendectomy, ventral hernia repair, bariatric surgery, or colectomy ($p<0.001$). Patients were more likely to travel more than 50 miles for hepatectomy, Whipple, distal pancreatectomy, and proctectomy ($p<0.001$). Multivariate logistic regression identified distance traveled and time of travel as the only 2 variables independently associated with readmission. For every additional 10 miles traveled from home, the probability of readmission increased by 3% after adjusting for patient characteristics, comorbidities, procedure performed, and postoperative complications.
Conclusions	The further patients travel from home, the more likely they are to be readmitted within 30 days. Patients are more likely to travel great distances for complex procedures. Targeted readmission prevention strategies may be needed in patients who travel from great distances for complex procedures.
Acknowledgements	I would like to thank the biostatistics department for their help during this project. I would like to specially thank my mentor Dr. Gould for all of his help and support.
Ancillary Materials	VIEW MY POSTER

Category	Technology, Imaging & Engineering, #73
Primary Author	Karthik Somasundaram, PhD
Secondary Authors	Frank A. Pintar, PhD
Title	Intervertebral Foramen Narrowing under Compressive loads
Introduction	Lumbar spine fractures occur in military environments, falls, and vehicle crashes. Each event encompasses pelvis acceleration/deceleration contributing to compressive loads as force transmitted through the pelvis compress the lumbar spine against the torso mass, leading to tissue deformation and injury occurs when local deformation exceeds injury tolerance. Injury to the lumbar region is of particular concern since the spinal cord, associated nerve roots, and the cauda equina can also be injured, resulting in a broad range of clinical outcomes. Even in the absence of severe vertebral body injury, persistent back and radicular pain may persist. The clinical evidence of the effect of vertebral compression fracture on the intervertebral foramen (IVF) parameters, however, is relatively sparce. This study evaluates IVF measurements associated with vertebral body fracture after traumatic axial loading.
Methods	A series of 30 isolated human cadaver lumbar spines underwent vertical dynamic loading using a drop tower. Axial CT scan was performed on the specimens, before and after the impact. Foraminal height (IVF Ht) and posterior disc height (PD Ht) were measured. Fractures were graded for presumed clinical significance using Abbreviated Injury Scaling (AIS) 2015 (AAAM 2016) scoring. Statistical analysis was done using one sample t-test with $p < 0.05$.
Results	There was a significant decrease ($p<0.05$) in the post-test IVF measurements compared to the pre-test. Furthermore, 45% of the total 22 less-severe cases (AIS2) and 88% of the total 8 more-severe cases (AIS 3) had IVF values below the clinical literature reported thresholds (IVF_Ht < 15 mm and PD_Ht < 4mm), indicating likely occurrence of foraminal stenosis.
Conclusions	This preliminary study provides a comparison between the vertebral body fracture scored using AIS coding, which is based on anatomy of the vertebral body and the IVF measurements, indicative of likely occurrence of nerve root compromise, often resulting in motor weakness, sensory loss, or radicular pain. Additionally, results underscore the need to assess foraminal geometry in low severity compression fractures of the lumbar spine from vertical dynamic loading
Ancillary Materials	VIEW MY POSTER

Category	Technology, Imaging & Engineering, #74
Primary Author	Jason W. Sidabras, PhD
Title	Beyond structure: Investigating paramagnetic states in protein crystals of nano-liter volumes
Introduction	Nature's inclusion of metals and metallo-cofactors in enzymes has led to the ability to perform very complex catalytic functions, such as, electron transfer/transport, nitrogen fixation, and biological hydrogen production, which are difficult to achieve with organic radical chemistry. Metallo-enzymes often employ first-row transition metals (Mn, Fe, Ni, Cu, V, etc.) in the active site. In order to fully understand the chemistry evolving within these enzymes, structural studies must be complemented with kinetic, spectroscopic, and computational studies. Synchrotron-based X-ray crystallography diffraction provides high-resolution structural snapshots of metallo-enzymes at different equilibrium states and can be used to distinguish small changes of the atomic structure as an enzyme is stepped through the catalytic cycle. The catalytic cycle of redox enzymes often contains paramagnetic intermediates that can be studied using electron paramagnetic resonance (EPR) spectroscopy. In combination with X-ray crystallography, the magnetic-interaction tensors obtained from single-crystal EPR experiments can be directly related to the protein geometry. From such studies, a wealth of information on the catalytic mechanism of the enzyme can be obtained. However, many protein crystals used in X-ray crystallography are of dimensions in the 50-300 μm range and, as such, are too small to be studied using commercial EPR instrumentation.
Methods	To study these limited sample volumes, new technical advances had to be developed. Here, I present a novel microwave resonant structure, the self-resonant micro-helix, for nanoliter samples that can be implemented in a commercial X-band (nominally, 9.5 GHz) EPR spectrometer. The use of finite-element modelling of microwave structures aided the design of the structure along with the initial comparison to commercial resonant probes. The micro-helix is fabricated by hand with 6-7 windings and is placed on a PC Board to couple the resonant probe the instrumentation. The protein crystal is placed in a 0.3 mm inner diameter, 0.4 mm outer diameter capillary and the whole probe head is rotated to obtain the series of angle dependent EPR spectra.
Results	The micro-helix is used in a first study with a 0.3×0.1×0.1 mm^3 (3 nL) single crystal of [FeFe]-hydrogenase from *Chlostridium pasteurianum* (CpI) in the Hox state that has enabled the determination of the full g-tensor within the molecular frame of the active site. The g-tensor is then used to validate quantum chemical calculations. Additionally, advanced pulsed EPR spectroscopy could be collected from the same protein single crystal, giving insight into the ^{14}N hyperfine and quadrupole coupling of coordinated ligands.
Conclusions	This work opens up, for the first time, the possibility of using advanced EPR techniques to study protein single crystals of dimensions typical for X-ray crystallography. Further applications of the new setup will be discussed.
Acknowledgements	This work was funded by the European Union Horizon 2020 Marie Skłodowska-Curie Fellowship (Act-EPR; No. 745702) and the Max Planck Society.
Ancillary Materials	VIEW MY POSTER

Category	Technology, Imaging & Engineering, #75
Primary Author	Mohammad Zarenia, PhD
Secondary Authors	Volkan Emre Arpinar, Andrew S. Nencka, L. Tugan Muftuler, and Kevin M. Koch
Title	Kinematic MRI Tracking of Wrist Carpal Bones
Introduction	A particularly challenging image registration problem is the mapping of a single or few 2D frames to a given volumetric (3D) reference image [1]. Here, this challenging problem is tackled in the context of kinematic sub-joint bone imaging, where only few moving frames (forming a slab structure) are available at each dynamic position [2]. In this study, a novel 4D MRI acquisition of the wrist is described and deployed to perform kinematic tracking of individual carpal bones during unconstrained wrist movement. In this paradigm, the acquired moving slab frames are registered to a high-resolution complete static volume that is used to define reference coordinates for kinematic tracking.
Methods	MRI: Imaging data were collected on a GE Premier 3T MRI scanner using a 16 channel large flex coil were used to capture dynamic and static images of the wrist. A healthy test subject was recruited into a locally approved IRB protocol and provided written consent to participate. The subject's arm was fixed with padding to give necessary range of motion for required tasks (i.e. ulanr-radial deviation in this feasibility study). No motion constraints were utilized. Instead, visual cues were used to pace the motion and the subject was trained prior to the exam using the same visual cues. Static fixed images were acquired using a 3D SPGR sequence with 0.6mm isotropic voxel with acquisition matrix size of 256x256x76. Other acquisition parameters were TE=1.7ms, TR=5.3ms, FA=10 degree , NEX=1, BW/Pixel=417Hz. An additional zero-echo time acquisition of identical resolution was acquired for future potential use in tracking cortical bone structures. Finally, 32 dynamic volumes with temporal resolution of 2.8s were acquired using 3D SPGR series with 0.78x0.78x2.5mm voxel size with 128x128x6 acquisition matrix size. The other acquisition parameters were TE=1.2ms, TR=4ms, FA=10 degree , NEX=1, BW/Pixel=977Hz. The visual guidance utilized to direct subject motion indicated 3 cycles of motion in the 90 second acquisition. This rate of motion was found to cause minimal motion artifacts in the described dynamic 3D acquisition. Registration: A novel approach to register sparse moving frames of carpal bones with the high-resolution MRI fixed volumes was developed. This model works on the boundary point cloud of segmented carpal bones, applies a rigid transformation, and minimizes a cost function matching the points at the boundaries. 6 degrees of freedom (DOF) rigid-body registration was applied. The fixed, F and moving sub-volumes (slabs), M , were transformed into discrete points of their boundaries and used to minimize the objective function O=F(x, y, z)-M(x'+Xc, y'+Yc, z'), where(x, y, z)are boundary points at a transferred/rotated position. (x', y', z') denote boundary points of the moving slab. Shifting x- and y-coordinates by the difference between the in-plane center of the fixed and the moving images (Xc, Yc), bypasses the search on the transfer degrees along x and y and results in a rapid registration approach.
Results	Using the dynamic registration of the static 3D volumes, a wide variety of metrics can be extracted and utilized for kinematic profiling. In this proof-of-concept demonstration, the kinematics of the Scaphoid-Lunate (SL) interval during an ulnar-radial deviation was investigated. During the 32 MRI cycle positions, volunteers were asked to move their wrist three times from a complete ulnar/radial deviation process. Figure 1 shows the resulting profiles of (a) SL interval and (b) SL center of mass distance. The results in (a) illustrate two points with a gap of ~2 mm (dashed line) at the static position (using high-resolution images and accounting for the cortical bone gap in the SPGR image contrast). This statically-defined gap is then navigated using the registered 3D volumes. In this analysis, an error estimate is also performed by registering artificial moving frames (with moving parameters estimated from real data) to the fixed volumes. The performance of the developed registration approach is visualized in Fig. 2 for one motion cycle. The black solid lines depict the boundaries of the moving frames, which are well-mapped to the 3D high-resolution volume. Figure 3 compares our results for the SL-interval kinematics with those obtained using the well-known and utilized registration software package ANTs [3]. While ANTs is accepted by the MRI community for efficient volume-to-volume registration problems, our results show that for our particular case of slab-to-volume registration, its accuracy is not enough to properly obtain the desired kinematic metric tracking of wrist carpal bones.
Conclusions	Through the use of an advanced 4D MRI acquisition technique and a novel boundary-based slab-to-volume registration approach, these results have demonstrated the feasibility of kinematic metric tracking of unconstrained wrist motion. In this demonstration study, sample kinematic profiling the scaphoid-lunate gap has been presented. Many more metrics across several more wrist motions can be tracked in similar fashion. Future work will continue to deploy these new technologies to explore more complete kinematic tracking and profiling of unconstrained wrist motion.
Acknowledgements	This study was supported by NIH R21AR075327. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.
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Reference 2	Foster B H, Shaw C B, et al. A principal component analysis-based framework for statistical modeling of bone displacement during wrist maneuvers. Journal of Biomechanics 2019; pages 1-9.
Reference 3	Avants B, Tustison N J, et al. A reproducible evaluation of ANTs similarity metric performance in brain image registration. Neuroimage 2011; 54(3):2033-2044.
Ancillary Materials	VIEW CORRESPONDING FIGURES

Category	Technology, Imaging & Engineering, #76
Primary Author	Sara Principi
Secondary Authors	Yonggang Lu, Yu Liu, Adam Wang, Alex Maslowski, Todd Wareing, Taly Gilat-Schmidt
Title	Experimental validation of a deterministic linear Boltzmann transport equation solver for rapid CT dose map generation
Introduction	The risk of inducing cancer to patients undergoing CT examinations has motivated efforts for CT dose reduction and CT dose monitoring, especially among pediatric population. The method investigated in this study is Acuros CTD (Varian Medical Systems, Palo Alto, CA), a deterministic linear Boltzmann transport equation solver aimed at generating rapid and reliable dose maps for CT applications. The present study aims at experimentally validating Acuros against measurements performed on clinical CT scanners, using physical anthropomorphic phantoms that simulate pediatric patients.
Methods	The study consisted of: (1) the acquisition of dose measurements on a physical CT scanner through thermoluminescent dosimetry chips (TLDs). The TLDs were located in selected organs' measurement points, such as stomach, liver, lungs, heart, and ribs, inside the pediatric anthropomorphic phantoms, for several examination protocols; (2) the modeling in the Acuros platform of the measurement set up, which includes the modeling of the CT scanner and of the anthropomorphic phantoms. The TLD chips were contoured in the phantom models as sensitive cylindrical volumes to provide dose estimates.
Results	The differences of the measured and estimated doses, in terms of absolute % errors, were within 10% for most measurement points. In few cases the absolute error increased to 13%, especially for TLDs located at the ribs. This may be due to the fact that TLDs at ribs' locations were at the interface between bone, lung, and soft tissue, where dose calculations are more challenging, especially for deterministic solvers. Root-mean-squared-error (RMSE) across all TLDs locations for all configurations were in the range 4% - 7%. Acuros, running on a GTX 1080 GPU, provided dose estimates in a time range of few seconds up to two minutes.
Conclusions	An overall good agreement between measurements and simulations is achieved, with average RMSE of 6% among all cases, and Acuros run time down to a few seconds. The proposed deterministic tool has then the potential to be a near real-time individualized dosimetry monitoring system for CT applications, providing patient-specific organ dose estimates. This would overcome the time constraint and the inaccuracy of the methods currently employed for dose monitoring in clinical practice.
Ancillary Materials	WATCH MY PRESENTATION

Category	Other Clinical Specialties, #77
Primary Author	Tyler Compton
Secondary Authors	Janine Struve, John Krolikowski, James T. Ninomiya, Dorothee Weihrauch
Title	Non-thermal infrared light demonstrates a protective effect in a murine hindlimb model of ischemia-reperfusion injury
Introduction	Ischemia reperfusion injury results in tissue damage and necrosis from acute inflammatory processes following a period of ischemia and subsequent restoration of blood supply. In skeletal muscle, ischemia reduces the aerobic energy capacity of muscle cells, leading to adverse biochemical alterations and an inflammatory response. Reperfusion then leads to the recruitment of macrophages and PMNs causing further inflammation and muscle damage. Chemokines involved in the process include CXCL1, a chemokine with neutrophil chemoattractant properties and CXCL5, a small chemokine that stimulates the chemotaxis of neutrophils that promote angiogenesis. The main macrophages involved in such pro-inflammatory responses are of the M1 phenotype, while M2 macrophages are predominantly anti-inflammatory and play a role in the healing response. Previous studies have demonstrated that exposure to non-thermal infrared (NIR) light increases angiogenesis in a mouse hindlimb model. Therefore, we hypothesized that exposure to NIR light during a period of ischemia decreases tissue damage in part by a decrease in the secretion of chemoattractant proteins along with phenotypic switching of tissue macrophages from an M1 to a protective M2 phenotype.
Methods	Eight-week-old, male C57/Bl6 mice underwent unilateral tourniquet-induced hindlimb ischemia for 3 hours followed by a period of reperfusion for either 15 or 30 minutes. The tourniquet consisted of surgical suture threaded through a 22-gauge needle cap to create a snare, which was clamped with a hemostat at the hip joint to induce ischemia. The light source consisted of an array of LED with a heat sink to minimize any thermal heating of the tissue (NIR Technologies, Brookfield, WI). The mice were randomly selected into 3 groups. Group 1 (n=8) underwent ischemia-reperfusion (IR) injury followed by reperfusion for 30 minutes. Group 2 (n=8) underwent ischemia-reperfusion (IR) injury followed by reperfusion for 15 minutes. Of each group, half of the mice (n=4) received no light treatment (No Light 15 min, No Light 30 min), while the remaining 4 mice received light treatment from a 670 nm LED light source (NIR 15 min, NIR 30 min) with an exposure to 50 mW/cm2 light for 5 minutes upon tourniquet application and at 1 and 2 hours during the ischemic period for a total exposure of 45 Joules (50 mW/cm2 x 300 seconds x 3 exposures). Control animals (n=8) were placed under anesthesia for 3 hours and did not undergo IR injury. Laser doppler flow imaging was performed on all mice for noninvasive measurement of blood flow to confirm ischemia. Flow data was expressed as the ratio of mean intensity between the ischemic limb and the contra-lateral control. After reperfusion, the mice were sacrificed, and the quadriceps and gastrocnemius were harvested distal to the tourniquet. Gastrocnemius samples were homogenized underwent ELISA analysis for neutrophil chemoattractants CXCL1 and CXCL5. Quadriceps samples homogenized and underwent immunoprecipation and Western Blot analysis of macrophage phenotypic markers CD68 (M1) and CD206 (M2). The macrophage markers were then normalized to the pan-macrophage marker CD14. Statistical analysis was performed using 2-tailed unpaired t-test and one-way ANOVA, with an alpha value of pâ‰¤0.05 being assessed as significant.
Results	Laser doppler imaging verified that the tourniquet was effective at inducing ischemia along with a return in blood flow to near baseline for both NIR treated and non-light treated hindlimbs. Thermal imaging also demonstrated there was no heating of the limbs from the LED arrays, suggesting that the observed effects were attributable to NIR light and not thermal heating. ELISA of homogenized gastrocnemius samples demonstrated a significant decrease in CXCL1 following 15 minutes of reperfusion in NIR light-treated gastrocnemius after IR injury compared to the non-NIR exposed gastrocnemius, and a decreasing trend in CXCL1 expression following 30 minutes of reperfusion. ELISA analysis of homogenized gastrocnemius samples demonstrated a significant decrease in CXCL5 levels in both the groups receiving 15 minutes and 30 minutes of reperfusion. CXCL1 and CXCL5 levels in non- NIR exposed gastrocnemius samples also demonstrated a significant increase as compared to control animals receiving no IR injury. Immunoprecipitation followed by western blot analysis of homogenized quadriceps samples demonstrated a significant decrease in CD68 normalized to CD14 in animals receiving ischemia and NIR treatment as compared to control animals and those exposed to ischemia alone. CD206 normalized to CD14 showed a significant increase in animals receiving ischemia and NIR treatment as compared to control animals and those exposed to ischemia alone.
Conclusions	These findings demonstrate that exposure to NIR light differentially affects inflammatory chemokine secretion, including decreasing the secretion of neutrophil chemoattractants CXCL1 and CXCL5. This suggests that a decrease in neutrophil migration is at least partially responsible for tissue protection following brief applications of NIR light during ischemia and reperfusion. Additionally, such exposure differentially affects macrophage phenotype, including a decrease in pro-inflammatory M1 (CD68 macrophages, and an increase in protective M2 (CD206) macrophages. These findings suggest that exposure to near infrared light alters inflammatory processes leading a tissue protective effect following a period of ischemia. This has significant implications regarding limb preservation following vascular injury as well as potentially increasing the time of tourniquet application during surgical procedures.
Acknowledgements	Thank you to Dr. Weihrauch for serving as my mentor throughout the research process.
Ancillary Materials	VIEW MY POSTER WATCH MY PRESENTATION

Category	Other Clinical Specialties, #78
Primary Author	Laura B Grogan**
Secondary Authors	Amy Domeyer-Klenske M.D. ; Megan Flatley, R.N.; Erika Peterson, M.D.
Title	Impact of patient safety bundle on timely treatment of severe hypertension in obstetric patients
Introduction	A California Pregnancy-Associated Mortality Review found 41% of all pregnancy related deaths in California from 2002-2007 preventable. Preeclampsia/eclampsia is a leading cause of pregnancy-related mortality in the immediate postpartum stage. Standardizing hypertension protocols based on Alliance for Innovation on Maternal Health (AIM) bundles in Illinois led to improvement in timely treatment of severe hypertension (41.5% to 78.9%). On November 1, 2019, Froedtert Hospital implemented a severe hypertension protocol, developed from the AIM patient safety bundle. This protocol outlines 3 algorithms with IV Labetalol, IV Hydralazine or Oral Nifedipine. We expected the protocol to increase the percentage of severely hypertensive patients receiving timely, evidence-based treatment. We evaluated obstetric patients with elevated blood pressures at Froedtert 6 months pre-protocol implementation compared to post-protocol implementation with ongoing monthly assessments.
Methods	Severely hypertensive patients were identified by two severe-range blood pressures (systolic ≥160 and/or diastolic ≥110) within 60 minutes, then evaluated to determine if they received acute treatment within 60 minutes of the 2nd elevated blood pressure and if they further adhered to the protocol. We collected Labetalol, Hydralazine and Nifedipine administration time, dose and route and considered Labetalol PO and Nifedipine XR non-acute. Adherence was defined as correctly following the sequence until the blood pressure fell into an acceptable range, or the protocol was completed. Deviation type was defined as late or absent blood pressure readings, late or absent medication administration, or incorrect medication dose or administration method. A 3 minute buffer was added to the protocol analysis to account for clinically insignificant delays between action and documentation.
Results	We initially reviewed 250 opportunities to treat severe hypertension between 4/23/19 to 10/31/19 and compared that to 250 instances between 11/1/19 to 7/4/20. Of the 250 prior to 11/1/19, 66% received acute treatment within 60 min compared to 71% from 11/1/19 to 7/3/20. Following the initial analysis and presentation of the pre and post implementation data, Froedtert modified their order sets to default to protocol defined medication orders, placed protocol procedure instructions in the provider workspaces and patient rooms. Of the 58 instances from 10/1/20 to 11/12/20, 85% received acute treatment within 60 min followed by 90% for the 81 instances from 11/13/20 to 12/29/20. The leading deviation from protocol throughout was late blood pressure reading, although starting 10/1/2020 no more cases of late medication administration have been recorded.
Conclusions	Standardizing the protocol decreased lack of medication administration and medication delay. Implementation of the protocol as well as subsequent efforts to streamline provide workflow has increased acute hypertensive medication treatments within 60 minutes of the 2nd elevated blood pressure. This effort will continue to evaluate and monitor adherence to the hypertension protocol bundle, and implement interventions to improve adherence.
Acknowledgements	Supported by the Collaborative for Healthcare Delivery Science (CHDS), which is funded by the Advancing a Healthier Wisconsin Research & Education Program and MCW Dean's Office
Reference 1	Burgess APH, Dongarwar D, Spigel Z, et al. Pregnancy-related mortality in the United States, 2003-2016: age, race, and place of death. Am J Obstet Gynecol. 2020;222(5):489.e1-489.e8. doi:10.1016/j.ajog.2020.02.020
Reference 2	The California Pregnancy-Associated Mortality Review. Report from 2002-2007 Maternal Death Reviews. Sacramento: California Department of Public Health, Maternal, Child and Adolescent Health Division. 2018
Reference 3	Main EK. Reducing Maternal Mortality and Severe Maternal Morbidity Through State-based Quality Improvement Initiatives. Clin Obstet Gynecol. 2018;61(2):319-331. doi:10.1097/GRF.0000000000000361
Ancillary Materials	VIEW MY POSTER

Category	Other Clinical Specialties, #79
Primary Author	Eric Hohenwalter, MD
Secondary Authors	Naif Alsaikhan, MD, Sarah White, MD, MS, FSIR
Title	NECESSITY OF IMAGING FOLLOW UP TO CONFIRMGASTROSTOMY TUBE POSITION PRIOR TO USE
Introduction	To assess the value of obtaining routine next-day radiographic contrast tube study following placement of percutaneous push-type gastrostomy tubes.
Methods	From January 2015 to February 2020, all primary percutaneous push-type gastrostomy tube placement procedures have been identified. Demographic data, purpose of procedure (feeding versus venting),periprocedural (one month) complications, and results of next-day radiographic contrast tube studies(performed prior to initiation of tube feeding) were recorded. Retrospective review of procedural and next-day radiographic images of patients with abnormal tube studies was performed.
Results	A total of 267 procedures were identified. 261 patients received next-day radiographic contrast tube studies. 7 patients (2.6%) of those had abnormal studies with only 3 patients (1.2%) requiring surgical/interventional management. Tube studies revealed tube dislodgement in 3 patients, deflated balloon in one patient, false positive interpretation of extraluminal contrast in one study (ruled out by CT scan), and two cases of benign pneumoperitoneum. Retrospective review of the 3 patients with tube dislodgment revealed extraluminal tube placement evident on last archived fluoroscopic procedural images, not recognized during the procedure. 254 patients had normal post procedure tube study and of those; 3 cases were complicated by tube dislodgment (2 in day-2 and 1 in day-12 post procedure). Subsequent imaging for non-tube related indications showed transhepatic tube placement in one patient and pneumoperitoneum in 12 patients (one with pneumatosis of the colon leading to negative surgical exploration). 6 patients did not receive next-day tube study; however, no periprocedural complications were encountered in this group.
Conclusions	Routine use of radiographic contrast tube studies following primary placement of push-type gastrostomy tubes revealed tube mis-placement in few cases, all of which could have been detected intra-procedurally.

Category	Other Clinical Specialties, #80
Primary Author	Molly Murray**
Secondary Authors	Joseph Zenga, MD
Title	Retrospective Analysis of Post-Tracheostomy Complications
Introduction	While overall infrequent, complications related to tracheostomies can be catastrophic. The aim of this study is to identify risk factors associated with short- and long-term tracheostomy complications at Froedtert Hospital. There is a lack of granular data regarding risk factors including the specifics of surgical technique and post-operative care. In particular, recent clinical experience suggests that certain tracheotomy techniques may limit both short- and long-term complications, but this idea requires robust multi-variable validation. Additionally, in several recent clinical adverse events, factors associated with the care team or tracheostomy changes have been identified as possible risk factors for complications. Exploring these gaps in current knowledge may help identify predictors of tracheostomy complications and aid in designing future prospective interventional trials.
Methods	A retrospective case series with chart review was performed at a single academic tertiary care center of patients undergoing tracheostomy by any technique for any indication between 2011 and 2018. Pertinent patient past medical history, tracheostomy procedural details, tracheostomy-related complications, hospital readmission and survival data were recorded.
Results	697 patients were included. The indication for tracheostomy was ventilator dependence in 590 (85%) patients. 521 (75%) patients had severe comorbidity (ACE-27 score of 3). 512 (74%) tracheostomies were performed open while 185 (26%) were percutaneous. 70 (10%) patients had a tracheostomy-related complication within 90 days, of which post-operative hemorrhage was most common (n=25). Tracheostomy related complications occurred at a median of 11 days after surgery (range 0 to 87 days). Of tracheostomy related complications 14 required immediate return to the operating room and 3 patients died of their complication, all within 3 days of their tracheostomy. In multivariable analysis only the presence of a known difficult airway was significantly associated with a 90-day complication (OR 0.41, 95%CI 0.20-0.86). Age, race, zip code, indications for tracheostomy, prior tracheostomy, surgical technique, and service performing tracheostomy were not associated with 90-day tracheostomy-related complications. 263 (40%) patients died within 30 days of tracheostomy.
Conclusions	While complications after tracheostomy are infrequent, occurring in 10% of the patients in this study, they are often severe. A heightened level of preparedness to immediately manage accidental tracheostomy decannulation or hemorrhage is required for patients with a known difficult airway pre-operatively. Importantly, 30-day mortality is high in patients undergoing tracheostomy. This reinforces the need for pre-operative multi-disciplinary, especially palliative care, evaluation to determine if the patient is a safe candidate for tracheostomy.
Ancillary Materials	VIEW MY POSTER

Category	Other Clinical Specialties, #81
Primary Author	Connor Ford
Secondary Authors	Rebecca Anderson, PhD, Professor, Department of Anesthesiology. Sarah Trost, PhD, Assistant Professor, Department of Anesthesiology. Amit Singh, DO, Department of Anesthesiology.
Title	Relationships among Treatment Expectancy and Positive Outlook and Spinal Cord Stimulation Success
Introduction	Spinal cord stimulation (SCS) is a pain management treatment modality for patients suffering from chronic pain. Past studies have shown that psychological evaluation tools are successfully used as predictors of SCS outcomes. Fama and Colleagues (2016) published a literature review consisting of nine studies on the use of preoperative psychological evaluations to predict SCS success. This review identified that the predictive value depends on the psychiatric factors used as well as which outcomes are measured. Finding factors with strong predictive value is significant because the predictive capacity can be used to treat patients holistically and may result in including psychiatric medication and consulting along with SCS treatment. In summary, existing literature supports the idea that psychological evaluation tools are relevant in SCS outcomes. This study will break this down further in regard to whether psychological tools are predictors in whether a patient has a successful SCS trial or not, specifically focusing on positive outlook (PO) and treatment expectancy (TE).
Methods	Retrospective chart review will be conducted on patients who have undergone SCS trial and have made the decision to move forward with a permanent implant, which is the definition of a successful trial, or not. Data collected includes patient score values for PO and TE, as well as whether or not the patient underwent a successful trial. The population of patients will be separated out into those with successful trials and those with unsuccessful trials, and the data will be analyzed to compare the two subgroups to determine if any of the variables play a significant role in SCS trial success.
Results	The mean PO scores for successful and unsuccessful trials were 25.05 and 25.72 respectively. The mean TE scores for successful and unsuccessful trials were 25.99 and 24.27. Both PO and TE scores had no significant impact on whether a trial was successful or not ($p = 0.34$, $p = 0.068$ respectively).
Conclusions	The results determined that PO are TE scores do not significantly impact the success of an SCS trial. While statistically insignificant, patients with successful SCS trials had a higher mean TE score and had a slightly lower mean PO score. Ultimately, the results suggest that patient scores for PO and TE should not influence the decision to move forward with SCS trials. Next steps include gathering more data to increase the sample size, as there were 11 patients with unsuccessful trials compared to 35 with successful trials. Additionally, pain catastrophizing and depression score analysis can be included to determine if either may influence whether a patient has a successful SCS trial. In conclusion, determining if any of these psychological tools significantly impact SCS success may lead to protocol changes to maximize the chances of patients undergoing successful SCS trials and moving on with permanent implantation.
Reference 1	Fama CA, Chen N, Prusik J, Kumar V, Wilock M, Roth S, Pilitsis JG. The Use of Preoperative Psychological Evaluations to Predict Spinal Cord Stimulation Success: Our Experience and a Review of the Literature. Neuromodulation. 2016 Jun;19(4):429-36. doi: 10.1111/ner.12434. Epub 2016 Apr 28. PMID: 27121447.

Category	Other Clinical Specialties, #82
Primary Author	Kaitlyn Sonnentag, MS3, MCW-GB**
Title	Emergency Department Utilization
Introduction	Past research looking at emergency department (ED) utilization found key reasons why patients come to the ED for non-emergent conditions are: •Lack of knowledge about affordable and convenient care outside of the ED. •Patients' perceptions of the acuity of their conditions being inconsistent with perceptions of the ED providers. The purpose of this research was: •To investigate the reasons for usage of the Bellin ED in Green Bay, WI for non-emergent conditions. • To provide patients with information on when they should seek care at an alternative healthcare facility and specific alternatives for care in the area. The ultimate reason for this is to decrease the number of patients presenting to the ED so that patients with emergent conditions can get faster and better care.
Methods	Patients who received an acuity level of 4 or 5 by ED provides were considered for the survey. At the end of the survey, patients were asked if they would like an informational handout on criteria for seeking care at an ED, urgent care, or primary care facility as well as addresses of these facilities in the area.
Results	75% of patients rated their problem as more severe than providers did. 87% stated that they would use reliable alternatives to getting care outside of the ED if these existed. 50% stated they wanted the informational handout.
Conclusions	Patients' perceptions of the acuity of their conditions are inconsistent with providers' perceptions. There is lack of knowledge about alternatives to the ED. Patients would be willing to use alternatives to the ED if they knew when they should go elsewhere and if they knew locations of other healthcare facilities. With educating our patients, we could reduce the number of people who use the ED for non-emergent conditions and have more resources for patients with emergent conditions.
Ancillary Materials	VIEW MY POSTER

Category	Other Clinical Specialties, #83
Primary Author	Harrison Mooers, MD
Secondary Authors	Sonali Srivastava, BA, Kaiwei Lu, MS, Thangam Venkatesan, MD
Title	Topiramate reduces the frequency and severity of cyclic vomiting episodes
Introduction	Practice guidelines recommend using topiramate for the prevention of moderate-severe cyclic vomiting syndrome (CVS) episodes in adults. However, the data supporting its use are limited to small studies in children. We aimed to determine the efficacy of topiramate for CVS prophylaxis in adults.
Methods	We conducted a retrospective review of patients diagnosed with CVS. Clinical characteristics, number of CVS episodes, emergency department (ED) visits, and hospitalizations the year before and after initiating topiramate were recorded. Response was defined as a global improvement in symptoms or > 50% reduction in the number of CVS episodes, ED visits, or hospitalizations.
Results	Seventy-six percent (77/101) of patients responded to topiramate. There was a significant decrease in the annual number of CVS episodes (17.9 vs 6.6,$p<0.001$) and CVS-related ED visits (5.0 vs 2.1, $p=0.021$). There was also a decrease in the annual number of hospitalizations (2.07 vs 1.06, $p=0.08$). On average, patients used topiramate for 10.6 out of the first 12 months and took a mean daily dose of 153mg. Eighty-two percent of patients used at least one additional form of CVS prophylaxis, including tricyclic antidepressants mitochondrial supplements, and aprepitant. Logistic regression revealed depression was associated with a good response to topiramate. Fifty-seven percent of patients experienced side effects. The most common side effects were paresthesia, cognitive impairment, and fatigue.
Conclusions	Topiramate is effective prophylaxis for patients with moderate-severe CVS, but its use may be limited by its side effects. Efforts to develop better-tolerated therapies for CVS are warranted.
Ancillary Materials	VIEW MY POSTER WATCH MY PRESENTATION

Category	Other Clinical Specialties, #84
Primary Author	Sonya Dave, MD**
Secondary Authors	Poonam Beniwal-Patel, MD
Title	Racial and Gender Disparities Exist in Influenza Vaccination Rates Among Patients with Inflammatory Bowel Disease
Introduction	Immunosuppressive therapies used to treat inflammatory bowel disease (IBD) are associated with an increased risk of infections, including vaccine-preventable diseases (VDP). Though patients with IBD have lower vaccination rates than the general population, no studies have assessed whether there are disparities in vaccination rates among patients with IBD. Determining if these disparities exist is important to assure high uptake of a COVID-19 vaccine. The aim of this study was to determine if racial or ethnic disparities existed in immunization rates among patients with IBD at two tertiary referral medical centers.
Methods	This was a retrospective case control study of patients with IBD at two tertiary referral IBD centers which included urban and rural patients. Patients who were 18 years or above and were seen in IBD clinic between 09/2019 and 02/2020 were included. Electronic health record extraction assessed demographic information and immunization rates. Each patient needed an active record in the Wisconsin Immunization Registry (WIR), which has very high rates of immunization documentation and is close to a comprehensive immunization record. For each patient, the WIR was accessed to obtain immunization data for pneumococcal 13 (PCV13), pneumococcal 23 (PPSV23) and influenza. Data analysis involved a Pearson's chi-squared test for categorical variables.
Results	In total 1968 patients with IBD were included in the study. Average age was 46.8 years. 53% patients were female and 47% were male. 90.7% were White and 6.3% were Black. There was no significant difference between the number of female vs male patients. Black patients had a significantly lower rate of influenza vaccination than White patients for two influenza seasons (2019-2020, 2018-2019). There was no difference in pneumococcal immunization rates among the groups. Female patients had a significantly higher rate of influenza vaccination rates than male patients for each season.
Conclusions	This is the first study to demonstrate racial and gender disparities in influenza vaccination rates among patients with IBD. Future studies are needed to determine causes for and strategies to remediate racial and gender disparities in immunization rates. Identifying these barriers is imperative especially since certain ethnic and racial groups are at increased risk for COVID-19 related illness and may display vaccine hesitancy. Efforts to ensure all patients with IBD have high uptake for COVID-19 vaccination is essential.
Ancillary Materials	VIEW MY POSTER

Category	Other Clinical Specialties, #85
Primary Author	Kevin Credille, BSE, MS
Secondary Authors	Siddhartha Singh, MD, MS, MBA
Title	Unequal Pupils in a Post-operative Trauma Patient: Check Your Reflexes
Introduction	Anisocoria is a physical exam finding associated with a variety of underlying pathologies affecting the oculomotor nerve or the pupillary sphincter muscle, but can also be caused by numerous pharmacological agents. The differential diagnosis includes potentially fatal conditions that cause damage to the oculomotor nerve such as cerebrovascular accident, intracranial hemorrhage, increased intracranial pressure, uncal herniation, carotid artery dissection, and cerebral artery aneurysms. To reduce unnecessarily aggressive testing when a neurological cause seems unlikely, other benign causes should be considered such as drug-induced unilateral mydriasis. This case study investigates a patient's sudden onset anisocoria in the post-operative setting.
Methods	A 31-year-old male presented with anisocoria and left pupil mydriasis less than 24 hours after an open reduction and internal fixation of a left tibial plateau fracture. This was accompanied by a reported sensitivity to light and blurry vision. Considering the mydriasis occurred acutely after surgery, there was initial concern for a stroke despite adequate perioperative anticoagulation. A detailed history and examination showed a left pupil unresponsive to light or accommodation and a complete absence of other neurological deficits. This diminished concern for a central nervous system etiology and heightened suspicion for a pharmacological agent. While several anesthetic agents administered are associated with mydriasis, the transdermal scopolamine patch was identified as a likely culprit given the unilateral nature of the mydriasis. After further patient questioning, the patient recalled removing the scopolamine patch with his left hand and then contacting his left eye while taking his contact lens out. In response, pilocarpine 1% ophthalmic eyedrop solution was diagnostically administered into the left eye.
Results	The pupil failed to constrict within 30 minutes, ruling out an oculomotor nerve palsy and indicating a pharmacological cause. The patient's anisocoria slowly but spontaneously resolved 48 hours later before being discharged from the hospital.
Conclusions	This case illustrates the importance of taking a thorough history and physical exam when a patient presents with a single dilated pupil and without obvious neurological symptoms. This condition can be caused in a perioperative setting especially with administration of anesthesia and other common inpatient drugs. Anisocoria can also occur secondary to multiple sclerosis or be the patient's physiologic baseline. The important clinical implication from this case is to consider benign etiologies of unilateral mydriasis in order to avoid expensive screening for cranial pathologies when a neurological diagnosis is unlikely.

Category	Other Clinical Specialties, #86
Primary Author	Brandon Key, MD
Secondary Authors	Thaddeus Maguire, MD, Sarah B. White, MD, FSIR
Title	Safety and Efficacy of Angio-Seal for Hemostasis after PTFE Graft Access
Introduction	To compare the safety and efficacy of Angioseal to manual compression in achieving hemostasis following direct percutaneous access of polyethylene terephthalate (PTFE) vascular bypass grafts.
Methods	This was an IRB-approved single institution, retrospective review of all patients undergoing endovascular evaluation and/or intervention performed on a peripheral bypass graft from June 2013 to July 2020. Cases in which the percutaneous access was not gained directly into the bypass graft, the bypass graft was not composed of PTFE, or in which closure was not obtained with either Angioseal or manual compression (e.g. planned primary surgical closure in collaborative hybrid cases) were excluded. Demographic data including patient age, sex, and co-morbidities, as well as procedural data including the type of procedure, type of graft accessed (femoral-femoral, axillary-femoral, femoral-popliteal or femoral-distal), method of access closure, peri-procedural anticoagulation and antibiotic use, and data regarding 30 day post-procedural complications were collected. For the purposes of this study, an â€˜angiogram with intervention' broadly includes all variety of angioplasty and stenting.
Results	A total of 373 cases involving lower extremity bypass interventions were reviewed. Of these, 119 unique cases resulted in 154 direct punctures of a PTFE bypass which met criteria for analysis. This included diagnostic angiograms (n=18 (12%)), angiography with intervention (n=66 (43%)) and utilization of catheter directed thrombolysis (n=70 (45%)). 116 accesses were closed with Angioseal and hemostasis was achieved with manual compression in the remaining 38. Overall, the access complication rate of direct PTFE puncture was 5.2%, with a major complication rate of 2.6%. A total of 4 (3.4%) complications were reported in PTFE accesses closed with Angioseal. Of these, 2 (1.7%) were considered major complications, including an abscess requiring surgical drainage and post-deployment stenosis requiring repair. A total of 4 (10.5%) complications were reported following manual compression, of which 2 (5.3%) developed pseudoaneurysms necessitating repair, which were considered major complications. Out of the 8 total reported complications, 6 (75%) arose after catheter directed thrombolysis, and the remaining 2 following an intervention. No complications were reported following diagnostic angiography alone.
Conclusions	Angioseal is safe and effective in achieving hemostasis following PTFE puncture and has a lower rate of overall and major complications.

Category	Other Clinical Specialties, #87
Primary Author	Amanda R. Smolock, MD, PhD
Secondary Authors	Aaditya Nagaraj, Sarah B. White, Christopher Johnson, Dean Klinger, Allan Roza,
Title	Evaluation of the Role of Antiplatelet Therapy in Hemodialysis Access Graft Patency Following Successful Percutaneous Thrombectomy
Introduction	The purpose of this study was to understand the role of antiplatelet therapy in maintaining arteriovenous graft (AVG) patency after successful percutaneous thrombectomy.
Methods	This was an IRB approved retrospective review of all dialysis access circuit evaluation orders placed over a 1-year period with a narrative keyword search of “declot”. A total of 152 encounters were found, 32 of which were excluded as the intervention performed was not a thrombectomy. The remaining 120 encounters were reviewed for patient demographics, details of procedure, and use of antiplatelet therapy prior to and after percutaneous thrombectomy. AVG failure was defined as re-thrombosis, graft abandonment, or surgical revision. The time to AVG failure was calculated from the date of declot to AVG failure. Technical success was defined as patency on angiography and palpable thrill at completion of the procedure.
Results	65% (n=78) of declots were performed on upper arm grafts, 3% forearm (n=3), 8% leg (n=9), 23% HeRO (n=27), and 3% ax-ax/ax-fem (n=3). Technical success was seen in 111 of 120 declots. Of the successful declots, 73 (65.8%) were already on antiplatelet therapy. 6 of 9 (67%) of unsuccessful declots were not on antiplatelet therapy at the time of procedure. 24.3% of successful AVG declots (n=27) were subsequently started on new or additional/increased antiplatelet therapy. Aspirin and clopidogrel were the most commonly used. Ticagrelor accounted for 18/61 cases of existing antiplatelet therapy and 5/27 cases of added/increased therapy. The median time to AVG failure without prior or subsequent antiplatelet therapy was 49 days (range 1-412 days) compared to 90 days (range 1-427 days) for those previously on antiplatelets without a subsequent change in therapy. For those cases that were started on new/additional antiplatelet therapy, the median time to graft failure was 94 days (range 2-407 days).
Conclusions	Antiplatelet therapy may provide additional patency gains for patients with AVG as evident by trends toward longer time to AVG failure and increased ability to successfully declot the AVG.

Category	Other Pre-Clinical & Lab Science, #88
Primary Author	Dilip Maddirela, PhD
Secondary Authors	Venkateswara Gogineni, PhD, Sarah White, MD, MS
Title	Inhibition of HIF-1a Sensitizes Primary and Metastatic Liver Cancer Cells
Introduction	The standard of care for primary liver tumors such as hepatocellular carcinoma (HCC) is transarterial chemoembolization (TACE), which includes tumor embolization with locoregional delivery of the chemotherapeutic doxorubicin. Embolization therapies often induce hypoxia, leading to proliferation of hypoxia-adapted cancer cells and develop chemoresistance. Although current guidelines suggest TACE as first-line treatment in patients with large or multinodular HCC, robust data in favor of clear superiority of chemoembolization over bland embolization is lacking. In this study, we aim to demonstrate that HIF-1ainhibition sensitizes cancer cells to doxorubicin and therefore can improve the outcomes of embolization.
Methods	Hepatocellular carcinoma (MCA-RH777), colorectal liver metastasis (CC-531) and immortalized liver (Clone 9) cell lines were grown in DMEM medium at 37^0C in a humidified atmosphere with 5% CO2 in normoxic and <1% O2 hypoxic conditions. Cells were exposed to doxorubicin, R59949 (HIF-1a inhibitor) or in combination. After 24h and 48h of incubation, images were acquired, and cell viability was determined by trypan blue staining. Migration Wound healing assay was performed on cells under similar conditions. Images of the cells migrating into the wound were captured prior to and after 16h.
Results	Combination of doxorubicin and R59949 showed greater than 12.5% cell death under hypoxic conditions compared to normoxic conditions in all cell lines. Combination therapy resulted in more cell death (>30%; $p<0.05$) and a greater inhibition of migration (>20%; $p<0.05$) under hypoxic conditions compared to normoxic conditions. Although migration was inhibited in both treatment arms, only combination therapy under hypoxia showed higher inhibition.
Conclusions	HIF-1a inhibition enhanced the cytotoxicity of doxorubicin and reduced cell migration under hypoxic conditions.

Category	Other Pre-Clinical & Lab Science, #89
Primary Author	Venkateswara R. Gogineni, PhD
Secondary Authors	Dilip R Maddirela, El-Sayed Ibrahim, PhD, Amit Joshi, PhD, Sarah B. White, MD, MS, FSIR
Title	Growth and characterization of orthotopic pancreatic tumor in a rat model
Introduction	Pancreatic cancer is the fourth leading cause of cancer-related mortality with less than 8% 5-year survival rates. Knowledge on pathogenesis and tumor microenvironment of pancreatic cancer has advanced largely because of mice models; however, a mouse model is unsuitable for site selective delivery. The purpose of this study was to develop an orthotopic rat model of pancreatic cancer suitable to evaluate localized delivery of therapeutics
Methods	10 immune compromised Dahl/Salt Sensitive rats were implanted with luciferase expressing Panc-1 cells into the tail of the pancreas. Tumor growth was monitored by weekly bioluminescence and dynamic contrast enhanced (DCE) magnetic resonance (MR) imaging. Quantitative R2* (1/T2*) MR maps were obtained from the multi-echo T2* images. Differences between normal and cancerous pancreas were determined to design treatment parameters using MR guided focused ultrasound. Rats were euthanized at 3 weeks, the pancreas explanted and gross and histological analyses were performed.
Results	All the 10 rats developed tumors within 1 week with tumor size ranging 2-4mm3 and by third week the sizes were 8-12mm3. Bioluminescence imaging showed a strong signal with a 4-fold increase in counts by week 3. DCE MR imaging revealed tumor growth
Conclusions	SS rat model allows the growth and monitoring of human pancreatic cancers and provide a treatment window for the interventional strategies.
Acknowledgements	Research grant from Focused Ultrasound Foundation supported this work.

Category	Other Pre-Clinical & Lab Science, #90
Primary Author	Sarah B. White, MD, MS, FSIR
Secondary Authors	Venkateswara Gogineni, PhD, Dilip Maddirela, PhD
Title	UPAR & MMP-9 EXPRESSION IS COUPLED TO HIF-1ALPHA AND INVASIVENESS OF HCC AND CRLM TUMORS
Introduction	Changes in the microenvironment coupled with extracellular matrix remodeling is essential for solid tumors to survive and metastasize. Unraveling the causal mechanisms allows for identification of novel targets and determination of efficacy of targeted treatments. The upregulation of uPAR and MMP-9 are known to be associated with tumor invasiveness, angiogenesis and tumor growth. The purpose of this study is to evaluate whether uPAR and MMP-9 expression is coupled to HIF-1A and whether suppression decreases the aggressiveness of HCC and CRLM tumors.
Methods	Hepatocellular carcinoma (MCA-RH777), colorectal liver metastasis (CC-531) and immortalized liver (Clone 9) cell lines, grown in DMEM medium at 37Â°C in a humidified atmosphere with 5% CO in normoxic and < 1% O hypoxic conditions, were assessed for the expression of HIF-1A, uPAR and MMP-9 by immunocytochemistry. Cells cultured in matrigel coated transwell were assessed for invasiveness under normoxic and hypoxic conditions. Cells were treated with a HIF-1A inhibitor (R59949) and doxorubicin, and matrigel invasion assays were performed In Vitro. Further, tumor sections explanted from rabbit and rat models of HCC and CRLM were stained for the expression of uPAR, MMP-9 and HIF-1A, and compared to normal liver sections after treatment with doxorubicin, R59949 or in combination.
Results	HCC and CRLM cells presented striking increases in HIF-1A, uPAR and MMP-9 expression under hypoxic conditions. Percentage of hypoxia induced invasive cells were higher among CRLM cells compared to HCC cells at 12h in Matrigel invasion assays. R59949 significantly reduced the invasion of both CRLM and HCC cells under hypoxic conditions. Immunohistochemistry revealed that rat and rabbit HCC tumors and rat CRLM tumors have abundant levels of HIF-1A, uPAR and MMP-9 compared to the respective normal liver sections.
Conclusions	Increase of CRLM and HCC cell invasion under hypoxic conditions is coupled with uPAR and MMP-9 expression.

Category	Other Pre-Clinical & Lab Science, #91
Primary Author	Ankan Gupta, PhD**
Secondary Authors	Karthikeyan Thirugnanam, Shubhangi Prabhudesai, Surya Nauli, Rahima Zennadi, Kevin Rarick and Ramani Ramchandran
Title	Quantifying Deciliation as Prognosis of Cerebrovascular Health
Introduction	The primary cilium is a microtubule-based sensory organelle having a dynamic structure that projects from the apical surfaces of various eukaryotic cells. In endothelial cells (ECs) of developing blood vessel, the cilium is projected into the vascular lumen and operates as a 'flow sensor'. When cilia are mutated in zebrafish, the mutants demonstrated compromised integrity in brain vessels and the defect is intrinsic to endothelial cells. This indicates that endothelial cilium is critical for cerebrovascular health. We previously demonstrated in zebrafish model that primary cilia are enriched in the earliest formed cranial vessels and in angiogenic hindbrain capillaries. We reported the abundance of cilia in primordial midbrain channel (PMBC) in developing brain of zebrafish at 24-hour post fertilization (hpf), the time point when blood flow is yet to begin. This observation spurred the possibility that primary cilium is functionally critical not only as flow sensor, but also beyond that. Primary cilia derived from EC are thought to be specialized sensors of low and oscillatory 'wall shear stress' (WSS). Throughout the vasculature, primary cilia are prevalent in regions that are exposed to WSS. However, upon shear stress some studies have reported the loss of endothelial cilia from cell surface. Emerging report suggests that the predominant mode of cilium loss was rapid deciliation, in which the membrane and axoneme of the cilium was shed from the cell. Thus, in this study, we tested our hypothesis that increased or altered shear stress causes deciliation in brain vasculature and quantifying EC-specific deciliation could be considered as prognostic marker of cerebrovascular health.
Methods	We monitored ciliary proteins from brain-derived ECs or body fluids and thus quantified deciliation under various experimental conditions in vitro or in vivo. To investigate whether increased shear stress would promote deciliation of EC in vivo, we adopted zebrafish model and treated zebrafish embryos with increased temperature. This treatment causes increased heart beats of the embryo that ultimately results in increased blood flow and flow-associated shear stress. We extended our investigation to experimental traumatic brain injury model as well as sickle cell disease condition to see if physical insult in brain or altered shear stress could result in shedding off cilia. We also validated our observation in vitro, under defined shear stress.
Results	Collectively, our data indicates that cilia derived from EC is sensitive to shear stress and ciliary proteins in body fluid are surrogate markers of cerebrovascular health. EC-derived cilia in brain could be considered as key player in maintaining BBB integrity. Cilia fragments or proteins can be detected in body fluids in various disease states where flow is compromised, ECs are injured, or tissue homeostasis is disturbed.
Conclusions	Our data also supports the emerging idea that physical stress to vessels in our body causes shedding off whole cilium. Our current data warrants extended investigation on how ciliary proteins in body fluids could be considered as diagnostic markers under various pathophysiological conditions.
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Category	Other Pre-Clinical & Lab Science, #92
Primary Author	Karthikeyan Thirugnanam, PhD
Secondary Authors	Shubhangi Prabhudesai PhD, Amy Pan PhD and Ramani Ramchandran PhD
Title	PDGF-BB induces brain endothelial cell cilia formation to promote vascular stability
Introduction	Primary cilia on the vascular ECs extend into the lumen of the blood vessel act as sensors and transmit extracellular signals. Recently, cilia mutants in zebrafish have been identified with intra cerebral hemorrhages (ICH). Vascular disruption is the initial cause of ICH followed by blood-brain barrier dysfunction. Previously it is known, platelet-derived growth factor (PDGF-BB) secreted by endothelial cells (ECs) recruit pericytes (PCs) expressing platelet-derived growth factor receptor B (PDGFRB). This cellular interaction regulates vascular formation, stabilization, remodeling, and its function. Dysfunction in EC-PC interaction leads to vascular instability which is often lethal. Thus, our overarching hypothesis is that PDGF-BB-mediated brain ECs signaling is associated with cilia in controlling brain vascular stability. To test this hypothesis and because in brain ECs PDGFRB were undetectable, we investigated the involvement of vascular endothelial growth factor receptor 2 (R2), a receptor on ECs to signal upon binding to PDGF-BB. The rationale for investigating the PDGF-BB and cilia connection is that mutations in either (PDGF-BB, PAK2 or ciliary proteins) causes brain hemorrhage. p21- activated kinase (PAK2), a downstream signaling molecule from R2 that regulates cytoskeletal rearrangement, and ciliary protein such as ARL13B which are known to induce ciliogenesis in mammalian cells and zebrafish. Finally, cilium in ECs has recently been implicated in pericyte recruitment in zebrafish. Therefore, it is important to understand the molecular mechanisms that govern EC- ciliogenesis and its effect on pericyte recruitment to facilitate vascular stability.
Methods	PDGF-BB ligand (10 ng/mL) and R2/PAK2 signaling were assessed by in vitro cell culture method in primary human brain microvascular endothelial cells (HBMVECs). Assays include western blot, siRNA mediated knockdown, small molecule inhibitor studies, co-culture (ECs-PCs) and immunofluorescence. Outcomes are cilia length, status of signaling proteins and PC recruitment.
Results	HBMVECs treated with PDGF-BB for 60 mins showed significant increase in the receptor protein levels of R2, and cytoplasmic protein levels of PAK2 and ARL13B. PDGF-BB treatment with R2 knockdown ECs show lower expression of PAK2 and ARL13B levels. To investigate the role of PAK2 in ARL13B ciliary protein synthesis, a selective small molecule PAK2 kinase inhibitor (AZ 13705339) at 10 nM concentration decreased the levels of ARL13B protein. However, PDGF-BB treatment with PAK2 inhibited cells, increase the levels of ARL13B protein. We next confirmed Pak2 on Arl13b in zebrafish model, where the Pak2 mutant embryos that display cerebral hemorrhages show less Arl13b protein levels.
Conclusions	These data suggest that VEGFR2 and PAK2 are the important mediators in PDGF-BB mediated ciliary signaling. Further, experiments such as measuring EC cilia length and PC recruitment will be tested to prove the hypothesis.
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Category	Other Research-Related Topics, #93
Primary Author	Clara Bosco
Secondary Authors	Fabrice Jotterand
Title	Ethical Framework for the Responsible Use of AI in Medicine
Introduction	Artificial intelligence is increasingly becoming a reality in healthcare. While it provides obvious benefits to clinical practice, patients, and society at large, it has the potential to challenge traditional ways of delivering healthcare, including how we train future healthcare professionals. We propose a set of ethical imperatives for the responsible development and implementation of AI into clinical practice and training of future healthcare professionals in the age of AI.
Methods	This presentation is based on literature review, weekly discussions, and two articles, one currently under development ["Artificial Intelligence and the Gift to Presence in Clinical Practice"] and the other published in the Journal of Science and Engineering Ethics ["Keeping the 'Human in the Loop' in the Age of Artificial Intelligence"].
Results	AI implementation into healthcare will require a transformation in the training of future physicians. Because of the nature of AI technology, medical education will require a stronger focus on the humanistic dimensions of medicine and the development of character traits, such as empathy, caring, compassion, and most importantly presence (the gift of human presence). Therefore, medical education must emphasize not only basic science knowledge and procedural abilities but likewise, the cultivation of character traits, critical thinking, and creativity should be a part of the core, pedagogical strategies of 21st-century medical schools. To this end, we propose six ethical imperative for the responsible implementation of AI in medicine and the training of future physicians: 1) *Humanity*: promoting human interaction, respecting personal identity, and serving human ends, 2) *Information*: gathering relevant information about AI, 3) *Transparency*: communicating risks and benefit of AI, 4) *Participation*: including all stakeholders for analysis of ethical, social, and policy implications of AI, 5) *Consensus*: establishing values and norms to determine standards of practice and public policy, and 6) *Accountability*: fostering responsible development and implementation of AI in health care.
Conclusions	The implementation of AI technologies in medicine will have its greatest effect on current and future medical trainees. As a result, medical schools and graduate medical education must adapt their curriculum to educate present and future generations of physicians in the responsible use of these groundbreaking technologies.
Reference 1	Keywords: Humanity, ethical imperatives, patient-physician relationship, artificial intelligence, medical education, physician identity

Category	Other Research-Related Topics, #94
Primary Author	Jennifer Ozawa
Secondary Authors	Jennifer Ozawa, Naomi Taylor, Kwame Opoku Akyeampong, Tifany Frazer, Sarah Ehlinger Affotey, Amber Rios, Joyce L. Sanchez, Stephen Hargarten
Title	The Local Economic Impact of Global Health: The Greater Milwaukee Global Health Landscape Study
Introduction	The Milwaukee metropolitan area is home to over 1.5 million people of diverse backgrounds and several major academic centers, hospital systems, and biohealth industries. A literature review revealed limited data describing the investment in local global health activities from these entities. The Milwaukee Global Health Consortium (MGHC), through partnership with RTI International (formerly Research Triangle Institute) sought to quantify this investment and its impact on the local economy in 2019. The data collected in this descriptive study is intended to showcase the investments' impact on Wisconsin's economy, make a case for increased investment in global health, and serve as a model for other metropolitan areas to consider.
Methods	Economic and educational data was collected from MGHC members and Milwaukee's largest global biohealth companies through interviews and surveys. Companies were selected based on available financial data and response to information request. Economic data collected primarily focused on employment, operating expenses, exports, and research relating to global health. Other data collected included organization type, global health activities, and global heath focus areas. Twenty greater Milwaukee area organizations were represented. In order to estimate the indirect and induced impacts of the direct employment and expenditure, the IMPLAN: economic impact modeling platform was used.
Results	Investment in Milwaukee's global health (GH) sector results in employment of 6,132 people and $2.9 billion of economic activity. After accounting for secondary and tertiary impacts of spending by organizations and their employees, the GH sector was estimated to support 16,961 jobs, $1.3 billion in labor income and $4.6 billion in economic output. Top disciplines of focus were infectious diseases (55%) and chronic diseases (50%), maternal, child, and newborn health (40%) and injury/violence (30%). Top activities included education, outreach and training (55%), clinical or professional services (40%), and research and feasibility studies (30%). Preparing future global health leaders, partnering to solve local and global problems, contribute to Wisconsin's health and economy.
Conclusions	This study describes the impact global health sector activities have in a defined metropolitan area and economy. Infectious disease was a top area of activity. This pandemic coupled with the economic data presented reinforces the need to enhance local investments in globally engaged institutions, companies, civil society, healthcare, and government.
Acknowledgements	The Milwaukee Global Health Consortium
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Category	Other Research-Related Topics, #95
Primary Author	Elizabeth Suelzer, MLIS, AHIP
Secondary Authors	Liz Witkowski, MILS: MCW Libraries; Jennifer Deal, MA, MLIS; Karen Hanus, MLIS, AHIP: Advocate Aurora Library; Barb Ruggeri, MLIS, AHIP: Carroll University Library
Title	Challenges to discovering the retracted status of an article
Introduction	Citing retracted literature has been a problem for some time. In a few recent studies in the field of library science, researchers have discovered that authors continue to cite literature after it has been retracted, sometimes in a positive light, and often without indicating the retracted status of the paper they are citing. The International Committee of Medical Journal Editors (ICMJE) provides recommendations for medical journal editors on how to retract an article. Publishers pass on retraction information to citation databases, and citation databases take steps in indexing retracted articles and notices of retractions to ensure that users are aware of the retracted status of an article. Despite the recommendations by the ICMJE and the steps taken by citation databases, it can be challenging for users to determine the retracted status of an article. Publisher websites and citation databases are not always consistent in how they display retraction information on their websites, thus users may be unaware of an article's retraction. The purpose of this study is to track how retracted articles appear on publisher websites and in citation databases.
Methods	In this study, we performed an analysis of 150 retracted articles to investigate how journals were labeling and disseminating article retractions and notices of retraction. To determine which articles to review, a search for articles that were indexed with a publication type "Retraction of Publication" was conducted in PubMed on Oct. 20, 2019. We limited to articles published in English since 2009. We identified the top 50 journals with the most retracted articles and chose 3 publications from each journal, giving us a set of 150 articles. We reviewed each article to document how the retraction information displayed on the journal publisher's website. Additionally, we searched the same set of 150 articles in six biomedical citation databases (PubMed, Ovid MEDLINE, Ebsco CINAHL, ProQuest PsycINFO, Scopus and Web of Science) to document how the retracted articles and notices of retractions were displayed.
Results	On publisher websites, our analysis found that of the ICMJE's seven recommendations for retracting an article, all seven recommendations were followed in only 47% (70 of 150) of the articles we looked at. Within a journal publisher's website, there was a lack of consistency in the way that retracted articles were labeled as being retracted. Abstracts were consistently labeled in the three examples we checked 78% (39 of 50) of the time, HTML versions were consistently labeled 70% (33 of 47) of the time, and PDFs on the publisher websites were consistently labeled as being retracted 64% (31 of 49) of the time. Criteria for analyzing the citation databases was largely based on PubMed's procedure for documenting retracted publications. PubMed had the best performance of the databases we analyzed, but even this database complied with all criteria in only 87% (131 of 150) of the articles we checked.
Conclusions	There is a need for clear labels and indicators of the retracted status of articles in the subsequent scholarly publications that cite them.
Reference 1	International Committee of Medical Journal Editors. Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals. Published online December 2019. Accessed May 14, 2020. http://www.icmje.org/recommendations/
Reference 2	Theis-Mahon NR, Bakker CJ. The continued citation of retracted publications in dentistry. J Med Libr Assoc. 2020 Jul 1;108(3):389-97.
Reference 3	Suelzer EM, Deal J, Hanus KL, Ruggeri B, Sieracki R, Witkowski E. Assessment of Citations of the Retracted Article by Wakefield et al With Fraudulent Claims of an Association Between Vaccination and Autism. JAMA Netw Open. 2019;2(11):e1915552.
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Category	Other Research Related Topics, #96
Primary Author	Robert Treat, PhD**
Secondary Authors	Kristina Kaljo PhD, Molly Falk-Steinmetz MS, Cheryl Crawford MS
Title	Medical Student Metacognition: The Predictive Personality Facets of Conscientiousness and Emotional Stability
Introduction	Metacognition is the awareness and regulation of thinking.[1] This involves goal setting, memory, comprehension monitoring, and strategy selection, which are salient features of effective learning.[2] It is important to examine how medical students regulate their own cognitive processes, so that if there are some underperforming elements, they can be assessed and improved. Medical student personality impacts metacognition,[3] but detailed associations at the higher resolution levels of these two constructs will provide greater insight into the features of learning. The purpose of this study is to analyze the impact of conscientiousness and emotional stability on medical student metacognition.
Methods	In 2019-20, 41 medical students voluntarily completed these self-reported surveys: Metacognitive Awareness Inventory (scale:0=false/1=true) to measure metacognition and Five-Factor Personality Inventory (IPIP-120, scale:1=very inaccurate/5=very accurate) to measure conscientiousness and emotional stability scores. Stepwise multivariate linear regression was used to predict metacognition scores from conscientiousness and emotional stability scores. Inter-item reliability determined via Cronbach alpha. IBM® SPSS® 24.0 generated statistical analysis. This research approved by the institution's IRB.
Results	The empirical range of metacognition (alpha=0.78) scores was 22-46 with a mean (sd)=39.0 (6.0) and were significantly (p<.001) above the instrument's midline score=26. Linear regression results for medical student metacognition was predicted (R^2=0.85, p<0.001) by two elements of conscientiousness (alpha=0.87): orderliness (beta=1.2) and achievement striving (beta=0.5). Linear regression results for medical student metacognition was predicted (R^2=0.46, p<0.001) by one element of emotional stability (alpha=0.90): immoderation (beta=0.7). Additional significant (p<.001) predictive elements of emotional stability emerged in the regressions when overall metacognition was split into knowledge and regulation, which included facets of anxiety, self-consciousness, vulnerability, and anger.
Conclusions	Medical student metacognition scores were predicted by personality facets of conscientiousness and emotional stability. However, emotional stability facets have greater predictive capacity at higher resolutions of metacognition, suggesting greater complexity and importance of emotions in metacognition.
Reference 1	Ohtani K, Hisasaka T, Beyond Intelligence: A Meta-analytic Review of the Relationship among Metacognition, Intelligence, and Academic Performance, Metacognition Learning 2019;13:179-212.
Reference 2	Rhodes MG, Metacognition, Teaching of Psychology 2019;46(2):168-175.
Reference 3	Karpov AA, Karpov AV, Karabushchenko NB, Ivashchenko AV, The Interconnection of Learning Ability and the Organization of Metacognitive Processes and Traits of Personality, Psychology in Russia: State of the Art 2017;.10(1):67-79.

Category	Other Research-Related Topics, #97
Primary Author	Michael Nagy, PharmD, BCACP**
Secondary Authors	Zach Pape, PharmD, BCACP
Title	Student pharmacist preference and perceptions of synchronous versus asynchronous virtual learning
Introduction	The Medical College of Wisconsin School of Pharmacy adapted to COVID-19 through a transition to virtual learning. Decisions for synchronous versus asynchronous methods of instructional delivery were left to individual course instructors. Past literature comparing these modalities in health professional education, while limited, show benefits of asynchronous virtual learning regarding quality of audio and visual environments, convenience, and limiting distractions with the "available anytime" format. 1,2 Moridani found asynchronous students performed slightly better in final course grades, possibly due to the opportunity for asynchronous learners to absorb content more completely and therefore better able to apply information in solving problems.3 As the pandemic subsides, future instruction may see an increased use of technology and alternative teaching methods in academia and clinical practice. Therefore, information gained from the pseudo-experimental shift to virtual learning is valuable. The purpose of this project is to evaluate student preferences, perceptions, and performance with synchronous and asynchronous virtual learning environments in didactic and skills-based coursework.
Methods	The retrospective mixed-methods study used data from a virtual learning survey (5-point Likert scale and open response questions) created by the assessment committee for student pharmacists to provide feedback during the early transition period in response to COVID-19. Study investigators analyzed anonymous survey data and compared subjective responses with course performance. Performance during virtual learning was compared with the prior year course data for didactic classes. Since patient care lab is consistent through all eight quarters, breakdown by quarter was evaluated for impact of virtual learning on a single cohort's performance. Survey responses were analyzed with mean and inter-quartile range for ordinal data and through content analysis for open response data.
Results	Overall, 32 of 96 (33%) P2 and P3 students voluntarily responded to the virtual learning survey. Technology functioned well for most respondents with live breakout sessions demonstrating the most issues. No significant differences existed between cohorts regarding technological function or the enhancement to learning based on instructional delivery. However, the P2 cohort reported preference for asynchronous learning over synchronous virtual learning [median 4.5 (IQR 4.0-5.0) vs. 3.0 (IQR 1.0-4.0), $p<0.05$]. Between the two student cohorts most common challenge was "not having a dedicated learning space at home" with 20 respondents indicating this as an issue. Overall, the highest support for virtual learning was related to the use of pre-recorded lecture material incorporated into instruction. Course performance data showed similar or slightly improved average performance for the virtual learning compared to the control group the prior year.
Conclusions	Health professional educators should consider student perspectives for optimization of virtual learning. Identified barriers, (lack of a dedicated learning space free of distractions and the function of technology) likely influence preference for asynchronous learning modality by providing flexibility while maintaining course structure.
Acknowledgements	Thank you to the School of Pharmacy assessment committee for developing and distributing the virtual learning survey. Additionally, we thank Erin Walcheske for collating survey and performance data for the project. Finally, we thank Dr. Mathew Letizia for assisting in the initial development of the project.
Reference 1	Buxton EC. Pharmacists perceptions of synchronous versus asynchronous distance learning for continuing education programs. AJPE. 2014;78(1)Article 8.
Reference 2	Kunin M, Julliard KN, Rodriguez TE. Comparing face-to-face, synchronous, and asynchronous learning: postgraduate dental resident preferences. J Dent Edu. 2013;78(6):856-866.
Reference 3	Moridani M. Asynchronous video streaming versus synchronous videoconferencing for teaching a pharmacogenetic pharmacotherapy course. AJPE. 2007;71(1)Article 16.
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Biochemistry

The research interests of our faculty span a broad spectrum of biochemistry ranging from cell and developmental biology to structural biology. The unifying theme defining us is an interest in biological processes at the molecular level. The department is home to state of the art facilities and instruments for X-ray crystallography, NMR spectroscopy, mass spectrometry, fluorescence microscopy, to name just a few. A collaborative and collegial atmosphere makes the Biochemistry Department an ideal place to do science and train for a wide variety of biomedical science careers.

Research Facilities

Biacore S200 SPR Instrument: The Biacore S200 SPR instrument can measure interactions of various sample types, from low molecular weight drug candidates to high molecular weight proteins (also DNA, RNA, polysaccharides, lipids, cells, and viruses) in various sample environments (e.g., DMSO-containing buffers, plasma, and serum).

Applications include:

- Fragment screening and LMW drug discovery
- Kinetic and affinity determination
- Competition assays
- Epitope mapping of antibodies
- Thermodynamics

The high sensitivity and low baseline noise of the Biacore S200 facilitate reliable affinity, kinetic, and fragment-screening data. The Biacore S200 is optimized for small molecule library screening, with automated software to evaluate non-specific binding, identification and prioritization of binders, and calculation of association (k_a) and dissociation (k_d) rate constants and affinity (K_D). The Binding Level Screen function provides a rapid overview of small molecule libraries, automatically identifying fragments above a defined cut-off level. The predefined template for Binding Level Screen was developed explicitly for a 384-well plate format, allowing 384 compounds to be screened in less than 16 hours.

The S200 software also offers a range of tools for kinetic analysis, including analysis of single-cycle kinetics where several concentrations of an analyte are injected in the same cycle. Multicycle injections can still be analyzed, but by eliminating surface regeneration between injections, single-cycle kinetics simplifies the analysis of targets that are unstable or difficult to regenerate. Single-cycle kinetics also reduces analysis time. By utilizing the predefined templates for kinetics, thirty different analytes can be run in as little as 16 hours.

The Biacore S200 also simplifies competition studies to validate small molecules' interaction site with the capability to use ABA injections. The ABA injection mode allows two different solutions to be injected over the surface in the same cycle consuming much less inhibitor than traditional SPR experiments. In addition, the ABA injection feature can help identify ternary complex formation with multiple ligands.

The Biacore S200 instrument is housed in the Biochemistry Department. It is available to all Medical College of Wisconsin faculty and staff who are trained and can demonstrate proficiency on the instrument. Training and consultation are available by appointment.

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BIAcore 3000 Instrument: The BIAcore 3000 instrument integrates surface plasmon resonance (SPR) technology with a microfluidics system to monitor molecular interactions in real time at concentrations ranging from pM to mM. This label-free technology can detect

a wide range of molecular masses from 180Da to >1000kDa. The high sensitivity and high through-put capabilities allows for the detection of drug-protein, hormone-protein, protein-protein, DNA-protein, carbohydrate-protein, and lipid-protein interactions. The ability to interface with mass spectrometers provides discovery-based research in proteomic studies. For more information about SPR technology, theory, and applications, please see the attached BIAcore presentation (PDF).

The BIAcore 3000 instrument is housed in the Department of Biochemistry and is available to all Medical College of Wisconsin faculty and staff who have been trained and demonstrate the ability to use microfluidic-based instrumentation. Training and consultation are available on an appointment basis.

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Biomolecular NMR at MCW: 600 MHz NMR spectrometer. Cryoplatform is visible to the left of the magnet, RF console and workstation to the right. The NMR Facility is an interdepartmental research service unit located in the Biochemistry Department. High-field NMR spectroscopy is a powerful technique for the study of biomolecular structure and dynamics. The facility provides service for routine 1D and 2D NMR methods, and can also provide consultation and collaborative assistance with the acquisition and analysis of multidimensional, multinuclear protein NMR spectra. The facility operates two Bruker 600 MHz and one 500 MHz NMR spectrometers, each equipped with 1H/13C/15N cryoprobes for enhanced sensitivity in biomolecular applications. In addition, a Bruker 300 MHz NMR spectrometer is available for routine analytical NMR of small molecules. For some long-term projects, the facility provides training for instrument operation and data analysis to investigators and research personnel. The facility operates on a fee-for-service basis and is open to faculty of the Medical College of Wisconsin and outside researchers.

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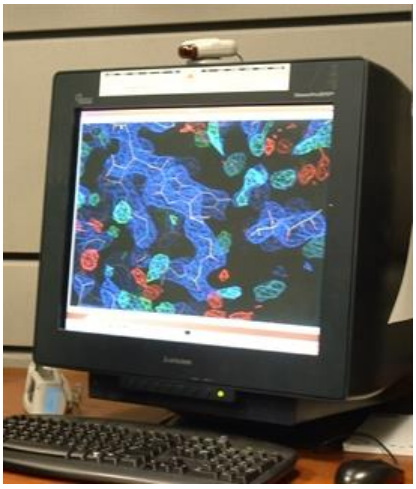
Macromolecular X-Ray Crystallography Facility: The department houses state-of-the-art instrumentation dedicated to Structural Biology research. The facility includes chromatographic systems for protein purification, an in-house X-ray diffraction core and an automated crystallization system for high-throughput screening and optimization. High-end computer workstations have been set up for 3-D graphic visualization and crystallographic analysis.

Automated Crystallization Systems: Hamilton (left) and Phoenix crystallizers (right)

In-house X-ray Diffraction Laboratory (*left*) and Graphics Workstations (*right*)

The facility is open to faculty members of the Medical College of Wisconsin. Various levels of training are available and collaborative arrangements can be made to scientists both inside and outside of the MCW community.

Linda Olson, PhD
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Shared Research Instrumentation

The Biochemistry Department maintains several instruments for isolation and physical characterization of biomolecules and detection of their interactions. All are located on the second floor of the TBRC and include:

Jasco J-710 Circular dichroism spectropolarimeter
The Jasco J-710 circular dichroism (CD) spectropolarimeter is equipped with a thermally regulated sample compartment. Monitoring of the far-UV and/or near-UV CD spectra can provide valuable information about the secondary structure, thermal stability, or conformational state of a protein.
Contact: Nolan Kennedy, nolkennedy@mcw.edu

Photon Technologies Inc. QuantaMaster™ spectrofluorometer
The QuantaMaster™ spectrofluorometer is outfitted with dual excitation and emission monochromators for high sensitivity, a thermally regulated sample compartment, and Glan Thompson polarizers for fluorescence anisotropy measurements. The instrument is suitable for emission/excitation scanning experiments, fluorescence experiments requiring synchronous scanning of the excitation and emission monochromators, time based fluorescence measurements, fluorescence resonance energy transfer experiments and fluorescence anisotropy measurements.
Contact: Francis Peterson, fpeterso@mcw.edu | Davin Jensen, djensen@mcw.edu

MicroCal VP - Isothermal Titration Calorimetry
The MicroCal VP-ITC is capable of measuring heat evolution as little as 0.4 nanoJ/sec. This instrument is suitable for the studies of protein-ligand and protein-protein interactions and provides the biochemists with reliable measurements of binding constants in the range of 10^3-10^9 M^{-1} as well as the enthalpy and stoichiometry of interactions. ITC is a preferred technique to demonstrate the interaction between newly discovered binding partners *in vitro*.
Contact: Brian Smith, brismith@mcw.edu

Perseptive Biosystems Voyager DE-Pro MALDI mass spectrometer
The matrix-assisted laser desorption ionization (MALDI) mass spectrometer is used for routine mass determination of peptides, proteins and other macromolecules.
Contact: Davin Jensen, djensen@mcw.edu

Promega Maxwell-16 robot
This benchtop instrument provides fast automation of routine DNA, RNA or protein extractions resulting in reproducible yields and purity. Parallel multi-channel operation permit automated purification of milligram yields of up to 16 different recombinant proteins in less than one hour.
Contact: Davin Jensen, djensen@mcw.edu

Molecular Devices Flexstation 3 microplate reader
This benchtop instrument is a 5-mode microplate reader for use in a wide range of biochemical- and cell-based assays for basic research and drug discovery. This instrument is equipped with an 8-channel pipettor for 96-well-based assays based on absorbance, fluorescence intensity, fluorescence polarization, luminescence, and time-resolved fluorescence assays. It has high-efficiency tunable monochromator optics and a dedicated photomultiplier tube for luminescence assays.
Contact: Chad Koplinski, ckoplinski@mcw.edu | Francis Peterson, fpeterso@mcw.edu

Program in Chemical Biology

The Program in Chemical Biology (PCB) provides resources in structure-based drug design, protein production, and organic synthesis to the MCW community for chemical biology and medicinal chemistry projects. The PCB is a valuable resource for faculty throughout the MCW research environment, supporting projects from the departments of Biochemistry, Biophysics, Cell Biology, Medicine, Microbiology and Immunology, Pharmacology and Toxicology, and Pediatrics. Collaborating centers and programs include the Cardiovascular Center, Cancer Center, Center for Infectious Disease Research, Genomic Sciences & Precision Medicine Center, National Biomedical EPR Center, Neuroscience Research Center, Research Computing Center, and Redox Biology Program. Different focus groups within the PCB meet weekly to discuss the progress of active projects and evaluate new collaborative opportunities. The PCB encourages investigators interested in the development and use of small molecules for basic and translational research to take advantage of its capabilities which include:

- Small-molecule library screening using NMR and other biophysical techniques
- Recombinant protein expression and purification
- Organic synthesis
- Computational docking and homology modeling of proteins and small-molecule:protein interactions

For more information or discussion contact:

Dr. Brian Volkman, Director (bvolkman@mcw.edu, (414) 955-8400)
Dr. Brian Smith, Associate Director (brismith@mcw.edu, (414) 955-5669)

Biomedical Engineering

DEPARTMENT OF BIOMEDICAL ENGINEERING

MARQUETTE UNIVERSITY

MEDICAL COLLEGE OF WISCONSIN

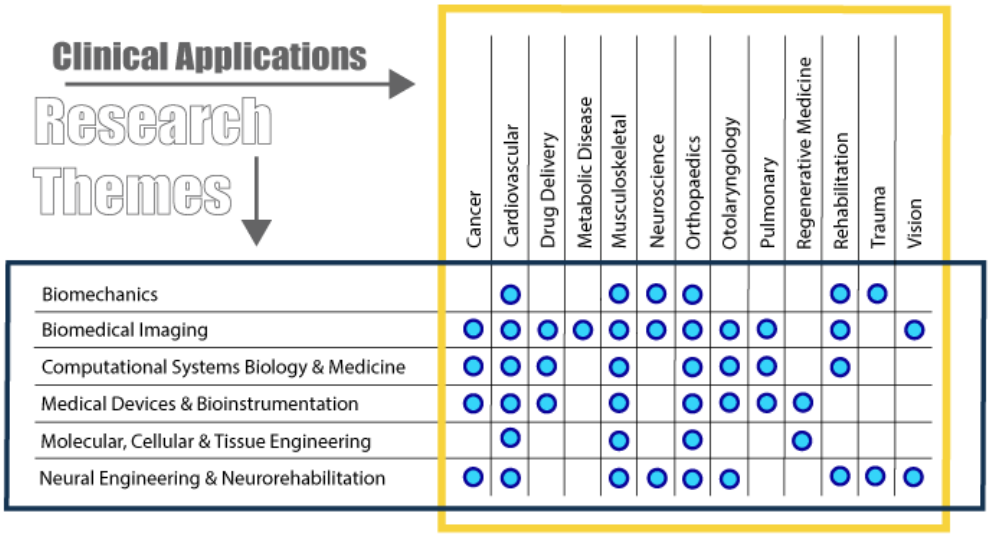
The Marquette University and Medical College of Wisconsin Department of Biomedical Engineering (Joint Department) provides a unique opportunity to grow southeast Wisconsin's biomedical engineering capabilities and reputation. Biomedical engineering is a multidisciplinary approach with unique influence, integrating education, research, patient care, industry and marketplace. The Joint Department presents many opportunities, investments and returns for various stakeholders including students, faculty, institutional and college leaders, donors, investors and industry partners.

Our mission is to serve our institutions, our community, and the world by applying engineering approaches to solving critical unmet biomedical research and clinical needs.

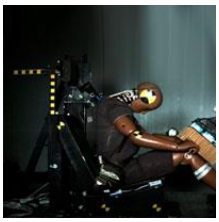
Clinical Collaborations

The Marquette-MCW Department of Biomedical Engineering provides tremendous opportunities to conduct research involving MCW clinical partner locations throughout the region. This exposure is second to none among biomedical engineering programs around the country, offering an amazing array of research opportunities in close proximity to your campus. Clinical collaborators include:

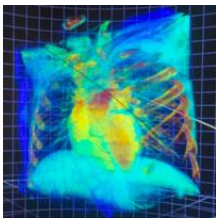
- Versiti (Blood Center of Wisconsin)
- Critical Care and Pulmonary Medicine – F&MCW
- Neurology- F&MCW
- Neurosurgery- F&MCW
- Ophthalmology- F&MCW
- Orthopedics – F&MCW
- Otolaryngology – F&MCW
- Physical Medicine and Rehabilitation- F&MCW
- Radiation Oncology – F&MCW
- Radiology – F&MCW
- Herma Heart Center & the Pediatric Genetics Groups at Children's WI
- VA Medical Center



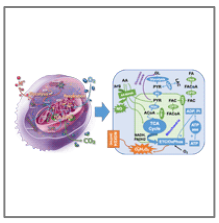
Research Themes



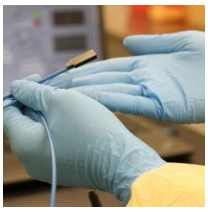
Biomechanics & Rehabilitation Bioengineering
Simply put, Biomechanics is the study of the structure, function and motion of the mechanical aspects of biological systems. When applied to the human body, biomechanics describes how muscles, bones, tendons, and ligaments work together to produce movement under neuromuscular control.



Biomedical Imaging
The Biomedical Imaging Engineering research groups in the MCW-MU Joint Department of Biomedical Engineering focus on developing new techniques to noninvasively visualize the structure and function of living objects for clinical analysis and medical intervention.

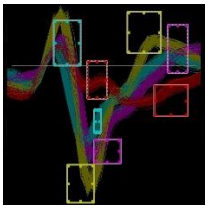


Computational Systems Biology & Medicine
Computational Modeling is the practice of using computer models and systems to simulate complex biological processes. Computational modeling has many applications in medicine, which include improving our understanding of human physiology, visualizing and interpreting experimental data, and designing novel therapies.



Medical Devices & Bioinstrumentation
Medical devices are at the heart of biomedical engineering, and faculty in the MCW-MU Joint Department of Biomedical Engineering have proficiency in instrumentation, biomaterials, medical device testing and design, and clinical and regulatory expertise. This broad base of skills and expertise positions our department at the forefront of medical device innovation.

Molecular, Cellular & Tissue Engineering
Tissues may become damaged due to injury or disease. Molecular, Cellular, and Tissue Engineering is a research specialization in Biomedical Engineering which seeks to repair or replace damaged tissues, such as heart valves, blood vessels, skin, cartilage, or bone by gaining understanding of the molecular and cellular mechanisms involved in the damage and regeneration.



Neural Engineering & Neurorehabilitation
The Neural Engineering and Neurorehabilitation research groups in the MU-MCW Department of Biomedical Engineering focus on the brain, the nervous system, and motor control. Researchers use a variety of engineering tools to analyze neurological function and with engineering solutions for problems associated with neurological pathologies, disabilities, limitations, and dysfunction.

Goals

- Develop new, highly innovative and translational programmatic areas of international excellence through collaboration with our partner institutions.
- Support entrepreneurial and industry activities that result in bringing biomedical engineering innovations to market
- Create seed funding to support developmental research using technological innovation to solve unmet clinical needs both globally and in our own community

Our faculty, staff, and students continuously strive to further advance the Joint Department's mission and enhance the impact of our discoveries and technology developments. Through their dedication and effort, the Joint Department will continue to contribute to scientific advances in biomedical research and explore clinical applications at Marquette University and the Medical College of Wisconsin.

Biophysics

The Department of Biophysics at MCW is dedicated to excellence in research and graduate and postdoctoral training. The research interests of our faculty are broadly based, with strong, innovative research programs in electronic paramagnetic resonance (EPR) spectroscopy, protein structure and function, biological membranes, redox biology, instrumentation development as well as novel magnetic resonance imaging (MRI) applications and data analysis for the study of cancer biology and Alzheimer's disease models for translation to clinical practice.

The Department of Biophysics has state-of-the-art facilities and equipment geared toward these programs. The department houses chemical and biochemical labs, two tissue culture labs, an engineering complex, a microwave lab, five EPR spectroscopy labs, and a machine shop.

EPR Research

The National Biomedical EPR Center at MCW is the most extensive EPR facility in the nation. It was supported by an NIH P41 research resource award from 1976 to 2019. The research conducted within the EPR Center includes technological innovation and application of new techniques to biological problems. The main areas of research are spin labeling of proteins and lipids, structural and conformational changes of proteins, redox changes at the active site of metallo-proteins, and oxidants and free radical formation in tumorigenesis and tumor progression and in drug resistance in cancer. The EPR Center houses an array of internally developed and commercial EPR instrumentation, a specialized engineering/development staff capable of steadily and significantly advancing the state-of-the-art technology for biomedical applications of EPR spectroscopy, and a scientific staff with broad expertise.

Redox Research

Scientists in the Department of Biophysics are internationally recognized for their expertise in and contribution to the field of free radical and redox biology. The main research focus is on establishing the role of free radicals and oxidants in pathophysiological conditions (e.g., in cardiovascular diseases, neurodegeneration, and cancer) and in normal cell function. The department provides an environment for development of novel, rigorous chemical probes and assays for monitoring the generation of free radicals in cells (in vitro) and animals (in vivo). These include fluorogenic and bioluminescent probes, EPR spin traps, and probe-free assays (e.g., redox immunoblotting [peroxiredoxins, thioredoxins] and low-temperature EPR studies of the redox status of cellular protein metal centers). Ongoing collaborative work within MCW (e.g., Cardiovascular Center, Cancer Center) and with other institutions utilizes these assays to understand the role of oxidants in cardiovascular diseases (e.g., stroke, ischemia-reperfusion), neurodegeneration (e.g., Parkinson Disease), and cancer (e.g., cancer cell proliferation, chemoprevention, and chemotherapy).

MR Physics & Brain Imaging Research

MCW Biophysics scientists have been engaged in MRI/functional MRI (fMRI) research for more than 25 years, publishing the first paper on fMRI in 1992 and on resting-state fMRI in 1995. The widely used fMRI software program AFNI (Analysis of Functional NeuroImages) was developed in Biophysics in 1994. Imaging technology development has been a hallmark in Biophysics, beginning with the introduction of the local gradient coil for fMRI. The current emphasis is on applications to cancer and neurological and psychiatric disorders (e.g., early disease detection, precision disease prevention, prediction of disease development, and assessment of treatment efficacy in tumorigenesis and Alzheimer's disease research). Strong interdisciplinary collaborations exist, centering on chronic pain mechanisms, psychiatric depression, and other fields in neuroscience.

Biophysics Graduate Program

The Biophysics Graduate Program features two primary areas of research: Magnetic Resonance Imaging and Molecular Biophysics. Our program is designed to assist young scientists in developing the research skills they need to thrive in academic, industry, and clinical settings. The Magnetic Resonance Imaging track places emphasis on MRI; fMRI of the human brain is an active research area (neuroscience, cancer, technical development). The Molecular Biophysics track encompasses the investigation, detection, and use of free radicals and paramagnetic metal ions in biological systems using EPR spectroscopy. Students with more of a physical background may specialize in EPR instrumentation.

Centers

The Department of Biophysics is home to the MCW Cancer Center Bioenergetics Shared Resource, National Biomedical EPR Center, and Redox Biology Program.

More Information

For more information about the department of Biophysics, visit our website (www.mcw.edu/departments/biophysics).

National Biomedical EPR Center

Current Director: Candice S. Klug, PhD
Founding Director: James S. Hyde, PhD

The National Biomedical Electron Paramagnetic Resonance (EPR) Center at MCW is the largest EPR facility in the nation. The National Institutes of Health (NIH) has made an enormous investment in EPR research at MCW over the past four decades. Most significantly, the NIH funded the EPR Center as a P41 Research Resource for more than 40 years to develop "the most extensive and advanced biomedical-oriented EPR facility in the world, with a complete range of EPR equipment, an engineering/development staff capable of steadily and significantly advancing the state-of-the-art technology for biomedical applications of EPR spectroscopy, and a scientific staff with broad experience across many fields."

EPR spectroscopy is a critically important technique in biomedical research. The fundamental power of EPR is its unique ability to detect unpaired electrons, either naturally occurring or engineered through site-specific labeling, in complex biological environments and its wide-ranging applicability to biomedically important areas of research such as structural biology, metalloproteins, redox biology, and rational drug design. EPR is also ideally suited to dynamic studies, as the wide array of EPR technologies that have been developed at MCW and elsewhere span the entire picosecond to millisecond timescale of protein motion. EPR provides detailed structural information on proteins, from helical rocking modes and loop fluctuations to large-scale tertiary rearrangements and protein-protein and protein-ligand interactions. In comparison with other biophysical approaches such as NMR (nuclear magnetic resonance) and fluorescence-based methods, EPR has distinct advantages in its ability to directly detect an unpaired electron attached to a protein in any environment, including macromolecular complexes, membrane proteins in their native lipid environments, distinct populations of protein states exchanging on the microsecond timescale, and on limited samples using short acquisition times. EPR technology also is central to characterizing metalloprotein structure and function, a gold standard for the detection of biological free radicals in redox biology, and a powerful method to reveal free radical and metalloprotein signatures in tumor and tissue samples as a diagnostic tool.

An impressive array of custom-built and commercial instrumentation is housed within the National Biomedical EPR Center in the Department of Biophysics at MCW. Our resources and expertise are available to scientists at MCW, regionally, nationally, and internationally. To take advantage of our instrumentation resources or collaborate with our faculty and engineers, learn more on our website: www.mcw.edu/departments/national-biomedical-epr-center

Cell Biology, Neurobiology, and Anatomy

Cell Biology, Neurobiology, and Anatomy Cell Biology, Neurobiology & Anatomy (CBNA) is one of the six Basic Science Research departments at MCW. CBNA faculty members and graduate trainees conduct fundamental research in the areas of cell biology, developmental biology and neuroscience, with expertise covering the brain, gastrointestinal tract, liver, retina and heart. Our Department is home to the Cell & Developmental Biology graduate training program as well as the Neuroscience Graduate program, and we prioritize the ability of our trainees to gain experience to a variety of cutting-edge methods from single molecule to whole organism assays and present their results at national meetings. CBNA's traditional focus on developmental pathway mechanisms caused it to evolve a major emphasis on stem cell biology, and its potential for regenerative medicine, during the past decade. CBNA is home to MCW's Program in Regenerative Medicine and Stem Cell Biology, which utilizes pluripotent stem cells to study pathways of normal development and disease. The Department has current expertise in neural, gastrointestinal, liver, and cardiovascular stem cell models. CBNA faculty members also play an essential role in the Medical School's Discovery Curriculum courses, including the first year Clinical Human Anatomy, Medical Neuroscience and Molecules to Cells courses, as well as several second-year courses. We have recently welcomed several new Faculty to MCW, who will enhance collaborative projects across our basic and clinical enterprise, and bring new technologies and capabilities to campus. For further information, please visit our department website: http://www.mcw.edu/cellbiology.htm

Microbiology & Immunology

Faculty research spans a broad range of interests including, viral and bacterial infection and pathogenesis, inflammation and immunology, enzymology and metabolism, molecular genetics, and signaling and gene expression. Our faculty address questions at the cellular and molecular level, using contemporary technology and approaches where more than 30-faculty serve as graduate student research mentors. Many graduates of our Program conduct postdoctoral studies and then serve as faculty at academic medical centers or scientists in research institutes, industry, and government.

Microbiology & Immunology

Departmental bacteriologists study a variety of organisms and topics, which include the identification and characterization of the delivery, trafficking and function of bacterial toxins that target key cellular processes of the eukaryotic host. Toxins under study include the botulinum and tetanus neurotoxins, and the ExoS and ExoU type-III effectors encoded by Pseudomonas aeruginosa. A variety of genetic, cell biological, biochemical, and structural approaches support the study of the biological functions of these toxins. Moreover, the toxins themselves and delivery machinery are components of potential vaccines. Faculty research interests also address intrinsic antibiotic resistance in Gram-positive bacteria such as E. faecalis where one major areas of study is a kinase/phosphatase system that mediates resistance to the cephalosporin family of antibiotics. Other faculty study host-pathogen interactions of spirochetes.

Departmental virologists study different research topics on members of the herpesvirus family. These topics include studies on the immune evasions encoded by human herpesvirus 6 and 7, host/ human cytomegalovirus interactions, using a combination of virology and mass spectrometry. MHV68, a mouse pathogen which is similar to the KSHV and EBV viruses that infect humans is also studied to understand the host DNA damage response and the interferon system to infection, and in how these viruses cause hematological malignancies.

Departmental immunologists address various aspects of the immune system. These topics include the study of chemokines, which are chemotactic cytokines that can affect the homing of various cell types to different organs. This work focuses on how the expression of chemokines and chemokine receptors affects tumor progression and metastasis; pancreatic cancer and other high-risk malignancies are a particular focus. Other studies address how the immune system combats infections by bacteria that establish granulomatous lesions, as seen in tuberculosis. These studies address the role of the cytokine IL12 and its cognate receptor. Departmental molecular geneticists' study various aspects of gene expression and fundamental cell biology. These studies focus on how differential mRNA splicing and polyadenylation regulate gene expression and modulate viral and cellular behavior, while other studies address mRNA localization, and the role of localization on cell fate, and studies essential cellular proteins that regulate mitochondrial protein import and lipid composition.

Center for Immunology

The Center for Immunology Program consists of a highly collaborative and integrated group of scientists from the Medical College of Wisconsin, Blood Research Institute and Children's Research Institute whose goal is to promote immunological education and research on campus at both the basic and clinical level. the Center for Immunology is composed of research laboratories focused on the immunological aspects of autoimmunity, infectious disease, allergy, immunodeficiency and cancer and is forging new links to physician colleagues at Froedtert Hospital and the Children's Hospital of Wisconsin. Graduate research training in immunology is offered through the Microbiology and Immunology graduate program. The Immunology Group sponsors a number of campus wide events offering additional training in immunology including a weekly journal club and Work-in-Progress. Immunology focused research seminars are available on campus through weekly Dept. of Microbiology and Immunology, Blood Research Institute and the Children's Research Institute seminar series. Now in its 12th year, the Immunology Group hosts an annual Immunology Scientific Retreat. The Center for Immunology held its inaugural retreat at Miller Park in March 2019 and will host its Retreat in Spring of 2020.

Faculty Research Expertise:

John Kirby, PhD: Chairman, major areas of research focus on signal transduction in diverse bacteria ranging from soil dwelling spore formers (Bacillus subtilis and Myxococcus xanthus) to biofilm forming pathogens, to microbial communities in the gut. Dr. Kirby is actively investigating interactions between M. xanthus and B. subtilis as a model for predator-prey interactions in vivo, primarily to assess the role of production of specialized metabolites, similar to antibiotics, on both sides of the predator-prey equation. Additionally, he has been examining the role of xenobiotics (antipsychotics, antihypertensives and antibiotics) for their capacity to disrupt the gut microbiota with deleterious consequences on metabolism.

Joseph Barbieri, PhD: research involves the study of bacterial toxins. Several families of bacterial toxins are under investigation: botulinum and tetanus neurotoxins; Certhrax, an ADP-ribosylating exotoxin from Bacillus cereus; and ExoS, a type III cytotoxin of Pseudomonas aeruginosa. Dr. Barbieri is also the Director for the Medical Scientist Training Program (MSTP).

Kenneth Brockman, PhD: Dr. Brockman's research is focused on understanding bacterial-host interactions within the human airways, with an emphasis on understanding the microbial regulatory mechanisms that underlie chronic diseases, such as otitis media and exacerbations of lung disease. One area of specific interest seeks to elucidate the role of the phase variable regulon (phasevarion) of nontypeable Haemophilus influenzae during disease. His lab utilizes a range of in vitro assays and experimental disease models to determine bacterial genes required for persistence and define their specific roles in pathogenesis in order to develop improved preventative and therapeutic strategies to combat infection and disease.

Weiguo Cui, PhD: The main goal of his research in the lab is to elucidate how TCR and cytokine signaling and their downstream transcriptional programs regulate pathogen-specific T cells to proliferate, differentiate into either short-lived effector cells or long-lived memory cells.

Bonnie Dittel, PhD: One goal of Dr. Dittel's research program is to investigate the cellular and molecular mechanisms involved in the regulation of the autoimmune immune response. Broadly, they are studying how the immune system regulates inflammation associated with the central nervous system autoimmune disease multiple sclerosis (MS). These studies are largely conducted using the animal model of MS experimental autoimmune encephalomyelitis (EAE). Specific areas of interest are regulatory mechanisms of B cells, immune-mediated neuronal damage and myeloperoxidase as a therapeutic target in CNS autoimmunity.

Michael Dwinell, PhD: Research in the Dwinell laboratory seeks to define the role for extracellular mediators in the progression and metastasis of solid and hematological cancers. Additional studies are examining the role for metabolic reprogramming to influence tumor progression and exploring new mitochondria-targeted compounds as inhibitors of cancer progression. Human and murine 2D and 3D cell culture systems and preclinical models are being used to investigate the cellular, biochemical, and metabolic signaling pathways that regulate cellular proliferation, programmed cell death and motility in inflammation and cancer.

Dara Frank, PhD: Dr. Frank's laboratory focuses on type III secretion systems (T3SS) and their effectors with specific emphasis on pathogens that inject patatin-like phospholipases causing severe lung pathology. P. aeruginosa and several other bacterial genera encode orthologous patatin-like PLA2 effectors that are highly toxic to eukaryotic cells. The founding member of this family is ExoU, which we have shown requires a noncovalent interaction with ubiquitin (Ub) or ubiquitylated proteins to express membrane destructive activity. Other than acting as overt toxins, the biological function of this family of enzymes is unclear. The mechanism of Ub-mediated activation has not been solved. Further, while there are crystal structures representing the inactive form of ExoU and a closely related ortholog, structural changes that result in activation are unknown. Understanding the mechanism of activation could lead to the development of therapeutics for a broad spectrum of organisms. To understand the structural changes that occur during membrane and ubiquitin association, we are using biophysical (continuous wave EPR and double electron-electron resonance), biochemical (mutagenesis and enzymology) and computational approaches (molecular dynamics and modeling).

Jack Gorski, PhD: Dr. Gorski is interested in understanding the molecular basis of T cell immunity in man, focusing on polymorphism and variability within this system. Work in his lab has involved one to many to one mapping of the principle components of the system: the MHC, antigen peptide, and TCR. He has been interested in the biophysics of binding of multiple peptides to a single class II MHC molecule, as well as the ability of a single peptide to bind multiple class II MHC. Similarly, he has a strong interest in the biophysics of many TCR interacting with a single peptide-MHC complex as well as the T cell cross-reactivity (one TCR binding many peptide-MHC complexes).

Amy Hudson, PhD: The Hudson lab is interested in how viruses escape detection by the immune system. As a response to selective pressures exerted by the host immune system, many viruses have developed an equally complex set of immune-evasive strategies.

Perhaps most interesting is the array of unique strategies that viruses employ to interfere with the presentation of viral antigens on the surface of host cells for recognition by cytotoxic T lymphocytes.

Nikki Johnston, PhD: Dr. Johnston's research laboratory measures pepsin, as a diagnostic biomarker for reflux and aspiration, in clinical tissue and secretion samples from patients with diseases of the upper airway, investigates the effects of nonacid pepsin on the airway using in vitro and in vivo models and the molecular signaling pathways through which nonacid pepsin elicits cell damage. In addition to investigating the role of pepsin in reflux-attributed inflammatory disease, her group has highlighted a potential role for refluxed pepsin in carcinogenesis of the laryngopharynx and for local acid and pepsin production in Barret's esophagus and its progression to esophageal adenocarcinoma. Her research team is currently investigating the mechanism by which pepsin causes inflammation and promotes carcinogenesis. Her team is also leading a drug discovery program to develop a therapeutic for reflux disease which specifically targets pepsin. They have developed high throughput screening assays, identified a FDA approved drug which also inhibits pepsin, and developed a mouse model to test the efficacy of these drugs for pepsin-mediated laryngeal inflammation in vivo. This work will pave the way for a clinical trial for a much-needed medical therapy for patients with airway reflux using a faster repurposing approach and allow us to provide proof of concept that a pepsin inhibitor will be effective for patients with airway reflux and thus de-risk the development of new compositions of matter, perhaps more potent with optimized formulation for local delivery by nasal spray.

Christopher Kristich, PhD: Dr. Kristich uses genetic, molecular, biochemical, and genomic experimental approaches to understand (1) the mechanisms by which Gram-positive bacteria sense internal and external stimuli (the input), (2) how these signaling systems control cellular processes in response to environmental conditions (signal processing); and (3) the biochemical mechanisms of antimicrobial resistance and gut colonization (the output). His goal is to understand all aspects of the sensory process: to define the signals that are sensed, to understand the signal transduction processes mechanistically, to identify the corresponding physiological or behavioral output, and to elucidate how that output – the product of the signal transduction processes – enhances the ability of the bacteria to survive and proliferate in their natural settings. He approaches problems of bacterial signal transduction in the context of basic bacterial physiology, host-microbe interactions, and microbial pathogenesis, with the goal of understanding how fundamental bacterial signaling processes serve to shape the outcome of interactions with human hosts and the environment.

Robert Lochhead, PhD: Dr. Lochhead is an immunologist studying the pathogenesis of Lyme arthritis, which is caused by infection with the tick-borne pathogen *Borrelia burgdorferi.* He conducted his postdoctoral fellowship at Massachusetts General Hospital and Harvard Medical School with Dr. Allen Steere where he studied inflammatory synovitis in patients with Lyme arthritis. In 2018 he accepted a faculty position at MCW in the Department of Microbiology & Immunology. His research focuses on understanding how bacterial infections may trigger immune dysregulation, arthritis, and autoimmunity, and he is involved in developing and testing a safe and effective Lyme disease vaccine for use in humans.

Mark McNally, PhD: Dr. McNally's laboratory uses molecular, genetic, biochemical, and cell biological approaches to study post-transcriptional mechanisms of gene regulation, including RNA splicing and polyadenylation control. One area of focus uses the simple retrovirus, Rous sarcoma virus (RSV), to understand the role of RNA processing in the virus life cycle. He is also exploiting antisense oligonucleotide technologies to alter RNA splicing as an approach to develop a breast cancer therapeutic.

Michelle Riehle, PhD: Dr. Riehle's laboratory uses genetic, molecular, biochemical, genomic and computational experimental approaches to understand (1) malaria resistance mechanisms and factors that naturally segregate in the wild mosquito vector (2) the role of non-coding genetic variation in the mosquito immune response and resistance to Plasmodium falciparum, the eukaryotic malaria parasite and (3) the role of the mosquito prokaryotic and eukaryotic microbiomes in shaping mosquito immune responses and Plasmodium infection outcome. The overall goal of her laboratory is to understand in totality existing natural mechanisms of Plasmodium resistance in the mosquito vector that have been molded through evolutionary time and to harness these mechanisms for vector and malaria control.

Vera Tarakanova, PhD: Dr. Tarakanova's current research focuses on gammaherpesviruses. Gammaherpesviruses infect a majority of adult population worldwide; this virus infection is never cleared. Importantly, gammaherpesviruses drive the development of several malignancies, including lymphomas. While it is clear that not every infected human will develop virus-driven lymphoma, the risk factors for viral lymphomagenesis remain poorly defined and it is next to impossible to predict individual's risk of developing gammaherpesvirus-driven cancer. Her research group utilizes a mouse gammaherpesvirus-68 (MHV68) model to study the entire spectrum of virus-host interactions: molecular mechanisms using cultures of primary immune cells --chronic infection of an intact host-- animal models of viral lymphomagenesis.

Scott Terhune, PhD: Dr. Terhune's laboratory is interested in determining the underlying molecular mechanisms of human cytomegalovirus protein function during infection. Our current projects focus on defining how viral proteins manipulate cellular processes early during infection to construct a permissive cellular environment for replication. He accomplishes his goal by combining targeted proteomics and viral genetic manipulations with basic approaches in cellular and molecular biology.

Demin Wang, PhD: Dr. Wang's research focuses on identifying and functionally characterizing signaling pathways and transcriptional regulators that control B cell development from hematopoietic stem cells (HSCs) and B cell function. His studies aim to understand the molecular mechanisms underlying immunodeficiency and autoimmune diseases, including heparin-induced thrombocytopenia (HIT). His research uses mouse models and human patient samples, and employs multiple cutting-edge approaches, such as targeted gene disruption, transgenic, bone marrow transplantation and high-throughput DNA/RNA sequencing technologies.

Tom Zahrt, PhD: Dr. Zahrt's laboratory uses a combination of genetic, molecular, biochemical, and proteomic approaches, along with various in vitro and in vivo model systems of infection, to understand the mechanisms by which two intracellular respiratory pathogens, Mycobacterium tuberculosis and Francisella tularensis, persist and/or cause disease within the lungs of infected individuals.

Pharmacology and Toxicology

The Department of Pharmacology and Toxicology at the Medical College of Wisconsin is dedicated to quality in research, graduate and postdoctoral training and medical education. The research interests of our faculty are broadly based in cardiovascular pharmacology, neuropharmacology, cancer pharmacology, toxicology, and molecular pharmacology. The research programs in the Department of Pharmacology and Toxicology are also multidisciplinary in nature and have strong associations with researchers of other basic science and clinical departments. In addition, our faculty members collaborate on research projects both nationally and internationally. The specific areas of research interest include:

Cardiovascular Pharmacology: The cardiovascular research focuses on the heart, kidney, and vascular biology. Emphasis is on molecular, signal transduction, immunological, cellular, and in vivo approaches to understanding heart failure, cardiac ischemia-reperfusion injury, endothelial regulators of vascular tone, lipoprotein regulation, renal injury, and mechanisms of hypertension.

Neuropharmacology: The neuropharmacology research involves studies of drugs of abuse and molecular mechanisms that underlie learning, memory, and behavior. Cellular, molecular, imaging, optogenetics and in vivo approaches are used to address the mechanisms by which addictive drugs, including cannabinoids, cocaine, ethyl alcohol and opiates, affect the brain; the roles of endocannabinoid signaling in stress-related disorders; and molecular mechanisms controlling memory.

Cancer Pharmacology: Basic mechanism regulating cancer cell growth and metastasis, chemoprevention and chemotherapy are studied. Emphasis is placed on identifying genes altered in cancer, regulation of cellular oxidant mechanisms, role of small molecular weight GTPases in cancer and immune mechanism regulating tumor growth. Studies to develop new treatment involve vaccines, antisense oligonucleotides, repurposing of existing drugs and combination therapies for chemoresistance.

The Drug Discovery Center is housed within the Department of Pharmacology and Toxicology. The primary focus of the Drug Discovery Center is to facilitate and accelerate drug discovery and the translation of new basic discoveries into therapies to improve human health. Research expertise in the Center will provide resources, knowledge, and services to complete the drug development process from target validation, drug design, and drug delivery to clinical application.

The MCW Shared Mass Spectrometry (MSMS) Facility – MSMS Facility is a research service unit managed by the Department of Pharmacology and Toxicology. The facility provides service and consultation for research projects requiring mass spectrometric analysis (fundamental, identification and quantitation) of a variety of compounds. The primary focus is on small molecules such as drugs, hormones, chemical intermediates, and cellular metabolites. The facility operates on a fee for service basis and is open for faculty of the Medical College of Wisconsin and outside researchers. State-of-the-art mass spectrometers with different configurations and 27 years of experience and expertise meet researchers' needs for sample analysis.

There is also a long history of quality graduate education in the Department of Pharmacology and Toxicology at the Medical College of Wisconsin. Our graduates are successful scientists in universities, pharmaceutical companies, and government. The size of the program encourages the development of a close working relationship between students and faculty. In addition, every effort is made to optimize and tailor training programs to meet individual student needs in preparation for successful careers in pharmacology and toxicology. Our doctoral program provides diverse research opportunities in the areas of cardiovascular pharmacology, molecular pharmacology, molecular toxicology, behavioral pharmacology, neuropharmacology, and cancer pharmacology. An emphasis is placed on cellular and molecular pharmacology and signal transduction and using in vivo models of disease. The primary objective of our program is to provide students with the academic background, state- of-the-art scientific approaches and professional development opportunities that are necessary to investigate and solve the important biological and biomedical problems for a successful biomedical research career in the 2000's.

Physiology

The Department of Physiology is dedicated to quality in three main areas: research, graduate and postdoctoral training and medical education. The interests of our faculty are broadly based, with strong emphasis on cardiovascular, renal, metabolic and respiratory physiology, physiological genomics, proteomics and computational biology, epigenomics, and related translational research. The research programs in this department are multidisciplinary in nature with strong associations with researchers in other basic science and clinical departments. The department is tightly integrated with several Research Centers on the MCW campus including the Cardiovascular Center, Genomic Sciences and Precision Medicine Center, Center of Systems Molecular Medicine, and Neuroscience Research Center. We are also closely aligned with the Marquette University and Medical College of Wisconsin Department of Biomedical Engineering.

There is a long history of quality graduate education in the Department of Physiology. Our graduates are successful scientists in universities, pharmaceutical companies and government. The size of our program encourages the development of close working relationships between students and faculty. Additionally, the Department has established the Master's in Medical Physiology (MMP) Program to improve a college graduate's academic record for application to medical schools. Every effort is made to optimize and tailor our training programs to meet individual student needs in preparation for successful careers.

The basic support for projects and programs in the department is provided by the Research Services Cores (RSC). The RSC facilities is serviced by a group of professional engineers, computer programmers, systems analysts, histologists, and animal technicians who provide infrastructure support to the research programs in the department of Physiology and other researchers at MCW. The main areas are: Chronic Monitoring Facilities (provide equipment, computer hardware and software, and service and support necessary for short term or continuous 24-hour-a-day measurement of hemodynamic variables from research animals in their home cages); Computer Core (an integrated computer environment to support research and other needs with specialized software, printers, and access to dedicated servers for online storage); Biochemical Core Service Center (provides a broad range of assays for biochemical measurements); and Microscopy and Image Processing Core (offers a broad range of imaging options as well as consultations and training).

Physiology is the home of two NIH Program Project Grants studying Blood Pressure Regulation; a Dissemination and Coordinating Center for a Somatic Cell Genome Editing (SCGE) Program; a Hybrid Rat Diversity Panel (HRDP) Program; and a T32 pre-doctoral training grant on Integrated Physiology Training: Molecular to Organism. Department trainees are the recipients of numerous training grants from the NIH and American Heart Association, among other agencies.

Summary of Faculty Research Programs:

Allen W. Cowley, Jr., PhD.: Research in the Cowley laboratory is dedicated to advancing our understanding of the physiological and genetic mechanisms that determine blood pressure in normal and hypertensive states with a specific interest in the role of the kidney. Research is currently focused on two major areas of research: 1) the role of the mTOR pathway and oxidative stress in the regulation of kidney function and blood pressure salt-sensitivity; 2) mechanisms whereby positionally cloned gene associated with blood pressure salt-sensitivity called Pappa2 influences kidney development and function.

- Kumar V, Wollner C, Kurth T, Bukowy J, Cowley Jr AW. Inhibition of Mammalian Target of Rapamycin complex 1 Attenuates Salt-Induced Hypertension and Kidney Injury in Dahl Salt-Sensitive Rats. *Hypertension* 70: 813-821, 2017.
- Kumar V, Evans LC, Kurth T, Yang C, Wollner C, Nasci V, Zheleznova NN, Bukowy J, Dayton A, Cowley Jr. AW. Therapeutic Suppression of mTOR (Mammalian Target of Rapamycin) Signaling Prevents and Reverses Salt-Induced Hypertension and Kidney Injury in Dahl Salt-Sensitive Rats. *Hypertension* 73: 630-639, 2019.
- Cowley AW Jr, Yang C, Kumar V, Lazar J, Jacob H, Geurts A, Liu P, Dayton A, Kurth T, Liang M. Pappa2 is linked to salt-sensitive hypertension in Dahl S Rats. *Physiol Genomics* 48: 62-72, 2016.

Melinda R. Dwinell, PhD: Dr. Dwinell's major focus is on the development of research resources for the scientific community. Current projects focus on 1) the development of the 96 strain Hybrid Rat Diversity Panel to be used to detect genetic loci associated with complex traits, 2) the establishment of the Somatic Cell Genome Editing (SCGE) Dissemination and Coordinating Center for the SCGE Consortium and 3) the development of Sry transgenic rats to study the phenotypic differences between males and females through isolation of differences in sex chromosomes and gonadal hormones.

- Smith JR, Bolton ER, Dwinell MR. The Rat: A Model Used in Biomedical Research. *Methods Mol Biol* 2018:1-41, 2019.
- Meurer JR, Whittle JC, Lamb KM, Kosasih MA, Dwinell MR, Urrutia RA. Precision Medicine and Precision Public Health: Academic Education and Community Engagement. *Am J Prev Med* 57:286-289, 2019.
- Shimoyama M, Smith JR, Bryda E, Kuramato T, Saba L, Dwinell M. Rat Genome and Model Resources. *ILAR* 58:42-58, 2017.

Aron Geurts, PhD: Dr. Guerts pioneers cutting edge genetic engineering technologies in stem cells and whole animals to model human cardiovascular diseases including heart disease, hypertension, type 1 diabetes, and more. His lab is strongly motivated by the challenges of understanding how genetic variation affects human disease and developing novel disease models primarily in rats and human stem cells. He is considered an expert in genetic engineering, especially gene editing of rodent genomes and was awarded a prestigious New Innovator Award from the Office of the Director of the National Institutes of Health in 2011 for his efforts to advance genetic engineering technology.

- Geurts AM, et al. Knockout rats via embryo microinjection of zinc-finger nucleases. *Science* 325:433, 2009.
- Endres BT, et al. Mutation of Plekha7 attenuates salt-sensitive hypertension in the rat. *Proc Natl Acad Sci USA* 111: 12817-12822, 2014.
- Mitzelfelt KA, et al. Efficient Precision Genome Editing in iPSCs via Genetic Co-targeting with Selection. *Stem Cell Reports* 8: 491-499, 2017.

Justin L. Grobe, PhD: The Grobe laboratory focuses on the cross-talk between obesity and hypertension, through dissection of the hypothalamic circuitry that mediates integrative control of blood pressure and resting energy expenditure. In addition, their work on hypothalamic contributions to blood pressure control has provided exciting new insights into the severely underserved hypertensive cardiovascular disorder of pregnancy, preeclampsia. Further, they are developing novel technologies to assess resting energy expenditure in vivo provides unique opportunities to understand the contribution of the gut microbiota to whole-organism energy homeostasis.

- Claflin KE, Sandgren JA, Lambertz AM, Weidemann BJ, Littlejohn NK, Burnett CM, Pearson NA, Morgan DA, Gibson-Corley KN, Rahmouni K, Grobe JL. Angiotensin AT1A receptors on leptin receptor-expressing cells control resting metabolism. *J Clin Invest* 127:1414-1424, 2017.
- Sandgren JA, Deng G, Linggonegoro DW, Scroggins SM, Perschbacher KJ, Nair AR, Nishimura TE, Zhang SY, Agbor LN, Wu J, Keen HL, Naber MC, Pearson NA, Zimmerman KA, Weiss RM, Bowdler NC, Usachev YM, Santillan DA, Potthoff MJ, Pierce GL, Gibson-Corley KN, Sigmund CD, Santillan MK, Grobe JL. Arginine vasopressin infusion is sufficient to model clinical features of preeclampsia in mice. *JCI Insight* 3:e99403, 2018.
- Soto JE, Burnett CML, Ten Eyck P, Abel ED, Grobe JL. Comparison of the Effects of High-Fat Diet on Energy Flux in Mice Using Two Multiplexed Metabolic Phenotyping Systems. *Obesity* 27:793-802, 2019.

Matthew R. Hodges, PhD: Dr. Hodges is focused on the neural mechanisms that control breathing during health and in animal models of human disease. He and his research team are specifically focused on the role of brainstem serotoninergic neurons as key regulators of breathing and global pH homeostasis, and how their dysfunction may contribute to unexpected death during development (SIDS) or seizure disorders (SUDEP). Through a strong multidisciplinary approach, he and his collaborators also are currently focused on how opioids such as fentanyl suppress ventilation, and are developing novel strategies and drugs for reversing these negative effects.

- Mouradian GC Jr., Alvarez-Argote S, Gorzek R, Thuku G, Michkalkiewiz T, Wong-Riley MTT, Konduri GC, Hodges MR. Acute and chronic changes in the control of breathing in a rat model of bronchopulmonary dysplasia. *Am J Physiol Lung Cell Mol Physiol* 316: L506-L518, 2019.
- Burgraff NJ, Neumueller SE, Buchholz K, Hodges MR, Pan P, Forster HV. Glutamate receptor plasticity in brainstem respiratory nuclei following chronic hypercapnia in goats. *Physiol Rep*, 7: e14035, 2019.
- Puissant MM, Muere C, Levchenko V, Manis AD, Martino P, Forster HV, Palygin O, Staruschenko A, Hodges MR. Genetic mutation of Kcnj16 identifies Kir5.1-containing channels as key regulators of acute and chronic pH homeostasis. *FASEB J* 33:5067-5075, 2019.

Alison J. Kriegel, PhD: Dr. Kriegel's research program is centered on understanding how alterations in microRNAs (miRNAs), protein coding genes, and metabolism influence cardiorenal syndrome, cardiovascular disease, and kidney disease progression. She often blends discovery-based next-generation technologies with classical physiology and molecular biology techniques to study these complex problems, with the goal of identifying novel translational interventions and/or therapies.

- Chuppa S, Liang M, Liu P, Liu Y, Casati MC, Cowley AW, Patullo L, Kriegel AJ. MicroRNA-21 regulates peroxisome proliferator-activated receptor alpha, a molecular mechanism of cardiac pathology in Cardiorenal Syndrome Type 4. *Kidney International* 93:375-389, 2018.
- Kriegel AJ, Terhune SS, Greene AS, Noon KR, Pereckas MS, Liang M. Isomer-specific effect of microRNA miR-29b on nuclear morphology. *J Biol Chem* 293:14080-14088, 2018.
- Nasci VL, Chuppa S, Griswold L, Goodreau KA, Dash RK, Kriegel AJ. miR-21-5p regulates mitochondrial respiration and lipid content in H9C2 cells. *Am J Physiol Heart Circ Physiol* 316:H710-H721, 2019.

Anne E. Kwitek, PhD: Dr. Kwitek's major research focus involves understanding the genetic susceptibility to complex human diseases, with a focus on obesity, hypertension, and cardiometabolic disease. The approach involves integrating genetics, genomics, and other 'omics' approaches to identify genes and mechanisms leading to complex disease using rat models and human populations. Her studies also involve how genomic variation affects and is affected by environmental stimuli to influence susceptibility to cardiovascular disease and metabolic syndrome.

- Mansilla AM, Sompallae RR, Nishimura CJ, Kwitek AE, Kimble MJ, Armstrong ME, Campbell CA, Smith RJ, Thomas CP, Targeted Broad-Based Genetic Testing by Next Generation Sequencing Informs Diagnosis and Facilitates Management in Patients with Kidney Diseases. *Nephrology Dialysis Transplantation* (in press) 2019.
- Ma MCJ, Pettus JM, Jakoubek JA, Mennie AK, Kwitek AE, Contribution of Independent and Pleiotropic Genetic Effects in the Metabolic Syndrome in a Hypertensive Rat. *PLoS One* 12:e0182650, 2017.
- Wang J, Ma MCJ, Mennie AK, Pettus JM, Xu Y, Lin L, Traxler MG, Jakoubek J, Atanur SS, Aitman TJ, Xing Y, Kwitek AE, Systems Biology with high-throughput sequencing revealed genetic mechanisms underlying the metabolic syndrome in the Lyon Hypertensive Rat. *Circ Cardiovasc Genet* 8:316-326, 2015.

Mingyu Liang, PhD: The current work in Mingyu Liang's laboratory focuses on three areas: regulatory RNA, cellular metabolism, and precision medicine and epigenomics, as they relate to hypertension and cardiovascular and kidney diseases. Dr. Liang uses a multidisciplinary, translational research platform to integrate human research with animal and cell model research using approaches of physiology, genetics, biochemistry, molecular biology, genome editing, and big data analysis.

- Xue H, Geurts AM, Usa K, Wang F, Lin Y, Phillips J, Henderson L, Baker MA, Tian Z, Liang M. Fumarase Overexpression Abolishes Hypertension Attributable to endothelial NO synthase Haploinsufficiency in Dahl Salt-Sensitive Rats. *Hypertension* 74:313-322, 2019.
- Liang M. Epigenetic Mechanisms and Hypertension. *Hypertension* 72:1244-1254, 2018.
- Widlansky ME, Jensen DM, Wang J, Liu Y, Geurts AM, Kriegel AJ, Liu P, Ying R, Zhang G, Casati M, Chu C, Malik M, Branum A, Tanner MJ, Tyagi S, Usa K, Liang M. miR-29 contributes to normal endothelial function and can restore it in cardiometabolic disorders. *EMBO Mol Med* 10: e8046, 2018.

Julian H. Lombard, PhD: The Lombard laboratory is currently investigating the mechanisms by which vascular dysfunction develops during chronic exposure to sub-physiological levels of angiotensin II, either as a result of a high salt diet or due to genetic factors, such as those encountered in humans with low renin hypertension. They found that chronic exposure to low levels of angiotensin II in the blood leads to oxidative stress and severe impairment of endothelium-dependent and endothelium-independent mechanisms of vascular relaxation and to a reduced density of microvessels that supply oxygen and nutrients to the tissues. To investigate these questions, they are employing novel rat genetic models including knockouts of the master antioxidant and cell-protective transcription factor (NRF2); the Mas1 receptor for angiotensin (1-7), and the AT1A receptor for angiotensin II.

- Priestley JR, Kautenburg K, Casati M, Endres BT, Geurts AM, and Lombard JH. The NRF2 knockout rat: A new animal model to study endothelial dysfunction, oxidant stress, and microvascular rarefaction. *Am J Physiol Heart Circulatory Physiology* 310:H478-H487, 2016.
- Raffai G and Lombard JH. Angiotensin (1-7) selectively induces relaxation and modulates endothelium-dependent dilation in mesenteric arteries of salt-fed rats. *J Vasc Res* 53:105-118, 2016.
- Allen LA, Schmidt JR, Thompson CT, Carlson BE, Beard DA, and Lombard JH. High salt diet impairs cerebral blood flow regulation via salt-induced angiotensin II suppression. *Microcirculation* 26:e12518, 2019.

Caitlin O'Meara: Dr. O'Meara's research is focused on understanding the cell biology of heart regeneration and cardiomyocyte cell cycle activity. They use pro-cardiac regenerative models such as neonatal mice and zebrafish to identify pathways and molecules that facilitate successful cardiac regeneration. The ultimate goal of this research is to develop new therapeutic targets for promoting cardiac healing in the adult heart following injury such as myocardial infarction.

- Wodsedalek DJ, Paddock SJ, Wan TC, Auchampach JA, Kenarsary A, Tsaih SW, Flister MJ, O'Meara CC. IL13 Promotes in vivo neonatal cardiomyocyte cell cycle activity and heart regeneration *Am J Physiol Heart Circ Physiol* 316:H24-H34, 2019.
- Flinn MA, Jeffery BE, O'Meara CC, Link BA. Yap is required for scar formation but not myocyte proliferation during heart regeneration in zebrafish. *Cardiovasc Res* 115:570-577, 2019.
- O'Meara CC, Wamstad JA, Gladstone RA, Fomovsky GM, Butty VL, Shrikumar A, Gannon JB, Boyer LA, Lee RT. Transcriptional reversion of cardiac myocyte fate during mammalian cardiac regeneration. *Circ Res* 116:804-815, 2015.

Curt D. Sigmund, PhD: Dr. Sigmund's major areas of research focus on 1) the mechanism by which the central nervous system and the brain renin-angiotensin system controls fluid balance, blood pressure and metabolism, and 2) vascular mechanisms of blood pressure regulation by the transcription factor PPAR-gamma, and its downstream effectors Cullin-3/RhoBTB1. He investigates these pathways using a combination of molecular biological, genetic and physiological approaches including the generation of unique transgenic and gene targeted mouse models.

- Mukohda M, Fang S, Wu J, Agbor LN, Nair AR, Ibeawuchi SC, Hu C, Liu X, Lu KT, Guo DF, Davis DR, Keen HL, Quelle FW, Sigmund CD. RhoBTB1 protects against hypertension and arterial stiffness by restraining phosphodiesterase 5 activity. *J Clin Invest* 130:2318-2332, 2019.
- Agbor LN, Nair AR, Wu J, Lu KT, Davis DR, Keen HL, Quelle FW, McCormick JA, Singer JD, Sigmund CD. Conditional deletion of smooth muscle Cullin-3 causes severe progressive hypertension. *JCI Insight* 5: e129793, 2019.
- Nair AR, Silva SD Jr, Agbor LN, Wu J, Nakagawa P, Mukohda M, Lu KT, Sandgren JA, Pierce GL, Santillan MK, Grobe JL, Sigmund CD. Endothelial PPARγ (Peroxisome Proliferator-Activated Receptor-γ) Protects From Angiotensin II-Induced Endothelial Dysfunction in Adult Offspring Born From Pregnancies Complicated by Hypertension. *Hypertension* 74:173-183, 2019.

Alexander Staruschenko, PhD.: Dr. Staruschenko's research is focused on understanding the mechanisms regulating ion channels activity and electrolyte homeostasis, respectively, in the control of blood pressure and various kidney diseases. His technical expertise is very broad and he applies in the laboratory physiological, biophysical, genetic, and microscopy methods to address unresolved questions regarding the regulation of renal transport processes in hypertension and kidney diseases.

- Ilatovskaya DV, Levchenko V, Pavlov TS, Isaeva E, Klemens CA, Johnson J, Liu P, Kriegel AJ, Staruschenko A. Salt-deficient diet exacerbates cystogenesis in ARPKD via epithelial sodium channel (ENaC). *EBioMedicine* 40: 663-674, 2019.
- Palygin O, Ilatovskaya DV, Levchenko V, Klemens CA, Dissanayake L, Williams AM, Pavlov TS, Staruschenko A. Characterization of purinergic receptor expression in ARPKD cystic epithelia. *Purinergic Signaling* 14: 485-497, 2018.
- Ilatovskaya DV, Blass G, Palygin O, Levchenko V, Pavlov TS, Grzybowski M, Winsor K, Shuyskiy LS, Geurts A, Cowley AW Jr, Birnbaumer L, Staruschenko A. A NOX4/TRPC6 pathway in podocyte calcium regulation and renal damage in diabetic kidney disease. *Journal of the American Society of Nephrology* 29: 1917-1927, 2018.

Physiology Biochemical Analytical Lab

The Physiological Biochemical Analytical Laboratory (Biochemical Assay Lab) provides a consolidated, highly specialized, well equipped and professionally staffed analytical laboratory capable of performing a wide variety of immunoassays, HPLC based assays, clinical chemistry and biochemical analyses. The priority of this laboratory is to meet the analytical needs of laboratories in the Department of Physiology, in other MCW departments, and collaborating individuals.

Anesthesiology

Departmental faculty members direct research teams at Zablocki VA Medical Center and the MCW campus labs, where we investigate a wide range of topics relevant to anesthesiology. These programs not only contribute fundamental new knowledge to the foundational basic science of anesthesia, but are also engaged in developing new therapies. Support for these labs, totaling $3,900,000 this past year, comes from the NIH, Veterans Administration, Advancing a Healthier Wisconsin, commercial affiliations, and internal departmental and MCW support. Research education is a key element in our research division, with participation by medical, graduate, and post-doctoral students. Our current projects are described below.

Amadou Camara, PhD studies the role of mitochondrial dysfunction in disease, particularly in ischemic heart disease, neurodegenerative diseases, diabetes and aging, with a focus on mitochondrial calcium handling and their regulation or reactive oxygen species, using a broad range of experimental approaches.

Caron Dean-Bernhoft, PhD performs research that is based in systems physiology, primarily the neurobiology of stress conditions. Recent research focus is on central neuronal circuitry at the interface of sympatho-sensory responses.

Julie Freed, MD, PhD uses physiological and pharmacological approaches to explore the regulation of microcirculation with particular interests in endothelial dysfunction, the coronary microcirculation, vasoplegia, endothelium-derived extracellular vesicles, and the role of ceramide signaling.

Quinn Hogan, MD examines mechanisms of chronic pain at the molecular and cellular level, and applies this in developing novel therapies for chronic pain. Additional studies involve coordination of autonomic activity and pain, and strategies to avoid loss of brain connectivity with sensory systems after injury.

Wai-Meng Kwok, PhD is focused on the modulation of ion channel proteins. His major areas of interest are investigating the roles of ion channels in mitochondrial dysfunction, and electrophysiological characterization of cardiomyocytes derived from induced pluripotent stem cells.

Bin Pan, PhD explores the organization of brain function at the network and synaptic level, focusing on the links between depression and pain, and the role of cannabinoid signaling in the control of these pathways.

Christopher Pawela, PhD investigates brain plasticity in neurological injury and disease using MRI. His current work focuses on the effect of chronic hypertension on neurovascular structure/function, brain reorganization after peripheral nerve injury/repair, and the physiologic basis of neuroimaging signals.

David Stowe, MD, PhD studies molecular aspects of mitochondrial channels and transporters involved in cell stress, and liver mitochondrial bioenergetics during ischemia/reperfusion during transplantation.

Astrid Stucke, MD examines the central mechanisms regulating breathing at the neuronal and network level. Her current focus is on the effect sites of opioids and potential differences between young and adult animals, which is of importance for perioperative patient care.

David Warltier, MD, PhD is an expert in the area of anesthetic effects on the circulation and heart function, with a current focus on the potential use of novel hemoglobin-based oxygen carriers (HBOCs) in the treatment of shock.

Dorothee Weihrauch, DVM, PhD studies coronary collateral growth and impaired angiogenesis in diabetes using techniques such as protein analysis, proliferation assays, migration assays on cultured cells as well as histology and immunohistochemistry.

Hongwei Yu, MD is an expert in molecular genetic techniques for controlling gene expression and signaling interactions, which he uses to design novel treatments for chronic pain, including arthritic and neuropathic etiologies.

Edward Zuperku, PhD studies the brainstem networks that control breathing, including the neurophysiology and pharmacology of respiratory neurons, the relevant pharmacology of agents that modulate respiratory control, and the effect of opioids and anesthetics on respiratory neurons and breathing patterns.

Dermatology

The Department of Dermatology at the Medical College of Wisconsin has a deep commitment to expanding the understanding of the physiology of the skin and new and novel treatments through research. Our faculty provide comprehensive and specialty clinical care in skin cancer and inflammatory diseases, first class cutaneous surgery and dermatopathology, and one of the most vital and important sections of pediatric dermatology, both nationally and internationally.

Our research portfolio includes projects with fellows, residents, medical students, and other collaborating researchers from numerous renowned institutions.

1. A Pilot Study of a Single, Easily Measurable outcome for Psoriasis in Pediatric and Adult Patients (Kenneth Gordon, MD)
2. A Pilot Study of a Single, Easily Measurable Outcome for Psoriasis in Pediatric Patients (Kristen Holland, MD)
3. A Phase 3 Multi-Center, Randomized, double-Blind, Placebo-Controlled Study to Assess the Efficacy and Safety of Apremilast in Pediatric Subjects from 6 through 17 Years of Age (Kristen Holland, MD)
4. A Phase 3, Multi-Center, Long-Term Extension Study Investigating the Efficacy and Safety of PF-04965842, with or without Topical Medications, Administered to Subjects Aged 12 Years and Older with Moderate to Severe Atopic Dermatitis. (Kristen Holland, MD)
5. A Phase 3, Randomized, Double-Blind, Placebo-Controlled, Multi-Center Study Investigating the Efficacy and Safety of PF-04965842 Co-Administered with Background Medicated Topical Therapy in Adolescent Participants 12 to <18 Years of Age with Moderate to Severe Atopic Dermatitis (Kristen Holland, MD)
6. A Prospective Observational Study of Adult Patients Receiving Dupixent for Atopic Dermatitis (Keri Chaney, MD)
7. Comparing Artificial Intelligence with Teledermatology in the Diagnosis of Pigmented Lesions in the Community (April Zhang, MD)
8. Development and Validation of a Gene Expression Assay to Predict the Risk of Recurrence Disease in Cutaneous Squamous Cell Carcinoma (Julia Kasprzak, MD)
9. Development of a Morphea Activity Measure (Yvonne Chiu, MD)
10. Efficacy, Safety and Pharmacokinetics of Topical Timolol in Infants with Infantile Hemangioma (Kristen Holland, MD)
11. Genomic Analysis of a Cohort with Infantile Hemangiomas Associated with Multi-Organ structural birth defects (Dawn Siegel, MD)
12. IL 19 and Hidradenitis Suppurativa (Gretchen Roth, MD)
13. Investigating NGLY1 as a promising anticancer target (Yu-Chieh (Jack) Wang, PhD)
14. Longitudinal Characterization of Pediatric - Onset Morphea (Yvonne Chiu, MD)
15. Multicenter Phenotype-Genotype analysis of Vascular Overgrowth Syndrome Cohort (Dawn Siegel, MD)
16. Prospective, observational, longitudinal study in pediatric patients with moderate to severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not medically advisable (Kristen Holland, MD)
17. Pustular Psoriasis in the United States (Kari Wanat, MD)

Emergency Medicine

The Department of Emergency Medicine at the Medical College of Wisconsin has a robust research portfolio and is at the forefront of emergency medicine research. The Department is one of the top 30 National Institutes of Health (NIH) funded emergency medicine departments in the country. Our faculty members are recognized nationally and internationally as leaders in emergency medicine research, and the department participates in the NIH sponsored Strategies to Innovate Emergency Care Clinical Trials Network (SIREN) and the HRSA sponsored Pediatric Emergency Care Applied Research Network. Our faculty has published hundreds of publications in the peer reviewed literature on a variety of topics ranging from disaster medicine to cardiovascular care and we are considered leaders in prehospital care research.

Our research portfolio includes numerous projects with fellows, residents, graduate and medical students. Our clinical research laboratory includes a 43 bed state of the art emergency department that treats over 70,000 patients per year and serves as the only adult level 1 trauma center in Southeastern Wisconsin. We work closely with the county EMS system to conduct both prehospital clinical trials and observational research that utilizes their medical record database which covers over a decade of EMS responses. We also work with numerous governmental and non-governmental organizations at the state, regional, and national levels to study injury rates and patterns, as well as treatment. We have international research relationships in China, Belize, and other countries. The Department's Research Director is a PhD epidemiologist with 20 years of emergency medicine research experience. The department also has a Research Manager, who works with the Director to assist faculty and students in all aspects of research. We also have Research Assistants stationed in the emergency depart 7 days a week/16 hours per day who identify and enroll research subjects.

The Department of Emergency Medicine provides numerous opportunities to engage in cutting-edge research.

Medicine

The Department of Medicine is nationally and internationally known for research and scholarship. Department of Medicine faculty members are active in numerous clinical trials and are primary or collaborating investigators on a number of NIH, Foundation and Industry grants. In total, the Department has over $35,000,000 in annual research funding, with all Divisions represented. Research efforts are based at the Medical College of Wisconsin campus, the Blood Research Institute/Versiti, and the Clement J. Zablocki VA Medical Center. Through investments and active recruitments, the Department continues to be poised for significant growth in research during the next several years.

Department of Medicine faculty members, spread across 10 Divisions, are actively pursuing numerous interdepartmental translational research projects and training opportunities, including in the Clinical Translational Research Institute (CTSI), the MCW Cancer Center, the Cardiovascular Research Center, the Genomic Sciences and Precision Medical Center (GSPMC) and the Center for Advancing Population Science (CAPS). The TOPS Obesity Center, in partnership with the Division of Endocrinology, is exploring the causes and treatment of obesity. The Center for International Blood and Marrow Transplantation, housed in the Division of Hematology/Oncology, is internationally known as a leader of outcomes research as well as a coordinating center for multi-center clinical trials.

These are just a few examples of the types of research activities taking place in the Department. To learn more about these and other research activities, please visit the Department Website (http://www.mcw.edu/Medicine/Research.htm) or our individual Division pages and click on “Research”.

Division of Cardiovascular Medicine

The Division of Cardiovascular Medicine maintains significant basic research programs with the purpose of generating and testing new hypotheses in the field of Cardiovascular Medicine and Physiology. Our physicians and investigators collaborate with many basic and clinical departments to advance MCW’s mission “to discover and translate new knowledge in the biomedical sciences”.

The research conducted by many of our investigators has national and international recognition. We are the recipients of funding through the NIH (including seven active R01s), the American Heart Association, the American Diabetes Association, and the Veterans Health Administration. Many of our investigators developed local collaborations through successful funding through the regional CTSI. Our research has been published in *Circulation, Circulation Research, American Journal of Physiology, Journal of the American College of Cardiology, EMBO Molecular Medicine, Free Radical Biology and Medicine, PLOS One, Journal of Molecular and Cellular Physiology, Hypertension.* Our areas of interest include atrial fibrillation, redox biology (nitric oxide and free radical), muscular dystrophy related cardiomyopathy, diabetes, hypertensive disease, congestive heart failure, endothelial dysfunction, peripheral arterial disease and wound management.

Active research-intensive faculty members include the following:

- **Andreas Beyer, PhD** studies the metabolic effects of aging, hyperglycemia, and oxidative stress on the peripheral microcirculation.
- **Sherry-Ann Brown, MD, PhD** is interested in shared decision making and application of machine learning for Cardio-Oncology patients.
- **Ivor Benjamin, MD** is interested in the genetic etiology of atrial fibrillation and the use of induced pluripotent stem cells in a dish for modeling disease.
- **David Gutterman, MD** examines the effect of atherosclerosis and diabetes on the coronary microcirculation.
- **Jacquelyn Kulinski, MD** is interested in understanding the physiological mechanisms between sedentary behavior and endothelial dysfunction, as well as the physiology of endothelial dysfunction in gestational diseases.
- **Nicole Lohr, MD, PhD** studies the mechanisms of cellular nitric oxide production and the effect of red light on vasodilation, as well as the physiology of endothelial dysfunction in gestational diseases.

- **Michael Widlansky, MD** has efforts focused on the relationship between altered mitochondrial bioenergetics and endothelial dysfunction. In addition, he studies the impact probiotic supplementation on vascular endothelial function in humans with coronary artery disease.
- **David Zhang, MD, PhD** seeks to identify cellular mechanisms by which the endothelium regulates blood vessel tone in both normal physiological conditions and disease states, such as ischemic heart disease and hypertension.

In addition, the Division boasts a robust clinical trials portfolio, including over 45 clinical trials involving all aspects of cardiovascular care including advanced structural heart disease, electrophysiology, advanced heart failure, and secondary prevention of cardiovascular events. In addition, the clinical trials group supports multiple investigator-initiated human translational research studies with the goal of eventually applying knowledge from these initial studies to improve the health of our patients.

Division of Endocrinology & Molecular Medicine

The Division of Endocrinology and Molecular Medicine has continued to maintain a high level of research and scholarly activity. Several of our current full-time faculty are currently involved in our clinical or basic-science research programs. We collaborate with many basic and other clinical departments in order to advance the research mission.

- **Zeljko Bosnjak, PhD, Professor of Medicine,** is interested in fundamental insight into the mechanisms responsible for greater susceptibility of diabetic hearts to ischemia-reperfusion injury using patient-derived cardiomyocytes. In addition, he is performing translational studies to identify biomarkers involved in anesthetic-induced neurotoxicity in children. Finally, studies are conducted to examine surrogate biomarkers of cardiotoxicity due to doxorubicin in breast cancer patients. His laboratory is currently funded by the NIH.
- **Ty Carroll, MD, Clinical Assistant Professor of Medicine**, is interested in novel tools to diagnose and treat Cushing syndrome. He is currently a co-investigator of multiple clinical trials for treatment of Cushing syndrome.
- **Yiliang Chen, PhD, Assistant Professor of Medicine,** has worked on the functions of a scavenger receptor CD36 and its role in chronic inflammation and atherosclerosis. Dr. Chen has a life-long passion in the study of metabolic diseases that are often associated with oxidative stress, abnormal lipid metabolism and chronic inflammation.
- **Carol Everson, PhD, Professor of Medicine,** is investigating the ways in which long-term sleep deficiency is physically harmful and increases morbidity and mortality. The laboratory has shown that long-term sleep deficiency in the animal model results in unique metabolic, immune, and hormonal abnormalities. Current studies are investigating the mediation of arrested bone formation and osteoporotic processes resulting from chronic sleep deficiency. Other organ systems—liver, lung, and intestine—show increased DNA damage; this provides potential biological linkage to epidemiological findings of cancer risk associated with chronic sleep deficiency. In a third area of concentration, sleep and sleep restriction, as well as other agents that affect cerebral blood flow and metabolism, are being studied as interventions in mild concussive injury. The interventions represent practical and low-cost means amenable to field implementation to improve outcomes from concussive injury, determined by changes to brain functional connectivity, hormone status, and behavior.
- **James Findling, MD, Clinical Professor of Medicine and Surgery** is interested in novel tools to diagnose and treat Cushing syndrome. He discovered the importance of inferior petrosal sinus sampling for the differential diagnosis of Cushing syndrome and introduced late-night salivary cortisol as a simple screening test for Cushing syndrome. He has been the PI of clinical trials for treatment and diagnosis of Cushing syndrome.
- **Benjamin Gantner, Assistant Professor of Medicine,** is interested in studying different types of inflammatory responses to understand how they impact the decisions of innate immune cells (e.g. macrophages and neutrophils) to injure surrounding host tissue. The lab uses microscopic observation of cells in living animals (i.e. intravital imaging) and in vitro culture systems to study the intracellular processes, intercellular communications, and behavioral responses of immune cells during bacterial infection and cancer.

- **Srividya (Vidya) Kidambi, MD, Associate Professor of Medicine,** is interested in the role of adiposity distribution, microRNA, and resting metabolic rate in obesity pathogenesis, epigenetic modifications in chronic diseases such as hypertension & cardiovascular outcomes. In addition, she is PI for multiple clinical trials for treatment of diabetes and metabolic syndrome.
- **Paul Knudson, MD, Associate Professor of Medicine,** is interested in evaluating outcomes of inpatient diabetes management team. He works with information technology for people with diabetes mellitus.
- **Theodore Kotchen, MD, Professor Emeritus,** is primarily on mechanisms and complications of hypertension. He is currently exploring the role of epigenetic modifications on cardiovascular outcomes. His research is funded by the AHA.
- **Lisa Morselli, PhD, MD, Assistant Professor of Medicine,** is interested in metabolic adaptation to weight loss, resting metabolic weight control and the impact of food insecurity on metabolic outcomes.
- **Hershel Raff, PhD, FAAAS, FAPS, Professor of Medicine,** is interested in two main research areas of interest. His basic research on the hypothalamic-pituitary-adrenal axis focuses on the short- and long-term consequences of neonatal hypoxia. His clinical research focuses on the development of diagnostic endocrine tests and, in particular, using the measurement of salivary cortisol to evaluate the hypothalamic-pituitary-adrenal axis in a variety of human stress models.
- **Daisy Sahoo, PhD, Professor of Medicine,** is interested in the role of scavenger receptors in cardiovascular disease, diabetes and obesity. Specifically, she relies on state-of-the-art biophysical and biochemical techniques to understand how the structural organization of SR-BI, the most physiologically relevant HDL receptor, facilitates HDL-cholesterol delivery to the liver for disposal. In other studies, she is trying to define the underlying mechanisms by which PCPE2, an extracellular matrix protein, facilitates the cholesterol transport functions of SR-BI in adipocytes. Other interests include the role of oxidized HDL in atherogenesis, as well as in beta-cell function. She also has a collaborative project to study the relationship between dyslipidemia and gammaherpesvirus infection. Dr. Sahoo is currently funded by the NIH and the University of Chicago Diabetes Research Training Center.
- **Jenna Sarvaideo, DO, Assistant Professor of Medicine,** is interested in optimal hormonal treatment for transgender patients in line with her clinical interest. She has received funding from the Endocrine Society, DOM Faculty Development Funds and MCW Research Affairs Committee. She was accepted into the Clinical Research Scholars Program for 2019-2021.
- **Mary Sorci-Thomas, PhD**, **Professor of Medicine,** is interested in examining the role of SR-BI and PCPE2 in adipose tissue lipid metabolism using a newly developed adipose tissue specific PCPE2 knockout mice and inducible adipose tissue specific PCPE2 knockout mice. Her other research is focused on molecular mechanisms involved in high density lipoprotein apo A-I-mediated protection against the progression of heart disease. She is currently funded by the NIH.
- **Ze Zheng, MBBS, PhD, Assistant Professor of Medicine,** is interested in understanding the role of hepatocyte-derived tPA and basal fibrinolysis in hemostasis, and to develop diagnostic/ preventive/ therapeutic strategies that can be used to combat atherosclerosis, thrombosis, and bleeding disorders. Specific areas of research interests include: 1) a new link between reduced fibrinolysis and dyslipidemia, 2) circadian regulation of basal fibrinolysis and the morning onset of thrombotic events, 3) the role of hepatocyte tPA and liver injuries, 4) increased fibrinolysis in hemophilia, and 5) a timely study of fibrinolysis in COVID-19.

Division of Gastroenterology & Hepatology

As part of the Department of Medicine at the Medical College of Wisconsin, the Division of Gastroenterology and Hepatology contributes to the MCW Research mission in several ways, spanning a variety of interests. The Division's active clinical, translational, and basic science research program involves gastroenterologists, hepatologists, advanced practice providers, research scientists, research fellows, post-doctoral fellows, and a myriad of MCW medical students and Department of Medicine residents. Our division places special emphasis on teaching and mentorship, as well as partnerships throughout the college. Basic, clinical, and translational research efforts are heavily supported by several successfully funded NIH awards, as well as internal funding from the Clinical and Translational Science Institute (CTSI) and Digestive Disease Center (DDC). During the 2019-2020 academic year, the Division of Gastroenterology and Hepatology has been involved in research spanningesophageal motility, IBD diseases including moderately to severely active Crohn's disease or ulcerative colitis, Cyclic Vomiting Syndrome, hepatic encephalopathy and esophageal obstruction

caused by intrinsic or extrinsic malignancies, refractory benign esophageal strictures or fistulas/perforations/leaks, and cystitis. This has resulted in many local, national, and international oral presentations and publications of articles and manuscripts. Below is a short highlight of some of our recent accomplishments:

- **Dr. Reza Shaker**, Division Chief, collaborated with Dr. Nita Salzman from the Division of Gastroenterology in the Department of Pediatrics, co-principal investigator, to successfully recruit a new fellow for the third year of his NIH Training Grant (T32) award. This grant allows for research intense training of 2 fellows each year in the area of gastroenterology, while still allowing for clinical exposure and training.
- **Dr. Reza Shaker** received a 5-year renewal of his Clinical and Translational Science Award.
- **Dr. Achuthan Souria** received a seed grant from the DDC for his proposal entitled "Effectiveness of point of care ultrasound liver imaging in the community for early diagnosis of fatty liver disease".
- **Dr. Jyoti Sengupta** received a seed grant from the DDC for his proposal entitled "Effect of angiotensin (1-7)/Mas receptor for the treatment of pelvic pain".
- **Dr. Thangam Venkatesan** received an award from Alnylam Pharmaceuticals, Inc. for her proposal entitled "Genetic Testing for Acute Hepatic Porphyria in the Cyclic Vomiting Syndrome Population".
- **Dr. Andres Yarur** received a grant from the Advancing a Healthier Wisconsin Endowment for his proposal "Presence of SARS-CoV-2 in stool samples of COVID-19 cases: Potential for Transmission Via Stool Shedding
- In May 2020, our Division presented a total of 25 posters during the virtual Digestive Disease Week.

Our ongoing clinical research studies in the Division currently include trials that assess the efficacy and safety of new medications and devices. They also assess new dosing regimens for currently approved medications. We currently have a total of thirty-seven active clinical trials in our Division. This includes twenty-eight active IBD clinical trials (two by **Dr. Poonam Beniwal-Patel**, three by **Dr. Amir Patel**, one by **Dr. Daniel Stein**, one by **Dr. Preetika Sinh**, twenty one by **Dr. Andres Yarur**), three active hepatology clinical trials (one by **Dr. Kia Saeian**, one by **Dr. Achuthan Sourianarayanane**, one by **Dr. Aiman Ghufran**), and 6 general gastroenterology trials (three by **Dr. Thangam Venkatesan**, one by **Dr. Ling Mei**, two by **Dr. Kulwinder Dua**). Overall, we are working with nineteen different pharmaceutical and device companies. Our division maintains our industry sponsored trials while continuously identifying and engaging in new drug and device trials for the future. The Division of Gastroenterology and Hepatology's philosophy has always been strongly rooted in MCW's research mission, as we believe this is the essential element to the advancement of medicine and innovation of patient-centered care.

Division of General Internal Medicine

The Division of General Internal Medicine (GIM), under the leadership of **Dr. Leonard Egede,** Division Chief**,** and **Drs. Barbara Slawski, Kurt Pfeifer, Theodore MacKinney, and Jeffrey Jackson,** Section Chiefs of Hospitalist Medicine, Perioperative & Consultative Medicine, Primary Care and GIM VA, respectively, has an active and nationally recognized research program focused on conducting innovative clinical and outcomes research. Research efforts by GIM are based at the Medical College of Wisconsin campus, the Clement J. Zablocki VA Medical Center, and in the local Milwaukee community. Research infrastructure includes affinity groups focused on building research capacity and mentoring faculty interested in research, statistical and design support to provide consultation and analysis for unfunded projects, and research conferences in collaboration with the MCW Center for Advancing Population Science (CAPS). Faculty in GIM are actively involved in dissemination of their work through peer-reviewed publications and participation in national and international conferences, including the Society of General Internal Medicine (SGIM) and the Society of Hospital Medicine (SHM). Faculty also conduct collaborative work with other Divisions, Departments, and the College of Pharmacy within MCW and local institutions.

Faculty in GIM incorporate a variety of research designs into their research including randomized controlled trials, community-engaged research, use of large administrative and clinical databases, and health systems based quasi-experimental research. GIM research faculty have expertise in both quantitative and qualitative research, community based participatory research, program evaluation, cost-effectiveness analysis, and implementation science. Research topics range from evaluating policy changes at the national level like the impact of Medicaid regionalization on disparities in breast cancer care, testing novel interventions to improve chronic care

such as financial incentives for improving glycemic control, addressing social determinants of health such as food insecurity, and recruiting participants for a national effort to expand the future of precision medicine.

- ***Leonard Egede, MD, Center Director, Chief, Professor**, Research focus in Type 2 Diabetes, Minority Health, Community Engagement, Health Services Research, Social Determinants of Health, Health Disparities, Mental Health Services, Global Health
- **Lolia Abibo, MD, Assistant Professor,** research related to chronic disease in global health, program development and evaluation of chronic disease in global health and evaluation of a diabetes self management and education program developed for a southern Nigerian population.
- **Haisim Abid, MD, Assistant Professor,** research related to hematology/oncology, especially multiple myeloma, immunotherapy and CAR-T.
- **Sarvpreet Ahluwalia, MD, Assistant Professor,** research related to high value care and quality improvement
- **Amer Al Homssi, MD, Assistant Professor,** research related to hematology/oncology, specifically benign hematology.
- **Todd Burner MD**, **Assistant Professor,** has a research interest in diabetic tendinopathy.
- **Jennifer Campbell, PhD, MPH**, **Assistant Professor,** research focusing on health disparities.
- **Evelyn Chan, MD, MS**, **Associate Professor**, board certified in lifestyle medicine, where she is actively pursuing research now. She is also pursuing research in Obesity
- **Paul Cimoch, MD, Assistant Professor,** research related to nutrition and the nutritional impact on health plus quality assurance methodologies and approaches
- **Brad Crotty, MD**, **Assistant Professor**, has research focusing on informatics, and has grants from AHW, CTSI
- **Aprill Dawson, PhD, MPH, Assistant Professor,** research focusing on health disparities.
- **Jake Decker, MD**, **Assistant Professor**, with grants and research in hereditary hemorrhagic telanciectasia and in statin us in the elderly
- **Amy Farkas, MD, MS, Assistant Professor,** with interest in women's health, mentorship, and medical education
- **Kathlyn E. Fletcher, MD MA, Professor,** Research focus on graduate medical education, patient safety, PTSD and using reflection as a tool for wellbeing.
- **Maryann Gillian**, **MD, MPH**, **Professor**, with active research and grants from the Kern Foundation in women's health, breast cancer and communications skills.
- **Laura Hawks, MD, MPH, Assistant Professor,** research focus on improving health outcomes for vulnerable populations, particularly those with criminal justice involvement.
- **Brian Hilgeman: Assistant professor**, research interest is developing systems of care to care for complex patients.
- **Robert Hoerner, MD, Assistant Professor,** areas of research focus on diagnostic reasoning, clinical decision support systems, and evaluation of medical evidence.
- **Jeffrey L Jackson, MD, Professor**, has research focusing on Depression, Health Services Research, Meta-Analysis, Somatoform Disorders, Patient Doctor Communication, and Qualitative Methods
- **Kory Koerner, MD, Associate Professor,** research related to quality improvement, rapid response/emergency response team
- **Julie Kolinski, MD, Assistant Professor,** research focusing on high value healthcare, utilization review and appropriate utilization of resources, clinical documentation and care transitions.
- **Geoffrey C. Lamb, Professor:** Current Research focus - Quality Improvement, Quality Metrics, Patient Safety.

- **Sebastian Linde, PhD, Assistant Professor,** Research focus on causality, economics, machine learning, collective bargaining, hospital charges, patient care team, cost-benefit analysis, hospital costs, statistics
- **Amalia Lyons, Assistant Professor,** with focus on outpatient graduate medical teaching and curriculum development.
- **Theresa C. Maatman, MD, Director, Associate Professor**, with research interest and grants from the Kern foundation (and internal grants) in the use of comics and other graphic representations in medicine
- **Theodore MacKinney, MD, Professor**, with (internal) grants and research in QI in developing countries.
- **Jennifer MacKinnon, MD, Associate Professor**, with research interest in the interface of music and medicine, especially
- **Ann Maguire, MD**, **Associate Professor**, with research interest in after care of patients with cancer
- **James McCarthy, MD, Director, Assistant Professor,** research related to medical education for learners at all levels with a focus on developing engaging and innovative ways to deliver curricula.
- **Marty Muntz, MD**, **Vice Chair, Professor**, with research interest in teaching techniques for medical students.
- **Kavita Naik, MD, Assistant Professor,** research focus on quality improvement, medical education and Hospital Medicine
- **Ann B. Nattinger, MD, MPH, Professor,** research focus on breast cancer outcomes and policy
- **Joan Neuner, MD, Professor of Medicine and Georgia Carroll Endowed Chair in Women's Health**, with extensive research in women's health. She is the acting program Leader/Program Leader for the Cancer Prevention and Outcomes Program. She has multiple current grants from NIDDK, NIA, NIH, and DHHS.
- **Kurt Pfeifer, Professor, MD, Section Chief, Professor,** has research focusing on medical education, undergraduate medical education, continuing medical education, perioperative care, and graduate medical education.
- **Joseph Puetz, MD, Assistant Professor** research related to bedside procedures; POCUS, and community health
- **Brian Quinn, MD, Assistant Professor,** research related to Perioperative Medicine, surgical outcomes for patients who have been either seen in our prep clinic or received co-management from medicine consult service.
- **Sushma Raju, MD, Assistant Professor,** research related to clinical medicine
- **Cecilia Scholcoff, Assistant Professor**, research focus in microaggressions, sexual harassment and gender discrimination.
- **Yogita Segon, MD, Professor**, has research focusing on Medical education, and Quality improvement
- **Barbara Slawski, MD, MS, FACP, SFHM, Professor,** research related to Perioperative Medicine
- **Melek Somai, MD, MPH Assistant Professor,** research focused on Informatics
- **Bipin Thapa, MD, Assistant Dean, Associate Professor,** research related to educational intervention, meta analysis
- **Heather Toth, MD, Professor,** research related to medical education, bedside rounding and inpatient care.
- **Corrado Ugolini, MD, Assistant Professor,** clinical research and medical student teaching. Ares of interest include complex patient care and management
- **Adrian Umpierrez. MD,, MPH, Associate Professor,** research related to bedside procedures and patient safety/quality improvement; bedside procedures and education
- **Lara Voigt, MD, Assistant Professor,** clinical research: procedural safety and improvements, such as our rate of post LP headache compared to national average, and education
- **Rebeka Walker, PhD, Assistant Professor,** research focusing on health systems and Type 2 Diabetes
- **Chad Wenzel, MD, Assistant Professor,** has research focusing on perioperative medicine, and medical education

- **Jeff Whittle, Professor,** chronic disease management
- **Joni S. Williams, MD, MPH, Assistant Professor,** research focus in community-based, patient-level interventions to reduce disparities and improve health outcomes among African American adults
- **Alice Yan, MD, PhD, Associate Professor,** research focusing on community-based participatory research, mixed method, qualitative, quantitative, cancer survivorship and quality of life, lifestyle behaviors (physical activity and healthy diet), diabetes self-management, and health disparities.

Division of Geriatric and Palliative Medicine

The Division of Geriatric and Palliative Medicine is a new division consolidated on January 1st, 2021. We are engaged in a variety of clinical and educational research areas which are intended to advance patient care and innovate/optimize geriatric and palliative education. Over the years, the Division has had a series of awards to support its efforts in Geriatrics Education; including funding from the National Institute of Aging-NIA (The Geriatric Medicine Academic Career Award), the Health Services and Resources Administration, The Department of Veterans Affairs, the Hartford Foundation and AAMC as well as the Society of General Internal Medicine, and 10 years of funding from the Reynolds Foundation for innovative geriatrics training.

For decades there has been funding for the Division from the Health Resources and Services Administration (HRSA) through a subcontract with Marquette University for the Wisconsin Geriatric Education Center. In July 2015, funding was competitively renewed for a new HRSA program to continue through 2020: The Geriatrics Workforce Enhancement Program (GWEP). The Division participates in the MCW NIA T-35 award which supports 10 undergraduate medical students in summer research each year including the summer of 2020.

- **Alexandria Bear, MD**, has research interests include experiential learning and development of end of life communication workshops. From 2019 through 2020, Dr. Bear was the Co-Investigator for "The Art of Observation," an evidence-based strategy to improve diagnostic and physical exam skills as well as empathy through the Kern Institute Innovative Ideas Initiative. She has been the Co-Investigator for "A Transdisciplinary Approach to Improving ICU Communication," a research grant aimed in team and project building through the Collaborative Research Grant at the University of Wisconsin-Milwaukee Office of Research which goes through 2021. In 2017, Dr. Bear designed an empathy workshop through a Kern Innovation Grant which she continues to host.
- **Angela Beckert, MD**, submitted an Advancing Innovation in Residency Education (AIRE) Proposal for disseminating the Medicine-Geriatrics Integrated Residency and Fellowship Program. Leading up to the submission, she co-chaired a national workgroup, led discussions with Association of Directors of Geriatric Academic Programs (ADGAP) leaders, and presented at national meetings and conferences. The AIRE proposal was approved in June of 2020.
- **Kathryn Denson, MD Edmund Duthie, MD and Steven Denson, MD** participated in grant funding through the Health Resources and Services Administration (HRSA) Geriatrics Workforce Enhancement Program (GWEP), partnering with UW-Madison, Marquette University, Advocate Aurora, and the Alzheimer's Association to (1) implement Maintenance of Certification (MOC) programs; (2) to expand *Geriatric Fast Facts*, (3) and to host the bi-annual Wisconsin Update in Geriatric Medicine and Board Review Course, a co-sponsored CME event between MCW and UW-Madison. By December 2020, 91 Geriatric Fast Facts were published; and in March 2020, the Alliance of Independent Academic Medical Centers (AIAMC) awarded *Geriatric Fast Facts* the Alliance Innovation Award.
- **Kathryn Denson, MD** partnered with Marquette University on a HRSA-funded grant for Home-Based Primary Care nurses at the Milwaukee VA.
- **Edmund Duthie, MD** has partnered with CTSI on the development of an interdisciplinary Ensemble addressing multi-drug resistant organisms and the interfaces between acute and long-term care facilities. He also partnered with Sylvia Munoz-Price in the Division of Infectious Diseases for an Advancing Healthier Wisconsin grant regarding PPE in community nursing homes during the COVID pandemic.

- **Jonathan Gully, MD** has research interests in the culture of palliative care, specifically, better integration of palliative care into medical student education. He is in the final stages of testing a palliative care app to augment educational efforts, with the hope of getting insights into how students and resident's interface with technology at bedside.

- **Sean Marks, MD**, has research interests in Palliative Care Education among physicians in training, prognostication, and psychological issues at the end of life. Dr. Marks is the Editor for Fast Facts and Concepts along with Associate Editor Dr. Drew A Rosielle from the University of Minnesota Medical School. By December 2020, 412 Fast Facts and Concepts were published to the Palliative Care Network of Wisconsin (PCNOW). As Director of Palliative Medicine curriculum for MCW's iTunes University, Dr. Marks has created on-point Palliative Medicine voice-over Power Point modules designed to be accessed by residents and medical students.

- **Cara O'Brien, MD**, was accepted into the Kern Institute KinetiC3 Scholars Program in July 2020. With the help of mentors Dr. Edmund Duthie, Dr. Kathryn Denson and Dr. Angela Beckert, she is conducting an evaluation of the Med-Ger Residency and Fellowship Program. This evaluation interviews current and previous Med-Gers to help Program Directors interested in adopting the Med-Ger model at their institutions and to promote benefits of going into Med-Ger compared to traditional residency and fellowship programs.

- **Wendy Peltier, MD,** has research interests in quality improvement models for 'upstream' palliative care in cancer and advanced heart failure and creating models for inpatient hospice in the ICU setting. She also serves on the Kern Faculty Pillar, with interest in educational programs that support Caring and Character in end-of-life care. Since 2001, Dr. Peltier has been the Principal Investigator for Neurology on the "Use of Rituximab in Sensorimotor Polyneuropathy Associated with Monoclonal Gammopathies and Antibody-Medicated Neuropathy (GM-1, Anti-MAG, and SGPG)" through Genentech.

- **Katherine Recka, MD** has research interests in palliative care education and bioethics. She has led quality improvement initiatives based upon key program data obtained from the quarterly, nationwide Department of Veteran's Affairs (VA) family bereaved survey. Her program has been selected to help other VA programs lead similar initiatives to enhance end-of-life care in the veteran population. Since 2011, Dr. Recka has been the Faculty Advisor for Hospice and Palliative Medicine Fellows' annual quality improvement (QI) projects. In 2020, the QI project was on pain intervention. Additional QI projects include ones that looked at palliative care patients with advance heart failure, who were seen by Emergency Medicine Residents, who were admitted into the ICU, and who "no-showed" to their clinic appointments.

- **Mary Rhodes, MD,** has research interests in identification of language and cultural barriers to quality palliative care services. She is particularly interested in the impact of limited English language proficiency on communication with patients with serious illness. Since 2019, she has participated in Student-Centered Pipeline to Advance Research in Cancer Careers through the National Cancer Institute. The PIs are OB/GYN Department Chair Janet S. Rader, MD, and Assistant Professor Kristina Kaljo, PhD.

- **Liza Thiel, MD, MS,** has research interests in Palliative Care Education in the community setting. She continues to work on improving Advance Directive incorporation into the inpatient setting through FH and FMF pilot programs.

Division of Hematology and Oncology

Building a robust clinical and laboratory research program is a primary mission of the Division of Hematology and Oncology. Under the leadership of **Parameswaran Hari, MD, MS**, Division Chief, **Dr. Mehdi Hamadani**, Director of Blood and Marrow Transplant (BMT) and Cellular Therapy Program, and**, Drs. Ehab Atallah, James Thomas, and Joshua Field,** Section Heads of Hematologic Malignancies, Solid Tumor Oncology, and Benign Hematology, respectively, the Division has been successful in creating a climate conducive to research and to developing high-quality, nationally recognized research programs. Below is a summary of the research interests and activities that occur throughout the Division.

- **Sameem Abedin, MD's** clinical and research interests are in the treatment of patients with myeloid malignancies including acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS), as well as Graft-versus-host disease after allogeneic HCT. He is developing clinical trials for patients with relapsed AML, with a goal of investigating methods to improve disease related outcomes. He additionally is developing trials related to GVHD.

- **Muhammad Bilal Abid, MD's** research interests include allogeneic bone marrow transplant, cellular therapy, and related infectious complications. Current efforts include retrospective studies and clinical trials evaluating the safety and efficacy of investigational agents. With expertise in transplant infectious diseases, malignant hematology, and drug development, he leads collaborative research efforts that examine the gut microbiome as a biomarker and potential therapeutic agent in enhancing responses to advanced immune-engaging therapy.

- **Gulrayz Ahmed, MD,** is an Internal Medicine trained physician with primary research interest in Pancreatic cancer, Multiple Myeloma, and non-Hodgkin's Lymphoma.

- **Abdel Alqwasmi, MD's** research interests include breast cancer.

- **Ehab Atallah, MD's** primary interest is in the treatment of patients with leukemia, myelodysplastic syndromes (MDS) and myeloproliferative disorders with special emphases on the treatment of patients with chronic myelogenous leukemia (CML). He is co-Principal Investigator (PI) with Dr. Kathryn Flynn, MD on an R01 from the National Cancer Institute (NCI) to evaluate stopping tyrosine kinase inhibitors in patients with CML who are in complete molecular remission. He is currently the administrative director of the Jean Khoury Cure CML consortium (HJKC3) which is housed at MCW. In addition, he is the clinical basket chair for patients < 60 with AML in the NCI myelomatch precision medicine initiative.

- **Lisa Baumann Kreuziger, MD, MS,** is a clinical and translational researcher with a focus in thrombosis. She has an interest in device and cancer-associated thrombosis. She started the US network for venous thromboembolism research (VENUS, https://www.htrs.org/HTRS/Research/Endorsed-Studies/VENUS-VTE-Network). Additionally, she is the institutional PI for cancer-associated thrombosis trials. Lastly, she works in collaboration with Alan Mast, MD, PhD, in the Recipient Epidemiology and Donor evaluation program (REDS-IVP) to understand outcomes of patients receiving transfusion for hematologic conditions. Dr. Baumann Kreuziger also developed a study to evaluate a mechanism of how blood clots form in left ventricular assist devices that is funded through a pilot grant from the CTSI. She works in collaboration with Alan Mast, MD, PhD, to complete the biomarker studies involved in her clinical trials and understand the clinical implications of tissue factor pathway inhibitor.

- **Juliana Perez Botero, MD's** research interest is in diagnosis and treatment of patients with inherited and acquired platelet disorders, specifically genotype-phenotype correlation in patients with inherited disorders of platelet number and/or function, development of new laboratory assays to evaluate platelet function and novel treatments of patients with immune thrombocytopenia.

- **John Burfeind, MD's** research interest includes enrolling patients with genitourinary malignancies in clinical trials. Additionally, he has a significant role in the development of the Community Cancer Network, serving as the liaison between the Division of Hematology and Oncology and the Cancer Care Network.

- **Kathryn Bylow MD's** research interest is in the treatment of genitourinary malignancies. She has a long-standing research interest in geriatric oncology and the long-term effects of cancer therapies. She is currently studying nutritional methods to forestall the loss of muscle mass seen in men treated with anti-androgen therapy in prostate cancer.

- **Karen Carlson, MD, PhD's** research focus is on hematopoiesis. Using a novel mouse model system, she has identified a requisite component of the early lymphopoietic niche. She is now working to elucidate the biochemical regulation of this niche and its spatial localization within the bone marrow. Her research activities provide information about the basic biology of the hematopoietic stem cell and early lymphocyte developmental environment and characterize new targets for niche-directed therapy. Her long-term goal is to identify novel targets for the treatment of bone marrow failure syndromes and hematopoietic malignancies. Dr. Carlson is the recipient of a K08 mentored career development award from the National Heart Lung and Blood Institute.

- **Sakti Chakrabarti, MD**'s primary interest is in treating patients with colorectal cancer, biliary tract cancer, and gastroesophageal cancer, with particular emphasis on translational research. He wants to highlight my research in treatment response assessment with ctDNA in rectal cancer patients. He recently opened an IIT to evaluate the feasibility of this approach (NCT04670588). In this observational study, patients with locally advanced rectal cancer (LARC) who are selected for the standard-of-care total neoadjuvant therapy (TNT) will be enrolled. After obtaining informed consent, a venous blood sample and the archival tissue block from the initial diagnostic rectal tumor biopsy will be sent to the Natera laboratory for designing patient-specific ctDNA assay, which will be used to measure ctDNA levels in the peripheral venous

blood samples at various time points coinciding with the standard studies to assess tumor response. The blood sample needed for designing the assay and measuring the baseline ctDNA level will be obtained within four weeks before neoadjuvant chemotherapy begins. Subsequently, for patients undergoing 16 weeks of neoadjuvant chemotherapy, blood samples will be obtained for ctDNA level measurement at t time points (after eight weeks/4 cycles of neoadjuvant chemotherapy within +/- 5 days of the magnetic resonance imaging (MRI) study, after 16 weeks/8 cycles of neoadjuvant chemotherapy within +/- 5 days of the MRI study, and one to 14 days before surgery). For patients who receive eight weeks of neoadjuvant chemotherapy, two blood samples will be obtained for subsequent ctDNA measurements (after eight weeks/4 cycles of neoadjuvant chemotherapy within +/- 5 days of the MRI study, and one to 14 days before surgery). All patients may also choose to undergo additional serial ctDNA level measurements for surveillance after the surgery every three to four months for two years (optional). Tumor response rate assessed by ctDNA (defined as reduction of ctDNA level at least by 90% compared to the baseline level) will be compared with the response rate assessed by the standard method (proctoscopic examination, pelvic MRI, etc.) to explore if a significant correlation exists between these two response assessment methods. If preliminary data support the hypothesis that peripheral blood ctDNA can be utilized for tumor response assessment in this scenario, a larger study will be conducted to validate this method. Once validated, ctDNA measurement can potentially replace expensive, uncomfortable, and time-consuming methods of tumor response assessment like MRI. Please contact him by email (schakrabarti@mcw.edu) if interested in participating in this area of research.

- **John Charlson**, **MD's** research interests are focused on the care of patients with sarcoma and young adult cancer patients. Current efforts include chemotherapy clinical trials, evaluation of several potential biomarkers of treatment response, and cancer care process improvement.

- **Lubna Chaudhary, MD, MS's** primary research interest is to better understand the biology of breast cancer tumors, as well as different hormone receptors and how they impact patient outcomes. She is working to identify new drug therapies to overcome cancer cell growth. Her investigator initiated clinical trial assessing neoadjuvant endocrine therapy and tumor molecular changes in patients with breast cancer was the recipient of funding from the Rock River Foundation and the MCW Cancer Center in 2017. Another investigator initiated clinical trial assessing the role of PD-1 inhibition in breast cancer patients undergoing neoadjuvant chemotherapy was recently funded by a CTSI KL-2 grant funded by Advancing a Healthier Wisconsin Research and Education Program (AHW REP).

- **Hui-Zi Chen, MD, PhD's** is a physician scientist and thoracic medical oncologist whose research mission is to enable discovery of new therapeutic vulnerabilities in advanced solid cancers by leveraging her expertise in translational genomics and rapid research autopsy. She was a recipient of the ASCO Conquer Cancer Foundation Young Investigator Award (2018-2019). Her research is currently supported by an NCI K08 Mentored Clinical Scientist Research Career Development Award (2019-2024) and focuses on elucidating mechanisms of therapeutic resistance in relapsed small cell lung cancer through multi-omics characterization of metastatic tumor tissues and pre-clinical validation studies. Dr. Chen was formerly a faculty member at The Ohio State University College of Medicine and Comprehensive Cancer Center in Columbus, Ohio (2019-2021). She is new to MCW and looks forward to forming new research and clinical collaborations to improve the care of lung cancer patients in Wisconsin.

- **Xiao Chen, MD, PhD's** research focuses on the role of micronutrients in regulating GVHD. His lab is investigating how vitamin A and vitamin D affect GVHD risk after allogeneic stem cell transplantation using animal models. He is also investigating how to target nuclear receptors including retinoic acid receptor and vitamin D receptor to mitigate GVHD.

- **Yee Chung Cheng, MD's** research interest is in the development of clinical trials focusing on the investigative use of chemotherapy and/or novel therapy in high risk breast cancer cases such as triple negative breast cancer or inflammatory breast cancer particularly in the pre-operative setting.

- **Saurabh Chhabra, MD, MS** is a BMT-trained clinician with interest in BMT and multiple myeloma. His current research interests include clinical trials for drug development in the areas of plasma cell neoplasms and improving outcomes of allogeneic hematopoietic cell transplantation. He is the Principal Investigator (PI) for an Investigator-Initiated study evaluating the utility of anti-IL-6 monoclonal antibody tocilizumab for prevention of Graft-versus-Host Disease (GVHD) in patients receiving allogeneic transplant for hematologic malignancy. He is also the site PI for a number of phase I and II clinical trials for treatment of newly diagnosed and relapsed/refractory multiple myeloma and for treatment of GVHD. He is

also actively involved with transplant registry studies, as Scientific Director of Regimen-Related Toxicity Working Committee of the Center for International Blood and Marrow Transplant Research (CIBMTR).

- **Rachel Cusatis, PhD** is an Assistant Professor of Medicine at the Medical College of Wisconsin, Division of Hematology and Oncology. She is a faculty member of the Center for International Blood and Marrow Transplant Research (CIBMTR). Her research focuses on the intersection of patient reported outcomes, social determinants of health, and time use patterns to understand patient and caregiver health outcomes. Through mixed methods approaches, she collaboratively works on projects analyzing patient reported outcomes, patient and provider communication, and decisional regret among transplant and cellular therapy patients and other contexts.

- **Sumana Devata, MD's** primary interest is in the treatment of patients with non-hodgkin (NHL) and hodgkin lymphomas. She is interested in the development of clinical trials and treatment strategies for these lymphomas.

- **Binod Dhakal, MD, MS's** research focuses on multiple myeloma and related plasma cell disorders. He completed two early phase studies in multiple myeloma: one looking at the novel drug combination in the management of relapsed/refractory multiple myeloma and the other on the pharmacokinetics of new Melphalan both of which were published. He has secured funding for 2 more early phase studies: one looking at the novel induction therapy in multiple myeloma patients with renal injury, and that also evaluates the role of novel biomarker for renal recovery. The other study is an entirely new drug targeting PIM kinase with the study evaluating a dual role of anti-myeloma and bone protective effect. He was awarded a pilot grant from American Cancer Society to explore the role of micro-RNA in multiple myeloma bone disease and the results looking promising to be tested in a larger setting. Additionally, in collaboration with investigator from University of Wisconsin Madison/UCSD, he was awarded a prestigious Translational Research Program grant from Leukemia and Lymphoma Society to explore the role of matrikines in the immune regulation of myeloma. This concept is being investigated prospectively through a nationally conducted multi-center BMT CTN study.

- **Jing Dong, MD's** research focuses on integrating high throughput "omics" data into epidemiological studies to develop approaches to reduce cancer burden and cancer disparities. She has applied genome-wide association study (GWAS), next generation sequencing (NGS), gene-environment interaction and Mendelian Randomization analysis approaches to identify genetic and non-genetic risk factors of cancer. After she joined MCW, she expands her interests to understand genetic determinants underlying outcomes of patients undergoing hematopoietic cell transplantation.

- **William Drobyski, MD's** laboratory evaluates multiple aspects of the immunobiology of allogeneic HCT with particular emphasis on Graft-versus-Host Disease (GVHD) biology. By employing murine models of stem cell transplantation, this research aims to understand the interplay between the inflammatory and regulatory arms of the immune system and how they impact the severity of GVHD. He is also the Leader of the Discovery and Development Therapeutics Program of the MCW Cancer Center. Dr. Drobyski has been continuously funded by NIH for this work since 1991. He currently has three NIH grants that are directed at understanding the pathophysiology of GVHD and is particularly interested in developing new approaches for the prevention of this disease in the gastrointestinal tract which is the major site of morbidity in patients. He also has an interest in the translation of pre-clinical studies into the clinic to attenuate GVHD and currently has two ongoing clinical trials designed to prevent GVHD in allogeneic hematopoietic stem cell transplant recipients.

- **Anita D'Souza, MD, MS,** is an Associate Professor of Medicine with a research focus in plasma cell disorders including multiple myeloma and amyloidosis. She is the Scientific Director of the Plasma Cell Disorders and Adult Solid Tumors working committee of the CIBMTR. In addition to conducting clinical trials, she also leads efforts to study quality of life and patient-reported outcomes in these diseases. She mentors multiple trainees on research projects in this area.

- **Mary Eapen, MD, MS's** research is in alternative donor and grafts for allogeneic HCT for acute leukemia and non-malignant diseases.

- **Timothy Fenske, MD, MS's** clinical and research interests focus on the care of patients with lymphoma. He has a strong interest in refining the use of hematopoietic cell transplantation (HCT) as a treatment for lymphoma. He is a co-chair of the Lymphoma Working Committee of the Center for International Blood and Marrow Transplant Research (CIBMTR). He is the co-chair of a national (Intergroup) trial evaluating the use of maintenance therapy with ibrutinib to prevent recurrence of diffuse large B-cell lymphoma after autologous HCT. He is also the national Principal Investigator for an Intergroup trial evaluating a deep sequencing minimal residual disease assay to help direct therapy for mantle cell lymphoma patients in first remission.

- **Joshua Field, MD's** research program focuses on of clinical studies in adults with sickle cell disease. Particular areas of interest include acute and chronic pain, pulmonary complications, transfusion, and therapeutic studies.
- **Kathryn Flynn, PhD** is the Senior Scientific Director for Patient-Reported Outcomes in the Center for International Blood and Marrow Transplant Research (CIBMTR). Her research focuses on the measure development and analysis of patient-reported outcomes as well as mixed methods approaches to understanding and improving patient-provider communication and patient decision making. She leads the NIDDK-funded Wisconsin Exploratory Center for Interdisciplinary Research in Benign Urology.
- **Patrick Foy, MD's** current research focuses on management of bleeding in patients with hereditary hemorrhagic telangiectasia with therapy designed to decrease blood vessel growth (VEGF inhibition). He also assists in ongoing clinical trials in hemophilia and thrombosis. He also is actively engaged in educational research designed to improve teaching of medical students, residents, and fellows in hematology and oncology.
- **Kenneth Friedman, MD** is a clinical laboratory investigator who is involved with numerous clinical trials with several academic institutions, Industry and the NIH investigating the role of diagnostic laboratory hemostasis and thrombosis testing in the evaluation of patient cohorts.
- **Ben George, MD's** research focus is on pancreatic and gastro-esophageal cancers. He is interested in experimental therapeutics, specifically, clinical trials targeting putative molecular mechanisms involved in the development and progression of gastrointestinal malignancies. He chairs the Molecular Tumor Board - a monthly meeting that analyzes genomic alterations in tumors to identify appropriate targeted treatment options. Further, he represents Froedtert and Medical College of Wisconsin at the Precision Medicine Exchange Consortium, of which MCW is a founding member. The goal of the consortium is to pool clinically annotated molecular data among member institutions and use that information to develop clinical trials aimed at actionable genomic alterations. He is the institutional Principal Investigator on several clinical trials in both Pancreatic and Gastro-esophageal Cancers.
- **Thomas Giever, DO, MBA's** main research interest is to enroll patients on genitourinary clinical trials. Additionally, he would like to build a robust general oncology clinical trial portfolio at the Drexel Town Square Health Center Cancer Center within the Froedtert Community Cancer Network and Division of Hematology and Oncology.
- **Guru Subramanian Guru Murthy, MD's** clinical and research interests focus on the outcomes of patients with leukemia and stem cell transplantation. He conducts retrospective and prospective clinical studies in patients with leukemia and stem cell transplantation with a goal of improving disease related outcomes"
- **Mehdi Hamadani, MD's** research interest includes lymphoma, GVHD, and alternative donor transplantation. He is the Scientific Director of the CIBMTR's Lymphoma Working Committee, and the Medical Director of MCW BMT and Cell Therapy Program. He has investigated the role of immunomodulation with HMG-CoA reductase inhibitors and TNF-alpha blockers for preventing acute GVHD as well as the role of the novel proteasome inhibitor MLN9708 in preventing chronic GVHD. As part of BMT CTN's Data Coordinating Center, Dr. Hamadani is intricately involved in the development and conduct of several cooperative group trials looking at prevention and treatment of GVHD, and mitigation of post-transplant relapse-risk in acute leukemias.
- **Parameswaran Hari, MD, MS,** conducts clinical research evaluating novel therapies for plasma cell disorders including myeloma and amyloidosis as well as novel approaches for transplantation. He is the Scientific Director of the CIBMTR's Plasma Cell Disorder Working Committee and co-Chair of multiple national trials for multiple myeloma. He is also an investigator on several novel drug phase I and II trials in multiple myeloma, several of which have led to FDA approval. In addition, he has projects in development for translational applications of cell-based therapeutics in malignancies, spinal cord injury, hemophilia and other immune therapies.
- **Mary Horowitz, MD, MS** is Deputy Cancer Center Director**.** Her career has focused on assessing clinical outcomes of blood and marrow transplantation (BMT) and other cell therapies through the Center for International Blood and Marrow Transplant Research (CIBMTR). She leads the BMT Clinical Trials Network (CTN), funded by NHLBI and NCI. The BMT CTN conducts large multicenter trials and enrolls patients from more than 100 centers in the US, Canada, France and Germany. Dr. Horowitz is co-PI, with Dr. Mary Eapen, of a grant from NHLBI for theCIBMTR to participate in NHLBI's Cure Sickle Cell (CureSC) Initiative. The CIBMTR works with the CureSC Data Consortium to build a research data ecosystem designed to

support investigator-initiated collaborative research. The CIBMTR also supports the design and launch of gene therapy sickle cell disease clinical trials using the infrastructure of the BMT CTN.

- **Siegfried Janz, MD, DSc**'s primary research interest concerns neoplasms of terminally differentiated, immunoglobulin producing B-lymphocytes called plasma cells. Relying in part on gene-insertion mice that mimic different fine structures of the human MYC-activating t (8;14) (q24;q32) translocation, he recapitulates important features of human plasma cell myeloma (multiple myeloma) in single and compound transgenic mice. His laboratory takes advantage of mouse models of this sort to elucidate mechanisms of neoplastic plasma cell development and evaluate new approaches to myeloma treatment and prevention. The long-term goal of Dr. Janz' work, which is supported by NCI R01CA151354, is to improve the outcome of patients with myeloma and related blood cancers. To that end, he collaborates with fellow investigators from HemOnc, the Department of Medicine and the MCW Cancer Center.

- **Bryon Johnson, PhD,** conducts basic/translational research on adoptive T cell immunotherapies for both hematologic malignancies and solid tumors. He is also Director of the BMT Cell Therapy Laboratories, which processes hematopoietic progenitor cells and immune cells for the MCW Blood and Marrow Transplant Program and participates in the development of novel immune cell therapies for patients with cancers and other diseases. The labs also provide some immune monitoring services for investigators involved in immunotherapy clinical trials.

- **Sailaja Kamaraju, MD,** has research interest in breast cancer and more specifically, how breast cancer mortality rates can be reduced in vulnerable, and underserved populations through community-based initiatives, for which she has received several Susan G. Komen grants. She works with Patient Centered Outcomes Research (PCOR) evaluating cancer treatment related toxicities and cancer survivorship disparities.

- **Mandana Kamgar, MD, MPH's** research focus is on pancreatic ductal adenocarcinoma, clinical trial development and translational research.

- **Tyce Kearl, MD, PhD's** research interest is in translational cancer immunotherapy. He is the Assistant Director of the BMT & Cell Therapy Laboratories and Co-Director of the new MCW Cancer Center shared resource—the Cell Therapy and Immune Monitoring Laboratory. The laboratory has developed expertise with in-house CAR-T cell manufacturing for early phase clinical trials. In addition, the laboratory provides cutting-edge immune profiling to support mechanistic and correlative studies of novel immunotherapies.

- **Deepak Kilari, MD's** research focuses on genitourinary cancers, including early phase and translational trials. Dr. Kilari and his collaborators are also studying how copper transport proteins play an important role in the sensitivity of cancer cells to platinum-based chemotherapy, as well as the role of exosomes micro RNAs in predicting treatment responses in men with prostate cancer. He is also the Principal investigator of a phase 2 study looking at the role of upfront enzalutamide and dutasteride for elderly men with systemic prostate cancer. He is actively involved in outcomes research at the Clement J Zablocki VA Medical Center.

- **Walter Longo, MD,** is interested in alpha/beta depletion with haploidentical donors to lessen complications of GVH but preserve graft versus tumor. He is also interested in CAR-T for lymphoma, myeloma, CLL and other hematologic malignancies.

- **Subramaniam Malarkannan, PhD's** research interests include signaling cascades that regulate the development and functions of human Natural Killer cells (NK) patients with malignancies, inherited diseases and infections, and developing translational models to improve the anti-tumor efficacy of human NK cells. His team uses cellular, biochemical, and transcriptomic (single-cell RNA-seq) approaches. Research in his laboratory is supported by NCI, NIH, MACC Fund, Nicholas Family Foundation, and Gardetto Family Endowed Chair.

- **Smitha Menon, MD's** research interest is in the role of novel agents and targeted therapy in the treatment of lung cancer. She is the PI of multiple clinical trials.

- **Laura Michaelis, MD's** research interests are in the care of patients with acute and chronic leukemias. She conducts research on novel agents in the treatment of these diseases and in ways to better manage the side effects and toxicities of therapies. She is the primary investigator of a national clinical trial being developed to test low-intensity therapy for older individuals who have acute myeloid leukemia.

- **Prabhas Mittal, MD's** research interests are in cooperative group clinical trials and drug development.
- **Ariel Nelson, MD's** primary research interests include genitourinary malignancies, immunotherapy and novel therapeutic and combination clinical trials.
- **Marcelo Pasquini, MD, MS's** research focus is on cellular therapies for the treatment of cancer. He oversees the CIBMTR cellular therapy registry and is the PI for the NCI-funded Cellular Immunotherapy Data Resource (CIDR). He also oversees clinical research on CT in the CIBMTR along with the conduct of long term follow up of commercial CAR T cells and other cellular therapies.
- **J. Douglas Rizzo, MD, MS's** research interest is in late effects after transplantation, quality of life, and financial impacts upon patients. He also performs the annual center specific outcomes analysis for US transplant centers and has an interest in hospital outcomes reporting.
- **Lyndsey Runaas, MD's** research interests include improving outcomes for patients undergoing allogeneic bone marrow transplant. Specifically, this includes understanding and preventing graft-versus-host disease, studying the role of the intestinal microbiome in bone marrow transplant, and trying to optimize communication between patients with advanced hematologic malignancies and their providers. She hopes to continue to foster a translational and collaborative research career incorporating both qualitative and quantitative methods to improve the outcomes of patients with advanced hematologic malignancies.
- **Wael Saber, MD, MS** conducts clinical research evaluating outcomes of autologous and allogeneic HCT. He is the Scientific Director of the CIBMTR's Chronic Leukemia, Acute Leukemia, and Health Services & International Issues Committees. His research primarily focuses on patients with MDS and on issues related to cost-effectiveness and access to HCT care. He is the protocol officer for a national clinical trial comparing transplantation to non-transplant therapies among older MDS patients (BMT CTN 1102). He is a co-principal investigator of an ancillary R01 grant to evaluate the cost-effectiveness of these two treatment approaches among older MDS patients participating in BMT CTN 1102.
- **Nirav Shah, MD, MSHP's** research interests includes lymphoid malignancies, cellular and immunotherapy, and bone marrow transplant. He is leading the internal CAR-T cell trial for non-Hodgkin lymphoma at MCW and is working on developing new treatment regimens for patients with relapsed hematological malignancies.
- **Bronwen Shaw, MD, PhD,** has an interest in health-related quality of life and survivorship issues in patients who undergo hematopoietic cell transplantation (HCT). She is especially interested in the ability of patient reported outcome (PRO) collection to predict patient experience and clinical outcomes. She also has an interest in hematopoietic cell donors, both in terms of their experience and in terms of determining factors which help to select the best donor for an individual patient.
- **Roy Silverstein, MD's** lab focuses on platelet and macrophage biology as they relate to common vascular diseases, including atherosclerosis and arterial thrombosis. His work centers on a cell signaling system mediated by the type 2 scavenger receptor CD36. As a receptor for long chain fatty acids CD36 mediates cellular metabolism in many cell types, including tumor stem cells and tumor infiltrating macrophages. As a pattern recognition receptor on macrophages and platelets for numerous "danger signals," including oxidized low-density lipoprotein (oxLDL), glycated proteins, cell-derived extracellular vesicles and bacterial cell wall components, CD36 mediates innate immune responses that contribute to inflammation, thrombosis and atherogenesis.
- **Robert Taylor, MD's** research interest is in head and neck cancers and malignant hematology.
- **James Thomas, MD, PhD's** research interest is in oncology drug development and the role of reactive oxygen species in cancer development and treatment.
- **Jonathan Thompson, MD, MS,** has interest in clinical and translational research related to thoracic malignancies, particularly regarding the use of immunotherapy and novel agents for the treatment of lung cancer. Recently, he has focused on the impact of the microbiome on immunotherapy outcomes in non-small cell lung cancer.
- **Li-Shu Wang**, **PhD,** conducts pre-clinical and clinical studies to investigate the mechanisms of nutritional-based approaches to prevent cancer through immunity and gut microbiome modulations.

- **Krista Wiger, MD's** research interests are in maintaining resiliency among practitioners as well as exploring quality improvement opportunities and hospital readmissions issues specific to inpatient oncology.

- **Stuart Wong, MD,** conducts clinical research evaluating novel therapies for head and neck cancer, and in particular, agents that are used concurrently with radiation therapy. His research efforts include NCI funded clinical trials. His research also focuses on national patterns of care for head and neck cancer treatment, and mitigation of toxicity from head and neck cancer treatment, and cancer prevention. Dr. Wong is the lead investigator for the Lead Academic Participating Site (LAPS) of the NCI's National Clinical Trial Network at MCW. MCW is one of the top 32 institutions in the country to receive a LAPS award. He also received an RO1 NIH grant with Ming You, MD. PhD, to study a new agent in patients with oral cancer.

- **Anthony Zamora, PhD's** research spans the fields of viral and cancer immunology, with a special focus on identifying ways to modulate the immune system to more effectively target and eliminate virally infected or cancerous cells. Along these lines, the lab utilizes cellular-based engineering approaches that aim to increase the specificity of immune cells for their targets and at the same time decrease the likelihood of off-target toxicities. A longstanding goal in the lab has also been to help address the current disparities in cancer research by developing reagents, assays, and tools that provide a deeper understanding of the underlying mechanisms that govern antitumor immunity across diverse demographic groups. Current research in the Zamora lab focuses on: (1) discovering tumor antigens that serve as immunogenic targets, (2) identifying the mechanisms involved in the immune system's ability to generate antitumor specificities, (3) characterizing the phenotypic, functional, and receptor repertoires of NK cells and neoantigen-specific T cells, and (4) exploring ways to translate these findings in order to expand on the current therapeutic options used to treat cancer.

Division of Infectious Diseases

The Division of Infectious Diseases is involved in multidisciplinary and collaborative research efforts with internal and external partners. Faculty are engaged in a variety of clinical research trials conducted in collaboration with research networks and industry sponsored trials. Several HIV treatment, HIV prevention, and Influenza Phase III drug trials and network trials are in active enrollment and will determine the safety and effectiveness of various new treatments. The Division also conducts studies in infection control and hospital epidemiology. In close collaboration with the MCW Center for AIDS Intervention Research (CAIR), the Division's behavioral and community research is supported by several key institutions including the National Institute of Mental Health, National Institute on Aging, Centers for Disease Control and Prevention, and the Wisconsin AIDS/HIV program. Division faculty work closely with CAIR to develop, conduct, and evaluate new interventions to prevent HIV among individuals most vulnerable to the disease. Several ongoing laboratory-based research projects headed by key members of the Infectious Diseases division. In addition, other research is aimed at addressing international health issues.

Primary research investigators include the following:

- **Dr. Bilal Abid's** research interest intersects in areas of both Oncology and Infectious Diseases. He heads projects dealing with immunotherapy, cytokine release syndrome, CAR T-cells, malaria, as well as the gut microbiome. He analyses haploHCT patients at MCW to study the association between CRS and infections. He spearheads a study in genomic profiling of a case of tumor hyper progression with pre-existing Li Fraumeni Syndrome that spans across both the Division of Infectious Diseases and Hematology and Oncology.

- **Dr. Sol Aldrete** is currently working on project in which the Retrospective observational study of patients who received BCG vaccination seeking to identify patient factors associated with Mycobacterium bovis infection after instillation of the vaccine for bladder cancer. This is a study in the VA along with Dr. Gundacker. Second project is looking at HIV Preexposure prophylaxis initiation and retention in care at an HIV health care system in Wisconsin.

- **Dr. Jenifer Coburn's** research interests focus on pathogenic spirochetes, a group of bacteria that are able to cause persistent, disseminated infections in immunocompetent animals, including humans. The Coburn lab is currently working with *Borrelia burgdorferi*, which is maintained in a tick-animal cycle in nature. They also work with another pathogenic spirochete, *Leptospira interrogans*. Leptospires are maintained in infected animals in nature but can also survive in water and mud. The focus of the work with both *Borrelia* and *Leptospira* is to identify and then test the biologic significance of bacterial proteins that help the bacteria bind to mammalian cell surface receptors, to identify the mammalian cell surface

receptors recognized by the bacteria, and ultimately the biological and pathologic significance of the bacterial-mammalian receptor interaction.

- **Dr. Carlos Figueroa-Castro's** projects include implementation of telemedicine consultation solutions in the inpatient setting, and its impact in patient's outcomes; use of open-source statistical software (RStudio) to perform analytics of electronic hand hygiene monitoring; and to study the correlation between data management organization strategies and infection prevention program effectiveness.

- **Dr. Michael Frank** is currently conducting two large NIH-funded clinical trials in individuals with HIV infection. The first is as an affiliate of the International Network for Strategic Initiatives in Global HIV Trials (INSIGHT), the START trial (Strategic Timing of Anti-Retroviral Treatment), which is answering the question of the optimal timing of initiation of antiretroviral therapy (ART) with regard to morbidity and mortality among HIV-1 infected patients. The second is the Randomized Trial to Prevent Vascular Events in HIV (REPRIEVE) trial through the AIDS Clinical Trials Group, which is examining whether use of an HMG-CoA reductase inhibitor improves outcomes in HIV-positive patients who are at low or moderate risk of cardiovascular events.

- **Dr. Mary Beth Graham's** clinical research interests including infections in immunocompromised hosts including HIV and transplant patients, orthopedic infections, and viral infections, including influenza, respiratory viruses, and novel coronaviruses. She has been the principal investigator for several clinical trials, including assessing the efficacy and safety of anti-SARS-CoV-2 convalescent plasma in hospitalized patients with acute serve respiratory symptoms and expanded access treatment protocol for Remdesivir in the treatment of COVID-19 Infection.

- **Dr. Gundacker** is currently involved in enrolling a study evaluating rabies, which is comparing human rabies immune globulin in post-exposure with different rabies exposure risks.

- **Dr. Jamie Green's** research interest are in the areas of infections of immunocompromised hosts including leukemia, lymphoma, stem cell and solid organ transplant. Past projects included immune reconstitution after stem cell transplant and herpesviruses (cytomegalovirus and human herpesvirus 6) as well as infections in heart or lung transplant recipients. Currently she is pursuing projects that aim to improve overutilization of antibiotics in neutropenic patients with leukemia, lymphoma or stem cell transplant, and creations of a comprehensive dataset on infections in heart and lung transplant recipients; specifically, to evaluate those who have an active infection at the time of transplant.

- **Dr. Michael Kron** is leading an NIH-funded collaborative study investigating compounds that might be useful in treating human filiarial diseases, which infect millions of persons. In collaboration with an international network of laboratories, the researchers are working to identify novel chemical scaffolds that inhibit recombinant parasite aminoacyl-tRNA synthetase (AARS) and predict the structure using computer modeling. Under an exploratory grant from the Fogarty International Center of NIH, research has also focused on the natural products and biodiversity issues of terrestrial and marine organisms in the Philippines. He also collaborates with the Viral Oncogenesis group at the US National Cancer Institute who are looking at the relationship between certain HHV8 genotypes and IgE levels. In a project that evolved from time as a US State Department Senior Science Advisor, and in collaboration with WHO mental health, he analyzed data in Global Mental Health in the 21 countries of APEC (Asia Pacific Economic Cooperation).He lead an MCW based project in collaboration with the Molecular Parasitology Research Unit, Queensland, Australia, comparing DNA sequence of parasite DNA extracted from a kidney-liver transplant recipient and mitochondrial DNA databases in order to determine the species of parasite and the country where our patient became infected.

- **Dr. Zouyan Lu's** research interest includes Adaptive Platform Treatment Trial for Outpatients with COVID-19, which is currently enrolling COVID-19 patients in ambulatory setting.

- **Dr. Sheran Mahatme** is involved in a variety of quality improvement and clinical research projects at ZVAMC. She has partnered with Allergy/Immunology, Emergency Medicine, and ID Pharmacy in reassessing beta lactam allergy listings and has supported ID Pharmacy in conjunction with Geriatric Medicine and Nursing in developing an algorithm to reduce the acquisition and unnecessary antimicrobial use in asymptomatic bacteriuria. Dr. Mahatme has worked with Inpatient Internal Medicine, Radiology and Nursing to initiate a Venous Access Team to provide a standardization process for long term venous access placement and has collaborated with ID Pharmacy in assisting the Department of Surgery's reassessment and update of antimicrobial surgical prophylaxis. She has spearheaded implementation of the ANNIE Program on a local level to improve the medical adherence, retention and linkage of care of people living with HIV and

those on pre-exposure prophylaxis. Finally, Dr. Mahatme is involved in two clinical studies, one looking at developing an improved interferon release gamma assay using specific T cell stimulation for the detection of *M. tuberculosis,* and the second as a site co-investigator for a National VA Cooperative Study assessing the optimal treatment for recurrent *C. difficile* infection by comparing the efficacy of oral Vancomycin, oral Vancomycin (taper and pulse) and Fidaxomicin.

- **Dr. Silvia Munoz-Price's** research deals with the horizontal transmission of organisms within the healthcare environment. This includes initial acquisition and development of infections with multidrug resistant organisms, microbiota disruption, antibiotic exposures, environmental contamination, and hand hygiene. Dr. Munoz-Price is also conducting clinical trials looking at prevention of *Clostridium difficile* colitis in patients colonized with *C. difficile*. She is the principal investigator for multiple COVID-19 studies, including understanding COVID-19 transmissibility in long-term care facilities and Effect of PPE on Incidence of COVID-19 in a Ventilator Capable Nursing Home. Additional topics of interest include analyses of time dependent variables (i.e. antibiotics) and quality and patient safety indicators, such as hospital readmissions. All activities are performed in close collaboration with the Enterprise Infection Control Departments, the Antibiotic Stewardship teams, the Quality Department and the Clinical Microbiology Laboratory. Using an array of approaches and data collection, research is focused on reducing the spread of infection among medical and surgical patients within the hospital environment.

- **Dr. Andrew Petroll's** research interests include understanding health care providers' knowledge and experience with HIV prevention methods and studying how to increase their awareness of such methods. Research is also examining factors that affect that affect medication adherence and retention in medical care among older HIV-positive patients in rural areas.

- **Dr. Joyce Sanchez's** main research interest is in illness related to international travel. She has collaborative projects with the Department of Microbiology and Immunology investigating immune responses to vector borne illnesses as well as with the Blood Center of Wisconsin analyzing of human immunity after vaccination to predict pathogen epitopes for improved vaccine development.

Division of Nephrology

The main research priorities of the Division of Nephrology include:

Kidney Stone Research: The kidney stone research group investigates the pathophysiologic mechanisms mediating the initiation and progression of urinary tract and kidney stone disease. Research is focused on: (i) studies on the epidemiological patterns of stone disease, (ii) mechanisms of stone initiation, (iii) genetic linkages between stone disease and hypertension, (iv) the development of new animal models to study calcium oxalate stone disease, and (v) composition variations in recurrent stone patients. Targeted research is also conducted on the physical, chemical and physiologic mechanisms of crystal nucleation, growth, and aggregation of crystals that form within the nephron and in related vascular tissue.

Research in Acute Kidney Injury: One area of laboratory research focuses on ischemic acute kidney injury (AKI), with goals to: (i) translate laboratory discoveries in AKI to clinical medicine, and (ii) perform experiments that further explore questions generated at the bedside. Current projects are aimed at: (i) the development of new therapies to prevent or treat AKI based on an understanding of the genetic, physiologic, and molecular mechanisms that underlie the ischemic kidney injury, and (ii) evaluation of the long-term effects of acute renal ischemia.

Research in Renal Cell Biology and Signaling: NIH funding supports multiple projects focused on cell signaling as related to pathobiology of kidney disease. Research is primarily focused on characterizing the molecular mechanisms underlying the activation and termination of signaling pathways, as well as defining the cellular consequences of specific stimulation of these cascades in systems relevant for the signaling from G-protein coupled receptors.

Clinical Research on Diabetic Nephropathy, Chronic Kidney Disease (CKD), End-Stage Renal Disease (ESRD), and Renal Transplantation: There are several areas of ongoing clinical research activity in subjects with CKD and ESRD. Recent trials in CKD and ESRD have studied new treatments for diabetic nephropathy, secondary hyperparathyroidism, and prevention of vascular calcification. The Division of Nephrology has participated in several large clinical trials investigating novel immunosuppressive agents and protocols in patients following kidney transplantation. Other studies have explored technologies for imaging of maturing dialysis vascular access and gene expression profiling, proteomics, and complex trait genetics in kidney transplantation.

Clinical outcomes-based research on cognitive and functional status in older adults on dialysis, focused on preventing cognitive and functional decline. This includes progression of cognitive impairment based on dialysis modality and evaluating changes in intradialytic cerebral perfusion and relationship with cerebral imaging parameters and performance on cognitive assessments.

Division of Pulmonary & Critical Care

The Division of Pulmonary and Critical Care Medicine has a rich research environment, where our faculty and research staff complement departmental goals of identifying ways and/or means of improving outcomes and quality of life for our patients.

Our current research support team features a full-time research manager, nine full-time clinical research coordinators, a full-time research assistant, one basic science support staff and two part-time data analysts to assist the faculty in conducting translational and clinical research and basic science. With this support, faculty and fellows conduct internally and extramurally funded research, publish and present findings which further highlight the Division's strong commitment to excellence in research and outcomes.

The Division strives to offer opportunities to our patients to participate in a variety of trials. The faculty, fellows, and research coordinators are engaged in many clinical and investigator-initiated research projects conducted in collaboration with several foundations, networks, and industry-sponsored partners. Additionally, our team assists others within the Department of Medicine as needed to onboard staff/faculty to research, assist in protocol preparation, submissions, regulatory, budgeting and other tasks as requested.

- **Cystic Fibrosis (CF) & Nontuberculous Mycobacterial (NTM) -** Working to improve outcomes and quality of life in patients. Focus in improving airway and breathing, reducing infections and inflammation, thereby increasing quality of life and survival time.
- **Pulmonary Hypertension (PH) -** Developing registries and new approaches in treatments with an emphasis on extending survival rates.
- **Idiopathic Pulmonary Fibrosis (IPF) -** Education by developing long-term care plans.
- **Chronic Obstructive Pulmonary Disease (COPD) -** Identifying safety and efficacy of medications in patients.
- **Critical Care (CC)** includes quality improvement**,** investigator-initiated, and industry-sponsored observational and randomized controlled trails evaluating therapeutics and outcomes related to sepsis, acute respiratory distress syndrome, ICU-related delirium, end of life care, family-provider communication, acute pulmonary embolism, diagnostic reasoning, and nutrition.
- **Interventional Pulmonary (IP) -** Incorporating research with the use of advanced diagnostic and therapeutic techniques.
- **Investigator-Initiated Trials (IIT) -** Finding ways to improve critically ill patients how we can provide maximum benefit and improved outcomes,

Pulmonary & Critical Care Medicine has over 82 active projects, 63 industry, 14 IIT, 5 grants; 1 $1.73M 3-year award through NCATS in collaboration with CTSI and 3 CF Foundation awards. Our research trials are primarily led by: J Biller MD, M Barash MD, B Benn MD, P Bergl MD, V Bonne MD, R Franco MD, D Ishizawar MD, E Jacobs MD, D Kogan MD, J Kurman MD, R Lipchik MD, MD, R Nanchal MD, J Patel MD, K Presberg MD, V Ramalingam MD, A Taneja MD, & J Truwit MD. Supported by; Jeanette Graf RM, Ashley Wuerl CRC III, Erin Hubertz CRC II, Amy Blair CRC II, Jennifer Peterson CRC II, Kiley Timler CRC I, Olivia Wenzel CRC II, James Zelten CRC II, and Ripna Parveen Data Analyst along with active recruitment for 3 additional team members; CRC I, Data Analyst and CRA III.

2020 has enlightened us with new challenges along with many new opportunities of research and collaboration for our Department, we look forward to the many new endeavors we have in store for 2021.

Division of Rheumatology

The Rheumatology Division at the Medical College of Wisconsin has a strong history of research, largely in crystal-related arthritis, and has continued this focus, while simultaneously pursuing work in Systemic Lupus Erythematosus (SLE) and scleroderma, and

participating in clinical trials of SLE and scleroderma. We are always interested in collaborations and have expertise that spans bench research, industry-sponsored clinical trials and investigator-initiated human studies. We have assistance from a clinical research coordinator in the department of medicine and expert laboratory personnel at the VA.

- **Ann Rosenthal, MD** continues to work on crystal arthritis, with a focus on calcium pyrophosphate deposition disease (CPPD). She runs a federally-funded research program at the Zablocki VA where she is delineating mechanisms of calcium crystal formation in articular cartilage. Dr. Rosenthal's current work focuses on the role of the multipass membrane protein known as ANKH, which was described as a novel mediator of ATP efflux in chondrocytes. She also has a project to explore the role of osteoprotegerin mutations in CPPD which involves studies of osteoclastogenesis and bone metabolism. Current local collaborators at MCW include Brian Volkman, Ph.D. Dr. Rosenthal is a standing member of the Skeletal Biology Development and Disease study section at the NIH, and a mentor for the US/Canada Bone and Joint Initiative Young Investigators Workshop. Additionally, she has published work on musculoskeletal complications of diabetes, osteoarthritis, and gout. She was the site PI for two clinical trials of cardiovascular risk in gout and osteoarthritis patients at the Zablocki VAMC, where she is Associate Chief of Staff for Research and Development.
- **Mary-Ellen Csuka, MD** is an expert in scleroderma and participates in many research initiatives with this rare disease at the national and international level. She has received funding with Dr. Kirkwood Pritchard to study IRE5 in scleroderma patient samples and currently collaborates with Dr. Polly Ryan on an NIH-funded study of health behaviors in osteoporosis patients. She has active clinical trials in scleroderma, Raynaud's and autoimmune overlap syndromes.
- **David Gazeley, MD** is developing a research program related to care models and adherence in high risk SLE patients. He has received funding to study apathy in lupus patients and the link to medication adherence and follow-up compliance.
- **Michael Putman, MD** is developing a research program related to vasculitis, with a particular focus on giant cell arteritis. He has received funding from the Rheumatology Research Foundation for multiple projects relating to GCA research.

Neurology

Research to improve health care for neurological illness is a major mission of the Department of Neurology, which maintains a wide range of basic and clinical research programs. Below is a list of just a few of our programs. More detailed descriptions and links to lab websites can be found on the Neurology website at http://www.mcw.edu/neurology.htm.

Autonomic Disorders: Directed by Dr. Thomas Chelimsky, research focuses on dysautonomias associated with pain such as functional abdominal pain, irritable bowel syndrome, interstitial cystitis, postural tachycardia syndrome, fibromyalgia, and cyclic vomiting syndrome. The aims of current studies are to ascertain the co-morbidities of these disorders, the familial occurrence patterns, and ultimately understand the genetic, epigenetic and environmental changes that influence their emergence across individuals.

Language Imaging Laboratory: Directed by Jeffrey Binder, this lab conducts basic research on normal and impaired language functions using functional (fMRI) and structural MRI, event-related potentials (ERP), magnetoencephalography (MEG), transcranial direct current (tDCS) and magnetic stimulation (TMS). Research focuses on quantitatively characterizing the structural and functional connections among brain regions in epileptic networks, language mapping prior to brain surgery, and on understanding and treating aphasia after stroke. Lab members have had continuous funding from the NIH since 1994 and have produced pioneering studies on the neurobiological basis of language.

Magnetoencephalography (MEG) laboratory: Both clinical and basic neuroscience research are conducted in the Froedtert MEG laboratory. Clinical research is directed toward developing and refining MEG methodologies for localizing regions of electrical dysfunction in epilepsy and mapping cortical functions.

Memory Disorders: Established by Dr. Piero Antuono in 1985, the Dementia Research Center employs fMRI techniques to develop noninvasive early diagnostic tools for predicting the risk of Alzheimer's disease and Mild Cognitive Impairment. Multiple clinical trials test the effectiveness of promising new therapeutics such as tDCS and drugs for the treatment of MCI and early AD as well as the prevention of AD in people with normal cognition but who are at high risk of developing the disease.

Multiple Sclerosis Translational Program: Dr. Staley Brod is researching optimal levels of oral ACTH (a natural endogenous protein showing intrinsic immunomodulation) which could be used as a disease modifying treatment for MS. He also conducts imaging work aimed at discovering a causal nexus between pro-myelinative proteins in the CSF and blood with decreasing brain activity as characterized by 7T MRI. The discovery of such proteins could provide future targets for CNS repair. There are also two clinical trials studying a monoclonal antibody that could stimulate neuronal regeneration.

Whelan Lab: Dr. Harry Whelan has been inducted into the NASA Space Technology Hall of Fame for his research on the use of near-infrared (NIR) LEDs for wound healing and the treatment of brain tumors and neurofibromatosis. The goal of his research program is the translational application of infra-red light technology to medicine. His work addresses cell culture, basic biochemistry, animal models, and human subjects, with active studies at all three translational levels of research.

Clinical Trial Program: Multiple subspecialties are evaluating the safety and efficacy of commercial products. The Amyotrophic Lateral Sclerosis Team is evaluating three compounds thought to have positive effect on breathing function. In Pediatric Muscular Dystrophy, several studies for Duchenne's are underway, including a new cellular therapy trial. Headache Medicine is testing two compounds for episodic and chronic migraine, and a device for migraine prevention. The Parkinson's Team is testing a drug for symptoms such as tremor, stiffness and slowness, and has an immune therapy study that targets cellular pathology. The Stroke Team has joined the NIH StrokeNet Consortium with two studies pending: a secondary prevention study in patients with cryptogenic stroke who have evidence of atrial cardiopathy, and a sleep study for stroke management and recovery.

Obstetrics & Gynecology

The Department of Obstetrics and Gynecology (OB/GYN) is dedicated to improving women's health care through our Women's Health Research Program (WHRP). Using WHRP as a vehicle of research, we have leveraged the expertise of MCW physicians and scientists, hospital partners, and affiliated organizations, to accomplish defined objectives in the field of gynecology oncology (GYN/ONC) and maternal fetal medicine (MFM). The research continues to grow strongly, and efforts to further support and serve the research needs of our faculty, fellows, residents and students. This includes monthly WHRP seminar series given by both internal and external speakers covering wide range of topics in women's health and twice monthly department meetings on work in progress.

Notable accomplishments include:

- Dr. Janet Rader, Professor and Chair of OBGYN along with Dr. Kristina Kaljo, assistant professor of OBGYN received an extramural $943,311 grant award for 5 years from NIH (R25) to conduct their project titled "Student-Centered Pipeline to Advance Research in Cancer Careers (SPARCC) for Underrepresented Minority Students". The first class of SPARCC students graduated on Aug 9th.
- Dr. Pradeep Chaluvally- Raghavan received a an R01 titled "Role of RNA activation in Tumor Progression and Metastasis" to start in August 2019 This was also supported by earlier internal MCWACS Pilot Research grant. "RNA activation driven ovarian cancer"
- Dr. Allison Linton received $450,00 grant award for 2 years from the AHW- Healthier Wisconsin for project titled, "Lower Uninsured, STI, & Unintended Pregnancy by Integrating Services at Milwaukee Co. Health Depts."
- Anna Palatnik, MD received a$75,000 grant award for one year from AMAG Pharmaceuticals for research "Involvement of micro- RNA 223 in the pathogenesis of preeclampsia through interference with epithelial-mesenchymal transition of the extravillous trophoblast"
- Gynecological Oncology Fellowship program was approved and fellows will start summer 2020.

Other key programmatic initiatives include:

- **WHRP SEMINAR SERIES:** This seminar series is held the third Wednesday at noon in the OBGYN conference room. Speakers from both within and outside the institution are invited, and often new collaborations, and initiatives emerge from these interactions.
- **CLINICAL TRIALS:** Overall, we have strong growth in clinical trials. Dr. Denise Uyar's investigator initiated multi-site trial for immunotherapy of primary ovarian cancer is actively recruiting and close to accrual. Dr. William Bradley's investigator initiated multi-site trial Combining Bevacizumab, Atezolizumab and Rucaparib for the Treatment of Previously Treated Recurrent and Progressive Endometrial Carcinoma was activated in July. We opened several phase I trials enabling cancer patients to receive novel drugs and early access to biologic agents. Maternal Fetal Medicine physicians joined one of the largest NIH consortiums, the MFMU. Also opened studies on fetal therapy and management of hypertension in pregnancy.
- **RESEARCH IN PROGRESS MEETINGS:** OB/GYN clinical and research faculty and staff meet twice a month to discuss work in progress and to critique pre-publication submissions. This interactive format has resulted in progress of research projects, and general awareness of lab methodology and expertise of members in OB/GYN department. Lab protocols, unpublished data and research in progress are shared at these meetings. Occasionally, speakers from other departments at MCW are invited to help with specific methodologies or relay new state-of-the-art methods to the group.
- **MFM/PREECLAMPSIA RESEARCH MEETINGS:** Dr. Nicole Lohr, Department of Medicine and Dr. Jennifer McIntosh, OBGYN faculty member are directing a monthly group meeting that is open to members interested in placenta/preeclampsia research. This meeting brings together clinicians from obstetrics and gynecology, cardiology, medicine and pediatrics with basic scientist studying fields related to preeclampsia. The group share ongoing research, discuss emerging topics, review grant proposals and develop inter-departmental collaboration.

- **PUBLICATIONS:** Highlight publication - Dr. William Bradley, associate professor is one of the highest enroller in the country for Solo 1 trail and an author in New England Journal of medicine titled “Maintenance Olaparib in Patients with Newly Diagnosed Advanced Ovarian Cancer” N Engl J Med. 2018 Dec 27;379(26):2495-2505.

Where are we heading?

Faculty recruitments in placental angiogenesis is ongoing, and this is a joint recruitment effort with MCW Cardiovascular Center. A joint GYN/ONC Cancer recruitment effort with MCW Cancer Center is also ongoing. Please visit our website at http://obgyn.mcw.edu/research.

Interested faculty should contact us for mentoring and collaboration opportunities with fellows, students and physician scientists in the department.

Ophthalmology & Visual Sciences

A broad spectrum of funding sources ranging from individual donations to National Institutes of Health grants enable our researchers to take a multidisciplinary approach to improving the fundamental understanding, diagnosis, and management of eye diseases. A leader in clinical and translational research, the Department of Ophthalmology & Visual Sciences supports a solid platform for innovation, collaboration, and discovery.

Significant accomplishments from the past year include:

- The department successfully recruited Dr. Shyam Chaurasia, PhD, whose major research interests are to identify the early key initiating oxidative, inflammatory factors/signaling molecules and immune cells which render metabolic derangements and eventually damage both neuronal and vascular cells in the pathophysiology of eye diseases.
- Dr. Joseph Carroll, PhD received a Clinical Innovation Award from the Foundation Fighting Blindness entitled, "Advancement of Ellipsoid Zone Intensity as a Surrogate Biomarker for Photoreceptor Structure."
- Dr. Ross Collery, PhD received a $240,000 grant over 3 years from the E. Matilda Ziegler Foundation for the Blind entitled, "Understanding Genetic Causes of Refractive Error Using Zebrafish."
- Ophthalmology & Visual Sciences expanded and renovated its space within MCW's Biomedical Resource Center (BRC) to support our growing animal and laboratory research program.
- The Eye Institute was one of only eight US sites to participate in a pivotal phase III trial for active thyroid eye disease. Teprotumumab, an insulin-like growth factor-1 receptor inhibitor, showed a dramatic reduction in proptosis and a substantial improvement in overall response rate in patients treated with teprotumumab compared with placebo. TEPEZZA (teprotumumab-trbw) was subsequently approved by the FDA for treatment of thyroid eye disease in 2020.
- In addition to our own research, the department continues to provide ophthalmology support for clinical trials from other groups across the Froedtert & MCW campus, including the Cancer Center, Pulmonary Medicine, Obstetrics and Gynecology, Nephrology, and Pediatrics.

Dennis P. Han, MD Advanced Ocular Imaging Program

The Dennis P. Han, MD Advanced Ocular Imaging Program (AOIP) was established in 2009 to promote the development and use of translational ocular imaging tools to improve detection, diagnosis, and management of eye disease. The founding directors were Joseph Carroll, PhD and Dennis Han, MD, and their initial focus was to create a culture of collaboration between our research faculty and physicians. What emerged was a truly unique infrastructure, where the common language was imaging. Expanding the arsenal of imaging equipment in the clinic, bringing the latest ocular imaging technology into the research labs, and establishing processes through which these resources could be shared were some of the biggest investments early on. The Department of Ophthalmology & Visual Sciences has made major investments to renovate the laboratory space on the 8th floor of the Eye Institute to house the AOIP. Space for multiple adaptive optics imaging systems, numerous image processing workstations, dedicated rooms for additional clinical imaging equipment and eye exams, and a separate research and development lab comprise the AOIP facilities. AOIP program members include vision scientists, clinicians, and engineers at the Medical College of Wisconsin. While the AOIP provides a solid platform for innovation, collaboration and discovery in ocular imaging, there remains the commitment to grow and expand. From image interpretation and analysis services, to offering hands-on training on new imaging technology or simply individual consultation on challenging clinical cases, we will accommodate the expanding needs of vision scientists and clinicians in an effort to advance knowledge and improve vision through advanced imaging.

Ocular Gene Therapy Lab

Founded in 2016 by Daniel M. Lipinski, DPhil, the Ocular Gene Therapy Laboratory (OGTL) aims to develop broadly applicable gene-based therapeutics to prevent human blindness arising from neurodegenerative or vascular diseases affecting the retina. Consisting of faculty, students and staff from a diverse range of academic backgrounds, the OGTL laboratory takes a highly multidisciplinary and collaborative approach toward research, working with basic science and clinical investigators worldwide to identify novel therapies for currently untreatable conditions that result in vision loss in humans, including diabetic retinopathy, age-related macular degeneration and glaucoma.

Orthopaedic Surgery

Biomaterials and Histopathology Laboratory

The Biomaterials Lab has done its most significant work in the study of calcium phosphate materials. In conjunction with the Medical College of Wisconsin's Animal Research Center and Clement J. Zablocki VA Medical Center, the lab studies new implant materials compatibility. The lab also collaborates with Marquette University's Biomaterials program.

- Equipment: To evaluate implants and implant materials, the biomaterials and histopathology lab is equipped with embedding stations, a rotary microtome, a Jung microtome and diamond saws, a tissue pathology laboratory, and a darkroom equipped for microradiography and autoradiography. Histomorphology and microdensitometry of bone also are performed.
- Personnel: The OREC Biomaterials Research Laboratory is directed by Jeffrey Toth, BSE, PhD, FAIMBE. Dr. Toth's research expertise includes: Bone histology and histomorphometry, Bone Grafts and bone graft substitutes, Fabrication, characterization, and evaluation of biomaterials, Characterization and pre-clinical testing of orthopaedic biomaterials, and Mechanisms and clinical uses for osteoinductive substances and materials.
- Research laboratory is staffed by Sara Landschoot, HTL. Sara is a registered histotechnologist. She is HTL certified by The American Society of Clinical Pathologists. Sara has experience in histologic techniques, including: routine and special staining; enzyme histochemistry; immunohistochemistry; electron microscopy; molecular pathology; cytogenetics; Mohs; cytology; grossing; and photography.

Biomechanical Laboratory

The Biomechanics Laboratory conducts a wide range of basic science and applied research projects in orthopaedic biomechanics. Research methods often encompass in-vitro experiments with human or animal specimens and the use of computer modeling and analysis.

- Space: The Orthopaedic Biomechanics Lab is designed and maintained to support basic science and applied research projects in orthopaedic biomechanics. Research methods often encompass in-vitro experiments with human or animal cadaveric specimens and the use of computer modeling and analysis.
- Equipment
    - MTS 809 servo hydraulic axial-torsion material testing system with a pair of hydraulic grips, 8 additional analogue data collection channels, and FlexTest 40 controller;
    - Optotrak Certus Motion Analysis System with 8 additional analogue data collection channels;
    - customized load frame for testing with static loads;
    - an equine portable radiograph unit;
    - Tekscan K-Scan joint pressure measurement system with software and five sensors;
    - AMTI six-axis load-cell and signal amplifier and other uni-axial load cells;
    - Microstrain 3mm micro-miniature DVRTs,
    - various LVDTs displacement transducers;
    - miniature pressure transducers,
    - assorted power and manual tools and surgical instruments.
- Personnel: The laboratory is staffed with a full-time engineer who holds a degree in Electrical Engineering and Computer Science and twenty years of experience of working in the lab.
- Funding: The laboratory is supported by the general operating funds of the Department of Orthopaedic Surgery and grants.
- Current research topics include
    - Studies of the stability of total-joint replacement
    - Acetabular cup and hip stem micromotion

- Joint mechanics
- Biomechanical analysis of subtalar motion
- Spine mechanics
- Experimental and computational evaluation of spinal instrumentation
- Bracing in scoliosis and spine fractures
- Planned projects include:
- Three-dimensional finite element modeling of the pelvis
- Strain measurement in the pelvis and ankle ligaments
- A study of femoral neck fractures

Cell Biology Laboratory

The Cell Biology Laboratory investigates the interactions between bone cells and orthopaedic implants. Research activities include studies into the role of orthopaedic wear debris in the generation of cytokines by cultured osteoblasts, as well as alterations in bone-associated proteins in response to orthopaedic implant materials. The cell biology laboratory in the Department of Orthopaedic Surgery provides a unique environment for collaboration between basic scientists and orthopaedic surgeons.

- cell2Equipment: Tissue culture equipment including incubator, hood, liquid nitrogen tank, centrifuges, water baths and refrigerators are available as well as gel electrophoresis equipment and software for quantitation, thermocyclers for reverse transcription and the polymerase chain reaction (RT-PCR), and an ELISA plate reader. Shared equipment includes ultracold refrigerators, ultracentrifuges, fluorescence spectroscopy, UV-visible spectroscopy, confocal microscopy and animal surgical facilities.
- Personnel: Dr. James Ninomiya (Lab Director) and Janine Struve (Research Associate) support residents and students in the laboratory.

Musculoskeletal Functional Assessment Center: Pediatric Orthopaedic Research Lab

The Musculoskeletal Functional Assessment Center supports basic science and clinically related studies involving orthopaedic conditions, focusing primarily on pediatric spinal deformities. The center is involved in research to better understand the etiology and effects of pediatric spinal deformities, to analyze and monitor spinal deformities progress using 3D surface topography and the EOS system, to design and evaluate new spinal implants in animals and in patients, and is collaborating with researchers in genetics to study children with scoliosis. The center provides research opportunities for medical students, biomedical engineering students, residents, and physicians. The center advances clinical transitional research that directly benefits children with orthopaedic deformities.

- Space: The Musculoskeletal Functional Assessment Center: Pediatric Orthopaedic Research Lab is located in the Pediatric Orthopaedic Clinic at the Children's Hospital of Wisconsin.
- Equipment: Recently the Milwaukee Spinal Scanner System has replaced the Quantec system for measuring spinal curvature. The Milwaukee Spinal Scanner System includes a hand held laser scanner, custom spinal curvature measurement software, a standing patient stabilizing apparatus, and a limb stabilization apparatus. The EOS 3D X-ray Orthopedic Imaging System that allows low radiation 3D spinal X-rays while the patient is standing.
- Personnel: The laboratory is supported and run by Dr. Xue-Cheng Liu (Lab Director) & Carlos Marquez-Barrientos MS (Research Associate).

Center for Motion Analysis

The Center for Motion Analysis (CMA) is designed to support a broad scope of both clinical and research oriented projects. Clinically, the center can provide gait analyses for both pediatric and adult patients, which enhance diagnoses and improve functional outcomes for neuromuscular and orthopaedic impairments as well as dysfunction caused by other deformities. Motion abnormalities include complex alterations imposed by the musculoskeletal and neuromuscular systems, as well as secondary adaptations that the patient makes in order to function. Identification of these patterns is extremely difficult, even for the trained clinician. Quantitative motion assessment includes specialty models for the distal extremities (foot and ankle, upper extremity, hand and wrist, trunk) sports

applications and higher speed analysis capability, and rehabilitation (assistive devices, prosthetics and orthotics.) Educational support through clinical training and research project participation is provided for research fellows, orthopaedic residents, medical students and engineering students. Numerous technical development projects are supported through close collaboration with the Department of Biomedical Engineering at Marquette University. The center also collaborates with Children's Hospital of Wisconsin, Froedtert Hospital, and other institutions (MSOE, UWM and CUW). Research applications include studies of surgical interventions, orthotic and prosthetic treatments, and therapy upon upper and lower extremity motion and control. Motion analysis provides a frame-by-frame analysis of the three-dimensional joint motion, limb kinematics, kinetics, and muscular activity. While changes from activity patterns of age-matched normals are used to formulate a clinical treatment plan, research studies of pathological motion and muscular control patterns are designed to increase our understanding and ultimately our ability to improve future diagnosis, treatment and injury prevention.

- Space: The CMA facilities provide a 2,325 sq. ft. test area, examination/preparation area, offices, and storage at the Children's Hospital of Wisconsin Greenway Clinic. A 30 ft. walkway is included in the test area for collection of ambulatory data. A 1,071 sq. ft. area is located adjacent to the testing area for support personnel and includes an examination room, equipment storage room and test bench, two offices and a working community area for research fellows and students.
- Equipment: includes twelve T40 Vicon MX cameras for motion capture, two AMTI 6 D.O.F force plates, two Bertec 6 D.O.F force plates,1 Novel EMED pressure platform, 1 Novel PEDAR insole pressure measurement system, F-Scan foot insole pressure measurement system, 16 channel Delsys Trigno wireless EMG system (surface and fine wire), 8 channel Noraxon surface and fine wire EMG system, Biodex extremity evaluation system, Vicon Nexus software for data collection and processing, Vicon Polygon software for constructing reports, Vicon Body Builder software for model construction, EMG analysis software for Delsys and Noraxon, FANDACAL – Foot and ankle motion analysis software, Walker Assisted Gait (WAG) torso and upper extremity motion analysis software, and Matlab software.
- Personnel: Educational support through clinical training and research project participation is provided by Dr. Roger Lyon (Medical Director), Dr. Xue-Cheng Liu (Co-Director), Dr. Gerald Harris (Co-Director), Jessica Fritz, PhD, (Research Assistant Professor) and Amie Chapoupka B.S. (Biomedical Engineer).

Sports Medicine Motion Analysis Laboratory

The Sports Medicine Motion Analysis Laboratory is used for developing, validating, and advancing injury prevention and performance enhancement in athletes. This facility is designed to be able to stimulate real-life sports environments such as a pitcher's mound, golfing tee box, or batting cage so that we can study the motion of the athlete's body and the forces acting at their joints. By understanding these motions and loads, we can learn to identify athletes at a greater likelihood of injury and measures of performance. The goal is to discover the mechanisms behind injury, rehabilitation, and performance, and apply them to improve the outcomes and optimize performance for the athletes that come through our lab, and to advance sports medicine research as a whole.

- Space: The 1600 square-foot Sports Medicine Motion Analysis Laboratory is located within the Froedtert and Medical College Sports Medicine Center.
- Equipment in the laboratory includes a Motion Analysis system with 8 Raptor cameras, 2 PointGrey high speed video cameras, 2 AMTI force plates, F-Scan foot insole pressure measurement system, EMG system, Biodex extremity evaluation system, Motion Analysis software for data collection and processing, and Matlab software.
- Personnel: William Raasch MD (Medical Director) & Janelle Cross PhD (Research Director).
- Areas of Research
    - Baseball pitching analysis
    - ACL injury studies
    - Biomechanics of landing/cutting/planting techniques among soccer, basketball, and volleyball athletes
    - Biomechanics of a batter's swing, golf swing, tennis serve, volleyball spike, speed skaters and ballet dance
    - Biomechanics of running

Otolaryngology and Communication Sciences

The Department of Otolaryngology and Communication Sciences has a robust and diverse research program. Many aspects of Ear, Nose, Throat and Communication Disorders in adults and children are being investigated. Research programs encompass basic science bench investigations, translational studies, and clinical trials. Funding sources include the NIH, public and private organizations and foundations, and corporate grant sponsorship.

Otology: Many disorders related to hearing and balance, as well as pathologic diseases of the ear, are under study. Basic science studies in the laboratory include investigations into the molecular mechanisms underlying otitis media, the pathogenesis of biofilms in the ear, and genetic diversity related to otitis media. Additional studies have identified a novel gene related to hearing loss and ongoing studies are characterizing this unique genetic locus. Clinical studies include investigations into cochlear implant performance and programming, auditory neuropathy spectrum disorder, cholesteatoma, and cardiovascular disease associations with hearing loss. Quality improvement studies include developing diagnostic protocols for vestibular disorders.

Laryngology: Basic science and clinical studies into disorders of, and affecting, the upper aerodigestive tract are a strong component of our research program. Basic science studies are examining the role of pepsin and laryngopharyngeal reflux in laryngeal injury and carcinogenesis. Clinical and translational studies are examining voice disorders, airway stenosis, extraesophageal reflux, dysphagia and related disorders, neurolaryngology, vocal fold paralysis, obstructive sleep disorders, outcomes with tonsillectomy, and modeling of the upper airway. These studies are being pursued in both adult and pediatric populations.

Rhinology: A major focus of research is modeling nasal air flow in the normal and pathologic conditions using computational fluid dynamics. These methods are also being extended to other regions of the upper airway. Additional clinical studies include the use of medication impregnated stents in managing rhinologic disease, the use of steroids in nasal inflammatory disease, chronic rhinosinusitis in children, and outcomes of nasal obstruction surgery.

Head and Neck: Many studies focus on cancer and on other soft-tissue anomalies in the head and neck. Clinical studies include head and neck oncologic and reconstructive outcomes, outcomes with minimally invasive head and neck surgery, treatment of salivary dysfunction and disease, cancer survivorship and quality of life issues, late effects of cancer treatment, and a number of other outcome and quality studies in pediatric or adult populations.

Quality: The Department of Otolaryngology and Communication Sciences has a strong commitment to quality outcomes. Many processes in all aspects of ear, nose and throat conditions are in effect to measure quality improvement initiatives. These range from patient outcomes, to operating room efficiency, to communication strategies, to use of the EMR, to effective instruction and teaching.

Education: The Department of Otolaryngology and Communication Sciences also has a strong commitment to education. The Department is a leader in studying the efficacy of objective surgical assessment tools (OSATs) to measure resident progress in acquiring technical surgical skills.

For information on Department of Otolaryngology and Communication Sciences research, for student opportunities to participate in research training, and for collaborators wishing to discuss opportunities, please contact:

David R. Friedland MD, PhD
Chief, Division of Research
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Pathology

Mission: The Medical College of Wisconsin Department of Pathology is dedicated to delivering state of the art, subspecialty laboratory diagnostics to our patients; providing comprehensive and practical pathology training; building a strong foundation for our medical students; advancing medical knowledge regarding the understanding, diagnosis, and treatment of human disease through advanced research; serving our community; and developing leaders.

Vision: A nationally recognized pathology department, leading the pursuit of cutting edge diagnostics, education, research, and community outreach.

Core Values

- **Commitment to Excellence:** We aim for excellence through a high-performance culture and self-motivation.
- **Continuous Improvement:** We strive to improve constantly based on evidence and data.
- **Diversity:** We are stronger because of the diversity in our department, both in us as individuals, and in the broad scope of work that we do.

Professionalism: We are respectful and considerate in all of our interactions. We hold honesty, integrity, and trust as pillars of everything we do.

Citizenship: We are all engaged in the pursuit of common goals, working as a collegial team in the fulfillment of the missions of our department and institutions.

As the provider of diagnostic services in anatomic (tissue) pathology and laboratory medicine, the department plays a critical support role for the entire medical center and its community of patients, physicians, paramedical personnel and researchers. Without the provision of high quality diagnostic services in surgical pathology and clinical laboratories, physicians and nurses in our system would not be able to properly evaluate patients admitted to the hospital or in the outpatient setting, perform surgery, or treat cancer and other patients.

In addition to patient care activities, pathologists are also critical in the education of the next generation of physicians and allied professionals. The pathology course for the medical students at the Medical College of Wisconsin provides the foundation for the understanding of mechanisms of disease, pathogenesis and the cellular substrate of human diseases. As such, our discipline serves as a bridge between the basic sciences and clinical medicine. In addition, we also educate our fellow physicians regarding mechanisms of disease and the biologic behavior of the various diseases we routinely examine and, as such, contribute to the continuing medical education of our peers.

Finally, pathologists play a critical role in biomedical research. In addition to constantly improving diagnostic methods, developing new criteria for a more accurate and simplified diagnosis, and redefining our understanding of disease processes, pathologists are uniquely positioned to apply many of the emerging modern biomedical techniques to the study of human disease. Because pathologists are custodians of the tissue samples obtained from patients admitted to our system, we are ideally positioned to carry out research that utilizes those tissues to advance our understanding of disease. In fact, because the natural setting for a pathologist is the laboratory where the diagnostic tests are normally carried out, laboratory research is merely a natural extension of our job.

In recent years biomedical research has tremendously expanded our understanding of the molecular and genetic mechanisms of disease. Modern science has exponentially advanced in terms of its ability to perform assay for molecular and genetic abnormalities that underlie most human disorders. Newer techniques such as DNA in-situ hybridization, polymerase chain reaction, fluorescence in-situ hybridization and molecular profiling have revolutionized the field of medical research. Pathologists are uniquely positioned to apply these techniques for the study of human tissues and, as such, to translate the knowledge gained from basic science to the bedside. As such, pathologists are the original and quintessential “translational researchers”.

Funded Research

A variety of funded research activities are carried out by the Department of Pathology at the Medical College of Wisconsin, including research that is funded by Government Agencies (NIH, DOD, and others), Advancing a Healthier Wisconsin (AHW) endowment, and various other private and commercial sources. The department also actively collaborates with several of the other departments on campus and with outside institutions in funded research. Funded research is also supported by the department through the activities of our MCW Tissue bank, which is housed and operated by the Department of Pathology.

For more information, please visit our webpage: http://pathology.mcw.edu/

Pediatrics

We support a diverse research agenda in the Department of Pediatrics (DOP) that is translational in nature and achieves focus through alignment with the priorities of our academic and hospital partners. Our goal is to improve the health of the children, both in our region and beyond. Toward that end, we incentivize collaboration across divisions to leverage Departmental strengths, we support a Grants Development Office and other widely used shared services, and we provide strong mentorship for new investigators. This strategy has resulted in over $69 M in new awards from extramural sources in the past 36 months.

Research in cardiovascular development is one of our key focus areas. Indeed, congenital heart defects are the most common type of birth defects, affecting nearly 1% - or about 40,000 – births per year in the United States. Our Herma Heart Institute (HHI) at Children's Hospital is one of the nation's top programs for medical and surgical treatment of congenital heart defects and heart disease in children. Founded in the early 1970s, The HHI team performs more than 13,000 diagnostic, therapeutic and surgical procedures annually and supports outreach programs in six additional locations outside southeast Wisconsin. **Dr. Joy Lincoln** joined our team in July 2019. She holds the Sommerhauser Chair for Cardiac Quality, Outcomes and Research and is the new HHI Research Director. Her work is focused on aortic valve development and calcific disease. **Dr. Janette Strasburger** recently received a new R01 to study cardiac development and conditions that result in fetal demise using fetal magnetocardiography. **Dr. Uli Broeckel**, another NIH-funded senior member of our cardiovascular research team uses IPSC- derived cardiomyocytes to study the mechanisms involved in left ventricle hypertrophy and the response of cardiomyocytes to different medications. **Dr. Ramani Ramchandran** uses mouse and zebrafish models to study the biology of endothelial cells and the role of cilia in vascular development. He brought the 2019 Vasculata Conference here to MCW, which educated trainees and highlighted some of the amazing research done on campus. **Dr. Peter Frommelt** directs the Echocardiographic Research Core Lab at CHW. He works closely with the national Pediatric Heart Network in ground-breaking clinical trials assessing children with Hypoplastic Left Heart Syndrome and the development of innovative echocardiographic tools for use in the assessment of children with heart disease.

Premature birth is the leading cause of infant death, and the rate continues to rise both statewide and nationally. Increasing survival and improving the clinical outcomes of infants born prematurely is a primary goal of our neonatology research program. **Dr. Ganesh Konduri**, Section Chief of Neonatology, recently received 2 R01 grants to study pulmonary angiogenesis and the cellular mechanisms driving persistent pulmonary hypertension. **Dr. Akiko Mammoto** has received 4 NIH awards (2R01, 2R21) in the past 3 years for her studies on pulmonary angiogenesis and the vascular remodeling driven by pulmonary hypertension. **Dr. Ru-Jeng Teng** studies hyperoxia-induced pulmonary injury and pharmacologic approaches to injury prevention that can be safely applied in premature infants. **Dr. Adeleye Afolayan** works closely with these investigators and is the recipient of a K08 award to study how phosphorylation of HSP70 regulates superoxide dismutase 2 function and controls the redox balance in the neonatal lung. **Dr. Nghiem-Rao** received a K23 award to study parenteral nutrition- associated liver disease in infants and **Dr. Joanne Lagatta**, another recent K23 recipient, is focused on outcomes research for infants with bronchopulmonary dysplasia.

Sickle cell disease (SCD) occurs in about 1 in every 365 Black or African American births while cancer remains the leading cause of disease-related death among children from birth through 14 years of age. Expanding treatment options while improving outcome for children with SCD, bleeding disorders and cancer is the focus of our Hematology, Oncology and Transplantation Research Program. **Dr. Julie Panepinto** and **Dr. David Brousseau** (Emergency Department) are recipients of a U01 award to conduct rapid cycle implementation research designed to improve the acute care of children with SCD. Another team comprised of **Dr. Amanda Brandow** and **Dr. Panepinto** recently received an R61 to develop a biomarker that both predicts and correlates with the clinical expression of pain in SCD. Other translational and preclinical studies have targeted bone marrow transplantation for the treatment of cancer and bleeding disorders. MACC Fund Professor **Dr. Jeffery Medin** is focused on the development of novel cancer immunotherapy strategies, including the manufacture of FDA approved gene therapy vectors that will accelerate preclinical testing and clinical trial implementation. In 2020, **Dr. David Wilcox** received funding from the NHLBI to conduct a Phase 1 clinical trial for the treatment of hemophilia A (FVIII deficiency) that employs a novel hematopoietic stem cell (HSC) gene therapy strategy. This strategy targets expression of the FVIII gene in megakaryocytes causing ectopic synthesis, storage and regulated-release of factor VIII from the α-granules of activated platelets. In closely related work, **Dr. Qizhen Shi** has longstanding funding from the NHLBI to study platelet delivery of factor VIII and other proteins, as well as the mechanisms by which this unique delivery system escapes allogenic immune responses that might otherwise limit its efficacy. Other investigators focused on hemostasis include **Dr. Veronica Flood**, who also has R01 funding from the NHLBI to study the interaction between Von Willebrand Factor and type 4 collagen.

As indicated by these and other NIH awards that include 7 active K-series grants, the DOP places great value on career development. The DOP offers multiple structured opportunities for junior faculty to develop competitive grant proposals. These include weekly conferences and a 3-day grant writing retreat which is held twice a year. Structured mentored activities are central to the success of both our junior and senior faculty.

Physical Medicine and Rehabilitation

The PM&R Research Program has been established to advance the science and the practice of physical medicine and rehabilitation by conducting research aimed at studying and reducing impairments and functional disabilities due to disease or traumatic events.

We have several collaborations focused on clinical and translational, and community engaged research. Current research areas include spinal cord injury, physical activity for individuals with disabilities, stroke rehabilitation, spasticity management, pain, and prosthetics. Our collaborators include faculty from Neurosurgery and Neurology at Froedtert Hospital/The Medical College of Wisconsin, Marquette University, UW-Milwaukee, and several community organizations.

Our Residency Program offers a Research Intensive Track with protected research time, funding, and significant mentorship opportunities. Please visit the Residency Program page for more information on resident research.

Research Administration Committee (PM&R)

The RAC is composed of Department of Physical Medicine and Rehabilitation faculty. The RAC is under the direction of the Research Director. The department sets an annual budget to support research endeavors of faculty, fellows and residents. These funds will support pilot research proposals, attendance at national and regional meetings to present results of research and / or accept awards, and to provide assistance with publication costs.

Orthopedic Rehabilitation & Engineering Center

The center was established in 1999 to facilitate research in support of the endeavors of the faculty, fellows, residents and graduate students participating in the programs of the MCW Departments of Orthopaedic Surgery and Physical Medicine and Rehabilitation and of the MU School of Dentistry and the MU Department of Biomedical Engineering. The center brings together common threads within the disciplines of engineering, biomedical sciences, materials sciences, and clinical dentistry. The result is a unique environment for interdisciplinary applied research.

Human Motion Analysis Laboratory (Gait Lab)

The Department of Physical Medicine and Rehabilitation has collaborated with the Department of Orthopaedic Medicine and Marquette University to establish the Gait Lab. An agreement with the Gait Lab allows for the use of the facility without charge for resident research. Funded research budgets provide for financial support of the gait lab.

Rehabilitation Robotic Research and Design Lab (RRRD)

Established in 2004, the RRRD Lab is dedicated to the design, development and therapeutic use of novel, affordable, intelligent robotic / mechatronic and domotic assistants. It is affiliated with OREC and the Falk Neurorehabilitation Center at Marquette University.

The lab is focused on:

- Examining underlying causes of upper limb impairment after neural disease, injury or cerebral accident.
- Discovering effective methods to retrain functional recovery on daily living activities.
- Developing new ways of facilitating independent living in daily living environments.

Plastic Surgery

The Department of Plastic Surgery is committed to providing innovative basic science and clinical research and service to our community. The Plastic Surgery Research Laboratory works collaboratively with other Medical College of Wisconsin clinical and basic science departments as well as other U.S. and international institutions to address issues such as treatment of vibration injury and nerve transfer. Our commitment to community service is noted in our annual medical mission trip and in our community education presentations. For more than 25 years, physicians and staff at MCW of plastic surgery have participated in annual mission trips to South America for the purpose of providing surgical services specialty care and medical collaboration and education to underserved areas.

Our faculty provide comprehensive and specialty clinical care in reconstructive surgery, breast surgery, cosmetic surgery, hand and upper extremity surgery, pediatric plastic surgery, craniofacial surgery, and cancer reconstruction.

Our research portfolio includes projects with fellows, residents, medical students, and other collaborating researchers from numerous renowned institutions.

1. A comparative effectiveness study of speech and surgical treatments using a Cleft (Robert Havlik, MD)
2. Brain rewiring mechanism in nerve transfer using vagus nerve graft (Ji Geng Yan, MD)
3. Changes in targeted muscle reinnervation in the transition from acute to chronic pain (Gwendolyn Hoben, MD, PhD)
4. Inflammation and Peripheral Nerve Regeneration (Gwendolyn Hoben, MD, PhD)
5. Model and mechanisms of surgical intervention for amputation related chronic pain (Gwendolyn Hoben, MD, PhD)
6. Neuroma to neuron: why is targeted muscle reinnervation less effective in chronic pain (Gwendolyn Hoben, MD, PhD)

Psychiatry and Behavioral Medicine

Joseph S. Goveas, M.D., Associate Professor

- Emotion Regulation in Complicated Grief
  Sponsor: The National Institute of Mental Health
  This novel study is expected to provide evidence that specific abnormalities in the emotion regulation brain circuitry that are associated with complicated grief symptom trajectories in individuals with acute grief. These brain circuit abnormalities could, in the future, serve as neurobiological indicators (or markers) of prolonged grief disorder (or complicated grief). Such biological markers could also be used to test the efficacies of treatment or prevention strategies that aim to prevent the development of prolonged grief disorder in acutely grieving individuals.

- Endocannabinoid System and Brain Network Function in Late-Life Depression
  Sponsor: The National Institute of Mental Health
  The major goals of this project are to determine components of the endocannabinoid signaling system (ECS) and brain network features associated with Late-life Depression (LLD) occurrence, and with persistent low mood and anhedonia, two core symptom dimensions of LLD. This NIH-funded study will set the stage for future seminal research that uses ECS and brain network function measures as biomarkers to aid diagnosis, predict and monitor outcomes to specific treatment interventions, and guide selection of optimal treatment for individual patients before initiation.

In addition, Dr. Goveas has contributed to multiple peer-reviewed publications, was selected as one of sixteen promising junior investigators in Alzheimer's disease research at the Charleston Conference on Alzheimer's Disease, was named in Best Doctors in America, is a scholar of the NIMH/Weill Cornell Advanced Research Institute in Geriatric Mental Health, is an invited reviewer for several journals, and is also the reviewer for the NIH Study Sections, Charleston Conference on Alzheimer's Disease pilot grants and Ad Hoc Reviewer for Alzheimer's Association New and Established Investigator Grants program. He is also a member of the Annual Meeting Program and Research Committees for the American Association of Geriatric Psychiatry.

Alan Nyitray, Ph.D., Associate Professor of Epidemiology

Dr. Nyitray's research has focused on the natural history of anal HPV infection and, most recently, anal cancer screening. The anal HPV epidemiology research has included studies with gay, bisexual, and other men who have sex with men, heterosexual couples, and heterosexual men. He has published more the 75 peer-reviewed papers on these topics and is funded by the National Cancer Institute. Prior to his HPV research, Dr. Nyitray delivered HIV prevention in a service capacity for 15 years. His current NCI-funded research assesses protocols for anal precancer and cancer screening including determining compliance with annual HPV DNA self-screening among HIV-positive and HIV-negative gay and bisexual men, assessment of a methylation biomarker for anal cancer screening, and assessing the sensitivity and specificity of self- and partner palpation for anal abnormalities.

- The Prevent Anal Cancer (PAC) Self-Swab Study: Men who have sex with men (MSM), especially MSM with HIV, have increased risk for anal cancer; however, screening for either anal precancers or anal cancers is not widely recommended. The PAC Self-Swab Study is recruiting 400 MSM and transpersons, aged ≥25 years in Milwaukee, Wisconsin into a clinical trial to assess screening modalities that seek to reduce morbidity and mortality from anal cancer. The Study (7R01CA215403), is a randomized clinical trial (NCT03489707) to evaluate compliance with annual home-based (self) vs clinic-based HPV DNA specimen collection among HIV+ and HIV- persons. Secondary objectives are determining factors associated with annual screening compliance; estimating the influence that home-based vs clinic-based screening has on the uptake of high-resolution anoscopy (HRA); estimate the association between high-risk HPV persistence and anal high-grade squamous intraepithelial lesions (HSIL); and estimate the association between HPV-16/host DNA methylation and anal HSIL. After the community advisory board advised on the design for the home-based self-swabbing kit, enrollment began two-months before COVID-19-required study suspension. Since study reactivation five community-based clinics in Milwaukee have contracted to do anal swab screening and Digital Anal Rectal Exams (DARE) for study participants (9 clinicians have been trained in swabbing and DARE). Initial study participants enrolled in January 2020 are now entering into final study activities including HRA. The outcomes will establish the level of screening compliance and factors associated with annual DNA testing including the effect of COVID-19; how home-based vs. clinic-based screening, in addition to other

characteristics like perceived susceptibility (e.g., HIV status), influences uptake of HRA; and the utility of anal HPV DNA persistence and viral/host DNA methylation testing. These outcomes will inform the delivery of future screening programs.

- The PAC Palpation Study: MSM, especially MSM with HIV, have increased risk for anal cancer; however, screening for either anal precancers or anal cancers is not widely recommended. The PAC Palpation Study is recruiting MSM and transpersons who have sex with men, aged ≥25 years in Chicago and Houston to test anal self-exams (ASE) and anal companion exams (ACE) that seek to reduce morbidity and mortality from anal cancer. The study (1R01CA232892) is recruiting 800 HIV+ and HIV- persons through 2022 with oversampling of Black MSM given their underrepresentation in HPV research and high risk for HIV. Participants will be taught about anal anatomy, pathology, and the procedure for an ASE or ACE, and then conduct the exam in private and record a result of either abnormal or normal. The primary objective is to compare the participant's ASE or ACE result at baseline with the clinician's gold-standard DARE to determine concordance, sensitivity, and specificity. The secondary objectives are to test the effect of practice on concordance after six months, and, using mathematical modeling, estimate the cost-effectiveness of ASE, ACE, and DARE and their impact on survival and health-related quality of life. The PAC Palpation Study will test the ability of ASE and ACE to detect early anal cancer tumors when they are much more treatable. Results could propel the development of a low-resource screening for rapid dissemination to populations with high anal cancer risk and no currently proven screening options.

Jeffrey A. Kelly, Ph.D., Professor and Director: Center for AIDS Intervention Research (CAIR)

The **Center for AIDS Intervention Research (CAIR)** in the Department of Psychiatry & Behavioral Medicine was first established in 1994; Kelly has been the Center's Director since its inception. CAIR is a multidisciplinary Center dedicated to advancing scientific and public health knowledge concerning HIV high-impact prevention that integrates biomedical and behavioral modalities and that accelerate their implementation in the field. CAIR's mission is to conceptualize, conduct, and scientifically evaluate the effectiveness and community impact of interventions to prevent HIV infection and alleviate adverse health consequences among persons living with HIV disease. Grounded in behavioral science and applied neuroscience frameworks, CAIR research also applies lessons learned in over 25 years of HIV prevention research to urgent community health challenges including COVID-19, cancer, health disparities and stigma, and systemic barriers to population health in underserved urban and rural areas. CAIR research emphasizes the discovery, development, and application of community-engaged behavioral interventions through multi-disciplinary and community partner collaborations, and the use of implementation science frameworks to ensure rapid dissemination and scale-up of effective interventions to improve the health and wellbeing of communities that are disproportionately burdened by disease.

CAIR's central fulltime faculty investigators devote almost their full effort to HIV prevention research. All fulltime faculty at CAIR have formal MCW faculty appointments in the Department of Psychiatry and Behavioral Medicine. Faculty from other departments, programs, or institutions are CAIR-Affiliated Investigators and devote part of their effort to HIV prevention research. CAIR investigators represent the disciplines of community, clinical, health, social, educational, and quantitative psychology; sociology; anthropology; biostatistics; health economics; pharmacology, psychiatry; infectious diseases; bioethics; community and family medicine; epidemiology and public health; and pediatrics. The work of CAIR investigators is supported by a team of approximately 12 fulltime research assistants, project coordinators, and research administrative personnel. CAIR expertise includes:

Intervention Support and Dissemination	Curriculum development, manualization of intervention protocols for studies, dissemination to service providers
International HIV Prevention Research	Establishing research collaborations abroad, translations of materials in English, Russian, Spanish; international logistics support
Qualitative Methods	Qualitative data gathering, coding, and analysis; development and use of appropriate qualitative methodologies
Impact Science	Feasibility of conducting economic efficiency, policy, or modeling studies; determination of applicable evaluation techniques and modeling analyses

Quantitative Methods	Study and assessment measure design, data collection procedures, analysis planning including evaluating efficacy and effectiveness
Developmental and Early-Stage Investigator Support	Proposal review and critiques, internal peer review of manuscripts, scientific presentation and grant applications, consultation and mentoring
Administration	Strategic planning, logistics and research operations, grant application preparation and submission, reporting, human subjects and IRB

CAIR's research agenda has integrated the advancements made in HIV prevention. Early identification of HIV infection coupled with immediate initiation and sustained use of antiretroviral therapy (ART) protects the health of persons living with HIV infection (PLH) and eliminates risk of onward transmission. The past decade also saw the discovery that high-risk but uninfected persons who use pre-exposure prophylaxis (PrEP) are almost fully protected from contracting HIV infection. Improved early HIV diagnosis with immediate treatment ("treatment-as-prevention"), scale up in PrEP use by high-risk uninfected persons, and responding to HIV outbreaks form the central pillars of the National End the HIV Epidemic (EtHE) Plan that targets counties and states with high HIV incidence.

CAIR's research incorporates biomedical, policy, behavioral, social science, and community perspectives needed to successfully scale up evidence-based interventions used by providers in the field; discovering and rolling out interventions that address critical gaps in the HIV care and prevention continuum; and reducing the country's longstanding HIV and other urgent health-related racial disparities.

CAIR's research vision is to prevent current, new, and emerging community health threats using evidence-based, behavioral intervention science. CAIR's research also develops improved strategies to promote health and alleviate adverse mental health consequences among persons living with HIV and other urgent community health challenges such as COVID-19, cancer, health disparities and stigma, and systemic barriers to population health in underserved urban and rural areas. CAIR is committed to disseminating its findings both to the scientific community and to public health providers so they benefit from Center research.

Our approach to achieving this vision is interdisciplinary, comprehensive, and multidimensional. The Center brings together outstanding investigators and draws upon models from the behavioral and social sciences, medicine, public health, mathematics, economics, communication, law, and infectious disease epidemiology to develop innovative prevention methods.

Grounded in behavioral science and applied neuroscience frameworks, CAIR's aims are:

(1) To advance the field in the development and evaluation of innovative behavioral, social, and structural interventions to improve PrEP uptake and to improve early identification of HIV infection, linkage and long-term retention of PLH in care, and attainment of durable viral suppression through ART adherence.

(2) To move the field forward by establishing the effectiveness of a new generation of multi-level HIV prevention approaches that combine behavioral, biomedical, social, structural, and systems interventions to achieve the greatest public health impact in disease reduction.

(3) To use dissemination and implementation science paradigms to quickly move HIV and other prevention interventions found effective in the research arena to service providers, policymakers, and the public health and provider sectors through an agenda of research that identifies ways to optimize scale-up and implementation.

(4) To develop strategies that reduce HIV and other health-related disparities and stigma through research that identifies and responds to the needs of racial and ethnic minority populations with greatest incidence and disease burden.

(5) To apply lessons learned in over 25 years of HIV prevention research to urgent community health challenges to develop, evaluate, and lead in the implementation of high-impact prevention; to serve as a resource to health departments, providers, researchers, and community constituencies to ensure rapid dissemination and scale-up of effective interventions to improve the health and well-being of communities that are disproportionately burdened by disease.

Jennifer M. Knight, MD, MS, FACLP

Knight Biobehavioral Oncology Research Program

Jennifer M. Knight, MD, MS, FACLP is an Associate Professor of Psychiatry, Medicine, and Microbiology & Immunology. She completed her undergraduate training at the University of Wisconsin-Madison in 1999 and her medical training at the Medical College of Wisconsin in 2004. Dr. Knight completed her residency in a combined Internal Medicine and Psychiatry program at Rush University in Chicago in 2009, and is dual board certified in both specialties. She finished a post-doctoral T32 research fellowship in Psychoneuroimmunology at the University of Rochester Medical Center in 2011.

Dr. Knight joined MCW in 2011 as an Assistant Professor of Psychiatry and Behavioral Medicine. She is currently an Associate Professor of Psychiatry, Medicine, and Microbiology & Immunology and Medical Director of the MCW Psycho-Oncology Program. Dr. Knight is an NIH funded researcher (R01CA238562) and is the elected Director of Research for the American Psychosocial Oncology Society, Co-Founder and -Director of the American Society for Transplantation and Cellular Therapy (ASTCT) Biobehavioral Oncology Research Special Interest Group, and elected fellow of the Academy of Behavioral Medicine Research. Locally she is the Co-Founder and -Chair of the MCW Biobehavioral Oncology Group and Chair of the MCW Cancer Center Population Sciences and Behavioral Health Disease Oriented Team (DOT). She mentors numerous students, residents, fellows, and junior faculty members both locally and nationally. Dr. Knight is a nationally and internationally recognized expert in biobehavioral HCT mechanisms.

Dr. Knight's research program aims to investigate biological risk and interventions – both pharmacologic and behavioral – for social health disparities in cancer, specifically among hematopoietic stem cell transplant (HCT) and cellular therapy recipients. Our lab does this by investigating how variations in immune function based on socioeconomic status (SES) – among other social health variables including depression, stress, sleep quality, and anxiety – contribute to differential patient responses and outcomes following HCT and cellular therapy. Reciprocally, we also investigate how these cancer therapies affect central nervous system function.

To accomplish these goals, we study biobehavioral mechanisms of cancer progression. Candidate mechanisms include the conserved transcriptional response to adversity (CTRA) transcriptome profile and associated molecular changes, inflammation, sympathetic nervous system activation, neurotoxic metabolites, and the endocannabinoid system, among others. These pathways are investigated as potential mediators of social health disparities among HCT recipients.

Dr. Knight's group has identified a potential effective candidate pharmacologic intervention for such social health disparities – propranolol. They have identified propranolol as an effective pharmacologic mitigator of CTRA gene expression among a cohort of patients with multiple myeloma undergoing HCT. Subsequent future research goals involve investigating whether propranolol is effective in ameliorating adverse clinical outcomes associated with reduced expression of these potential biomarkers. We have also recently confirmed preliminary findings that these CTRA-related transcriptome dynamics are associated with adverse clinical outcomes among HCT recipients. Examples of ongoing and future work include investigating the following:

- Bidirectional neuroimmune effects of tocilizumab, an IL-6 antagonist used to treat
- Biobehavioral implications of chimeric antigen receptor (CAR) T cell therapy
- Mindfulness to improve sleep and related symptomatology and inflammatory markers among hospitalized HCT recipients
- Effect of donor SES on recipient HCT outcomes
- Propranolol as an intervention to reduce cancer progression

Our research program continues to inform the clinical field of Psycho-Oncology as we increasingly understand how the central nervous system regulates cancer disease and progression.

Dr. Jeffrey Engelmann

Dr. Engelmann has a research interest in using neuroscience to better understand behaviors that put individuals at risk for cancer, with the aim of developing more effective cancer prevention strategies. His research focuses on using functional magnetic resonance imaging (fMRI) to identify brain systems and processes involved in the development and maintenance of nicotine dependence, with the long-term goal of translating these laboratory findings into safer, more effective, and more specific behavioral and pharmacological interventions for tobacco use and abuse.

Dr. Engelmann completed his Ph.D. in cognitive and biological psychology at the University of Minnesota and a postdoctoral fellowship in addiction neuroscience and cancer prevention at the University of Texas MD Anderson Cancer Center. His prior research, supported by the National Institute on Drug Abuse, used fMRI to study how smokers respond to smoking-related and other emotional stimuli, both when smoking was not possible and when smoking was imminently possible during the fMRI session. He found that smokers with greater brain responses to pleasant stimuli than to smoking-related stimuli were more likely to successfully quit, whereas smokers who showed the opposite pattern of brain response had difficulty quitting, suggesting that they might need additional smoking cessation support such as medication. He also found that the imminent possibility of smoking resulted in greater brain responses to smoking-related cues, especially among participants who reported the most severe withdrawal symptoms. This effect was observed in the insula, which adds to a growing body of evidence that this brain region is important for the development and maintenance of smoking behavior. Dr. Engelmann currently has funding from the Greater Milwaukee Foundation to extend these findings to a more diverse sample of smokers. Recently, Dr. Engelmann received a grant from Advancing a Healthier Wisconsin to test the feasibility and efficacy of providing on-site smoking cessation support in multifamily public housing in the city of Milwaukee. This study will provide important information about how to best partner with communities to increase smoking cessation rates.

Radiation Oncology

Cancer Center Clinical Trials

Froedtert & the Medical College of Wisconsin Cancer Center physicians and staff are dedicated to providing their patients with the most up-to-date cancer treatment options. Radiation Oncology participates in offering eligible patients access to clinical trials that investigate improved survival and quality of life for patients with cancer. The link to related studies is provided below.

http://www.froedtert.com/research/clinical-trials/cancer

Cancer Cell Biology Research

Cancer is a leading cause of morbidity and mortality for Wisconsin residents. Cancers that are aggressive and that become resistant to therapies lead to recurrence, metastasis, and even death. Cancer cell biology research is studying the manipulation of oncogenes and tumor suppressor genes to enhance the effectiveness of cancer therapy. This knowledge can be used to identify and create novel therapeutic strategies to reduce the human burden of cancer in Wisconsin and in the United States.

Radiation Biology Research

Radiation is required in the treatment of approximately 50% of all cancer cases at diagnosis; for 75% of patients at some time during their disease course. The radiation biology group is developing ways to decrease toxicity associated with therapeutic uses of radiation in cancer treatment. In addition, they assess the risk of exposure to ionizing and non-ionizing radiation and study medical countermeasures that mitigate radiation injury from radiation accidents and potentially from acts of terrorism.

Radiation Oncology Medical Physics Research

The Radiation Oncology Medical Physics section works to research and develop the most accurate and efficient manner of delivering radiation therapy to patients. Some of these innovative developments include adaptive dosimetric planning, magnetic resonance image (MR)-based planning and other image-guided techniques for delivering a highly conformal radiation tumor and target dose, while minimizing dose to normal structures. Most recently this team is working to develop MR image-guided linear accelerator delivery techniques; a breakthrough technology at the cutting edge of modern radiation therapy.

Radiology

The MCW Department of Radiology, under the leadership of Dr. Vince Mathews, Chair of Radiology, has continued to demonstrate the values of innovation and discovery that are hallmarks of Froedtert and the Medical College of Wisconsin. The scientific accomplishments of both the Radiology department and the Medical College promote a strong relationship with our community and peers both nationally and internationally.

Over the past year, the Department of Radiology has restructured our research program. Kevin Koch PhD, the current Director of the Center for Imaging Research, and Sarah White, MD, MS, FSIR have been named Co-Vice Chairs of Radiology Research. In their roles, Dr. Koch will oversee the basic and translation research laboratories, and Dr. White will focus on Clinical Research and developing relationships with external collaborators including other departments and industry partners. In order to expand the research mission, a new infrastructure has been developed. Each section has named a Director of Research (DoR) to serve as a liaison between research administration and clinicians. Drs. Koch and White will meet with the DoRs quarterly to provide and receive updates regarding research in each division.

In addition to the DoRs, the Department of Radiology has and continues to grow a robust administrative research infrastructure to support research. Brad Condon serves as the Research Administrator for Radiology. He manages all the research staff, including the research coordinators as well as providing financial and compliance oversight and program budgeting. With 10 years at MCW, Brad has the institutional savvy to help facilitate research endeavors on this campus. Jodi Nicolai-Johnson is the Radiology Program Manager and is an expert in grant submission and post grant award follow-up. After the grant is awarded, Jodi will track the budget and time lines for the follow-up of deliverables. Jodi has been with Radiology for almost 5 years and brings a perspective of a scientist and former lab manager to her role. Due to the large volume of research currently being performed, Melissa Hollister and Christi Reichert were recently hired as Clinical Research Coordinators. In their roles they will help navigate the regulatory processes necessary to conduct research and recruit and consent patients. Melissa and Christi were previously radiology technologists and their knowledge of radiology provides for an extremely efficient work flow. Elizabeth Weil continues to serve as Research Coordinator for Vascular & Interventional Radiology (VIR), navigating the regulatory processes for all VIR research including chart reviews to multi-center international randomized trials. This year Elizabeth began a new role as Research Ambassador through MCW's Office of Research new Research Ambassador Program. Elizabeth and Dr. Sarah White will also serve as committee members on MCW's Office of Research Committee on Regulatory Burden which will work to reduce administrative burdens associated with regulatory compliance. Lastly, Diana Kane serves as Radiology's Database Administrator. Diana has made manual chart reviews a thing of the past. If given data elements, Diana has the IT knowledge necessary to build databases and populate the databases with the necessary data elements. This allows the extraordinarily laborious chart review to be fast and allows the researcher to focus on data analysis.

Together Drs. Koch and White have obtained MCW IRB approval for an umbrella protocol that can be used by all radiology faculty. This radiology umbrella protocol was modeled after the VIR umbrella protocol which has been in use for 2 years. The radiology umbrella protocol allows research of all imaging studies and their comparators to be reviewed. In addition, Dr. Andrew Nencka is the PI of an umbrella MRI protocol that allows for clinical and research technology investigations. This protocol can be used for investigations of new sequences and processing applications on consenting volunteers and clinical subjects.

The benefits of an increased and strengthened research support staff are already apparent with many process innovations and new opportunities. Dr. Koch was awarded a DOD (Department of Defense) Grant for Quantitative MRI of the Post-Injury Instrumented Spinal Cord, beginning soon. Dr. Peter LaViolette received a supplement to his NIH Brain Cancer MRI R01 to study Alzheimer's Disease. Dr. Yang Wang Received a Multi-PI R01 with Dr. Michael McCrea for Effects of Head Impact Exposure During Contact Sport on Middle School and High School Athletes.

The overall research activity within the Department of Radiology continues to grow. Within the past year, the Department has submitted approximately 44 grant applications, and has collaborate on over 38 other grant applications. Current fiscal year research revenue includes $880K NIH funding, we also have several multi-PI Federal Grants submitted with other institutions.

Other Extramural revenue stayed strong at $446K, but was less than prior years due to timing of milestones and extension of several projects. Several multi-year projects are ongoing with GE Healthcare, Novocure, Guerbet, and the Focused Ultrasound Foundation. Sponsors with recognizable names such as Radiological Society of North America, Siemens, CR BARD, Cook Medical, Penumbra, DFINE, W.L. Gore and Associates, Medtronic, InSightec, Instylla, BTG, The Froedtert Hospital Foundation, Myocardial Solutions, and PRISM, have new and ongoing collaborations with the Department of Radiology.

We continue to receive awards on campus from the Cancer Center, CTSI, and the Center for Imaging Research (CIR) Pilot grants. The Department is also continuing Investigator Initiated Studies, to further the partnership with Industry.

Taken together these many initiatives and successes being in Radiology Research should enable both physician and PhD researchers to provide even more benefit to the community in a more timely and efficient manner.

For the 2018-2019 academic year, the MCW Division of VIR continued to expand its clinical and translational research activities. Dr. White's translational Interventional Oncology (IO) lab published 3 papers (and 2 in progress), 7 abstracts, 6 ongoing grants, awards from JVIR and SIO and 3 invited lectures. The Division opened 2 new clinical trial and continued research activities in 7 ongoing clinical trials. Their research endeavors have resulted in 1 publication, 3 grants, 10 abstracts and 8 poster presentations at national and international meetings. Herein we will highlight some of the pivotal trials our faculty have been involved with over the past year:

- **Vice-chair, Clinical Operations-Image Guided Procedures, William S. Rilling, MD, FSIR** continues to build his research interests, which are focused on image guided therapy for cancer. We received IRB approval for a phase 2 HCC study evaluating a new drug combating the hypoxic response in combination with transarterial embolization. Dr. Rilling will be national PI for an upcoming multi-center clinical trial looking at an arterial embolization medical device system. He will also be PI for a multi-center, randomized cancer trial comparing CIS-GEM chemotherapy with and without Y-90 as first line treatment in patients with unresectable intrahepatic cholangiocarcinoma.

- **Vice Chair, Radiology Faculty Affairs, Sean M. Tutton, MD, FSIR** continues to work on the development of techniques for image guided orthopedic applications. Dr. Tutton also has the largest cohort of patients with extra-abdominal desmoids in the country and recently published, in the Journal of Surgical Oncology, his innovative approach to treat this incurable cancer. Additionally, he is the PI on all MR guided Focused Ultrasound clinical trials currently underway here at MCW/FH. He is currently developing an international registry to track safety and efficacy of MSK interventions. He is also collaborating on a protocol evaluating the abscopal effect of ablation in combination with immunotherapy in a mouse model. Dr. Tutton developed a research protocol that surveyed, on a national level, the current training that interventional radiologists get in palliative care and a manuscript is in process.

- **Chief of the Clement J. Zablocki VA Medical Center, Robert A. Hieb, MD, FSIR** is serving as PI for the JET RANGER study which is evaluating whether Jetstream atherectomy followed by drug coated balloon improves target lesion revascularization at 1 year compared to balloon angioplasty followed by drug coated balloon in the treatment of complex lesions in femoropopliteal arteries. Dr. Hieb is also the lead in a local study that applies a novel software system to post process angiographic images in patients with critical limb ischemia (CLI). The software "removes" the blood vessels to view the underlying parenchyma for blood flow and assess for changes post treatment.
- **VIR Division Chief, Eric J. Hohenwalter, MD, FSIR** is PI for several clinical trials. He completed enrollment of patients in the PRESERVE study which evaluated the safety and effectiveness of IVC filters. He is also PI for a prospective study of a novel class of software working with Siemens Medical Solutions, USA, Inc. Dr. Hohenwalter is actively recruiting for the C-TACT trial. CTRACT is a NIH-funded randomized controlled trial that is examining new treatments for vein damage caused by blood clots (DVT). Patients with established moderate to severe Post-Thrombotic Syndrome will be randomized to either endovascular therapy (EVT) or No-EVT treatment groups. All study patients in both groups will receive active treatment for their leg problem and will be monitored closely. This trial aims to understand which treatment strategy is most effective in improving patients' symptoms and quality of life. Later this year, Dr. Hohenwalter plans to start enrollment in an investigator initiated trial in collaboration with cardiology and GI physicians. Funded by the Radiological Society of North America (RSNA), the study will determine the impact of the transjugular intrahepatic portosystemic shunt (TIPS) procedure on cardiac function.
- **Parag J. Patel, MD, MS, FSIR** serves as PI for BEST-CLI which is a multicenter trial of endovascular vs. open surgical revascularization in patients with CLI and infrainguinal peripheral arterial occlusive disease who are candidates for both treatments.

- **Co-Vice Chair, Radiology Research, Sarah B. White, MD, MS, FSIR** continues work in her translational research laboratory at MCW with an emphasis on interventional oncology. She recently started her second term on the MCW IACUC committee. She continues to run the Medical Student Summer Research program, and this year the Division welcomed 2 medical students. Through the Society of Interventional Radiology (SIR) a third medical student was funded to spend time in VIR participating in research. Additionally, Dr. White organized Radiology's participation in hosting 2 SPARCC (Student-

Centered Pipeline to Advance Research in Cancer Careers) students. The 2 students each had a 2-week rotation observing and learning about interventional and digital radiology and the research done in the department. Dr. White continues to be PI for the RETNET trial, evaluating the efficacy of liver directed therapy in metastatic neuroendocrine cancer. On a national level, Dr. White continues to serve as the Chair of the Clinical Research and Registries for the Society of Interventional Radiology.

- **Alexandra H. Fairchild, MD** has been working on a quality improvement project with the purpose of educating Radiology and VIR residents on procedural consenting skills. Dr. Fairchild has been instrumental in manuscript development for a project that evaluated the palliative care education among interventional radiology fellows.
- **Matthew J. Scheidt, MD** recently joined the group. He will be PI for an upcoming study assessing the safety and effectiveness of a new type of IVC filter. Dr. Scheidt has also provided research mentorship to trainees and medical students. Due to his excellent instruction he was awarded the 2019 Teacher of the Year by the 2018-2019 VIR fellows.

Surgery

The Medical College of Wisconsin Department of Surgery, led by Chairman Douglas Evans, MD, is dedicated to laboratory, translational, and clinical research in all nine clinical divisions including Adult Cardiothoracic Surgery, Colorectal Surgery, Congenital Heart Surgery, Minimally Invasive General Surgery, Pediatric Surgery, Surgical Oncology, Transplant Surgery, Trauma and Critical Care, and Vascular and Endovascular Surgery, as well as the Division of Research. Research efforts by faculty, residents, and medical students continue to have resulted in numerous research manuscripts published, research talks and posters presented, scientific meetings conducted, collaborations fostered and funding received.

Surgery faculty worked one-on-one with a significant number of medical students in the Scholarly Pathways program during the 2019-2020 academic year. In addition, a large number of the student–faculty pairings were undertaken in the "Physician Scientist Pathway" whereby the surgeon mentors a student on his or her own research project throughout the academic year.

Division of Research

The Division of Research leads the research strategic planning and implementation for the Department of Surgery with the vision to be a nationally recognized institution in surgical research. Core responsibilities of the Division of Research (DoR) include faculty development, advocacy for research infrastructure development and expansion, enhancing department extramural funding, maximizing the quality and quantity of peer-reviewed publications, optimizing the resident research experience, and identifying and supporting constructive collaborations within the department and the institution.

The DoR hosts a monthly Surgery Research Conference, featuring faculty and trainee scientific presentations as well as talks on available research resources on campus. DoR releases a monthly research e-newsletter, "*On the Cutting Edge*," featuring research highlights, funding opportunities, abstract deadlines, important news, and tips. SurPASS, our Surgery Pre-Award Support Services, provides grant administrative support to Department of Surgery faculty. DoR also leads in clinical research operations, providing core resources and training.

For students interested in identifying a research mentor in the Department of Surgery and do not have an established connection, please contact Krissa Packard at kpackard@mcw.edu, who may facilitate an introduction with a faculty member.

Division faculty and their research interests:

- **Gwen Lomberk, PhD**, serves as the Chief for the Division of Research, Director of Basic Research and Associate Professor of Surgery and Pharmacology & Toxicology. Dr. Lomberk's research program is broadly focused on the epigenetic landscapes that characterize subtypes of pancreatic cancer (PDAC) and refining the utility of epigenetic inhibitors for treatment and re-sensitization to conventional therapies. Epigenomic-based pharmacology has the potential to serve as a robust tool to improve the treatment of PDAC. Her laboratory seeks to contribute to the field of experimental therapeutics through combined inhibition of genetic-to-epigenetic pathways, as an important and provocative consideration for harnessing the capacity of cell cycle inhibitors in efforts to enhance future use of epigenetic inhibitors.
- **Young-In Chi, PhD,** Assistant Professor, recently joined us from Kyongpook National University Medical Center in Daegu, Korea where he was a Research Professor in the Center for Drug Discovery and Development for Diabetes and Metabolic Disease. Dr. Chi is a member of Dr. Raul Urrutia's team in the Genomic Sciences and Precision Medicine Center and will be conducting basic science research in the areas of molecular modeling, variant analysis, and precision medicine of pancreatic cancer.
- **Angela Mathison, PhD,** Assistant Professor, joined the Department of Surgery in August 2018 from the Genomic Sciences and Precision Medicine Center where she is the Technology Development Director. Dr. Mathison's research focuses on the role epigenetics play in the development and progression of pancreatic cancer and the potential to target these cellular mechanisms for novel therapies.
- **Raul Urrutia, MD,** serves as the Director of the Genomic Sciences and Precision Medicine Center, Warren P. Knowles Professor of Genomics and Precision Medicine and Professor in the Department of Surgery. Dr. Urrutia's laboratory focuses on precision medicine as it applies to pancreatic cancer, as well as other diseases. Precision Medicine is a clinical discipline that was born from basic science in genetics, as well as engineering, representing a translational science "par excellence"

with an actual marriage of basic science with clinical science. Through the combination of three innovative tools of Cancer Precision Medicine, namely multi-omics, computational modeling, and patient-derived models, his research program seeks to identify new mechanisms, diagnostic markers, and therapeutic targets for pancreatic cancer. His laboratory has been focused on investigating how epigenomic regulators work as nuclear effectors of common mutations (e.g. KRAS) associated with human pancreatic diseases.

Division of Cardiothoracic Surgery, Adult

Dr. Paul Pearson leads the "CryoLife PROACT Xa" clinical trial. The trial compares apixaban to warfarin for the anticoagulation of patients who have an On-X prosthetic aortic valve. The trial randomizes participants who have had an On-X aortic valve implanted at least three months ago to either apixaban or warfarin (INR goal 2-3). Given the challenges associated with long-term warfarin use, including both quality-of-life factors as well as difficulties maintaining a consistently therapeutic INR, the possibility of being able to safely manage mechanical valve patients with a DOAC, like apixaban, has the potential to greatly improve the future care of these patients.

Dr. David Joyce leads the "Transmedics DCD Heart CAP" clinical trial. Its objective is to enable continued clinical access to DCD heart transplantation in the U.S. and to continue to collect additional data on the performance of the OCS Heart System to resuscitate, preserve and assess hearts donated after circulatory death for transplantation to increase the pool of donor hearts available for transplantation. While the demand for heart transplantation globally has increased significantly each year, the utilization or recovery of available donor hearts for transplantation has been limited. Currently, the TransMedics' OCS Heart technology is the only portable system available for ex-vivo maintenance of the donor heart in a metabolically active and beating state.

Dr. David Joyce leads the "SynCardia 70cc Total Artificial Heart (TAH-t) for Destination Therapy (DT)" clinical trial at MCW. The Total Artificial Heart is a pulsatile biventricular device that replaces the heart's two ventricles and four heart valves, relieving the heart's workload by pumping blood to both the lungs and the body. The purpose of these studies is to evaluate whether the TAH-t can support patients with life-threatening irreversible biventricular heart failure who are not candidates for a left ventricular device or heart transplantation.

Dr. Lucian Durham leads the "Extracorporeal Membrane Oxygenation for 2019 novel Coronavirus Acute Respiratory Disease" (ECMOCARD). In response to the COVID-19 outbreak and to assist in pandemic planning both locally and globally, a research collaborative has been assembled. The study aims to describe clinical features; severity of pulmonary dysfunction; incidence of ICU admission and use of mechanical ventilation and ECMO; ECMO technical characteristics; duration of ECMO; complications; and survival of patients with COVID-19.

Dr. Lucian Durham leads the "Registry of CytoSorb Therapy in COVID-19 ICU Patients" (CTC Registry". SARS-CoV-2 infections and the associated morbidity and mortality from severe residual effects of this infection (COVID-19) are currently increasing in the US. Based on real-world evidence, the FDA granted Emergency Use Authorization (EUA) for CytoSorb therapy for adult COVID-19 ICU patients. Under the EUA, CytoSorb therapy is provided via integration of the CytoSorb device into extracorporeal membrane oxygenation (ECMO), continuous renal replacement therapy (CRRT), or hemoperfusion alone extracorporeal circuits.

Chart Review Studies:

- *Component-Based Case Logging for Improvement and Innovation in Surgical Resident Operative Training (D. Joyce)*
- *Outcomes of Alternative Surgical Treatments for Atrial Fibrillation: a Retrospective, Single-Institutional Experience (D. Joyce)*
- *Comparison of Traditional Transhiatal Esophagectomy to Transhiatal Esophagectomy with Transcervical Endoscopic Esophageal Mobilization: One Institutions Experience* (TEEM Study) *(D. Johnstone)*
- *Percutaneous Right Ventricular Assist Device with Oxygenation as Treatment Compared to Endotracheal Intubation in COVID-19 ICU Patients (D. Joyce)*
- *Determining if Use of Bipolar Sealers During LVAD Implantation Reduces Take-Back Rates for Bleeding (D. Joyce)*
- *Differences in CardioMEMS Pulmonary Artery Pressure Readings in Heart Failure Patients with Reduced vs. Preserved Ejection Fraction (D. Joyce)*
- *Case Study Report of Patient Outcomes in Mechanical Circulatory Support in Cardiogenic Shock: Comparing Impella, IABP, and ECMO (D. Joyce)*
- *A Bridge to the Fridge? Changes in BMI Post Left Ventricular Assist Device Implant (D. Joyce)*

- *Long Term Efficacy and Safety of Epicardial Ablation for Paroxysmal Atrial Fibrillation (D. Joyce)*

Division of Congenital Heart Surgery

The Division of Congenital Heart Surgery is actively involved in clinical and translational research to improve outcomes for children with congenital heart disease (CHD). Our team of highly skilled scientists are successful principal investigators, mentors and co-investigators on numerous studies in collaboration with many MCW departments and external institutions.

Viktor Hraska, MD, PhD leads a multi-disciplinary team that is testing and validating a NIR imaging system meant to provide adequate contrast for anatomical and functional assessment of thoracic duct during surgery. Dr. Hraska received We Care funding to support a pilot study that is studying neonates undergoing the Norwood operation with the intent to optimize cardiopulmonary bypass to support cerebral and somatic perfusion during arch reconstruction. Dr. Hraska is also studying pulmonary cell plasticity during single ventricle palliation and the hydrodynamics of arch reconstruction in HLHS. In addition, Dr. Hraska is a Co-Investigator on the STRESS trial, which is looking at the impact steroids have on the reduction of systemic inflammation following neonatal surgery. Finally, he has been instrumental in the implementation of the utilization of the technical performance score to measure the effects of surgeon technical Skill on outcomes and resource utilization for children with congenital heart disease.

Dr. Ronald K. Woods, MD, PhD is an investigator on 16 active clinical or basic science studies. His research includes clinical, surgical, quality of life, and value improvement/ quality assurance initiatives, as well as laboratory surgical investigations that utilize animal models. He is the site PI for 2 large multicenter studies and has organized a multicenter registry to evaluate mechanical circulatory support in single-ventricle patients. He regularly mentors medical students on clinical projects which often lead to podium presentations and publications. Additionally, Dr. Woods is actively engaged in innovation to develop new technology to improve the quality and safety of surgical care.

Michael E. Mitchell, MD and Aoy Tomita-Mitchell, PhD lead the Mitchell lab. The long term goal of the Mitchell lab is to understand how the integration of genetic and genomic information with clinical variability and clinical outcomes in CHD can be used to identify predictors of clinical outcomes in CHD, and to understand mechanisms of healing and plasticity following surgical repair. The lab employs patient specific induced Pluripotent Stem Cells (iPSCs) to investigate the genetic etiology of CHD. Dr. Michael Mitchell is PI of the CHD Tissue Bank, a biorepository of DNA and surgical discards from CHD patients. He is a Co-PI of the new Herma Heart Institute Cord Blood Bank aimed at advancing the science and practice of cell-based clinical therapies for high risk patients with CHD. He is the PI of a HHI Innovation grant investigating the role of the MYH6 gene in Hypoplastic Left Heart Syndrome (HLHS) using patient specific iPSCs. Dr. Tomita-Mitchell and her collaborators have also received a grant from the CTSI to bioprint patient-specific cardiac cells on a 3D tissue construct. Other significant studies in the Mitchell lab include investigating the genetic etiology of Ebstein's Anomaly with Left Ventricular Noncompaction, and publishing regarding a Newborn Screening assay for 22q11.2 Deletion Syndrome. The lab is also exploring the role of metakaryotic stem cells in transplant atherosclerosis, coronary artery disease, and progressive pulmonary venous stenosis. The Mitchell lab has studied the science of cell-free DNA extensively. Currently Dr. Aoy Tomita-Mitchell and her collaborators are conducting research funded by an HHI Innovation Pilot award from AHW to study cell-free DNA in pediatric sepsis.

Professor John Baker's research program serves as a nexus to translate basic science discoveries into clinical applications. Dr. Baker is studying why survivors of childhood cancer, who have been treated with radiation therapy are at increased risk for heart disease. His findings demonstrate targeted irradiation of organs below the diaphragm such as the kidney, cause pathologic remodeling of the non-targeted heart in rats. This non-targeted effect appears to be mediated in part by the immune system. Dr. Baker is funded by NASA to determine the increased risk for developing degenerative cardiovascular disease from exposure to components of space radiation. During exploratory missions to the Moon and Mars, astronauts will be exposed to penetrating galactic cosmic rays and solar particles. Ground-based animal studies are being used to assess the increased risk for developing degenerative cardiovascular disease.

Division of Colorectal Surgery

The research efforts within the Division of Colorectal Surgery remain robust. Dr. Kirk Ludwig continues as the institutional principal investigator (PI) for a Cooperative Group Colorectal Cancer Trial at Froedtert and MCW Cancer Center. The purpose of the trial is to explore the use of neoadjuvant chemotherapy for treatment of locally advanced rectal cancer. Dr. Ludwig is also involved in two early stage projects studying the safety and efficacy profile of each new product. One study drug is to be used in conjunction with an enhanced recovery pathway for gastrointestinal recovery on the resolution of postoperative ileus following bowel resection. The other product is

a new formulation of an anti-infective drug to be used to prevent surgical site infection following elective colorectal surgery involving colon or rectal resection. Dr. Ludwig also serves as the Division Chief and holds the Vernon O. Underwood Endowed Chair. Under his supervision, the Division has begun to carefully track functional outcomes in those undergoing resections for rectal cancer and the treatment of anal cancer. Dr. Ludwig has a national reputation as an expert in the surgical treatment of rectal cancer with special emphasis on sphincter sparing techniques.

Dr. Mary Otterson maintains a primary clinical and research focus on inflammatory bowel disease. She is currently the MCW site PI for a prospective, multi-institutional study evaluating bowel and sexual function following ileal pouch anal anastomosis surgery with the hopes of identifying surgical and disease-specific factors predictive of improved function. Furthermore, she, along with the other faculty in the Division of Colorectal Surgery, are participating in the ADMIRE-CD II trial, a phase III, randomized, double blind, parallel group, placebo controlled, international, multicenter study assessing the efficacy and safety of adult allogeneic expanded adipose-derived stem cells for the treatment of complex perianal fistula(s) in patients with Crohn's disease.

Dr. Timothy Ridolfi recently completed a 3-year project aimed at evaluating the changes in enteric nervous system following low anterior resection. This work allowed him to complete a Master's Degree in Clinical and Translational Science. He is also interested in the evaluation for complete response in the setting of neoadjuvant therapy for rectal cancer. This work is done in collaboration with the Departments of Pathology, Radiology, and Biophysics and relies heavily on advanced MRI techniques that are currently offered only at MCW. This project was awarded funding from the Association of VA Surgeons Foundation Karl Storz Award. In other research, Dr. Ridolfi is using the Vizient dataset, which includes outcome data from more than 100 medical centers, to evaluate the most beneficial aspects of enhanced recovery after surgery programs in regard to colon and rectal surgery. Lastly, Dr. Ridolfi is involved in a collaborative study which is aimed at self-examination techniques for identifying anal cancer.

Dr. Carrie Peterson is the site PI for a national randomized superiority trial of elective colectomy versus best medical management for patients with quality of life (QoL) limiting diverticular disease. The goal of the trial is to answer the question: For patients with QoL-limiting diverticular disease, is elective colectomy more effective than best medical management? Dr. Peterson also continues to pursue her research interests in minimally invasive colorectal surgery and surgical outcomes. She is heavily involved in several research projects evaluating improvements in quality and perioperative process improvements. Along with the others in the Division of Colorectal Surgery, Dr. Peterson is participating in a prehabilitation project in the frail undergoing colon resection. The project is aimed at both improving frailty preoperatively as well as improving postoperative functional recovery.

Dr. Kent Peterson is our 2020-2021 Colorectal Research Resident. Dr. Peterson is completing his General Surgery residency at MCW and will be working with the Division for 1 year. He has a very active role in the multitude of current ongoing projects within the Division. He is currently investigating specialized anesthetic techniques used in anorectal surgery, as well as radiomic data as it pertains to rectal cancer.

Kathryn Hoffman continues in the position of Clinical Research Coordinator to assist in the organization and successful completion of the ever-expanding list of research projects within the Division of Colorectal Surgery.

Division of Minimally Invasive Gastrointestinal Surgery

The Division of Minimally Invasive Gastrointestinal Surgery supports the Department's commitment to excellence in education and research. Over the 2019-2020 academic year, faculty and research staff collaborated to develop 7 new research protocols and showcased the institution's innovative efforts through virtual presentations at local, regional, and national meetings. Additionally, Tammy Kindel, MD was named the 2020 Michael H. Keelan Jr., MD Scholar, and received a $50,000 grant. Throughout the academic year the division faculty mentored 9 medical students and 7 general surgery residents. Our research is focused in the domains of foregut surgery, bariatric surgery, and hernia surgery.

Bariatric Surgery

The bariatric surgery program at Froedtert and the Medical College of Wisconsin is accredited as a Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program (MBSAQIP) Comprehensive Center with Adolescent Qualifications. The 2019-2020 Quality Improvement project, Opioid Reduction in Bariatric Surgery, was led by Jon Gould, MD and Tammy Kindel, MD, PhD. This project focused on reducing opioid use and replacing with non-opioid pain management treatments following bariatric surgery. This project was part of the MBSAQIP BSTOP protocol initiative that was designed with the help of Jon Gould, MD. The division published

multiple peer-reviewed bariatric surgery manuscripts in journals that including Surgery for Obesity and Related Diseases, JAMA Surgery, Surgical Endoscopy, Obesity Surgery, the American Journal of Surgery, and Surgery.

Foregut Surgery

In the 2019-2020 academic year, the division participated in numerous multi-institutional sponsored trials on gastroesophageal reflux disease (GERD) surgical outcomes using implantable medical devices. We continued to review long-term outcomes for patients following surgery that received an implanted magnetic sphincter augmentation device (LINX). Faculty continued to examine long-term patient experiences following implantation of a gastric electrical stimulation device (Enterra) in patients with medically refractory gastroparesis. In addition, the Tailored Myotomy to Reduce the Incidence of Post-Procedure Reflux after Peroral Endoscopic Myotomy (POEM) trial was approved for enrollment. The Division presented findings in foregut surgery outcomes at Wisconsin Surgical Society, Academic Surgical Congress, and Society of American Gastrointestinal and Endoscopic Surgeons (SAGES). Peer-reviewed manuscripts were accepted to Surgical Endoscopy, the Journal of Gastrointestinal Surgery, and Surgery.

Hernia Surgery

Sponsored and investigator-initiated studies in the hernia domain included studies designed to evaluate quality and recovery outcomes following implantation of various types of mesh. In the 2019-2020 academic year, the division continued long-term follow ups for the Medtronic Parietene™ DS Composite Mesh in Ventral Hernia Repair Study under Dr. Matthew Goldblatt. The Division continues to participate in the Americas Hernia Society Quality Collaborative, a national quality improvement effort aimed at improving the quality of care provided to hernia patients. The Division's hernia research efforts were presented virtually at MCW, the Wisconsin Surgical Society, and nationally at Academic Surgical Congress, Southwest Surgical Association, and the International Hernia Congress.

Division of Pediatric General and Thoracic Surgery

The Division of Pediatric General and Thoracic Surgery houses a highly successful and thriving research program with prestigious studies in both the bench and clinical science.

In our bench research, Dr. Kirkwood Pritchard has an NIH R01 grant to research mechanisms of oxidative stress and inflammation in sickle cell disease. His interests also include examining the role of oxidative stress and inflammation in murine models of stroke, multiple sclerosis and rodent models of hyperoxic lung injury in neonatal rat pups. Dr. Pritchard established the licensing agreement for MCW startup ReNeuroGen, LLC to develop and test a novel treatment for secondary brain injury after stroke. ReNeuroGen has been funded by the NIH Small Business Innovation Research (SBIR) program.

Dr. Brian Craig's primary research interest is in establishing pre-clinical experimental models to understand the impact of the perioperative stress-inflammatory response on the tumor immune microenvironment in neuroblastoma, in order to identify innovative immune-modulating therapeutic strategies. In addition, he helps to represent the division as an active member of the Pediatric Surgical Oncology Research Consortium, a national network of pediatric surgeons who investigate high-priority clinical questions via a multi-institutional approach.

With support from Dr. Tom Sato, our clinical research program is one of the founding members of the Midwestern Pediatric Surgical Consortium (MWPSC). As part of the MWPSC, a number of our surgeons participate in multi-institutional clinical studies examining biliary atresia, hernias, esophageal atresia and tracheoesophageal fistula (EA/TEF), adolescent breast masses, pediatric adenexal masses, and appendicitis.

One of the first major initiatives of the MWPSC was led by Dr. Dave Lal to examine the treatment of EA/TEF, which resulted in the development of a best practice care bundle to reduce complications. Dr. Lal is also the site PI for the MWPSC clinical trial funded by PCORI to investigate parental choice in the operative versus non-operative management of acute appendicitis.

Under the direction of Dr. David Gourlay, MWPSC developed a protocol to prospectively study venous thromboembolism prophylaxis in trauma patients. Dr. Gourlay also has a grant from the Advancing a Healthier Wisconsin REDIRECT Program which is currently building institutional data sharing relationships between Children's Wisconsin Trauma Registry and community partners to study social determinants of health and outcomes in pediatric trauma patients.

The MWPSC is doing a study of non-accidental trauma during COVID spearheaded by Dr. Katy Flynn-O'Brien. Dr. Flynn-O'Brien is an experienced data scientist who analyzes large local and national datasets to study outcomes in pediatric trauma.

Dr. Casey Calkins is our site's PI in an NIH-sponsored study led by Vanderbilt University examining early versus late repair for neonates with inguinal hernias, in what is known as the HIP study. Dr. Calkins is also a steering committee member of a national registry of anorectal malformations (Pediatric Colorectal and Pelvic Learning Consortium; PCPLC). This multi-center consortium investigates variations in care that lead to optimal outcomes. PCPLC recently began a study to investigate Patient and Parent Reported Outcome Measures of patients with colorectal disease.

Dr. Amy Wagner oversees the Gastroschisis Outcomes of Delivery study, a large, multi-institutional randomized control trial endorsed by the North American Fetal Therapy Network examining the outcomes of early versus late delivery in prenatally diagnosed gastroschisis. Dr. Wagner has built a comprehensive multi-institutional gastroschisis research program which studies short and long term clinical outcomes via a registry, as well as the genetic relationship driving gastroschisis via a biobank.

Drs. Sabina Siddiqui and Keith Oldham are the division's global health liaisons, studying surgical illness across the world. Both are members of the Global Initiative of Children's Surgery, where they work on establishing partnerships to examine improvement in global surgical care.

Dr. Siddiqui is also a founding Board member (and Chief Medical Officer) of Brio Device LLC, a company who develops technology to increase efficiency and effectiveness in airway management. Brio is currently working on their second SBIR, which includes partnership with a psychometrician to develop a valid and reliable survey tool to assess intubation devices, and using that tool to test the effectiveness of their new pediatric intubation stylet.

Dr. John Densmore has a strong clinical interest in Congenital Chest Wall Malformations and is currently investigating the use of non-operative means to correct chest wall anomalies. He is active in research related to identifying variabilities that impact the cost of pediatric surgical care. Dr. Densmore is also spearheading groundbreaking innovations in treatment of tracheal agenesis, with emphasis on studying the impact of embryology on development of this rare diagnosis.

Access to quality pediatric surgical care in resource poor settings is the focus of Dr. Kyle Van Arendonk's current research. Dr. Van Arendonk is a skilled data scientist who works with large national databases to understand disparities in pediatric surgical care. He is also the leader of the division's ERAS initiative, and represents the division for participation in projects through the national Pediatric Surgical Research Consortium (PedSRC). PedSRC is currently investigating the impact of COVID on hernia and appendicitis care, as well as coordinating a cluster randomized trial studying the outcomes of povidone-iodine irrigation for abscess prevention in perforated appendicitis.

Pediatric Surgery houses a Clinical Outcomes Registry, which collects annual quality of life data from over 500 neonatal surgery patients. The division supports various investigator initiated chart reviews, case reports, and systematic reviews. Pediatric Surgery also has a robust quality improvement program which prospectively follows the clinical details of all surgeries performed within the practice and any associated morbidity/mortality, with special emphasis on data driven quality initiatives with quantifiable outcomes.

Division of Transplant Surgery

Introduction

The Organ Transplantation and Hepatobiliary Surgery Research Program in the Division of Transplant Surgery, Department of Surgery at Medical College of Wisconsin (MCW) was established on October 1, 2012 under the leadership of Johnny C. Hong, M.D., Professor of Surgery, Chief of the Division of Transplant Surgery and Director of the Solid Organ Transplantation Service Line at Medical College of Wisconsin, Froedtert Health and Children's Wisconsin.

The overarching goal of the research program is to provide a solid framework for discovery and innovation of novel therapies to improve the lives of patients suffering from end stage organ failure and surgical diseases of the liver and bile duct. The Research Program conducts basic science, as well as clinical and translational investigations on transplantation immunobiology, organ preservation and resuscitation, liver, kidney, and pancreas transplantation, as well as surgical diseases of the liver and bile duct. The Research Program has also established strong collaborative research partnerships and affiliations with other scientists at MCW and other academic institutions.

Basic Science Research

While a significant number of patients awaiting liver transplantation die each year due to lack of suitable donor organs, similar number of donated livers are being discarded because of poor organ function caused by ischemia and reperfusion injury (IRI). The primary goal of our basic science research program is to develop novel bench to bedside therapies that would circumvent IRI. These therapies

would expand the organ donor pool by converting high-risk liver organs (currently being discarded) to normal-risk transplantable organs and thus, saving more human lives.
The primary area of study is on the mechanisms of liver IRI as it relates to transplantation immunobiology. Our research laboratory utilizes experimental animal (mouse, rat, and swine) models to study the physiologic, immunologic, metabolic, and transcriptomic profiles of liver IRI. After nearly a decade of work, Dr. Johnny C. Hong has developed and recently patented a new liver resuscitation treatment, regulated hepatic reperfusion (RHR), to revive severely damaged livers. Based on a large animal experimental model, RHR mitigated liver IRI and improved liver function and prolonged survival. The MCW Organ Transplantation Team will soon bring this innovation to clinical trials.

Clinical and Translational Science Research
The Research Program maintains a comprehensive medical database for patients (adults and children) in our clinical transplantation program. In 2014, the MCW Institutional Review Board (IRB) approved a transition of that clinical database to a REDCap database, now known as the Solid Organ Transplantation Data Bank. This information is valuable for program management, performance improvement, quality assurance, and clinical and translational research.
Recent advances in epigenetics (the study of natural and environmental causes of genes being turned on and off) may provide insight on how liver IRI regulated which genes are active or dormant. These epigenetic phenomena are dynamic and potentially modifiable, making it attractive therapeutic targets. A collaborative translational study has been designed by Drs. Johnny C. Hong and Raul Urrutia, MD, the Warren P. Knowles Endowed Chair of Genomics and Precision Medicine, Professor of Surgery, and Director of the MCW Genomic Sciences and Precision Medicine Center. This study aims to understand the epigenetic changes in the liver during the transplantation process so that targets can be identified for development of new treatments. The research project received the Medical College of Wisconsin Department of Surgery Maggie Z. Schultz We Care Award for Medical Innovation and Research.

Current ongoing studies involving Divisional Faculty and Advanced Practice Provider (APP) in academic year 2020-2021

1) Determine the effect of regulated hepatic reperfusion in a DCD swine liver transplant model and mitigate IRI through novel treatment.
2) Assessment of hepatic IRI measured by bile transporter expression in a rat IRI model with hepatic steatosis.
3) Investigate the influence of extracellular adenosine signaling on leukocyte-mediated hepatic injury in a mouse IRI model.
4) Impact of A Specialized Transplant Critical Care Model on Short-Term Outcomes Following Liver Transplantation in High Acuity Patients
5) Multi-Institutional Validation of a Novel Prognostic Nomogram Predicting Hepatocellular Carcinoma Recurrence after Liver Transplantation
6) Everolimus-based immunosuppression in pediatric liver transplantation.
7) Staged Biliary Reconstruction After Liver Transplantation (SBRALT) Reduces Post-Transplant Biliary Complications in High-Acuity Adult Patients
8) Staged Biliary Reconstruction after Liver Transplantation (SBRALT): A Novel Surgical Strategy for High Acuity Pediatric Transplant Recipients
9) Incompatible Organ Transplantation in High Risk Donors.
10) The Effect of Donor Specific Antibodies and Positive Crossmatch on Outcomes after Combined Liver- Kidney Transplantation
11) Intraoperative Renal Replacement Therapy in High Acuity Liver Transplant Patients
12) Impact of Transplantation Mental Health Group Therapy on Outcomes after Solid Organ Transplantation
13) Outcomes of Liver Transplantation for Acute Alcoholic Hepatitis
14) Safety and Utility of Cycle Ergometer Therapy (CET) in a Transplantation Intensive Care Unit (TICU): A single-blinded Randomized Controlled Trial
15) Pre-Habilitation in Patients Awaiting Liver Transplantation: Impact of formal physical activity program on nutritional status, psychological factors and physical fitness prior to liver transplantation and subsequent impact on morbidity, mortality, compliance and quality of life after liver transplantation.
16) Efficacy of combination neoadjuvant therapy followed by orthotopic liver transplantation in treatment of patients with unresectable cholangiocarcinoma
17) Outcomes in Cirrhotic Patients Undergoing Major Abdominal Surgery
18) Platelet Refractoriness and Alloimmunization in Liver Transplantation
19) Liver Biopsies to study Ischemic Reperfusion Injury
20) A Randomized, Controlled, Open Label Clinical Trial of Thymoglobulin Induction and Extended Delay of Calcineurin Inhibitor Therapy for Renal Protection after Liver Transplantation.
21) Neurocognition in Heart Failure and Relationships with Mechanical Circulatory Support and Transplant Outcomes.
22) Platelet Refractoriness and Alloimmunization in Liver Transplantation
23) The Effect of Race on Transplant Outcomes. A single center experience.
24) Nutritional effects and 30 Day Readmission in Liver and Kidney Transplantation

25) Recognition of Advanced Providers in the Transplantation Intensive Care Unit.
26) Early Liver Transplantation for Severe Alcoholic Hepatitis.
27) Evaluation of a new transplant surgical workforce paradigm: A transplant surgeon- advanced transplant provider practice model
28) Impact of the role of advanced transplant provider (ATP) on patient experience in liver transplantation

Division of Trauma & Critical Care

The Division of Trauma and Acute Care Surgery focuses its research in several areas of expertise including: emergency intervention, evaluation of current practices for improved outcomes/recovery of trauma related injuries, measuring patient outcomes after injury, cost effectiveness, surgical infections, palliative care, early diagnosis for symptoms of post-traumatic stress disorders, ethics, educational research, quality, health disparities, patient safety, geriatrics, nutrition, and disease modeling. These clinical entities fall under the three chief timeframes during the continuum of patient care from Pre-Hospital/Acute to Subacute to the Long-Term Recovery/Rehabilitation phases. Throughout the 2019 academic year, we have had internal and external funding, including from non-profit, government and industry sources.

- **Dr. Marc de Moya's, Chief of Trauma & Acute Care Surgery,** research focus is in prospective controlled trials for improving surgical outcomes in trauma, acute care surgery, and surgical critical care patients. In addition, he is growing his research experience in Global Surgery.
- **Dr. Marshall Beckman's** research and education in emergency general surgery data collection and registry development, using that data to improve patient care and update emergency general surgery practice management guidelines.
- **Dr. Tom Carver's** research focuses on non – opioid pain medications in trauma. The treatment of chest trauma, and surgical education.
- **Dr. Panna Codner** is currently funded to research dysbiosis in the traumatically injured patient, as well as focusing on the role of nutrition and frailty in patient outcomes.
- **Dr. Terri deRoon-Cassini** is funded to focus on developing acute neurobiological risk factors and treatment targets for PTSD and depression in adult injured trauma survivors.
- **Dr. Christopher Davis, MD, MPH** is the Chair of the Injury Prevention Committee for the Division, which is focused on comprehensive injury prevention including but not limited to injury from violence, falls, and motor vehicle crashes. He is also Chair of the Bleeding Control Initiative of Wisconsin which aims to train all of Wisconsin's citizens how to stop life-threatening hemorrhage through the American College of Surgeons' "Stop the Bleed" course.
- **Dr. Chris Dodgion's** research focus involves work to strengthen trauma systems, expand quality improvement initiatives in low resource settings and address the global surgical workforce shortage through education innovation. He is currently involved in collaborative projects in Haiti, Ghana, and Ethiopia.
- **Dr. Anu Elegbede** is studying the impact of a dedicated Geriatric Trauma co-management program with internal medicine. She is also studying penetrating injury in the Geriatric population, as well as mentorship of medical students and surgical residents.
- **Dr. David Milia's** research focus includes both primary and secondary prevention of urban firearm violence as well as real-time mapping and geospatial analysis of foci or violence in and around Milwaukee.
- **Dr. Mary Elizabeth "Libby" Schroeder's** research focuses on the development of curriculum to teach surgeons in LMIC's how to perform basic clinical research. In addition, she is working to evaluate barriers to accessing trauma care in Ethiopia.
- **Dr. Todd Neideen** studies necrotizing soft tissue infections, evaluation of beta blockers in geriatric trauma patients, and medical student perceptions of important residency attributes.
- **Dr. Colleen Trevino** leads research focused on understanding the transition from acute to chronic pain in adult injured patients and developing novel models of holistic multidisciplinary care to prevent chronic pain and psychological distress.
- **Dr. Travis Webb** is leading research related to frailty in the geriatric trauma population and the impact of traumatic brain injury on the elderly patient, as well as a focus on small bowel obstruction in the acute care surgery patient.
- **Dr. Rachel Morris** is funded to focus on developing a prediction model for the triage of the severly injured trauma patients and outcomes in geriatric trauma patients.
- **Dr. Andrew Schramm's** research focus includes sociocultural influences on recovery from traumatic injury, posttraumatic stress disorder, and suicide prevention.
- **Dr. Patrick Murphy's** research is to understand the perspective of patients diagnosed with emergency general surgical conditions and define and measure high-quality of care using traditional and non-traditional outcomes.

- **Continuing Research Education:** Dr. Panna Codner have completed the first year of the MCW CTSI Clinical Research Scholars Program. Dr. Panna Codner has also started in the MS in Clinical and Translational Science program at MCW.

Division of Vascular Surgery

The MCW Division of Vascular and Endovascular Surgery has continued to expand its clinical research activities throughout the Academic Year 2020-2021 by continuing a NIH trial in collaboration with the Division of Vascular and Interventional Radiology, and with multiple aortic device trials in various stages of data collection. Additionally, the division participated in several retrospective studies, vascular device registries, and other device trials.

Dr. Neel Mansukhani has been working with postdoctoral fellow Ayo Olowofela, MD on analyses of outcomes after repair of ruptured aortic aneurysms, a novel machine learning quality improvement project to decrease length of stay after endovascular aneurysm repair (EVAR), and analysis of type 2 endoleak, the most common complication after EVAR. Dr. Mansukhani has taken the leading role in the division in coordinating several medical student and resident efforts on research projects and helping shepherd these through to presentation and publication. Finally, Dr. Mansukhani is the deputy medical director for the Upper Midwest Vascular Network and facilitates collaboration on regional research and quality improvement projects focused on elective and ruptured aortic aneurysm repair.

Peter Rossi, MD, Chief of the Division of Vascular/Endovascular Surgery, as site PI (Principal Investigator) at FH (Froedtert Hospital), led the division to be the top enroller nationally for "A Prospective, Multicenter, Non-Blinded, Non-Randomized Study of the RELAYPRO® Thoracic Stent-Graft in Subjects with Traumatic Injury of the Descending Thoracic Aorta" with Terumo Aortic. Dr. Rossi continues to oversee the GREAT Registry (Global Registry for Endovascular Aortic Treatment Outcomes Evaluation). This registry, sponsored by WL Gore, collects data on Gore vascular grafts utilized by the vascular surgeons at FH. Dr. Rossi is also site PI for Gore's study entitled "Evaluation of the GORE® EXCLUDER® Iliac Branch Endoprosthesis for the Treatment of Common Iliac Artery Aneurysms or Aorto-iliac Aneurysms." In this project, Dr. Rossi oversees the collection of data to assess the outcomes associated with the use of the GORE® ILIAC BRANCH EXCLUDER®, an FDA-approved bifurcated iliac graft.

Vascular/Endovascular Surgery also completed enrollment with Parag Patel, MD, Interventional Radiologist, in the NIH-sponsored study entitled "BEST-CLI." This trial is a randomized, multicenter, controlled trial, comparing the Best Endovascular versus the best Surgical Therapy in patients with Critical Limb Ischemia. National enrollment reached over 1800 patients with MCW as one of the top enrolling sites. The Divisions of Vascular and Endovascular Surgery and Vascular/Interventional Radiology continue to collaborate on several active trials.

Vascular surgeons, Brian Lewis, MD, Kellie Brown, MD, Michael Malinowski, MD, Joseph Hart, MD, Shahriar Alizadegan, MD and Abby Rothstein, MD, are co-investigators on open and accruing Vascular and Endovascular Surgery protocols and continue to author and co-author articles and presentations with other division faculty including former Division Chief, Dr. Gary Seabrook and Charles Edmiston, PhD. Dr. Hart is our regional representative to the Arterial Research Advisory Committee for the VQI. Several of our faculty are also involved in research at the Clement J Zablocki VA Medical Center where they have privileges and conduct research trials.

Contributions to the division's research efforts have also been made by MCW 2020/2021 Vascular/Endovascular Surgery fellows, Simon Fraser, DO and Nathan Kugler, MD. Dr. Fraser is investigating conversion to open aneurysm repair after EVAR in veterans, and Dr. Kugler has published and presented at several conferences. Finally, our research Nurse Coordinator, Beth Weseman, RN, and select medical students are invaluable and remain critical elements to the success of the Vascular Surgery research program.

Division of Surgical Oncology

Section of Breast Surgery

The Section of Breast Surgery includes Amanda L. Kong, MD, MS (Section Chief), Chandler S. Cortina, Caitlin R. Patten, MD, and Tina W.F. Yen, MD, MS. The group has an active clinical, translational and outcomes research program, addressing the treatment and outcomes of both benign and malignant diseases of the breast. Funded health services research related to breast cancer, its treatment and outcomes is performed in affiliation with MCW's Center for Advancing Population Science. Our faculty also collaborate with the basic science faculty at the medical school on translational research projects. In collaboration with the Kern Institute, our faculty are also invested in educational research as well as methods of improving medical education.

As active members of the Cancer Center, our faculty participate in numerous clinical trials sponsored by industry and the National Cancer Institute through cooperative groups, including the Alliance for Clinical Trials in Oncology, NRG Oncology, and ECOG-ACRIN cancer research group. Tina Yen, MD, MS, serves as the institutional principal investigator for the Alliance for Clinical Trials in Oncology cooperative group. These trials examine different ways to improve breast cancer treatment involving new surgical approaches, combination therapies, the delivery of radiation, and new drug agents. In addition, the Breast Surgery Program maintains a multidisciplinary breast clinical research database that is maintained by a dedicated program database coordinator, overseen by Amanda Kong, MD, MS, and is an active participant in MCW's Central Tissue Bank, which stores blood as well as healthy and tumor tissue for research purposes.

Section of Endocrine Surgery

The Section of Endocrine Surgery has a robust research program, active in clinical, translational, and outcomes research, focused on benign and malignant diseases of the thyroid, parathyroid, and adrenal glands. During the 2014 – 2019 academic years, the Endocrine Surgery research program had nearly oral/poster presentations at the national/regional/local level and published >35 peer-reviewed publications and book chapters. During the 2019-2020 academic year, the research program continues to work with MCW medical students and Department of Surgery residents and fellows.

The Section of Endocrine Surgery maintains three prospectively-collected clinical databases (thyroid, parathyroid, and adrenal), which serve as the foundation for the research program. In addition, the Section participates in the American Association of Endocrine Surgeons (AAES) Collaborative Endocrine Surgery Quality Improvement Program (CESQIP), a quality improvement program that allows for collection of longitudinal outcomes specific to Endocrine Surgery. Institutional members of CESQIP include faculty from the Department of Surgery, Division of Surgical Oncology (Endocrine Surgery and Hepatobiliary Surgery) and Department of Otolaryngology, Head and Neck Surgery.

The program is also currently involved in several clinical trials, utilizing new technology in the operating room to minimize postoperative complications and using molecular testing to determine the optimal extent of surgery for patients with thyroid cancer. The Endocrine Surgery program was also one of the fourteen founding members of the Australian-American-Asian Adrenal Alliance (A5), a multi-institutional collaborative on the study of adrenal disease.

Section of Gastrointestinal (GI) Surgery

The Gastrointestinal (GI) Section of the Division of Surgical Oncology's active clinical, translational, outcomes and basic science research program involves six GI surgeons, research scientists and staff, fellows, post-docs, and a myriad of medical students. The GI section has been involved in research projects spanning both benign and malignant diseases of the hepatopancreaticobiliary system (liver, pancreas, gall bladder) as well as sarcomas, peritoneal carcinomatosis, and other gastrointestinal cancers as well as palliative care. This has resulted in multiple national oral presentations and publications.

The section is committed to developing novel investigator-initiated clinical trials. These include the current PANC trial, which is an adaptive clinical trial utilizing biomarkers to guide total neoadjuvant therapy in pancreatic cancer and the SOFT trial, which is a randomized controlled trial comparing neoadjuvant stereotactic body radiation as compared to conventional radiation for pancreatic cancer. The pancreatic cancer trials are the top accruing clinical trials in the cancer center. As active members of the MCW Cancer Center, Surgical Oncology GI Faculty also participate in numerous NIH-sponsored cooperative group clinical trials coordinated by the Cancer Center Clinical Trials Office.

Since its inception the Surgical Oncology Tissue Bank has enrolled over 2800 patients. This bank stores blood throughout a patient's oncologic treatment from the time of diagnosis and throughout treatment. Benign and malignant pancreas, liver and adrenal tissues that would otherwise be discarded at surgery are banked. The bank has been instrumental in a multi-center NIH collaborative examining non-coding RNA for early detection of pancreatic cancer. Specimens have also been utilized the development of a novel platform to perform chemotherapeutic testing on pancreatic cancers ex vivo and to examine the germline variants of uncertain significance in patients with sporadic pancreatic cancer. The bank supports one of five Post-mortem Tumor Donation Program which allows patients to donate their remains for pancreatic cancer research following death. The Tissue Bank collaborates with multiple research collaborations including external collaborations with MIT, Van Andel Institute, University of Wisconsin-Madison, and City of Hope, as well as internal collaborations within MCW.

Clinical databases maintained in GI Surgery Oncology included efforts in gastric, sarcoma, liver, pancreas, and regional therapies. Outcomes research projects and manuscripts are abundant and have been extremely productive. Faculty have contributed to over 26 peer-reviewed publications and 18 book chapters since 2017. Pancreatic cancer research has been presented at 12 national meetings during this time, including the 138th American Surgical Meeting. Furthermore, the clinical program supports infrastructure for innovative quality programs including the development of ERAS pathway following pancreatectomy, longitudinal quality of life surveys for patients with pancreatic cancer, and the implementation of universal genetic testing.

Urology

Biomedical research is a core component of the mission of the Department of Urology. To this end, the Department is actively involved in both clinical and basic science research ranging from self-initiated to industry sponsored trials and single site to collaborative, multi-institutional efforts. Urology residents and fellows are expected to actively participate in ongoing research projects throughout their training.

Current research projects within the Department of Urology include:

Bladder cancer

- Evaluating various measures of oxidative stress associated with Bacillus Calmette–Guérin's (BCG) effect on bladder cancer
- Optimizing immunotherapy in the treatment of bladder cancer
- Outcomes of robotic assisted bladder cancer surgery
- Quality of life after urinary diversion

Prostate cancer

- Use of MRI as a tool in the surgical planning for prostate cancer
- Evaluation of robotic techniques to decrease the morbidity of radical prostatectomy
- Outcomes comparison between open and robotic prostatectomy
- Factors leading to readmission after prostatectomy

Kidney cancer

- Multicenter outcome assessment of robotic partial nephrectomy for large renal tumors

Genital issues/benign prostate disease

- Studying complications of HoLEP (holmium laser enucleation of prostate)
- Outcomes of surgery for buried penis
- Outcomes of surgery for giant genital condyloma

Urinary stone disease

- Outcomes of urinary stone treatment (multicenter study)
- Comparison of 2 different types of lithotripsy (stone disruption) for bladder stones
- Dietary modification in the management of urinary stones in obese patients
- Comparison of different laser fibers with respect to damage to ureteroscopes

Infertility

- Testicular tissue harvesting for research in stem cell isolation/cryopreservation with the hopes of reimplantation after cure
- Genetic testing for evaluation of severe male factor infertility
- Outcomes research for men with male infertility and varicoceles
- Research in characteristics of men undergoing vasectomy

Voiding dysfunction

- Comparison of different injection techniques for injecting onabotulinum toxin (Botox) in the management of neurogenic bladder
- Assessment of patient characteristics in neurogenic bladder patients with recurrent urinary tract infections
- Assessment of adequacy of improvement criteria in predicting long term efficacy of sacral neuromodulation for overactive bladder

Education

- Use of robotic simulators in residency training
- Accuracy of resident surgical case logs
- Familiarity trends in successful urology residency match applicants

Cancer Center

MCWCC is the only academic cancer research center in Southeastern Wisconsin, a distinct region that includes large underserved minority populations with significant disparities in cancer incidence, mortality and outcomes. The MCWCC serves over 2 million residents in a seven-county area, providing the people of Southeastern Wisconsin with access to nationally recognized physician scientists, the latest research-driven treatments, and over 200 cancer clinical trials. The heart of our service area is the city of Milwaukee, the most segregated urban area and 9th-poorest city in the U.S., with 30% of residents living at or below the poverty line. The nearest cancer centers are in Madison and Chicago, 75-90 miles away, making MCWCC the only academic cancer center accessible to these underserved populations. One of MCWCC's top priorities is to address and eliminate cancer disparities in Southeastern Wisconsin, and we are lucky to have a 47-member Community Advisory Board to help direct efforts in this area.

MCWCC has over 250 faculty research and clinical members from five institutions and 24 MCW departments who are aligned within three established Research Programs; Cancer Biology, Hematologic Malignancies & Immunotherapy and Cancer Control & Outcomes. The MCWCC provides members with access to shared research resources – labs, cores, equipment, data, and expertise. These resources are critical to successful cancer research but not usually available to individual researchers because of cost, complexity or lack of space. Some of these resources are labs and equipment; some resources are expertise, knowledge, or access to data. The MCWCC provides eight shared research resources; Bioenergetics, Biomedical Imaging, Biostatistics, Clinical & Translational Research Laboratory, Flow Cytometry, Lymphocyte Propagation Lab, Observational Methods, and Tissue Bank. Helping to direct the science of the MCWCC are thirteen Faculty Research Committees that focus on disease-specific clinical research, in addition to external, internal and community advisory boards.

MCWCC physician scientists treat over 4,000 new cancer cases each year. There are over 200 cancer clinical trials underway, with our researchers funded by over $35 million in peer-reviewed cancer research grants. The clinical cancer programs are housed in the Clinical Cancer Center, where care is delivered in this 340,000 square feet building dedicated to cancer services. This state-of-the-art ambulatory care facility houses multidisciplinary clinics, diagnostic and treatment imaging facilities, operating rooms, the Quality of Life Center, and Breast Care Center. Designated clinical research facilities provide dedicated space for research coordinators, biosampling, and processing, and a Translational Research Unit designed just for patients participating in early phase I/II cancer clinical trials.

An important part of the MCW Cancer Center is the Nicholas Family Foundation Translational Research Unit (TRU). The TRU is a space devoted to early-phase investigator initiated cancer research trials, one of only a few in the nation with the capability to conduct early phase cancer clinical trials in dedicated space with experienced research staff. The TRU was built to accommodate complex and novel cancer treatments and support pharmacokinetic and pharmacodynamic research. The TRU encompasses 4,700 sq ft of space, with 13 infusion bays and a sub-waiting area with room for 2 patients. The TRU is staffed with 10 experienced chemotherapy infusion nurses who have received additional training in the care of patients on early-phase clinical trials. The location within the Clinical Cancer Center provides nearby access to the resources of the entire center, including a dedicated research pharmacy, full laboratory, day hospital and 76-bed dedicated inpatient oncology space. MCWCC is the only center in the state and region to have this type of dedicated unit, making it a unique resource for patients throughout the upper Midwest.

To learn more, visit the MCWCC website at www.mcw.edu/cancercenter

Cardiovascular Center

The Cardiovascular Center (CVC), founded in 1992 at the Medical College of Wisconsin (MCW), is at the forefront of scientific discovery in cardiovascular health and disease, ranking in the top 10 in the U.S. for federal dollars for cardiovascular research in medical schools. Over 32,000 square feet of space is dedicated to over 20 laboratories and housing offices, conference rooms, and equipment cores primarily located on the fourth floors of the Health Research Center (HRC) and Medical Education Building (MEB). The CVC is staffed by full- and part-time personnel who maintain core equipment, coordinate academic research, funding, and community outreach initiatives, and provide support to the more than 165 CVC members from 25 departments and institutes on the Milwaukee Regional Medical Campus.

The CVC's mission is to improve cardiovascular health in southeast Wisconsin and beyond through cutting-edge research, cost-efficient and high-quality healthcare delivery, rigorous training of the next generation of diverse and proficient cardiovascular scientists and physicians, and engaging the community to eliminate disparities in health outcomes.

At the CVC, an emphasis is placed on collaborative, multidisciplinary research centered around our faculty's expertise in thematic areas of research called Signature Programs and Affinity Groups, which are:

Signature Programs:
Atherosclerosis, Thrombosis & Vascular Biology
Cardiac Biology & Heart Failure
Hypertension
Precision Cardiovascular Medicine

Cross-Cutting Affinity Groups:
Cardio-Oncology
Prevention

The CVC is directed by Ivor Benjamin, MD, Professor of Medicine at Froedtert Hospital and MCW, and 2018-2019 President of the American Heart Association, who has over 25 years of experience and expertise leading cardiovascular clinical and research programs. David Gutterman, MD, the Senior Associate Director of the CVC and Distinguished Professor of Cardiovascular Sciences, also brings more than 25 years of experience including 8 years as Senior Associate Dean for Research with broad responsibility over research development and infrastructure. The CVC is also supported by its four Associate Directors: Mary Sorci-Thomas, PhD, Professor of Medicine, who directs Training and Education; Curt Sigmund, PhD, James J. Smith & Catherine Welsch Smith Professor and Chair of Physiology, who directs Team Science; Michael Widlansky, MD, MPH, Northwestern Mutual Professor in Cardiology, who directs Adult Translational Science; and Jeanne James, MD, Professor of Pediatrics (Cardiology); who directs Pediatric Translational Science. Moreover, as an MCW "Green Center", the CVC is also guided by an external scientific advisory board, internal scientific advisory board, and institutional leadership.

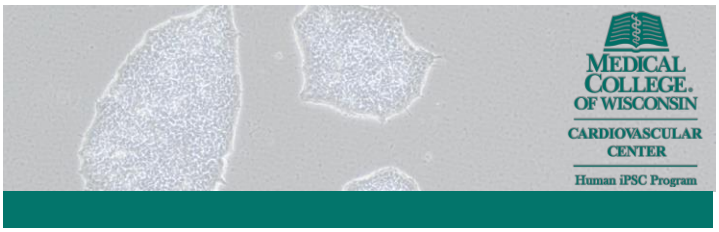
Along with its exceptional leadership, the CVC receives extensive institutional support in addition to a $4 million grant from the Advancing a Healthier Wisconsin Research and Educational Endowment Program, and from philanthropic gifts by the A. O. Smith Foundation, the Michael H. Keelan, Jr., MD, Cardiovascular Research Fund through the Greater Milwaukee Foundation, and the Cullen Family Healthy Heart Research Program, among others. In 2017, the CVC was awarded a $1.6 million postdoctoral training grant from the National Heart, Lung, and Blood Institute (NHLBI), one of only four T32 postdoctoral training programs on campus.

T32 Training Grant:
Building on excellence in cardiovascular research, the CVC's T32 postdoctoral training program, "*Training in Signature Transdisciplinary Cardiovascular Sciences,"* is funded by the NHLBI that provides support for six postdoctoral training slots each year. The grant provides up to three years of training for appointed postdoctoral fellows in the CVC with an MD, PhD, PharmD, or DO degree. Complementary support for trainees is provided by a grant given to the CVC by the A.O. Smith Foundation for the A.O. Smith Fellowship Scholars Program, a program designed to support talented cardiovascular researchers and physicians to overcome the barriers that exist in launching and sustaining a successful research career.

In its first 4 years, the CVC-based T32 training program has been highly successful in training 11 postdoctoral fellows, 36% that belong to underrepresented groups, continuing to work toward our ultimate goal of training the next generation of cardiovascular scientists and physicians, including individuals from underrepresented groups, by incorporating broad-based, personalized, diversity-conscious, supportive, and rigorous training opportunities. Our graduates have published over 20 manuscripts with 100% remaining in academia and almost 75% obtaining federal funding thus bridging their path to independence.

For more information on the training program, which typically has two application cycles occurring in October and March of each year, contact cvc@mcw.edu or visit: www.mcw.edu/departments/cardiovascular-center-heart/postdoctoral-fellowship

Human Induced Pluripotent Stem Cell (iPSC) Program



To advance translational and precision medicine research, the CVC has established the Human Induced Pluripotent Stem Cell (iPSC) Program funded by the Advancing a Healthier Wisconsin Endowment. Over 600 square feet within the center is dedicated to providing quality iPSCs from a matching biorepository, consisting of somatic cells obtained from a multi-ethnic cohort of patients, representative of the region/community in which we serve. The core offers reprogramming of somatic cells into iPSCs, the production of human iPSC-derived myocardial, endothelial, and other cells, and quality maintenance and differentiation services for investigators campus-wide. For services, contact Gracious Ross, DVM, PhD at gross@mcw.edu.

Specialized Services and Infrastructure

The CVC offers its primary members and their trainees and staff access to core facilities including microscopy, imaging, other core equipment, the Cardiovascular Tissue Bank, a quarterly newsletter, weekly seminar notices, funding e-newsletter, conference rooms for meetings and presentations, eligibility for CVC grant awards, and access to the CVC Seminar Series and Trainee Development Seminar Series, which are held on an almost weekly and quarterly basis, respectively, during the regular school year in the CVC's main conference room on the fourth floor of the HRC. CVC members and their trainees and staff are also given many educational and networking activities throughout the year, including the annual CVC Research Retreat.

Last year, the members of the CVC were awarded more than $96 million in total funding, with $50 million being funded by the National Heart, Lung, and Blood Institute of the National Institutes of Health. More than 100 trainees were mentored and more than 500 scientific articles were published in peer-reviewed journals.

For more information, visit our webpage:
http://www.mcw.edu/Cardiovascular-Center.htm

CVC Core Equipment
Axion Microelectrode Array System
Beckman Coulter DU640 Spectrophotometer
Bio-Rad Cell Counter TC-10
Bio-Rad CFX96 Touch Real-Time PCR Detection System, 2 Units
Bio-Rad CFX384/C1000 PCR Detection System
Bio-Rad ChemiDOC MP Imaging System
BMG Labtech CLARIOstar Microplate Reader
BMG Labtech Fluorstar Omega Microplate Reader
Chemical Hood, Built-in
Chromium 10x Single Cell Sequencing System
Li-COR Odyssey CLx Infrared Imaging System
Protein Simple WES Western Blotting System
Tech One Biomedical Services Microm Cryostat
Microscopes & Accessories
Nikon Eclipse 55i
Nikon E600/spot RT
Nikon A1R+ Confocal
Nikon A1R+ Environmental Chamber/Cell Stage
Nikon TE-2000
Computer with Software for Analyzing Nikon Images
Centrifuges & Rotors
Beckman Coulter Ultracentrifuge XPN-100
Sorvall Superspeed RC 6+, 2 Units

MEDICAL COLLEGE OF WISCONSIN

CARDIOVASCULAR CENTER

Year in Review

28 YEARS AS A CENTER

165 MEMBERS WHO ARE RESEARCHERS AND DOCTORS

#1 IN WI FOR FEDERAL DOLLARS FOR CARDIOVASCULAR RESEARCH

OVER **25** DEPARTMENTS/INSTITUTES

ECONOMIC IMPACT IN THE COMMUNITY OF APPROXIMATELY **$211M**

$96M IN FUNDING (TOTAL COSTS)

GENERATING **37%** OF MCW'S RESEARCH INCOME

TOP 10 IN THE US FOR FEDERAL DOLLARS FOR CARDIOVASCULAR RESEARCH IN MEDICAL SCHOOLS

Schools of Medicine	NHLBI
1. Univ of Massachusetts	$138.1M
2. Univ of Pennsylvania	$74.7M
3. Univ of California, San Francisco	$67.6M
4. Columbia University	$62.5M
5. University of MI at Ann Arbor	$62.2M
6. Univ of Pittsburgh at Pittsburg	$60.9M
7. Stanford University	$55.4M
8. Medical College of Wisconsin	**$50.5M**
9. Yale University	$46.8M
10. Northwestern University	$46.8M

OVER **530** PUBLICATIONS IN PEER-REVIEWED SCIENTIFIC JOURNALS

181 FUNDED RESEARCH PROPOSALS

OVER **300** RESEARCH PROJECTS

OVER **40** CLINICAL TRIALS

MENTORED OVER **100** TRAINEES

HOME TO 1 OF ONLY 5 NIH T32 POSTDOCTORAL TRAINING PROGRAMS AT MCW, INVESTING **$1.6M** IN TRAINING

8701 Watertown Plank Rd • Milwaukee, WI 53226 • 414.955.6716
www.MCW.edu/Cardiovascular-Center

Center for Advancing Population Science

The Center for Advancing Population Science (CAPS) develops, tests, and implements innovative strategies for transforming healthcare that optimize quality, value, and cost. Through innovative research, analysis, implementation and impact, CAPS is set to be become a global leader in healthcare transformation.

CAPS focus on population science and global health, enhanced faculty and collaborator recruitment, and a desire to improve community engagement, conducts research on patient care services and related health outcomes, facilitates a supportive environment for new MCW investigators, determines the need for and recruit new faculty in targeted methodologic areas, and sponsors a health services research seminar series for the exchange of ideas.

CAPS Strategic Goals

MCW Strategic Priorities	MCW Strategic Goals	CAPS Strategic Goals	CAPS Metrics & Tactics
Health Starts from Within	Inclusive Excellence	Recruit and mentor a cadre of multi-disciplinary investigators	Inclusive & equitable center practices Increase collaboration opportunities Expand infrastructure for mentoring, coaching
Preferred Choice	Best Quality	Disseminate and implement evidence-based strategies to transform healthcare	Annual State of Science Conference Works in Progress & Grand Round Seminars Publications/Posters/Papers
Accelerate Discovery	Nationally Recognized	Build a cohesive and dynamic research infrastructure that rapidly adapts to the changing environment	Strengthen center research infrastructure Streamline research data & tracking Grant Submissions & Awards
Think Next Gen	Future Healthcare Excellence	Create a pipeline of health services researchers and innovators	Student/Resident/Doctoral Opportunities Center unit activities and collaboration Employment Pathways & Professional Development
Health of Our Community	Redefine Health	Build healthier communities and eliminate inequalities in health at local, national and international levels	Diverse faculty, staff and center membership Community partnerships & Participants served Diverse vendor pilot participation

Center Units

Six center units are organized around a particular approach or content area. Leaders of each unit will help set the CAPS strategic plan and work towards its goals as well as serve as a resource for CAPS by representing their unit to people both within and outside of CAPS. Unit leaders also support existing CAPS investigators and help to identify new core investigators, associate investigators, and trainees. Unit leaders use rigorous research methodology to pursue competitive grant funding and develop the next generation of researchers.

Biostatistics/Health Economics; Global Heath; Veteran Affairs; Population Health; Health Systems Research; Health Disparities/Community Engagement

Health Systems Consulting Service Center – The Health Systems Consulting Service Center aids in the development, design, analysis, and interpretation of quantitative study results. Investigators throughout MCW, Froedtert, University of Wisconsin – Milwaukee, and

Marquette University can use this service to obtain biostatistical support. This service supports CTSI mini-grant population health projects and investigator-initiated projects billed to MCW departments.

Career Development – CAPS is dedicated to creating a pipeline of health services researchers and innovators. This is done through strategic efforts and a supportive environment for students, trainees, and junior faculty to grow. A bi-monthly seminar series is held from September through May each year. Seminars are divided into Grand Rounds where leaders in the field discuss advances in their area of research and describe new innovations, and Works in Progress where junior faculty present a grant they are working on and obtain feedback on their idea from the multidisciplinary team of investigators attending. CAPS support students through summer research opportunities for high school through undergraduate students, support of the medical student Pathway program throughout the year, and service as mentors and advisors for Masters and PhD students in a variety of disciplines. Finally, mentorship within Units and in smaller writing and mentoring teams is available to junior faculty members.

Areas of research focus for the center include:

- **Health Systems Research**, particularly related to the most effective ways to organize, finance, and deliver care, as well as the translation and implementation of research findings into everyday clinical practice.
- **Health Disparities**, focusing on increasing awareness on health disparities in the populations and communities we engage in research and considering the impact of interventions on disparities.
- **Community Engagement**, focused on engaging communities in research through identifying relevant issues to the community, conducting research in collaboration with communities, and evaluating and sharing results with the community.
- **Cancer control and outcomes**, particularly related to breast cancer therapy and survivorship issues and understanding ways in which outcomes may vary for underserved populations, and ways to ameliorate these disparities.
- **Cardiovascular outcomes**, including projects designed to improve care for hypertension, diabetes, and obesity.
- **Surgical care outcomes**, involving outcomes related to breast and spine surgery.
- **Patient-physician communication and medical decision making**, including such diverse populations as pediatric and adult ICU patients and veterans.
- **Patient safety**, consisting of issues related to shift handoffs, resident training, inpatient documentation, and the role of hospitalists.
- **Use of the electronic medical record (EMR),** especially as it relates to communication between the doctor and patient.
- **Maternal Health Outcomes**, including addressing racial/ethnic disparities in material and birth outcomes.
- Social Determinants of Health, including addressing individual and structural factors impacting health outcomes, and incorporating social risk factors into health focused interventions.
- **Measurement of patient-reported outcomes**, including health-related quality of life, with applications in both research and clinical care.

Center for Advancing Population Science (CAPS)
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Center for Biomedical Mass Spectrometry Research

Scope & Mission

The Center for Biomedical Mass Spectrometry Research, founded in 2017 at the Medical College of Wisconsin (MCW), is a collaborative research hub for scientific discovery. We integrate state-of-the-art instrumentation, innovative methodologies, advanced bioinformatics, and unique expertise to promote basic, translational, and clinical research programs. Our goals are to catalyze interdisciplinary research, foster technology development, and provide education regarding the applications of mass spectrometry in biomedical research. Our technologies and expertise are applied to targeted and untargeted analyses of biological molecules including: identification, characterization, and quantification of peptides, proteins, metabolites, and small molecules. With more than 50 established project workflows to choose from, we work together with investigators in a flexible and collaborative model, to apply the most advance methods available in an individualized approach. Ultimately, the MS Center is well-equipped with state-of-the-art instrumentation and recognized expertise that collectively provide a competitive edge for investigators at MCW and partner institutions. To learn more, visit our website to learn more about our capabilities. All projects begin with a consultation with MS Center experts.

To schedule your free consultation, please visit our website. You can also contact us at mscenter@mcw.edu, or Michael Pereckas, Research Associate, at mpereckas@mcw.edu.

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Center for Biomedical Mass Spectrometry Research

Center for Healthy Communities and Research

The Center for Healthy Communities and Research (CHCR) was established to meet the growing need for rigorous scholarship, teaching, and engagement to address health care gaps and advance health equity for underserved and vulnerable populations. The CHCR is an integral part of the department, closely aligned with its affiliated family medicine residency programs and MCW regional campuses. The CHCR is driven by three core commitments that are cornerstones for its work: partnerships, education, and research.

CHCR faculty have a diversity of backgrounds, including sociology, psychology, adult education, anthropology, medicine, and public health. The CHCR also houses strong expertise in qualitative research methods. The CHCR has built a regional and national reputation for research in these areas, with faculty serving as principal or co-investigator roles for numerous internal and extramurally funded awards (over $8M) since 2016.

The CHCR has the following major areas of research activity:

- **Health Equity and Disparities,** examining from a critical sociological perspective the mechanisms by which social institutions perpetuate disparities.
- **Mental Health,** prioritizing the study of trauma among military veterans, and resilience, peer mentoring, and the influence of behavioral health on physical health outcomes.
- **Physical Activity and Nutrition,** focusing on inadequate food access, increasing physical activity in schools, and innovative utilization of farmers' markets for healthy food options.
- **Veterans' Health,** as an emerging area of research excellence focused on examining factors that affect vets' health and intentionally engaging them in research and education.

CHCR faculty and staff develop, implement and evaluate educational courses across the continuum of medical education, graduate and post graduate education. This includes support and sponsorship of primary care research training through the **Academic Fellowship in Primary Care Research**. CHCR faculty and post-doctoral fellows teach and mentor medical students each summer supported by a National Research Service Award from the National Institute on Aging. CHCR faculty also mentor students in MCW's Scholarly Pathways program on longitudinal research and service-learning projects.

For more information about the CHCR, please visit: www.mcw.edu/chcr

For more information about the Academic Fellowship in Primary Care Research, please visit: https://www.mcw.edu/Family-Medicine/Primary-Care-Research.htm

Center for Imaging Research

Our Mission:
The mission of the Center for Imaging Research (CIR) is to unite basic and clinical scientists of various disciplines to further the development and application of imaging in health and disease. Investigators from institutions across the Midwest utilize the resources available within the MCW CIR. Our state of the art facilities and technical support infrastructure provide users with tools required to perform basic and clinical imaging research studies. Investigative projects at the CIR span a wide variety of disease states and topics of technological development.

Services Offered:
The CIR maintains 3 research-dedicated MRI systems, including a 3.0T GE Healthcare Discovery MR750 located in the Froedtert Pavilion, the newest generation 3.0T GE Healthcare Signa Premier located in the MRI annex to the MACC Fund Building, and a pre-clinical 9.4T Bruker Biospec located in the MRI annex.

The CIR is structured to enable the use of MRI in a broad range of research studies. Support is available from staff and faculty level physicists on a fee-for-service model. This support can be used to protocol experiments, develop novel image acquisitions, and assist in image analysis. For pre-clinical work, an animal "drop-off" service is available to aid in the preparation and handling of small animals in imaging studies. With these services, the goal of the CIR is to lower the "barrier to entry" for imaging studies. Ultimately, researchers with questions that can be answered with MRI can use the services of the CIR to tailor an imaging experiment and understand its outcome.

The CIR has an imaging study pilot award funding opportunity. Renewable $5,000 awards are available, and are reviewed and awarded on a rolling basis. Funds from these awards are available for study setup, general physics support, data analysis, and imaging expenses. For application details, please see the CIR webpage: www.mcw.edu/CIR.

The following imaging equipment is dedicated for research use and is available to all funded researchers associated with the MCW CIR:

- GE Healthcare Advantage Workstation with VolumeShare 7.0
- GE Healthcare Discovery MR750 3T MRI
- GE Healthcare Signa Premier 3T MRI
- Bruker 20cm 9.4T pre-Clinical MRI

Contact Us:
Center for Imaging Research
Medical College of Wisconsin
8701 Watertown Plank Road
Milwaukee, WI 53226
414-955-4663

Center for Immunology

The Center for Immunology under the Directorship of Dr. Michael Dwinell, was established in 2018 and built on a strong decade-long informal group known as the Committee on Immunology that spanned investigators at the Medical College of Wisconsin (MCW), the Children's Research Institute and Versiti, Blood Research Institute.

The Center for Immunology combines expertise in basic and clinical immunology to accomplish two goals across MCW:

- Integrate immunological resources around emerging needs in clinical care that will constitute the personalized healthcare of tomorrow
- Coordinate immunological research investment capacity by coordinating Center communications and interactions

The comprehensive Center for Immunology will coordinate the resources, investments and research strengths in immunology to build additional capacity in basic and translational research to enhance patient care and strengthen MCW's connection to the community.

To achieve these goals the Center for Immunology will empower clinicians and basic scientists to collaborate in translational research, to understand immune pathology and pathophysiology, and to develop individualized and effective treatments for our patients. Congruent with these translational goals the Center will streamline the education of tomorrow's physicians so that they are conversant in the use of immune-based therapies and confident in initiating cutting-edge trials with new therapies.

Center for Infectious Disease Research

The mission of the Center for Infectious Disease Research (CIDR), is to enhance research efforts that focus on understanding the molecular mechanisms of pathogenesis related to infection with all types of microorganisms, viruses, fungi or parasites. These efforts also include programs to define host factors contributing to disease resistance or susceptibility, host recognition of foreign materials and the innate and adaptive immune responses following exposure to infectious organisms. Overall, the long-term goals are to integrate basic and translational research for the development of new therapeutics, vaccines and diagnostic tests.

CIDR was established in 2002 as the Center for Bioterrorism and Infectious Diseases (CBID) under the leadership of Dr. Dara Frank, Founding Director. Dr. Frank established a core of highly successful investigators whose research focuses on bacterial pathogens, viral pathogens, and parasites. Dr. Frank also established the highly interactive and collaborative nature and culture of CIDR that persists today. CBID was also dedicated to the set up and maintenance of a state of the art Biosafety Level 3 laboratory and development of a select agent research program. Select agents are those of particular concern from the standpoint of potential use as biological weapons. The name of the Center was changed in 2010 to reflect broadening appreciation for the importance of infectious diseases that are caused by organisms that would be difficult to weaponize.

CIDR remains dedicated to fostering collaboration that will lead to new insights into a number of infectious diseases. These insights are essential to formulating strategies to combat infectious diseases, including vaccines and new therapeutic approaches guided by comprehensive understanding of the pathogenic mechanisms of bacteria, parasites, and viruses.

Please visit the CIDR website at https://www.mcw.edu/Center-for-Infectious-Disease-Research-CIDR.htm to learn more about who we are and what we do.

Center for International Blood & Marrow Transplant Research

The Center for International Blood and Marrow Transplant Research (CIBMTR) collaborates with the worldwide scientific community to advance the fields of hematopoietic cell transplantation (HCT) and cellular therapy (CT). A research collaboration between MCW and the National Marrow Donor Program/Be The Match, the CIBMTR facilitates important clinical research to increase survival and enrich the quality of life for thousands of patients.

The CIBMTR's research arises from a base of collaborative scientific and statistical expertise, a network of >330 centers across the globe, a clinical database containing information from >575,000 patients, and a biospecimen repository containing >175,000 samples. Information from the database, and the support provided by the CIBMTR Coordinating Center to analyze it, have led to the successful completion of hundreds of studies that have significantly impacted clinical practice worldwide. At any given time, the CIBMTR has >200 observational studies and >25 prospective studies ongoing. Since inception, the organization has published >1,500 articles and chapters in scientific publications. In 2020, the CIBMTR generated 89 peer-reviewed publications and presented 63 abstracts at national and international conferences.

The CIBMTR has six major areas of research activity:

- **Clinical Outcomes**. Fifteen international Scientific Working Committees oversee most of the CIBMTR's clinical outcomes research. Each committee focuses on a specific disease, use of HCT or cellular therapy, or complication of therapy. They utilize the CIBMTR's clinical database to answer clinically important questions in a timely manner. CIBMTR data and expertise are also used to address other specific questions in a variety of settings, often in collaboration with other research partners.
- **Clinical Trials**. The CIBMTR supports prospective research to evaluate new transplant and cellular therapies. The Blood and Marrow Transplant Clinical Trials Network conducts multicenter Phase II and III national trials. The Resource for Clinical Investigations in Blood and Marrow Transplantation supports Phase I-III trials, providing investigator support services, survey research, and clinical study management.
- **Immunobiology**. The CIBMTR maintains a repository of paired tissue samples (from donors and recipients, related and unrelated) used in studying the genetic, cellular, and immunologic factors that influence the outcomes of transplantation and cellular therapy.
- **Health Services**. The CIBMTR facilitates studies regarding economic and health-related cost analyses, disparities in and barriers to access, treatment decision making and support, health care utilization, quality and value of care, and survey research.
- **Bioinformatics**. The CIBMTR analyzes genetic data, particularly the major histocompatibility complex; research activities include improving the transplant match algorithm and data standards as well as conducting donor registry modeling.
- **Statistical Methodology**. In conjunction with the MCW Division of Biostatistics, the CIBMTR Coordinating Center not only provides advice and statistical consultation to researchers writing proposals and developing protocols for HCT and cellular therapy studies but also investigates new statistical approaches and techniques for analyzing their data.

The CIBMTR serves as the data repository for the Stem Cell Therapeutic Outcomes Database for HRSA's C.W. Bill Young Cell Transplantation Program. As such, it collects data for all allogeneic HCTs performed in the US. The goal is to make blood and marrow transplants available to all who need them and to increase the safety and effectiveness of HCT. The CIBMTR also collaborates on the NHLBI-funded Cure Sickle Cell Initiative to accelerate promising genetic therapies to cure sickle cell disease.

Center for Microbiome Research

What Do We Do?

The Center for Microbiome Research (CMR) facilitates collaborative research, provides specialized research resources, and promotes education. A microbiome is defined as the totality of microorganisms and their collective genetic material present in or on the human body or in another environment. This ecological community consists of bacteria, viruses, fungi, yeasts, and protozoa. Each body site has a distinct microbiome, but the vast majority of the microbiota reside in the GI tract. The precise composition of a physiological microbiome is affected by host diet, age, genetics, exposure to drugs, and other environmental factors. Disrupted microbiomes have been correlated with a number of disease states including obesity, diabetes, asthma, eczema, heart disease, celiac disease, colitis, neuropsychiatric disorders, and some cancers.

Benefits:

- Collaboration with MCW, CHW & BRI investigators
- Gnotobiotic Core Facility (GCF) resource
- Training and assistance in biota-focused sample collection, processing & sequence coordination
- Invited speaker seminar series, journal club, & bioinformatics workshops

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Center for Microbiome Research

Microbiome-Focused Services Offered

- Consultation: Study Design & Funding Applications
- Sample Collection & Processing specific to microbial targets
- Gnotobiotic Core Facility: Axenic and gnotobiotic rodent husbandry & experiments, including choice of isolators or iso-caging as appropriate for your study.
- Bioinformatics & Biostatistics support and training

Contact Us:

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CRI Wing, TBRC, 3rd floor bay, #C3368; Email for an appointment
https://www.mcw.edu/Center-for-Microbiome-Research.htm

Center for Neurotrauma Research

The Medical College of Wisconsin recently launched the Center for Neurotrauma Research (CNTR) with the Department of Neurosurgery. The CNTR's multidimensional mission is to advance the science of neurological trauma and related diseases, enhance the translation of brain and spinal trauma research into clinical care innovations, foster the professional development of future scientists, and improve the health of communities throughout the region and state. Within MCW, the CNTR functions as a collaborative hub for neurotrauma research and will create a synergistic collaboration with other MCW Centers such as the Comprehensive Injury Center, Neuroscience Research Center and the Center for Imaging Research.

The CNTR builds upon the successful track record of the neurotrauma research program in the Department of Neurosurgery spanning more than 25 years, including dramatic growth over the past 10 years. The creation of the CNTR reflects MCW's scientific progress in this field and the program's current standing in the international neurotrauma research community. The CNTR is co-directed by Shekar Kurpad, MD, Sanford J. Larson Professor and Chair of Neurosurgery; and Michael McCrea, PhD, Professor of Neurosurgery, Eminent Scholar, Vice Chair of Research and Director of Brain Injury Research.

Spinal Cord Injury Research

Spinal Cord Injury (SCI) is a relatively frequent event, with estimates suggesting that 12,500 new cases of SCI occur every year in the US alone. In the US, approximately 276,000 persons live with SCI, which has a huge impact on their lives and families, as well as tremendous socioeconomic and medical costs. Additionally, approximately 500,000 persons in the US are living with non-traumatic SCI, brought on by degenerative diseases, tumors, and other causes.

The current theme in SCI research is interdisciplinary cooperation with a strong emphasis on a multi-pronged solution to increase functional recovery. The Department of Neurosurgery is conducting research in diagnostic, interventional, and therapeutic areas of SCI. Our researchers are examining Diffusion Tensor MR Imaging of traumatic SCI and of cervical myelopathy, giving clinicians more information about prognosis at earlier time points. We are investigating the mechanisms that contribute to secondary tissue damage tissue damage following SCI with the aim to reduce this damage and thereby improve functional outcome. The Department of Neurosurgery is also involved in clinical trials investigating stem cell intervention in SCI patients.

Traumatic Brain Injury Research

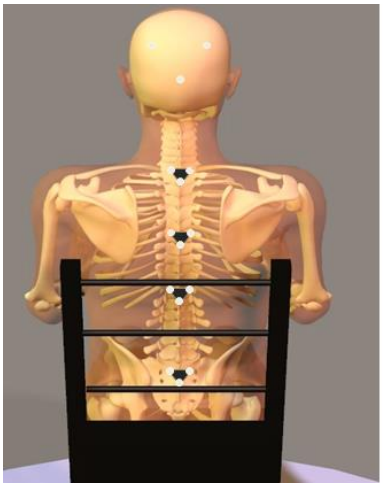
Traumatic Brain Injury (TBI) is a significant public health problem with national estimates of TBI in the United States range anywhere from 1.4 million to 4 million brain injuries per year, depending on the study and methods used to define and include cases. About 75% of TBIs that occur each year are concussions or other forms of mild traumatic brain injury (mTBI). The Brain Injury Research Program was established in the Department of Neurosurgery in 2011 and focuses on investigating the acute and chronic effects of traumatic brain injury (TBI). With funding from the Department of Defense, National Collegiate Athletic Association, the National Institutes of Health and other sources, current research employs basic and applied methods to study civilian, military and sport-related brain injury. Ongoing projects focus on understanding individual differences in TBI recovery, refining TBI outcome measurement, investigation of advanced multi-modal MRI techniques, identifying the acute effects of mTBI on brain biochemistry and physiology using blood biomarkers, and determining the short- and long-term effects of mTBI. The Brain Injury Research Program is also involved in various large scale national efforts to study TBI, such as the NCAA-DOD CARE Consortium, TRACK-TBI, and the TBI Endpoints Development Initiative.

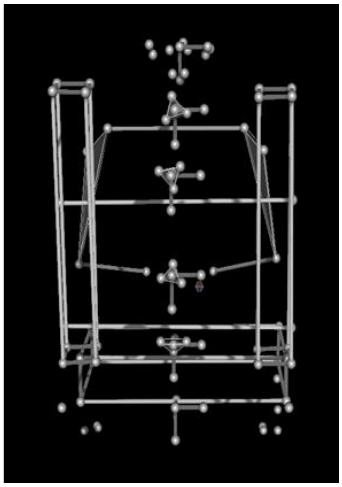
Head and Spine Biomechanics

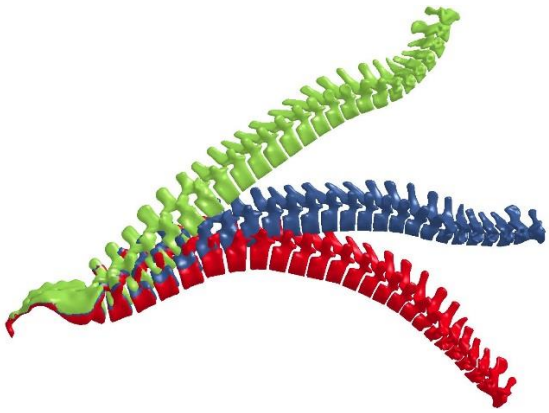
One of the longest running research programs in the Department of Neurosurgery has focused on head and spine biomechanics, with emphasis on trauma and disease. This research area brings together engineering scientists specializing in biomechanics and neurosurgeons to determine how the spine and the head-neck complex are compromised in traumatic events and through disease progression. Current efforts in this area include: examination of spinal trauma in underbody military vehicle blast events, development of lumbar spine injury criteria in vehicle and other types of crashes, comparison of available artificial cervical discs and their viability in active military personnel, investigation of head supported mass and the effects of wearing advanced combat helmets for prolonged periods of time, and the development of spine injury criteria for female military personnel.

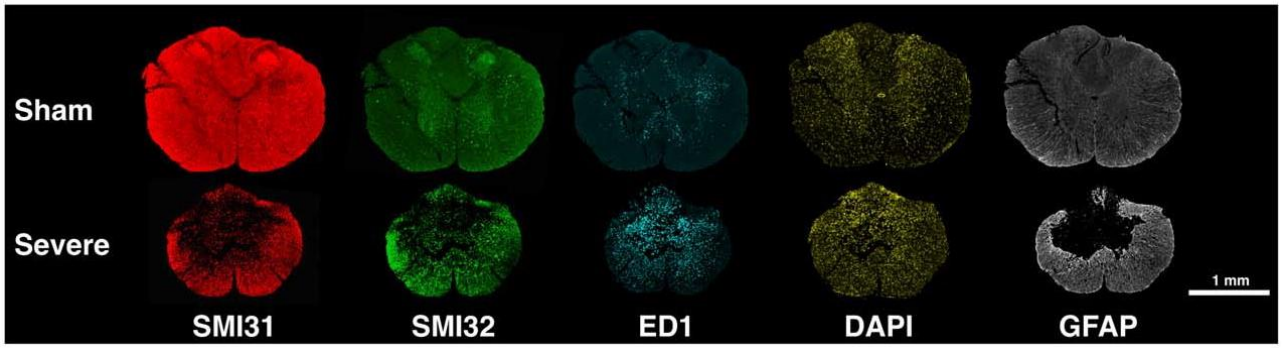
Patient Specific Modeling

Surgical Intervention in the spine to optimize neurologic function has a measurable effect on the biomechanics of the spine with possible neurologic sequelae. In general, current intervention and treatment plans are based on rough estimates of outcomes, primarily based on results of clinical trials. One explanation for variation in outcome is differences in local anatomy between patients. Personalized finite element (PFE) modeling is the development of accurate computer models that use patient specific data. Researchers in Neurosurgery are working to develop and validate a clinician friendly tool that can perform patient specific pre-clinical evaluations to aid with the treatment planning process.









Center of Systems Molecular Medicine (CoSMM)

The Center of Systems Molecular Medicine (CoSMM) is an intellectual incubator for research and project development in molecular systems medicine.

Molecular systems medicine is an emerging discipline that is rooted in the recognition that humans are molecular systems. Humans are molecular systems in which molecules interact to take on emergent properties in the context of cells and organ systems. One must understand humans as molecular systems to understand human biology, health, and disease.

The CoSMM membership is open to any MCW faculty who is involved or interested in molecular systems medicine research or practice. CoSMM currently has 35 faculty members from 12 departments and 6 divisions across MCW. CoSMM provides innovative venues for scientific interactions.

CoSMM is the intellectual home to several standing or extramurally funded programs, including Program for Medicine and AI Research (MARs), Dynamic Systems Modeling Program, a recently completed, AHA-funded center program on the basic, clinical, and population sciences of the epigenomics of hypertension, and an NIH-funded Program Project on Genetics and Epigenetics of Blood Pressure Regulation.

Visit our website for more information: http://cosmm.org/

Children's Research Institute

Children's Research Institute represents the investment of Children's Hospital of Wisconsin in pediatric research. The Children's Research Institute (CRI) advances state-of-the-art pediatric health care through translational research programs designed to find life-saving discoveries, interventions and cures for the diseases that affect children. Additionally, our researchers are studying ways to improve the quality of life for children living with chronic diseases. Investigators are involved in nearly 1,000 active clinical research studies, and pediatric researchers have approximately $29 million in extramural funding.

The CRI currently has numerous cores and shared services to help pediatric investigators, including:

- BioBank and Analytical Tissue Core
- Histology
- Confocal Imaging
- Flow Cytometry
- Pediatric Translational Research Unit
- Quantitative Health Sciences (Biostatistics)
- Grants Development Office

For more information on the cores and how their capabilities can enhance your research, contact Bill Sweeney at 955-5773 or Nick Kampa at 955-2339.

Children's Research Institute is organized in Research Units to promote team science. Research Unit Leaders are charged with strategically growing and advancing science in their disciplines through programmatic development and collaborative efforts. The CRI Research Units are:

- Developmental Genetics & Genomics
- Infection, Inflammation and Immunity
- Cardiovascular and Lung Development
- Patient-Centered Research.

Examples of research awards for ongoing CRI investigations include:

- Ulrich Broeckel, MD, professor of Pediatrics at MCW and a research unit leader of the CRI was awarded a $3 million dollar NIH grant "Characterization and Genetics of Kinase Inhibitor toxicity in iPSC-derived cardiomyocytes"
- Amanda Brandow, DO, professor of Pediatrics at MCW and CRI member was awarded a $2.7 million dollar NIH grant "The Inflammatory Index as a Biomarker for Pain in Patients with Sickle Cell Disease"
- Amy Drendel, DO, professor of Pediatrics at MCW and CRI member was awarded a $2.9 million dollar NIH grant "The Effect of Emergency Department and After-Emergency Department Analgesic Treatment on Pediatric Long Bone Fracture Outcomes"
- Martin Hessner, PhD, professor of Pediatrics at MCW and a research unit leader of the CRI was awarded a $2.7 million dollar NIH grant "Reducing innate inflammation in new onset T1D with Lactobacillus plantarum"
- Michael Lawlor MD PhD, professor of Pathology at MCW and CRI member assumed the lead PI role for a $1.78 million NIH grant "Developing Nicorandil and Companion Biomarkers for DMD Cardiomyopathy Therapy"
- Janette Strasburger, MD, professor of Pediatrics at MCW and CRI member received a $2.4 million dollar NIH award titled "Fetal Electrophysiologic Abnormalities in High-risk Pregnancies Associated with Fetal Demise"
- Rosemary White-Traut, PhD, RN, FAAN, Children's Director of Nursing Research and CRI member, was awarded a $3.1 million NIH multicenter R01. She will study implementation of H-HOPE, a novel developmental behavioral intervention for preterm infants.

Children's Research Institute researchers have also received recent funding from several local and national foundations including American Diabetes Association, American Cancer Society, American Heart Association, Cystic Fibrosis Foundation, Lillian Goldman Charitable Trust, MACC fund and the W.M. Keck Foundation. CRI researchers also serve as investigators in clinical trials sponsored by Children's Oncology Group and various industry sponsors.

Clinical & Translational Science Institute

Clinical & Translational Science Institute
of Southeast Wisconsin

The Clinical & Translational Science institute of Southeast Wisconsin (CTSI) is dedicated to transforming the biomedical research enterprise in southeast Wisconsin to advance patient care and education. The 8 member organizations, the Medical College of Wisconsin, Marquette University, the Milwaukee School of Engineering, University of Wisconsin-Milwaukee the BloodCenter of Wisconsin, Children's Hospital and Health System, Froedtert Hospital, and the Clement J. Zablocki VA Medical Center, create a borderless, synergistic research enterprise that accelerates the translation of research discoveries into new, innovative medical treatments.

The CTSI serves as a nexus for services that support clinical and translational research, including:

- The Faculty Collaboration Database fosters collaboration between the CTSI member institutions through detailed faculty profiles.
- Biomedical Informatics supports the collection and management of data from CTSI supported protocols, offers image de-identification services, and is the clearinghouse for access to clinical data through the data warehouse.
- Statistical support for investigators on study design, data management, data entry, and statistical software usage and analysis
- Cores Search – A centralized database of core facilities and technical expertise available at MCW and partnering institutions
- Clinical Trials Office (CTO) – The MCW CTO is a central resource available to investigators to facilitate implementation of clinical studies and trials. The CTO operates at MCW, CHW and at our partner institutions in Greater Milwaukee area to provide fully trained study coordinators who assist with all aspects of clinical trial implementation, including but not limited to, IRB submissions, budget and contract negotiations, recruitment of patients into trials and any other activity required for completion of research protocols. We also provide assistance with IND/IDE applications, study monitoring and audit, OnCore implementation and educational programs such as BootCamp for new research staff.
- Translational Research Units (TRUs) – CTSI has three TRUs: the Adult TRU at Froedtert Hospital, a Pediatric TRU at Children's Hospital of Wisconsin, and an Adult/Geriatric TRU at the VA Hospital. Research support includes nursing care for research participants, Boinutrition and Body Composition Cores, Exercise Physiology Lab, Pediatric Echocardiography Core Lab, Sleep Lab, and a Translational Cardiac and Vascular Function Unit.
- CTSI's website serves as our virtual portal. All information related to our mission, from educational to funding opportunities and clinical research resources to workshops and conferences is located on the site. Membership is required to access CTSI resources. Please join: ctsi.mcw.edu/join

The CTSI supports and promotes efforts to enhance multidisciplinary collaborations within our institution and with others, including:

- Collaboration consortia with UWM, MU and MSOE to focus on administrative, informatics, educational, and project/program initiatives
- Virtual Community with online tools for investigator collaboration (web conferencing, group document sharing, virtual white board, instant messaging, etc.)
- Common IRB – one set of forms and one meeting for multi-site studies with area academic collaborators (MU, UWM, MSOE)
- Shared research facilities, staff, other resources
- Infrastructure for promoting translational research that includes the community as active partners (community based physicians, advocacy groups)

The CTSI funds innovative, multidisciplinary programs that advance clinical and translational research, including:

- Clinical and Translational Pilot Grants for collaborative teams of researchers
- Core support for facilities conducting research in novel methodologies
- Infrastructure support for services that promote clinical and translational research
- Support for the enhancement of technology transfer services and expertise
- Co-funding grant opportunities with *Advancing a Healthier Wisconsin*

The CTSI provides training opportunities that will prepare individuals to function effectively on multidisciplinary research teams:

- Mentored Clinical and Translational Research Awards (KL2)
- MS degree in Clinical and Translational Sciences
- PhD in Basic and Translational Science
- PhD and MS in Clinical and Translational Rehabilitation Health Science at Marquette University, Jointly sponsored with CTSI
- Clinical Research Scholars Program
- Lecture series on Grant Preparation, Biostatistics, and Collaborative IRB Training Initiative (CITI)
- Workshops on training human research team members on basic knowledge necessary to conduct research safely, ethically, and efficiently

For more information about CTSI, please visit our website at https://ctsi.mcw.edu/

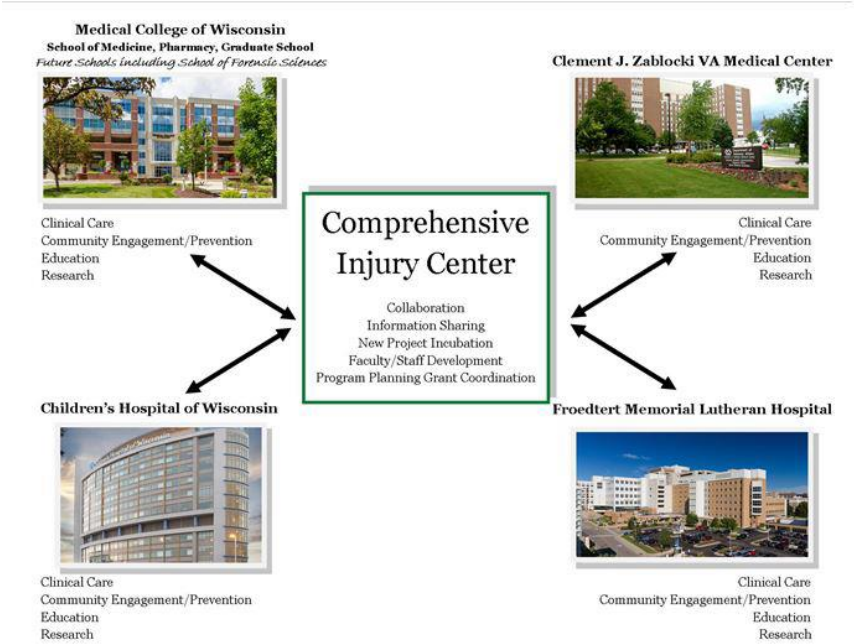
Comprehensive Injury Center

The mission of the Comprehensive Injury Center (CIC) is to create a platform to engage campus and community partners in the advancement of injury control and prevention science. The CIC is particularly focused on the public health model of prevention, focusing on injury, violence, and suicide. The CIC will build on the history of the Injury Research Center as well as the strengths of our faculty and staff who work in many sectors across campus to advance all four missions of the Medical College of Wisconsin with a focus on injury control and prevention.

The goals of the CIC are to:

- Advance injury prevention and control science by facilitating, conducting, and disseminating interdisciplinary injury prevention and control **research** that makes new discoveries in injury prevention, acute care, and rehabilitation;
- Catalyze, leverage, and advance the value of our Level I Trauma Centers by translating research into **clinical practice** by partnering with faculty and staff to advance the care and rehabilitation of the injured patient through discovery, translation, and training, as well as contribute to efforts to maintain national and state-level trauma verification, which require advanced care and sustained research and prevention efforts;
- Utilize and leverage our campus resources including our experienced faculty and staff to **train** the next generation of injury prevention and control researchers, practitioners, and educators by developing, implementing, and evaluating multi-disciplinary educational opportunities; and
- Prevent injury, suicide, and violence in vulnerable and underrepresented populations through strong **community** partnerships.

The CIC will serve as the convening body for ongoing injury prevention and control work at our two Level I Trauma Centers, the Medical College of Wisconsin, and the VA Medical Center, facilitating interdepartmental partnerships and providing a platform for collaboration. This will enhance both the breadth and depth of the advances that can be made by leveraging talent and investments that exist across this campus as well as become a beacon for attracting new talent and investments to our campus.



Genomic Sciences & Precision Medicine Center

Since 2017, the MCW genomics center has continued its transformation into the **Genomic Sciences & Precision Medicine Center (GSPMC)**—a robust family of specialized yet interconnected Precision Medicine Laboratories with the ***Mission*** *to prevent, diagnose, and treat diseases, as well as improve the wellness of our patients and the community through scientific investigations and their rapid translation to the medical practice*. All efforts strive to achieve the Center's ***Vision*** *to provide educational, clinical, and research support infrastructure to the Milwaukee Regional Medical Center, establishing MCW and its partnering health care providers as the premier Precision Medicine provider in the state of Wisconsin and one of the top in the nation*. Core to realizing this vision is the critical role of research, wherein the GSPMC will arm MCW researchers with the advanced science necessary to increase funding and establish the Institution as a national leader in Precision Medicine research.

Modernized Precision Medicine Laboratories to Enable Research and Clinical Practice:
The GSPMC's Precision Medicine Laboratories (PML) boast **over 40 precisely-recruited, expertly-trained laboratory leadership and staff**, who enable an expansive and diverse menu of services with **over 300 clinical, translational, and basic science research assays** and, through the constant evaluation, reconstruction, and maximization of infrastructure, equipment, technology, and project management, have created **a capacity of over 3 million samples a year**. Continuous development of assays, methods, and services is an ongoing, Center-wide effort. Presently focusing these development efforts on research-enabling assays and services in the areas of genomics, epigenomics, pharmacogenomics, microbiome, data science, and undiagnosed and rare diseases, these offerings are scheduled to be fully developed by 2022. In FY19 alone, GSPMC completed nearly **400 projects** for **56 different PI's** in **18 different MCW departments**, and the number of projects completed in FY20 is expected to increase significantly.

The aggressive development and offering of services require the following matrix of Precision Medicine Laboratories and Units:

- Germline Sequencing Laboratory
- Somatic Molecular Oncology Precision Medicine Laboratory
- Epigenomic Laboratory
- Research and Development Laboratory
- Bioinformatics Research & Development Laboratory
- Functional Validation Laboratory
- Precision Medicine Simulation Unit for New Methods of Interpretation of Genomic Information

Robust Bioinformatic and Data Modeling Research, Development, and Services:
In order to expand the reach of its services and collaborative network, the GSPMC continues to grow its bioinformatics workforce, with **5** active recruitments alongside a present headcount of **15** (**6** PhD-level, **4** Masters-level, and **2** Bachelors-level bioinformaticians as well as **2** IT managers and **1** software engineer). This **engine of Bioinformatics** is at the heart of these "connector" service lines that are enhancing research, translation, and patient care.

Services:

The GSPMC offers whole exome and genome sequencing as well as many additional services, including RNA-Seq, ChIP-Seq, RRBS, and 10x Genomics Single Cell sequencing. In the field of precision diagnostics and therapeutics, the PML offers assays in pediatric and adult solid tumors, liquid biopsies, and myeloid diseases. The Center also provides robust bioinformatics, quality control, and validation for all assays and will work with investigators to develop custom research and translational sequencing analysis.

Facilities:

The GSPMC occupies a 20,000 square foot facility on the 5th floor of MCW's Health Research Center. These facilities have modern design, state-of-the-art equipment, and expert personnel to allow the efficient implementation of next generation sequencing methodologies to Cancer Genomics, Non-Cancer Clinical Genomics, Pharmacogenomics, Epigenomics, Molecular Pathology, and Rare Diseases.

Our Technology:


Illumina NovaSeq 6000


Illumina HiSeq 2500


Illumina MiSeq


Life Technologies QuantStudio 12k Flex


Pac Bio Sequel


PerkinElmer Sciclone G3 NGSx


10x Genomics


Life Technologies GS Prime


Biocartis Idylla

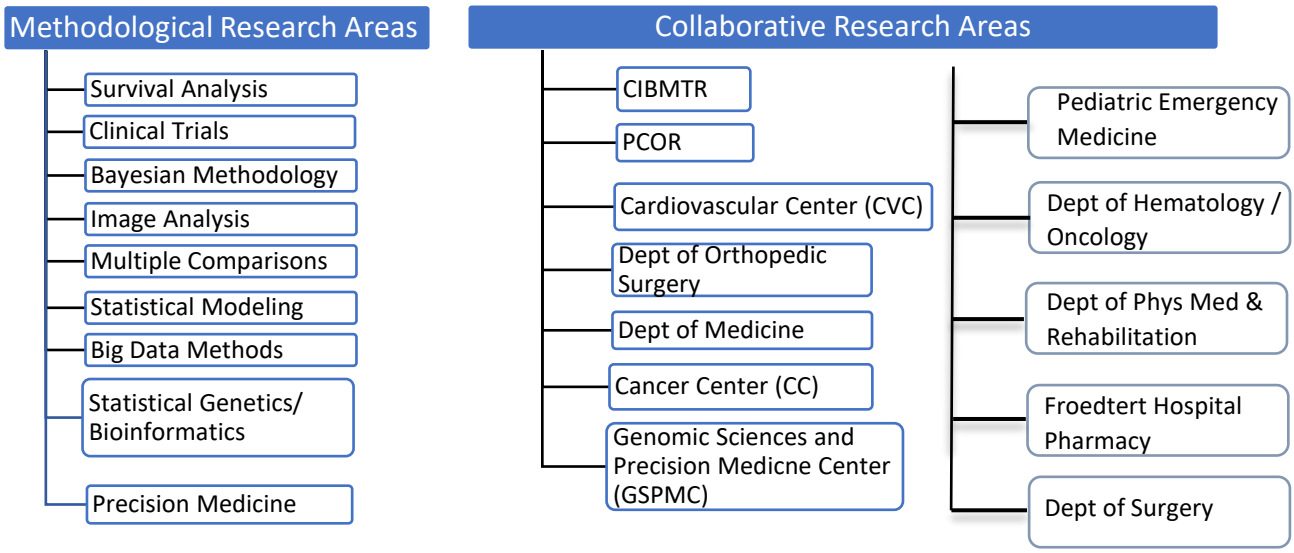

PerkinElmer Chemagic 360


Nanostring

Institute for Health & Equity

Biostatistics Consulting Service

The Division of Biostatistics is part of the Institute for Health and Equity at the Medical College of Wisconsin. The Division's faculty, staff, and students are dedicated to providing basic biostatistical support for biomedical researchers. The Division focuses on three missions: *Methodologic research* into novel techniques for analyzing biomedical data, *Collaborative research* with biomedical researchers such as through the Biostatistics Consulting Service, and *Education* including a PhD program in Biostatistics and other training opportunities.



Research Accomplishments & Activities:
In 2017, the Division of Biostatistics helped bring in over $152 million dollars to the Medical College of Wisconsin from various grants they were included on. In calendar year 2017, the Division published 14 methodological papers that appeared in the statistical literature either online or in print. The Biostatistics Consulting Service collaborated on 430 projects which resulted in 73 Publications. Of those 430 projects, 70 were grant preparation.

Research Support Services Available:
The Biostatistics Consulting Service can handle projects requiring expertise in any area of statistic, such as:

- Sample size determination
- Grant proposal preparation
- Assistance with study design
- Help with funding proposals
- Modeling
- Randomization
- Design of clinical trials
- Analysis of experimental data
- Statistical graphics
- Interpretation of results
- Help with data management
- Assistance with manuscripts

Useful Links:
Division of Biostatistics websites
Biostatistics Faculty
Biostatistics MCW YouTube Page

Contact Us:
Jennifer Ward
jward@mcw.edu | 414-955-7439

Center for Bioethics and Medical Humanities

The Center for Bioethics and Medical Humanities (CBMH) has pursued a variety of interdisciplinary research and scholarly activities since its establishment in the early 1980s. This commitment to research and scholarship continues today and will be a part of the CBMH's future endeavors. Past research activities and scholarship by CBMH faculty have addressed a wide range of bioethics issues, including discovery and dissemination of new knowledge and best practices for addressing and managing the ethical concerns raised in research and clinical application of new genetic technologies; patient refusal of recommended treatment in the emergency department; responses to law enforcement demands of health care personnel, comparing clinical consent and research consent; political authority in a bioterror emergency; vaccination and objection; and, disabling cardiac devices.

Currently, CBMH faculty are engaged in research aimed at developing a conceptual framework for health equity, analyzing ethical implications of contributing factors and interventions to address health disparities, constructing a flexible curriculum for community engaged research as an alternative to CITI training and also creating simple, strong consent translation policies; examining the attitudes and personal expectations concerning psychiatric advance directives of stakeholders; and, examining the ethical, legal/regulatory and social issues arising from the use of neuroimaging biomarkers as a new diagnostic tool for Alzheimer's Disease in asymptomatic individuals.

CBMH faculty provide research ethics consultation services to investigators before, during, and after engaging in research activities. CBMH faculty and staff also serve as members and leaders of a number of Froedtert and the Medical College of Wisconsin institutional review boards.

Faculty Scholarly Expertise

- **Arthur R. Derse, MD, JD**, *Professor and Director* – Informed consent; decision making capacity; medical futility; ethics in emergency medicine; legal issues in end of life care; ethics and humanities in medical education; health care ethics committees and ethics case consultation.
- **Mary Homan, MA, MSHCE, DrPH**, *Assistant Professor* – Pediatric ethics; public health ethics; social justice; vulnerable populations; health equity.
- **Fabrice Jotterand, PhD, MA**, *Associate Professor* – Neuroethics; ethical issues in psychiatry and mental health; the use of neurotechnologies in psychiatry; medical professionalism; neurotechnologies and human identity; and bioethics and moral/political philosophy (justice and health care).
- **Cynthiane Morgenweck, MD, MA**, *Associate Professor* – Ethical issues and the surgical experience; informed consent; clinical trials and placebo surgery; treatment limitation during procedures, including use of cardiac devices; spirituality in medicine; and ethics case consultation.
- **Ryan Spellecy, PhD**, *Professor* – Research ethics and scientific integrity; community engaged research ethics, informed consent in research; advance directives; psychiatric advance directives; ethics and mental health care; pediatric ethics; exception from informed consent in emergency research.
- **Julia A. Uihlein, MA**, *Assistant Professor* – Humanities in medical education; ethical issues in pediatrics

Division of Epidemiology

The Division of Epidemiology is comprised of seven faculty members and thirteen staff members, along with the PhD in Public & Community Health and Master's in Global Health Equity education programs. Members of the Division engage in a wide variety of research and education activities and collaborate with a multitude of internal and external partners, both locally and globally.

- **Laura Cassidy, MS, PhD,** Professor and Director of the Epidemiology Division and Founding Director of the MS Program in Global Health Equity in the Institute for Health and Equity. She has expertise in pediatric trauma, clinical research, community health, health disparities and global health. She is the MCW PI of the Great Lakes Native American Research Center for Health (GLNARCH) - Expanding Community and Academic Partnerships. As part of NARCH she is also the PI of an NIH funded grant, Building a Menominee-Centric Trauma Resilience Model that measures adverse childhood experiences and resilience in middle and high school students at Menominee Indian High School. She is also funded by the Childress Institute for Pediatric Trauma to lead a national initiative to create a smartphone app, pediatric trauma pre-arrival checklist for trauma centers. As one of the PI's of the AHW Redirect grant, she leads a team that analyzes citywide data on social

determinants of health and academic achievement in Milwaukee Public School students. Her global health projects include measuring early childhood development in Uganda using the Malawi Developmental Assessment Tool (MDAT), barriers to immunizations in Ugandan children and depression in young mothers in Uganda.

- **Kirsten Beyer, MPH, PhD, MS:** Dr. Beyer's current research focuses on the impacts of neighborhood environmental characteristics such as residential racial segregation and green space on cancer outcomes, particularly through pathways that include stress, time spent outdoors, social interaction, and food and physical activity behaviors. Dr. Beyer's work includes disease mapping, social and spatial epidemiology, and mixed methods approaches that aim to identify spatial patterns of disease and injury and understand the complex human-environment processes that create them. Her goal is to conduct research that leads to the development of community-based interventions and policies to reduce health disparities. Her primary research project (NIH R01CA214805) is focused on the contemporary problems of institutional racism and residential racial segregation and investigates whether these social structures contribute to the magnitude of racial and ethnic breast cancer survival disparities. The project uses a community engaged research framework that draws upon existing partnerships with community organizations in Milwaukee, WI, which often tops the list of America's most segregated cities.

- **Matt Dellinger, MS, PhD:** Dr. Dellinger has collaborated with ITCM and ITFAP on fish consumption outreach since 2004 and is a recognized researcher in the Great Lakes region. He a co-investigator and co-director of the Great Lakes Native American Research Center for Health (GLNARCH) Community Scientific Advisory Committee and the Bemidji Area Environmental Public Health Advisory Committee. He has worked extensively with Native American youth education programs through digital storytelling and art, combining academic research and cultural perspectives. His current initiatives include: digital storytelling as a tool for exposure reduction to toxic, GLNARCH outreach, and adapting mobile technology to improve environmental health literacy. He currently has an R01 through NIEHS entitled "Gigiigooinaan (Our Fish): A New Advisory to Promote Anishinaabe Health and Wellness"

- **Julia Dickson-Gomez, PhD:** Dr. Dickson-Gomez studies HIV prevention among drug users in the United States and El Salvador and is also interested in the influence of structural factors on HIV risk. Her research explores the effects of housing policy on drug users' access to housing, variations in housing status and housing options of drug users, and levels of HIV risk related to these factors. Dr. Dickson-Gomez's work also explores macro- and micro-social contexts of crack use and HIV risk in communities in El Salvador. Her work develops and evaluates the impact of structural and multi-level interventions in the U.S. and Latin America. Currently, Dr. Dickson-Gomez is leading a three-state study that examines the effects of state law and policy on illicit opioid users and their transition to the use of heroin. She has three international projects in progress, two in Uganda and one in Tanzania, exploring the informal settlements of each county and constructing a buprenorphine intervention for opioid users in Uganda. She's also the MCW lead for the Great Lakes Node of the Clinical Trials Network and has started the Substance Use Working Group.

- **Constance Kostelac, MS, PhD:** Dr. Kostelac joined MCW in 2019 with a background in criminal justice research and analysis. Her current work primarily focuses on violence and overdose prevention, with a lens to the importance of understanding and addressing demographic and place-based disparities. Dr. Kostelac provides training and technical assistance to multi-disciplinary Overdose Fatality Review (OFR) teams across Wisconsin. She directs the Milwaukee Homicide Review Commission as well as DataShare, an integrated system connecting data across sectors including public health, public safety, education and others. Most recently, she is the lead research partner for a new project in Milwaukee County focused on identifying overdose trends and developing prevention opportunities with funding from the federal Bureau of Justice Assistance (BJA), Comprehensive Opioid, Stimulant and Substance Abuse Program (COSSAP).

- **Mallory O'Brien, MS, PhD:** Dr. Mallory O'Brien is the former Founding Director of the Milwaukee Homicide Review Commission (MHRC) and DataShare, an integrated data system for Milwaukee, linking public health, public safety and education data to improve the lives of Milwaukee residents. Dr. O'Brien participates in death reviews and conducts trainings across the country on these reviews. She is working on a variety of research projects on violence prevention and firearm use funded by both federal agencies and private foundations. Dr. O'Brien is using her extensive experience to partner with the State of WI and at the federal level to develop opioid overdose reviews and sexual assault reviews.

- **Liliana E. Pezzin, PhD JD:** Dr. Pezzin is an economist specialized in Econometrics and Public Finance, with a long-standing interest in issues related to healthcare delivery, its measurement, antecedents, and consequences. A significant part of her early work centered on the economics of aging, with a special focus on the interplay between public policy and family

decisions regarding living and caregiving arrangements of older persons, a field that enabled her to explore, both theoretically and empirically, the notion of public policy as a means to influence family dynamics and potentially overcome inefficiencies in the provision, cost, and quality of post-acute and long-term care. Through a fascination with economics applied to health, she became interested in outcomes research, particularly the comparative effectiveness of different care settings and medical treatments. Understanding the effectiveness of health care often requires the use of advanced methods of causal inference applied to carefully designed study experiments. Funded by NIA, NCI, NHLBI, VA, and other federal agencies, she has used national surveys, prospectively-collected observational data and health insurance claims to examine the effectiveness and cost-effectiveness of alternative public policies and health care delivery modes.

Community Health Division Research

The IHE Community Health Division includes many research projects and 4 graduate education programs led by 11 community engaged faculty and staff.

- **Jess Olson, PhD, MPH**, research focuses on determining the cause of exercise response variability to tailor lifestyle interventions to individual survivors of breast cancer. She was first author of an AHW crosscutting team paper on community and research perspectives on cancer disparities in Wisconsin in *Prevention of Chronic Diseases.* Dr Olson directs the CTSI PhD in Basic and Translational Science program. Dr Olson was recently appointed Associate Director in the MCW Office of Diversity and Inclusion. She has been active in the National Lung Cancer Roundtable.

- **Jamila Kwarteng, PhD,** research focuses on improving wellbeing, quality of life, and survivorship for African American cancer survivors and cancer prevention for African Americans and Latinos. She uses a community-engagement approach by partnering with local and state organizations to develop programming. This includes providing resources to address unmet needs of cancer survivors; facilitating education and training for churches to better support cancer survivors within faith-based communities; and providing programs for cancer prevention. She is the co-principal investigator of a recently awarded Health and Human Services grant that partners with Milwaukee Recreation to prevent cancer through education in nutrition and physical activity.

- **John Meurer, MD, MBA**, is director of the Institute for Health & Equity. With a dozen primary care health centers, the faith community, and community agencies, he is co-PI of a major NIH grant to CTSI to study the seroprevalence of COVID among adults in Milwaukee, the duration of antibodies, the individual and neighborhood risk factors for severe illness, and the impact of vaccines. With a decade of CDC funding, Dr Meurer is co-investigator of studies of the effect of variations in state Medicaid expansion on diabetes outcomes. He is co-PI of AHW-funded research in early childhood development by improving resiliency and equity (REDIRECT). He leads an evaluation of STRY365 trauma-informed sports programs on scholars at Milwaukee Academy of Science.

- **Jenny Geurts, MSGC,** is director and Jess Bell, MPH, is coordinator of the accredited ***MS Genetic Counseling Program*** enrolling students in the fall 2021.

- **Dale "Bud" Beatty, PhD,** is evaluation director of the Kern National Network of Transforming Medical Education.

- **Greer Jordan, PhD**, is Director of the MCW Office of Diversity and Inclusion.

- **David Nelson, PhD**, is director with the support of **Terry Brandenburg, MPH, MBA**, **Kim Contardi, MPH,** and **Sarah Curry, MEd,** of the new online ***DrPH program*** enrolling students in the fall. They are also leaders of the online MPH program.

John Meurer is director and **Kellie LeGrave** is coordinator of the ***Precision Medicine MS and Certificate program*** enrolling clinician students in the fall.

Neuroscience Research Center

The mission of the Neuroscience Research Center (NRC) is to facilitate the discovery and translation of new knowledge in the neurosciences, with a focus on discoveries that will improve the health of the communities served by our clinical programs.

Overall Goals:

1. **Impactful research.** The NRC is made up of outstanding biomedical scientists who are experts in neuroscience knowledge and are carrying out research projects that are supported by extramural funding and have the potential to improve the health of the communities we serve.

2. **Leverage resources through collaboration.** NRC scientists are engaging in collaborative research projects that bring scientists with complementary expertise and interests together, promoting collegiality, sharing of data and ideas, and raising the caliber of research of all participants.

3. **Provide support.** NRC members have access to high quality support staff, seed funding, statistical support, equipment and expertise to carry out their research.

How does this help me?
As part of our strategic initiatives, the NRC hosts seminars, data sharing events, research in progress and symposia, all with the goal of providing MCW faculty, students, staff and fellows up-to-date knowledge and connecting members for the purposes of collaboration.

The NRC has established a Rodent Behavioral Core that is available to all MCW investigators. The core is equipped with apparati and software for the measurement of simple and complex rodent behaviors using tests such as the elevated plus maze, open field, radial arm mazes, prepulse inhibition, and fear conditioning. To learn more about the Rodent Behavioral Core, please contact Jenny Sterrett at jsterrett@mcw.edu

The NRC also runs a Microscopy Core with Multiphoton Microscope services and a Leica Sp8 Confocal Microscope. More information and the ability to book our equipment is available on iLab, or you may contact Suresh Kumar at skumar@mcw.edu.

Please visit our **Intranet area on Infoscope** for details on our cores, grant opportunities and membership:
https://infoscope.mcw.edu/NRC-Intranet.htm

If you are interested in becoming a member of the NRC and receiving email updates of seminars, events and grant opportunities, please contact Amy Calhoun at acalhoun@mcw.edu.

Versiti Blood Research Institute

From its beginning in 1947, Versiti (formerly known as BloodCenter of Wisconsin), has supported basic, translational, and clinical research to advance patient care. Research at Versiti today excels in Thrombosis, Hemostasis and Vascular Biology, Immunobiology, Transfusion Medicine, and Stem Cell Biology. Research activities are housed primarily in the Blood Research Institute (BRI) on the Milwaukee Regional Medical Center (MRMC) adjacent to the Medical College of Wisconsin (MCW), an 87,000 sq. ft. facility. The BRI is home to 34 investigators and more than 120 research staff, including fellows, graduate students, technologists, and administrative personnel. Total extramural funding for research in 2018 was $16.1 million, including a Training Grant in Transfusion Medicine, currently in its 40th year, which provides stipends for outstanding postdoctoral fellows engaged in NIH-funded research.

BRI research in Thrombosis, Hemostasis and Vascular Biology focuses on the cellular and molecular mechanisms of normal blood clotting, pathological thrombosis and event impacting the integrity of vascular and blood vessel development. Studies have given rise to a number of important breakthroughs in understanding mechanisms of the regulation of blood clotting. The work of our clinical investigators has led to improved outcomes for patients with blood-related diseases including Sickle Cell Disease, Hemophilia, and von Willebrand Disease. Research in Transfusion Medicine focuses on immune responses to transfused blood and the underlying immunologic mechanisms as well as practices related to blood storage and safety. Currently, investigators in this area focus on the basic biology and clinical implications of a wide range of transfusion-related issues. Historically, Versiti research in Immunobiology focused on understanding the mechanisms involved in antibody/antigen recognition. Versiti investigators played an important role in the first allogeneic bone marrow transplant performed at Children's Hospital of Wisconsin and the creation of the national marrow donor program. Today, BRI investigators are exploring the immune system in a variety of areas, including neuro-immunology, T- and B-cell development and regulation and the development of cell-based immunotherapies targeted to malignant hematopoietic and solid tumors. The Translational Glycomics Center focuses on the important and understudied role sugars play in the biology and pathobiology of various blood cells. The Translational GlycOmics K12 Program, part of the National Career Development Consortium for Excellence in Glycosciences, trains emerging generations of researchers to pursue basic and applied glycobiology research. Stem Cell Biology is the newest and fastest-growing area of research at the BRI with studies focused on transcriptional and epigenetic regulation of stem cells and normal/malignant hematopoiesis biology.

In addition to its research laboratories, the BRI maintains 12 state-of-the-art Core Laboratories within the BRI, which provide cutting-edge technology and expertise to BRI investigators and others on the MRMC campus. Core Labs include Biophysics, Histology, Hybridoma, Microscopic Imaging, Molecular Biology, Protein Chemistry, Viral Vector, Thrombosis, and Flow Cytometry. The Cores are supported by a PhD-level Director, who oversees a staff of experienced, cross-trained technologists available for consultation with researchers on experimental design and data analysis related to products and services provided by the Core Labs. In addition, the BRI provides expertise in Transgenic Mouse production and maintenance and in Gene Editing and Bioinformatics. Finally, the BRI houses a fully staffed Clinical Trials Research Office.

Adult Translational Research Unit (A-TRU)

What Do We Do?

The Adult Translational Research Unit (ATRU) provides optimal clinical research environments for participants and investigators to conduct a wide range of patient-oriented studies from pilot to multi-center to community-based studies. The infrastructural support and access to space, resources and expertise of research personnel have proven to be an essential hub for CTSI investigators.

The unit is conveniently located in Froedtert Hospital and includes 5 exam rooms, 3 suites, 2 lab processing areas, 1 DXA exam, and 1 metabolic kitchen. The unit's hours are Monday- Friday 8:00am - 5:00pm with after-hour and weekend appointments offered, as needed. Special arrangements can be made for studies requiring TRU support in a hospital setting. Additionally, the ATRU offers community and mobile services which support the establishment of temporary research facilities throughout the Greater Milwaukee Area to ensure that unrepresented and minority community centers and agencies have the resources necessary to conduct community and participatory based research.

The leadership of the ATRU includes a Medical Director, the Clinical and Translational Research Center Administrator, and mangers for clinical services, lab core, and bionutrition core. The ATRU administration supports all stages of clinical research from study design review, IRB submission, data management, FDA approvals, and compliance.

Services Offered:

Clinical Services: • Vital signs/height/weight • Phlebotomy • IV insertion • Study drug administration and monitoring • Injections/Infusions/Vaccines • 12 lead EKG recording (without interpretation) • Glucose tolerance • Point of care testing • Focused nursing assessment • Assist with punch biopsies • LP and Post LP Evaluations • Six minute walk test • Mantoux Tuberculin (TB) skin test • SARS-CoV-2 specimen collection and treatments

Bionutrition Services: • Anthropometry • Body composition (DXA & BIA) • Energy expenditure • Dietary assessments: nutritional analysis, food frequency questionnaires & food diaries • Lifestyle counseling • Research meal design: preparation & distribution • Controlled feeding trials

Lab Services: • Simple or complex processing and shipping of biospecimens • Study kit creation for specimen collection needs • Long and short term storage and inventory control of samples (4C/-20C/-80C freezers) • Point of care lab assessments • Access to bench space and specialized lab equipment • Coordination & assessment of 100+ specialized lab tests

Contact Us:
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Shankar Srinivasan, Administrator CTRC, ssrinivasan@mcw.edu
Jill Theobald, Medical Director, jtheobald@mcw.edu

Regular Hours: Monday – Friday 0800 – 1700 **After Hours:** Evenings and weekends by appointment
Website: https://ctsi.mcw.edu/investigator/ctsi-cores-facilities-services/a-tru/

All of Us Research Program

What is the *All of Us* Research program?

Initiated by Barack Obama as part of the Precision Medicine Initiative, the *All of Us* Research Program is a historic, longitudinal effort to gather data from one million or more people living in the United States to accelerate research and improve health. By taking into account individual differences in lifestyle, socioeconomics, environment, and biology, researchers will uncover paths toward delivering precision medicine – or individualized prevention, treatment, and care – for all of us.

What is the promise for researchers?

1. The opportunity to save time and resources and accelerate your research breakthroughs by leveraging:
    a. A rich resource of data, including biospecimens and robust electronic health records.
    b. A longitudinal dataset that will follow participants as they move, age, develop relationships, get sick, and try treatments.
    c. A diverse cohort of participants, including people both healthy and sick, from all walks of life and all parts of the country.
    d. Data that is already cleaned and curated.
    e. Robust computing and analytic tools to support complex data analyses in a secure data environment.
    f. A group of engaged participants who may be eager to participate in ancillary studies.
2. The ability to easily share workspaces and analyses with research partners and reviewers.
3. The chance to learn from the program's pilots and experiments and leverage innovations for other studies and cohorts.

What do the participants look like?

https://www.researchallofus.org/data-tools/data-snapshots/

As of today – 273,307 people have provided access to EHR, completed 3 core surveys and donated biospecimens

- 52.5% ethnic/racial minorities
- 0.5% non-binary, transgendered or other categories
- Median age mid-50's
- All 50 states represented
- Over 12,000 in Wisconsin

What kind of data is available?

https://databrowser.researchallofus.org/

- Electronic health records
- Vital signs, Body Mass Index, and waist and hip circumference at the time of enrollment
- Biospecimens
    - Whole blood, Plasma, Serum
    - RNA, cfDNA, DNA
    - Urine
- Surveys regarding personal and family medical history, health habits, COVID experiences, and other topics https://www.researchallofus.org/data-tools/survey-explorer/

How do I sign up to access this?

https://www.researchallofus.org/apply/

You need to:

- Be at an institution with a Data Use Agreement – e.g, MCW
- Have an ERA commons account
- Complete All of Us specific humans studies research training.

Here's a full playlist with all of the Researcher Workbench videos:
https://www.youtube.com/playlist?list=PLR8euOCc1JWjJK_Dy8f5_mWyOk-oH7pug

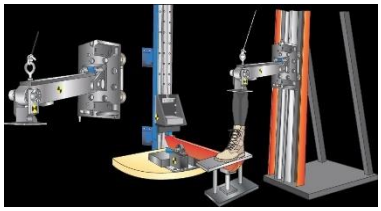
Biomechanics Core

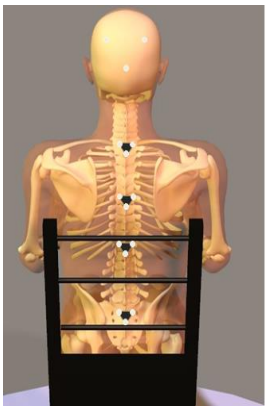
What Do We Do?

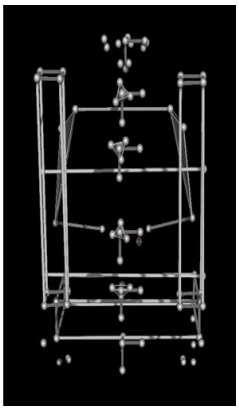
Multiple specialty labs serve as the "Biomechanics Core" facilities. We are equipped with multiple small-animal injury models, including custom-designed equipment to deliver blunt or blast brain injury to rodents and tissue. We also have facilities and equipment for investigators who want to obtain mechanical or physical testing of specimens. Resources include bi-axial and uni-axial electrohydraulic pistons that apply simple or complex loads to biological or material specimens of various sizes. Additional devices include drop towers, pendulum impactors, pneumatically driven servo-sled accelerator, and a full-scale vehicle crash lab. High speed and 3D motion capture capabilities complement over 400 channels of data acquisition equipment.

Equipment Available

- 3D Motion Capture System
- High-speed video systems
- High-rate data acquisition systems
- Servo-sled accelerator to study occupant response
- Full-scale vehicle crash lab
- Shock-wave tubes for blast simulations on rodents, cells, and tissue
- Rotational acceleration brain injury device for rodents
- Behavioral lab: Morris Water Maze, Elevated Plus Maze, Open Field Test, Barnes Maze, Rotarod assessments
- Split-Hopkinson Pressure Bar
- Finite Element Mechanics Software







Contact Us:

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Cancer Center Biomedical Imaging Shared Resource

What Do We Do?

The Biomedical Imaging Shared Resource (BISR), led by Amit Joshi, PhD, and Peter LaViolette, PhD is a Cancer Center resource that provides access to in vivo biomedical imaging instrumentation, customized imaging technologies, and image processing/analysis services for the basic and clinical cancer researchers. The shared resource was founded in 2010 to complement the MCW Center for Imaging Research (CIR) by providing additional small animal imaging technologies with an emphasis on cancer research, and provide access, training, and collaboration interface to MCWCC members. The equipment utilized by the BISR are centrally located and easily accessible to MCWCC members in both the clinical and basic science departments, with convenient and protected access to animal facilities.

Equipment Available

The BISR has small-animal and human imaging systems dedicated for research purposes.

PerkinElmer IVIS-100 Bioluminescence Imaging System | Located in the Biomedical Resource Center
The IVIS system allows in vivo bioluminescence imaging in mice and rats with an enzymatic bioluminescence expressing tag (e.g., luciferase).

IVIS Spectrum CT
Key features of the IVIS Spectrum-CT include:

- Integrated optical and micro-CT technology
- 3D optical tomography for fluorescence and bioluminescence
- Bioluminescence
- Multispectral fluorescence and spectral unmixing
- Cerenkov imaging for optical radiotracer detection
- Low dose and ultrafast micro-CT
- Dynamic enhanced imaging for real time distribution studies of both fluorochromes or PET tracers

Contact Us:

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Cancer Center Redox & Bioenergetics Shared Resource

The Medical College of Wisconsin Cancer Center (MCWCC) Redox and Bioenergetics Shared Resource (RBSR) was established in 2012, as part of the Cancer Biology research program, to provide state-of-the-art instrumentation, cutting-edge techniques, and sophisticated expertise dedicated to investigating cancer cell metabolism and redox signaling.

The mission of the RBSR is to enable researchers to assess cellular bioenergetics, metabolism, ROS generation, and intracellular redox status. The RBSR provides an environment for education and training in research on oxy-radicals and cellular redox and bioenergetic status. The resource supports and guides investigators in the development of anticancer treatments, based on the redox profiling of cancer cell and bioenergetic status. The RBSR is directed by Jacek Zielonka, PhD, with oversight by an advisory committee responsible for reviewing all services provided by the resource.

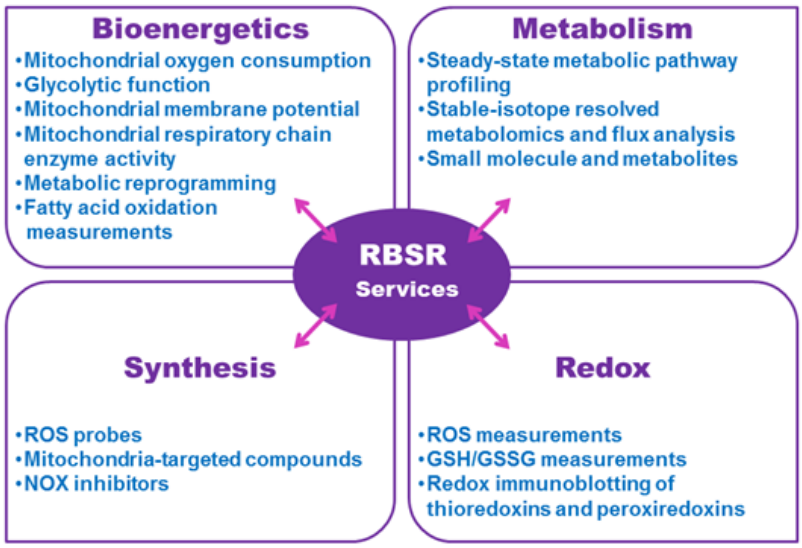

Figure 1. The RBSR promotes the understanding of cancer cell bioenergetics, metabolism, reactive oxygen species, and redox signaling, which are central to several areas of cancer research.

The RBSR offers services and instrumentation to assess many aspects of redox signaling and metabolic function in cancer cells (**Figure 1**). These include ***1)*** detection of superoxide radical anions, hydrogen peroxide, and peroxynitrite; ***2)*** measurements of redox status of key cytosolic and mitochondrial antioxidant proteins including peroxiredoxins and thioredoxins; ***3)*** measurements of mitochondrial respiration and glycolytic function; ***4)*** analysis of metabolic intermediates; and ***5)*** identification of altered metabolism using stable isotope-based metabolite flux analysis.

The five main goals of the MCWCC RBSR are as follows: ***1)*** Investigate cancer and immune cell metabolism and redox signaling, and understand how cancer cells exploit metabolic pathways for survival, proliferation, differentiation, and drug resistance. ***2)*** Provide a better understanding of the bioenergetic pathways and oxidant production in cancer cells cultured under normoxic and hypoxic microenvironments. ***3)*** Develop new, rigorous, and cost-effective assays to measure the production of reactive oxygen species, redox, and bioenergetic status in cancer cells *in vitro* and in tumors *in vivo*. ***4)*** Develop new redox- and metabolism-based strategies to inhibit cancer cell progression and metastasis, and to promote cancer prevention and therapy. ***5)*** Promote increased collaboration in cancer metabolism research between basic scientists and clinical researchers at MCW.

The RBSR labs are centrally located for cancer researchers at MCW, Froedtert, and the Versiti Blood Research Institute, on the second floor of the MACC Fund Research Center (MFRC, Room 2013) in the Department of Biophysics.

The resources and facilities of the RBSR have been utilized in numerous grants, including program project grants, over the past decade, and more than 80 research publications have utilized the RBSR facility. Examples of recent papers follow:

1. Cheng G, Hardy M, Topchyan P, Zander R, Volberding P, Cui W, Kalyanaraman B. Potent inhibition of tumour cell proliferation and immunoregulatory function by mitochondria-targeted atovaquone. *Sci Rep*. 2020 Oct 21;10(1):17872.
2. Cheng G, Hardy M, Zielonka J, Weh K, Zielonka M, Boyle KA, Abu Eid M, McAllister D, Bennett B, Kresty LA, Dwinell MB, Kalyanaraman B. Mitochondria-targeted magnolol inhibits OXPHOS, proliferation, and tumor growth via modulation of energetics and autophagy in melanoma cells. *Cancer Treat Res Commun*. 2020 Sep 17;25:100210.
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For more information, contact Jacek Zielonka, PhD (955-4789 or jzielonk@mcw.edu) or visit the RBSR website (https://www.mcw.edu/departments/redox-and-bioenergetics-shared-resource).

Clinical Research Data Warehouse (CRDW)

What Do We Do?

The CTSI's Clinical Research Data Warehouse (CRDW) provides **no-cost self-service tools** to CITI-trained research teams for study feasibility, cohort discovery and data extraction. CRDW tools include the i2b2 Cohort Discovery Tool, TriNetX (a pharma-sponsored cohort query and analysis tool) and the Honest Broker data extraction tool. Data sources include Epic, GE/IDX (physician billing system), Froedtert legacy systems (Affinity, Intellidose & SIS), MCW Tissue Bank biospecimens, NAACCR tumor registry, and genetic testing vendors (Foundation Medicine and Tempus).

The query tools help to answer the question "Does the CRDW contain a cohort of patients with certain characteristics?"

How Can Investigators and Their Teams Get Access?

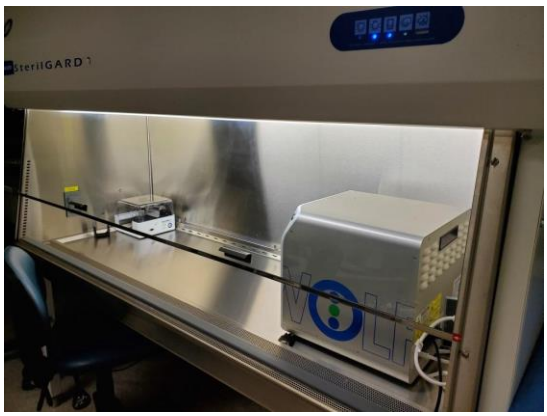
1. Join the CTSI at https://ctsi.mcw.edu/about/join-ctsi/
2. Complete MCW's CITI Training Modules for Human Subjects Research
3. Complete an Access Form at https://ctri.mcw.edu/cda/i2b2-cohort-discovery-tool/
    a) CRDW Query Tool Access (for query tools only)
    b) CRDW Data Release Agreement (for query and extract tools)

Contact Us:
Kristen Osinski, MS
Business Analyst, Biomedical Informatics
kosinski@mcw.edu | (414) 805-7245
https://ctsi.mcw.edu/investigator/ctsi-tools/i2b2/

CRI/CC Flow Cytometry Shared Resource

What Do We Do?

The Children's Research Institute and Cancer Center Flow Cytometry Shared Resource is an advanced technology facility primarily serving MCW and CRI investigators. The facility provides secondary support to on-campus colleagues at the BRI, as well as collaborators off campus at institutions in the Upper Midwest. Our facility provides 24/7 access to analytical cytometers and operator-assisted cell sorting by appointment. In addition to these services, we provide assistance to both new and established investigators with protocol and assay development, including selection of antibodies and fluorochromes, proper staining and compensation controls, and selection of appropriate buffers. Data analysis assistance using FlowJo and DIVA software is also available by appointment. In 2020, we added the 10X Genomics platform to the Flow Core to enable scRNAseq analysis of sorted cells.



Equipment Available:

- BD LSRFortessa X20 – 5-laser (18-color, 20-parameter) Flow Cytometer
- BD LSR II – 4-laser (12-color, 14-parameter) Flow Cytometer
- BD FACSAria II – CC 4-laser (10-color, 12-parameter) Cell Sorter
- BD FACSAria IIu – CRI 4-laser (12-color, 14-parameter) Cell Sorter
- NanoCELECT WOLF-Sorter – 1-laser (3-color, 5-parameter) Cell Sorter
- HemaVET 950 - CBC Analyzer (24 parameters, including platelets; multi-species)
- 10X Genomics Chromium
- Agilent 4200 TapeStation
- ThermoFisher Applied Biosystems QuantStudio Pro 7 Real Time-PCR
- BioRad C1000 Thermocycler
- FlowJo Software

Contact Us:

Galina Petrova, PhD
Research Scientist I /Manager
gpetrova@mcw.edu | (414) 955 5793

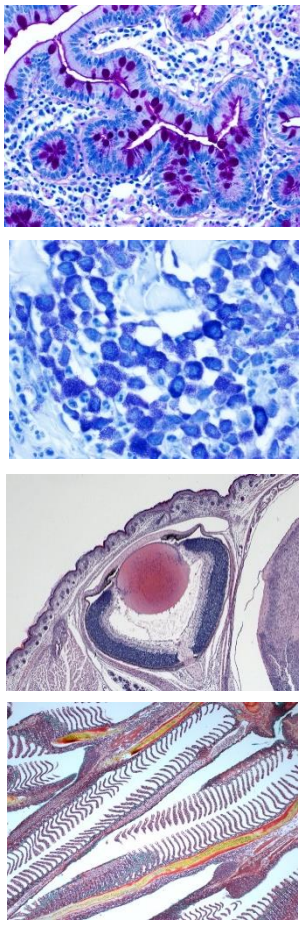
Calvin B. Williams, MD, PhD
Director
cbwillia@mcw.edu

MACC Fund Research Center, 5th Floor, #5052
Monday – Friday, 9:00 a.m. – 5:00 p.m.

CRI Histology Core

What Do We Do?

The CRI Histology Core offers a broad range of high quality histological and immunohistochemical services on a fee-for-service basis to investigators from CW, MCW and off-campus institutions. Our staff includes ASCP certified Histologists and American Board of Pathology certified Pathologists who provide service, assistance, and quality control. Our services include grossing specimens, frozen and fixed tissue sectioning, routine H&E and specialized histochemical staining, cytospin preparations, IHC/IF and antibody optimizations using investigator provided antibodies. We also provide training for immunohistochemical and histochemical techniques.



Histology Core Equipment:

- Leica BondMAX Immunostaining Platform
- Leica BondRX Immunostaining Platform
- Leica Slide Printer and Labeler
- Micron HM355S Automated Microtomes (x2)
- Sakura Automated Tissue processors VIP5(x2) and VIP6
- Sakura Glass Coverslipper
- Sakura Prisma Automated H&E stainer
- Sakura Tec-5 EMA1 Embedding Center
- ThermoShandon Cytospin2

**Please note: Histology Core equipment is used by staff only; work is completed on first-come-first-serve basis.

PHONE: (414) 955-8624
LOCATION: TBRC/CRI 4th Floor, #C4305
OPERATING HOURS: Monday – Friday 8 a.m. – 3:30 p.m.

Histology Core Staff

Christine Duris BS, HTL(ASCP)CM, QIHC (ASCP)CM
Supervisor/Technologist
cduris@mcw.edu

Tanya Bufford, HT(ASCP)
Histotechnician
tbufford@mcw.edu

Daraphone Zieske HTL(ASCP)CM
Histotechnologist
dzieske@mcw.edu

Qiuhui Yang, MD, PhD, HTL(ASCP)CM
Research Scientist/Histotechnologist
qyang@mcw.edu

Histology Core Directors

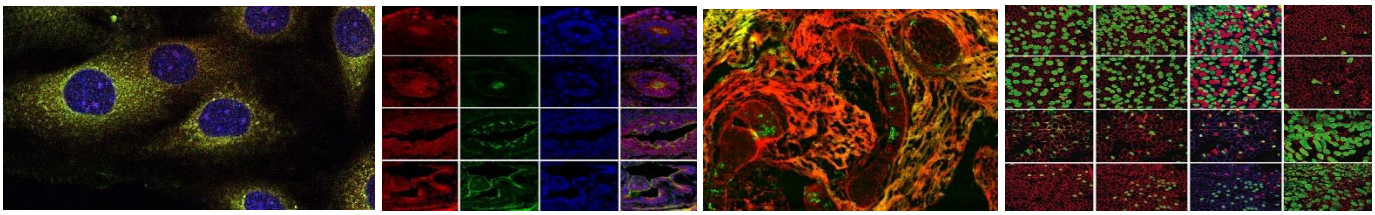
Jason A. Jarzembowski, MD, PhD
Interim Chief Executive Officer, Children's Specialty Group
Vice Chair (Pediatric Pathology) and Professor, Department of Pathology, MCW
Interim Senior Associate Dean of Clinical Affairs, MCW
Medical Director, Pathology and Laboratory Medicine, Children's Wisconsin
Chair, Pathology Discipline Committee, Children's Oncology Group

Paula E. North, MD, PhD
Professor of Pathology, MCW
Department of Pathology (Pediatric Pathology)
CRI-Histology Core – Scientific Director

CRI Imaging Core

What Do We Do?

Children's Research Institute's imaging core is a fee per use facility with a variety of state-of-the-art microscopic imaging systems listed below. Operated by the Pediatric Pathology Division at the Medical College of Wisconsin and Children's Research Institute, the imaging core is open to all investigators including those at our collaborating institutes. Core users will be trained and consulted on the instrumentation, software, and analysis. Access to microscopes and imaging systems are monitored, and unassisted use of imaging core equipment requires prescribed training. Trained users access the core by calender booking, card reader entry, and individualized computer account sign-on. Untrained users utilize the core through assisted use method.



Equipment Available

- Zeiss Axio Imager Z1: widefield side imaging
- Zeiss Axio Vert 200M: slide, culture dish & plate imaging
- Zeiss P.A.L.M. Microbeam III: isolating specific regions/single cells from tissue section
- Zeiss LSM510 Confocal: confocal slide imaging0
- Zeiss LSM510 META NLO multiphoton: live cells, small animals, deep tissue & more
- Hamamatsu Nanozoomer Slide Scanner: high-res slide scanning & analysis
- Olympus VS100 Fluorescent Slide Scanner: high-res scanning & analysis of fluorescent slides
- Compucyte iCys: flow cytometry-like analysis
-

Contact Us:

Suresh Kumar PhD | Director of CRI Imaging Core
skumar@mcw.edu
Ph# 414-955-2448

https://mcw.ilab.agilent.com/service_center/show_external/4968/cri_imaging_core

Echocardiography Core – Clinical & Small Animal

What Do We Do?

Echocardiography is the cornerstone of cardiac imaging. Its highly versatile nature makes it the non-invasive tool of choice. This form of non-invasive assessment is ideal for performing serial evaluations of cardiac function or real-time monitoring during and after pharmacological or therapeutic intervention. The Core serves investigators affiliated with MCW. We provide consultation on image acquisition and analysis based upon American Society of Echocardiography (ASE) recommendations for the performance and evaluation of a comprehensive transthoracic echocardiogram.

Services Offered

- **Adult Echocardiography Core:** High-quality cardiovascular imaging along with quantitative and qualitative imaging analysis for cardiovascular clinical trials and investigator initiated protocols**.**
- **Small Animal Echocardiography Core:** Imaging resource for cardiovascular phenotyping efforts

Contact Us:
Lindsey Kalvin
lkalvin@mcw.edu

https://mcw.ilab.agilent.com/service_center/show_external/5065/echocardiography_core

Electron Microscopy Core Facility

What Do We Do?

The Electron Microscopy Core Facility is an interdepartmental research service unit managed on behalf of the Medical College by the Department of Microbiology and Immunology and the Department of Cell Biology, Neurobiology and Anatomy. The facility provides service, consultation for research and some training for projects requiring transmission electron microscopy. Services include complete tissue processing facilities, immunoelectron microscopy, negative staining, enzyme cytochemistry and ultrastructural Electron Tomography. The Facility operates on a fee-for-service basis and is open to all MCW faculty, staff, and students, and investigators at affiliated and non-MCW institutions.

Equipment Available

- JEOL 2100 electron microscope equipped with a 2K x 2K ultrahigh resolution digital camera
- Hitachi 600 electron microscope
- Leica EMPact 2 high pressure freezing apparatus
- Leica Automated Freeze Substitution Apparatus
- RMC PowerTome & Leica Ultracut UCT ultramicrotomes

Contact Us:

Clive Wells, CBiol, FRSB, FRMS
Director
cwells@mcw.edu | (414) 955-8141

Rob Goodwin, BS
Technician
rgoodwin@mcw.edu | (414) 955-8344

https://mcw.ilab.agilent.com/service_center/show_external/5443/electron_microscopy_facility

Epidemiology Data Resource Center

What Do We Do?

The Epidemiology Data Resource Center (EDRC) is MCW's centralized resource for secondary health and demographic data. The EDRC also provides assistance in the use of spatial data and geographic information systems, or GIS. Since opening its doors in 1994 (as the Epidemiology Data Service Center), the EDRC has provided data assistance to faculty, staff, and graduate and medical student researchers in epidemiology, health services, health policy, and other related disciplines.

Services Offered

- Provides summary statistics and prepares data set extracts
- Lends data management and preparation expertise
- Assistance with long-term secondary data research projects
- Mapping and other GIS services
- Use of REDCap Survey for primary data collection
- Use of HCUP, NIS, and KID Databases
- Assistance with accessing secondary data from other sources such as US Census, NCHS, etc

Contact Us:
Tom Chelius, MS
EDRC Coordinator
edrc@mcw.edu | (414) 955-8040

https://www.mcw.edu/departments/epidemiology/edrc

Geospatial Epidemiology & Outcomes (GEO)

The Geospatial, Epidemiology, and Outcomes (GEO) Shared Resource at the Medical College of Wisconsin (MCW) Cancer Center provides access to population-based data, cancer epidemiology and database expertise, information on the cancer burden in the catchment area, and geospatial mapping and analysis to catalyze population-based cancer research at MCW, with an emphasis on cancer disparities. GEO serves numerous departments and centers on and off campus.

Geospatial Services

Geographic Information Systems (GIS) and Spatial Analysis Services

- Spatial Data Acquisition, Preparation and Management
- Cartography, Mapping and Data Visualization
- Geocoding, Distance Estimation and Routing, Geographic Access Estimation
- Disease Mapping, Small Area Estimation, Spatial Pattern and Cluster Analysis
- Modeling Including Spatial and Clustered Data
- Web-Based Mapping
- Data analysis in R, STATA, Esri software
- Geographic Information Systems (GIS) and Related Technology Support
- Software license(s) for GIS and related software (Esri, STATA)
- Geospatial analysis techniques and data sources

Epidemiology Services

General epidemiologic information about cancer burden

- Boiler plate information for grant applications about cancer burden and GEO center
- Basic epidemiologic data (Froedtert-MCW, Southeastern Wisconsin, Wisconsin, U.S.)
- Catchment Area/WI cancer maps
- Website (updated cancer data, maps, links to publicly available data, related sites)
- Specific epidemiologic information
- Preliminary data for grant applications
- Anticipated accruals to clinical trials
- Consultation on study design and methodology
- Cancer knowledge, database expertise
- Study design, aims, measurement/variables, feasibility

Outcomes Services

Data acquisition, preparation, management and analysis

- Database acquisition, licensing and use agreements
- Database repository and maintenance
- Database cleaning
- Variable creation
- Data manipulation/linkage
- Preparation of dataset for analyses
- Preparation of data dictionaries/metadata
- Data analyses
- Computer and statistical programming (R, SAS, Python, etc.)
- Specific database knowledge
- Variable creation and data analysis strategies

Contact Us:

geo@mcw.edu | https://mcw.ilab.agilent.com/service_center/show_external/5621/geospatial_epidemiology_outcomes_geo

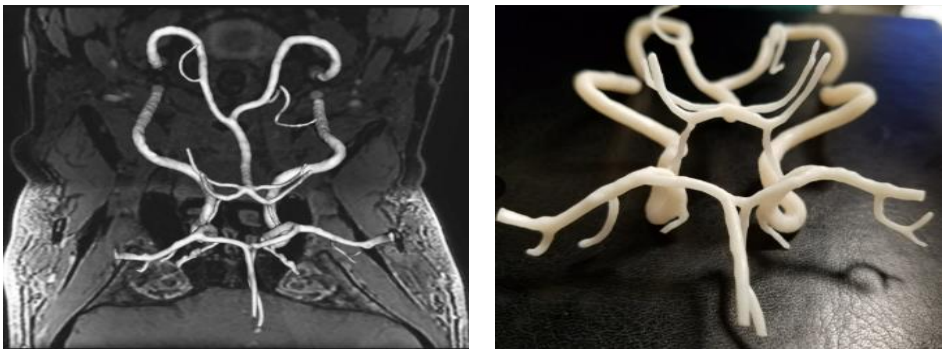
MCW Engineering Core

What Do We Do?

The mission of the MCW Engineering Design and Fabrication lab is to support the medical research effort carried out by our research labs and clinical partners through a range of services including custom research device design and fabrication, laboratory equipment calibrations and repair, 3D-Printing services including anatomical models from CT and MR data, and new protocol development. Simply put, we can do more than we can list on a flyer! Please ask about our services and we will be happy to work with you to determine if our services are a good match for your research needs.

Services Offered

- Equipment repair
- Instrument calibration
- Custom device design and fabrication
- 3D printing services: Patient-specific anatomical models from CT or MR; Novel devices; Student teaching aids
- Equipment preventive maintenance
- New equipment installations



LEFT: Patient CT of brain aneurysm; RIGHT: 3D model of same aneurysm printed from CT data

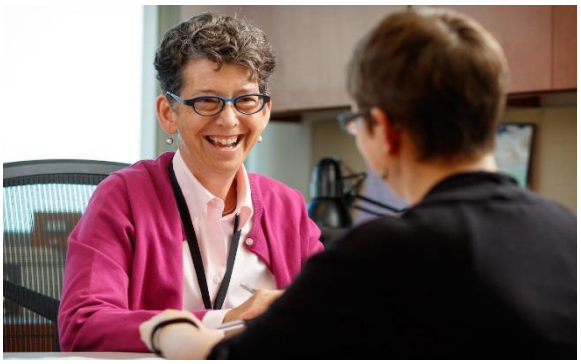
Contact Us:
Bonnie Freudinger, ME
MCW Engineering Lab Supervisor
bfreudinger@mcw.edu | (414) 955-4722

https://mcw.ilab.agilent.com/service_center/show_external/5143/mcw_engineering_core

MCW Libraries

What Do We Do?

With locations at MCW, Froedtert Hospital, and Children's Hospital (CHW), MCW Libraries is the primary provider of information services to 19,000+ MCW faculty, residents, students and staff, and hospital employees of CHW and Froedtert. We also provide information services/health care information to patients and their families. All three libraries are open to the public. As a designated "Resource Library" within the Regional Medical Library program, we are also responsible for providing medical information services to the 5.5 million people of Wisconsin.



Services Offered

- Searching for Grant Funding
- Reaching NIH Public Access Policy Compliance
- Finding Journal Rankings and Showing Research Impact
- Searching for Literature
- Poster Printing

Contact Us:
Todd Wehr Library
MEB, 3rd Floor; Monday – Friday, 7:30 a.m. – 6 p.m.
MCW badge access available 24/7

Library Information
asklib@mcw.edu | (414) 955-8302
https://www.mcw.edu/Libraries.htm

Poster Printing Service
posterprinting@mcw.edu | (414) 955-8300
https://www.mcw.edu/Libraries/Forms/Poster-Printing.htm

MCW Tissue Bank

What Do We Do?

The MCW Tissue Bank is a secure storage facility that collects, processes and distributes blood and tissue for research here on campus. We consent for one additional blood draw during a regularly scheduled clinic procedure and the collection of any future surgery discard samples such as tumor, bone marrow and normal tissue. Our streamlined, IRB-approved process allows researchers to query available samples and de-identified clinical data with the help of CTSI's i2b2 Cohort Discovery Tool. We also work to accommodate researchers in prospective studies.

Services Offered

- DNA/RNA Isolations
- Snap Frozen Tissue
- Plasma
- Buffy Coat
- Unstained Slides
- Sample QC
- 24/7 Monitored Storage
- -80°C Freezers
- H&E Stained Slides
- OCT Embedded Tissue
- Fresh Cord Blood
- Fresh Tissue Procurement
- Frozen Bone Marrow
- Matched Tumor/Benign

NOTE: COVID-19 samples available through the MCW Tissue Bank.

Contact Us:
Mary Rau
Tissue Bank Manager
mrau@mcw.edu | (414) 805-9569

https://mcw.ilab.agilent.com/service_center/show_external/4613/mcw_tissue_bank

NRC Microscopy Core

What Do We Do?

The Neuroscience Research Center (NRC) Imaging Facility owns a state of the art custom built 2 photon microscope from LaVision biotech. The double header microscope has inbuilt capability to collect images at 60fps (256x256 pixels) using resonant scanner (system I) and deep tissue imaging using PMT galvo scanners (System II). The system is equipped with two, spectra Physics HP Ti: Sapphire laser that have patented Deep See technology, mode-lock capability, femtosecond power duration and tuning range of 690-1040nm. An external beam optimizer and negative chirp compensator is also installed to combine the two lasers beams and condition the laser pulse shape. Simultaneous imaging (resonant scanner) and treatment (IR or Vis) capability is enabled through an additional galvo scanner on system I. Patch clamp experiment is facilitated by the IR Dodt contrast imaging. The scope is controlled by ImSpector software that controls imaging data collection (64bit) and analysis and the following lenses from Nikon and Zeiss are available for imaging –PlanApo10x / 0.45NA (2.0WD), Planfluor10x / 0.3NA (16.0 WD), CFI-Apo NIR 60x / 1.0NA (2.8WD) and PlanApo20x / 1.0NA (2.4WD).

Instruments:

- Leica SP8 Upright Confocal Microscope
- LaVision TrimScope II Multiphoton Microscope

Contact Us:
Suresh Kumar, PhD
Scientific Director
skumar@mcw.edu

https://mcw.ilab.agilent.com/service_center/show_external/4824/nrc_microscopy_core

NRC Rodent Behavior Core

What Do We Do?

The Neuroscience Research Center's Rodent Behavior Core was established to enable MCW labs to perform behavioral analysis on rodents without having to buy costly equipment themselves. Our goal is to foster a collaborative environment to enhance neuroscience research at MCW. The center is equipped with up-to-date experimental devices, analysis software, multifunctional rooms, and the ability to reserve time, space and equipment for your own research needs. Test types focus on Aggression & Dominance, Anxiety & Depression, Avoidance & Social Interaction, Coordination & Motor Abilities, Learning & Memory, Reward Seeking and Sensation. Funding was provided by the Research and Education component of the Advancing a Healthier Wisconsin Endowment.

Equipment Available

Mouse (sample listing)

- Elevated Plus Maze
- Prepulse Inhibition Chambers
- Fear Conditioning Chambers
- Radial Arm Maze (wet/dry)
- Grip Strength Meter
- Remotely-Monitored Running Wheels

Rat (sample listing)

- Open Field Chambers
- Rotarod
- Conditioned Place Preference Chambers
- Morris Water Maze
- Gait Analysis Chamber
- Forced Swim Apparatus

Contact Us:

Jennifer Sterrett
414-955-8620

Breanna Glaser
414-955-2226

behavioralcore@mcw.edu
https://www.mcw.edu/departments/neuroscience-research-center/services

Office of Technology Development

What Do We Do?

The MCW Office of Technology Development (OTD) is MCW's "technology transfer" office. The OTD nurtures intellectual creativity, stimulates research, develops and protects intellectual property, transfers intellectual property to entities best equipped to develop and take the product to market, and strengthens the Medical College of Wisconsin brand with the business community. The OTD is housed administratively within the Medical College of Wisconsin Office of Research. The overall mission of the OTD is to support and educate MCW faculty, postdoctoral fellows, interns, students and staff. The OTD engages inventors, as well as internal and external stakeholders to bring Patents to Patients®.

Services Offered:

- Intellectual property evaluation and protection
- Patenting
- Licensing
- Start-Up company development

Contact Us:

Kevin Boggs, MBA, PhD
Director
(414) 955-4381 | kpboggs@mcw.edu

Landon Olp, PhD
Licensing Manager
(414) 955-4884 | lolp@mcw.edu

Ann Amidzich
Intellectual Property Manager
(414) 955-8660 | aamidzich@mcw.edu

https://www.mcw.edu/departments/technology-development

Pediatric Echocardiography Core

What Do We Do?

Established in 2005, the CW/MCW Pediatric Echocardiography Research Lab is currently located in the Herma Heart Institute and Children's Wisconsin. The lab has successfully performed echocardiograms and analyzed echocardiographic data for internal and external research projects. We have trained staff with expertise in congenital heart disease and pediatric and adult echocardiography (including 2D, 3D, and myocardial deformation imaging). The lab has received multiple NIH sub-contract grants from the Pediatric Heart Network (PHN) to act as an echo core lab for large, multi-institutional trials focused on pediatric heart disease.

Equipment Available

Hardware:

- TomTec Arena workstations (3)
- Syngo® Ultrasound Workplace

Software:

- TomTec Arena v2.40.00: Diagnostic and report management system specifically designed for 2D echo image review, archiving, and reporting with password-protected access.
- 2D Cardiac Performance Analysis: Myocardial deformation analysis tool that is integrated into TomTec Arena.
- Left ventricular, right ventricular, and left atrial autostrain integrated into TomTec Arena.
- 2D Image, Speckle tracking Velocity Vector Image, Syngo-Software, (Siemens®, US); integrated into the SC2000 ultrasound platform

Ultrasound Equipment:

- 10 Siemens SC2000 ultrasound machines (4 MHz 2D imaging and 4 MHz 3D imaging probes)
- 1 Philips Epiq 7c ultrasound machine and 1 Philips IE33 ultrasound machine (12, 8, 5 MHz 2D imaging and 7 and 3 MHz 3D imaging probes)
- 1 GE Vivid IQ ultrasound machine (9MHz and 13 MHz linear imaging probes)

Contact Us:

Megan Schoessling, RDCS, BS
Echo Research Lab Manager
Email: mschoessling@chw.org

Pediatric Translational Research Unit (P-TRU)

The Pediatric TRU is a unique unit within Children's Wisconsin, located conveniently on C4S – located between the S elevators and Day Surgery skywalk.

We are open Monday/Thursday 0730-1700; Tuesday/Wednesday 0730-1800 and Friday 0730-1600. Additional requests for services outside these times can be discussed with Cristen Berry, Pediatric TRU Manager (414-266-7233).

The TRU provides a variety of services, including:

- Research Coordination Training Support
    - EPIC Research Trainer and consultant
    - IRB Navigation (IRBnet) assistance
    - Budget consultation
    - Study monitoring
    - Well versed with FDA Regulations (IND/IDEs/audits)
- Nursing support
    - Nursing study support
    - Nursing coordination
    - 12 Lead ECG support (not reading/interpreting)
- Phlebotomy
- Simple lab spinning and storing. P-TRU has experience working with plasma, serum, buffy coats, and vortex mixing. We are open to expanding our lab services as requests arise. We have both refrigerated and standard centrifuges along with a Baker Hood for more sterile alliquoting of the specimens we process. We also have the ability to draw clinical labs at time of the research draw and obtain DNA samples for pick up and processing. -80oC, -30oC, and research fridge available for short term use.
- Specimen shipping – all staff are IATA/DOT trained; dry ice available for research shipping.
- 6 dedicated exam rooms for research study participants
- Investigational drug administration
- IV starts
- Data Entry (REDCap aware, open to supporting new systems based on requests)
- All RNs are PALS certified nurses and the non-nursing staff are CPR certified
- Staff are comfortable working with neonates through geriatrics

Whenever you wish to initiate a study using the TRU or are considering using the TRU, please contact:

Cristen Berry (P-TRU Supervisor) 266-7233 and/or Jeff Crawford 266-7254 (P-TRU Operations Specialist) to set up a meeting for initial conversations

Qualitative Research Consulting Service

What Do We Do?

The Qualitative Research Consulting Service is part of the Center for Healthy Communities and Research (CHCR) within the Department of Family and Community Medicine at the Medical College of Wisconsin and provides comprehensive consulting in qualitative research methodologies to MCW faculty, staff, and trainees. Our center is made up of qualitative methods experts focusing on community-engaged research, with extensive grant preparation on projects funded by NIH, NEH, Robert Wood Johnson Foundation, Advancing Healthier Wisconsin, CTSI, HRSA, and VA.

Services Offered:

- Research design
- Interview and focus group questionnaire development
- Qualitative data collection and analysis
- Grant language
- Community-based dissemination
- Publication review.

Our services are provided through hourly consultations on an appointment basis, faculty FTE on grant-funded projects, and professional training.

After the initial consultation, a time estimate and cost are provided. Please fill out a service request form and submit to schedule a consult.

Contact Us:

Staci Young, PhD	Katinka Hooyer, PhD	Melissa DeNomie, MS
Director	Co-Director	Staff Researcher

Karen Krause, Core Administrator
kkrause@mcw.edu
https://mcw.ilab.agilent.com/service_center/show_external/5073/qualitative_research_consulting_service_core

Quantitative Health Sciences (QHS)

What Do We Do?

Our mission is to provide scientifically valid, efficient and dependable research support for study design, data management and analysis of lab, animal and clinical studies. In partnership with Children's Research Institute, QHS will help train junior researchers, work with more mature researchers in obtaining and maintaining funding and develop standardized data management protocols which facilitate collection of quality data. All Pediatric researchers are eligible to receive service for no charge. Other researchers should contact QHS.

Specialties:

- Statistical Analysis: longitudinal[1] & Omics data[2]
- Weighted analysis for big databases (i.e., HCUP) [1]
- Precision medicine: statistical issues in microbiome & genetic analysis[2]
- Data conversion/analysis support[3]
- Designing data management protocols[3]

Services Offered

- Study design
- Biostatistical consultation, design & analysis
- Data collection tool development
- Survey development
- Database development
- Collaboration on proposals: IRB, grants & CTSI

QHS also provides access to many statistical programs on a shared computer.

Contact Us:

Pippa Simpson, PhD[1,2,3]
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psimpson@mcw.edu

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Amy Yumei Pan, PhD[2]
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Jody Barbeau, BS [3]
Sr. Data Manager
jbarbeau@mcw.edu

Cindy Feltz
Consultation Contact
cfeltz@mcw.edu

CRI/TBRC, 3rd Floor, #C3135; Monday – Friday, 8:30 a.m. – 5 p.m.

Redox Biology Program

The mission of the Redox Biology Program is to foster communication and an exchange of expertise among clinicians and basic science researchers in the spirit of collaborative research. To that end, the Redox Biology Program unites a broad, interdisciplinary group of researchers who are interested in the role of redox processes in physiology and pathology. These scientists have extensive research experience and technological skills, and their laboratories contain cutting-edge resources. The goal is that data and novel hypotheses resulting from interdisciplinary collaboration will yield funded grant proposals, published manuscripts, and course curricula.

The Redox Biology Program collaborates and consults with interested faculty around MCW to provide a scholarly scientific environment to conduct redox-related research, and provides training for students, who are the medical and science leaders of tomorrow. Areas of expertise include bioenergetics, cancer, cardiovascular disease, fetal brain injury, nitric oxide and its interactions, reactive oxygen species, thiol biochemistry, free radical chemistry and biochemistry, EPR (electron paramagnetic resonance) spin trapping, and inflammation, infection, and immunity.

To facilitate the exchange of expertise and ideas, the Redox Biology Program delivers high-quality education events for busy physicians and scientific investigators. One such event is the upcoming 3rd MCW Redox Biology Symposium/SfRBM Regional Symposium, which will be held virtually May 13–14, 2021. This two-day symposium will feature presentations by well-recognized speakers in the field as well as poster presentations, and will focus on new frontiers in immunology and inflammation, metabolomics and metabolism, epigenetics, and redox systems. Additional details are available at the SfRBM website: https://sfrbm.org/meetings/regional-symposium/.

Learn more about the Redox Biology Program at www.mcw.edu/departments/redox-biology-program.

Research Computing Center

The Research Computing Center (RCC) provides the infrastructure and campus-wide access to high performance computing (HPC) resources required for computationally-intensive biomedical research. RCC is institutionally supported and available to all MCW students, staff, and faculty. RCC services and operations are governed by representatives of the MCW Faculty in partnership with RCC leadership.

Services

HPC:

RCC maintains a Linux-based HPC cluster ideal for both massively parallel and high throughput workloads.

- 50 nodes
- 1200 cores
- 44 GPUs
- 10TB of memory
- Infiniband Interconnect

Storage:

RCC also provides petascale data storage to support both data-intensive computing and long-term retention.

- High-performance parallel file system
- Long-term storage for completed projects
- 10GigE interconnect

Consulting:

RCC provides consulting services for users, groups, and projects regarding a variety of research computing related topics.

- Training on HPC systems
- Software installation and setup
- End-user support and trouble-shooting
- Grant assistance and boilerplate language
- Consulting on IT needs of computational research projects

Staff and Facilities:

RCC has full-time dedicated staff with extensive experience in system administration and computational research. All hardware is housed in professionally managed MCW datacenters. RCC also collaborates with and is supported by MCW's excellent central IT teams.

- 2 Datacenters
    - Redundant power and cooling
    - Biometric access control
- Professional staff
    - Experience in research computing, system administration, network, and security

Shared Mass Spectrometry Facility

What Do We Do?

The MSMS Facility is an interdepartmental research service unit managed on behalf of MCW by the Department of Pharmacology & Toxicology. It provides service and consultation for research projects requiring mass spectrometric analysis. Two mass spectrometers are available to analyze samples. We operate on a fee for service basis. The facility provides quantitation using SRM (MRM) for known compounds. In addition, the facility can identify unknown small molecules using MS/MS techniques. The facility will implement reported procedures for analysis and quantitation and will develop new methods that answer investigator-driven questions.

Equipment Available

Agilent 6460 Triple Quadrupole-LC Mass Spectrometer: LC/MS/MS has Jet Stream source interfaced to a 1290 Infinity liquid chromatograph and autosampler. Mass analyzer uses both positive and negative detection modes with data-sampling rate of up to150 SRM/s. The 6460 routinely achieves fmol sensitivity.

Thermo Scientific Triple Quadrupole-GC Mass Spectrometer: TSQ 8000 (GC/MS/MS) is equipped for electron impact (EI) and chemical ionization (CI). Analyzer has a mass range up to 1100 m/z in both positive and negative ion detection modes. Interfaced to Trace 1310 gas chromatograph equipped with a TriPlus autosampler.

Typical Analyses:

- Complex Lipids
- Smaller, volatile lipids
- Endocannabinoids
- Drugs of Abuse
- Metabolites
- Peptides

Contact Us:
Michael J. Thomas, PhD
Director
mjthomas@mcw.edu | (414) 955-8605

Therapeutic Accelerator Program

The Medical College of Wisconsin (MCW) Therapeutic Accelerator Program (TAP) was launched in 2017 as a major initiative for the Drug Discovery Center. TAP's mission is to facilitate and accelerate therapeutics and drug discovery by translation of new basic discoveries into therapies. Tremendous progress has been made by TAP in three years of existence with support from our partners, the MCW Cardiovascular Center Smith Family Program for Enhanced Precision Therapeutics, CTSI-AMPD Module and the Wisconsin Economic Development Corporation (WEDC), Targeted Industry Projects Program. TAP is expanding services to Southeast Wisconsin regional research institutions.

SERVICES INCLUDE

- Providing project-based funding opportunities
- Facilitating collaborations
- Independent scientific review and guidance
- Resource planning advice
- I.P. disclosure assistance
- Project execution

TAP Service Center

Launched in 2020 to fill in the unmet need of support to execute investigator funded projects that will enable PI's to develop their translational therapeutic project. We are involved projects that support clinical trials by facilitating procurement of drug product for clinical trials, generating pre-IND data like PK profile, metabolism and stability profile.

Versiti BRI Flow Core

What Do We Do?

The Flow Cytometry Core Laboratory provides flow cytometric analysis and cell sorting. An experienced Flow Cytometry Specialist is in charge of the lab and will help with experimental design, data analysis and will train new users. We primarily serve internal investigators on a first-come, first-serve basis, and assist outside users as capacity permits. New users must attend a free training session prior to using the analysis instruments. Sample preparation is always critical to success, therefore we invite researchers to discuss their protocols with us in advance.

Equipment Available

- **BD LSRII Flow Cytometer:** 10 color & 12 parameter acquisition; 4 laser system; BD HTS can be used on this instrument; reads 96 well & 384 well microtiter plates.
- **BD LSRII Special Order System:** 12 color & 14 parameter acquisition; 4 laser system; BD HTS can be used on this instrument; reads 96 well & 384 well microtiter plates.
- **BD FACSAria Cell Sorter:** 10 color & 12 parameter acquisition; 4 laser system.
- **BD FACS Melody Cell Sorter:** 9 color & 10 parameter acquisition; 4 laser system; self-service after training.
- **Accuri C6:** 4 color & 6 parameter acquisition; 2 laser system

Software Available:

- FlowJo
- FCS Express
- FACSDiva
- CFlow Plus
- Miltenyi Biotec Magnetic Cell Separation Workstation also available

Contact Us:

Benedetta Bonacci
Flow Core Lab Operator
(414) 937-3843
Blood Research Institute, West Wing, #269 – 270
https://www.versiti.org/research/blood-research-institute/core-labs/flow-cytometry-core-lab

Versiti BRI Protein Chemistry Core

What Do We Do?

The Protein Core Lab at the Blood Research Institute provides services in the areas of custom FMOC solid phase peptide synthesis, peptide purification, mass spec verification, coupling peptides to carriers for antibody production and labeling peptides. Other core services are consultation on sequence selection for antigenicity, and consultation on project design and feasibility.

Modifications Available:

- C terminal labeling: Amidation
- N terminal labeling: Acetylation; Biotinylation; Fluorophores and Myristylation
- Cyclization: Disulphide; End to End; Hydrocarbon Stapling
- Backbone Modifications: D-enantiomers; N-methylamino acids; Peptoids
- Conjugation and Labeling: Carrier Proteins; Stable Isotope Labeling; Click Chemistry and PEGylation
- Special Amino Acids: Phosphoamino Acids; Dipeptides to Overcome Aggregation; Pseudoproline Derivatives and Non-Natural Amino Acids

Contact Us:

(414) 937-3847
Blood Research Institute, West Wing, Room #273
https://www.versiti.org/research/blood-research-institute/core-labs/protein-chemistry-core-lab

Versiti Viral Vector Facility

What Do We Do?

The MCW/BCW cGMP Vector Production Facility is a state-of-the-art gene therapy vector production cleanroom facility housed at the Blood Research Institute (BRI) on the Milwaukee Regional Medical Center campus here in Milwaukee. The MCW/BCW-VPF opened its doors in early 2016 and aims to provide gene transfer vectors and scientific expertise to investigators interested in conducting pre-clinical research. The facility is also developing the capacity to provide vectors and expertise to clinicians and scientists interested in acquiring/implementing clinical grade vector for early phase gene therapy trials.

Services Offered

Our original services are based in lentivector technology:

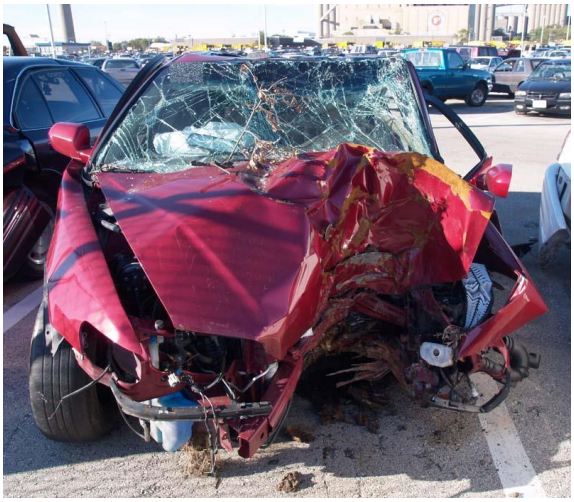
- Clinical grade cGMP lentivector for usage in early stage gene therapy clinical trials
- Pre-clinical grade lentivector produced using the same SOP's as for clinical preparations, suitable for large scale laboratory projects, and GLP toxicity studies
- Laboratory grade lentivector for research projects
- Gene Therapy project development consultation.

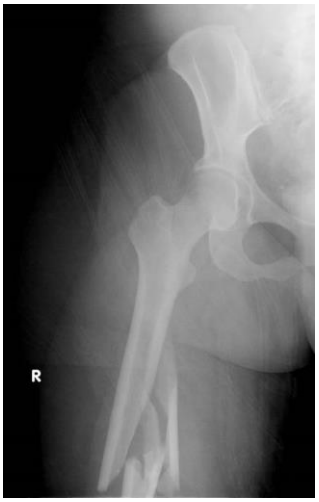
Contact Us:

Brad Best
414-937-3814
https://www.versiti.org/research/blood-research-institute/core-labs/viral-vector-core-lab

Wisconsin CIREN: Crash Injury Research Engineering Network

Narrative: The CIREN center contributes to the National Highway Traffic Safety Administration's (NHTSA) mission to prevent and reduce deaths, injuries and economic losses resulting from motor vehicle travel on our nation's roadways. The CIREN Center at MCW is one of seven national centers. It conducts crash injury research collecting and analyzing relevant data in the interest of public health. Real-world crashes are investigated to further the following objectives: Reconstruct and understand crash and injury causation, improve prognosis and treatment for crash trauma patients, reduce time of recovery and treatment costs, simulate crash scenarios in laboratory environment, disseminate data to industry, regulatory, and public agencies, develop strategies to reduce fatalities and injuries in automobile accidents, provide information to improve public infrastructure to reduce accidents, develop and disseminate safety messages to the public and train health care providers in vehicular safety and associated care.





Available Equipment: FARO 3D LIDAR scanner

Contact:
Dale Halloway
Program manager
dhalloway@mcw.edu
(414) 384-2000 x47171