Research Day 2018

Event Catalog

Monday, September 24

Welcome to Research Day!

On behalf of the Office of Research, we welcome you to Research Day 2018. This annual event brings together MCW scientists, clinicians, staff and students for an afternoon of networking and discovery. Research progresses through growth, collaboration, and change, and this year's program effectively illustrates this principle.

We are thrilled to welcome Keynote Speaker Joseph Takahashi, PhD, Howard Hughes Medical Institute Investigator and the Loyd B. Sands Distinguished Chair in Neuroscience at the University of Texas Southwestern Medical Center. Dr. Takahashi is a is a mammalian geneticist with a focus on circadian rhythms, and we look forward to his talk, "Molecular Architecture of the Circadian Clock in Mammals: Implications for Metabolism and Longevity." Join us for lunch and the opportunity to learn from a nationally renowned neurobiologist.

This year's poster session will take place in the Hub Gallery. We invite anyone and everyone to connect and conversate with 80+ researchers representing 24 different departments, institutes, and centers. We hope this environment can stimulate the openness and collaboration that leads to exciting new research projects.

This catalog not only contains the research showcased on Research Day, it also includes an institutional overview across our many departments and centers. You can also meet a diverse cross-section of MCW investigators in the monthly Research Publication Series.

Thank you for joining us as we celebrate all things research!

Ann B. Nattinger, MD, MPH, MACP
Associate Provost for Research

Cecilia Hillard, PhD
Associate Dean for Research

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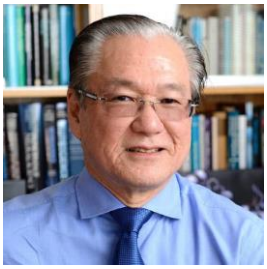
Research Day Schedule

Monday, September 24

12:00 – 1:00 p.m.
Doors open at 11:45
Lunch provided

Keynote Address in MCW Alumni Center
"Molecular Architecture of the Circadian Clock in Mammals: Implications for Metabolism and Longevity"



presented by

Joseph Takahashi, PhD

Investigator, Howard Hughes Medical Institute
Loyd B. Sands Distinguished Chair in Neuroscience
The University of Texas Southwestern Medical Center

Read Dr. Takahashi's Bio

1:00 – 3:00 p.m.

Poster Session in Hub Gallery (1st floor)
Posters will be judged for cash prizes

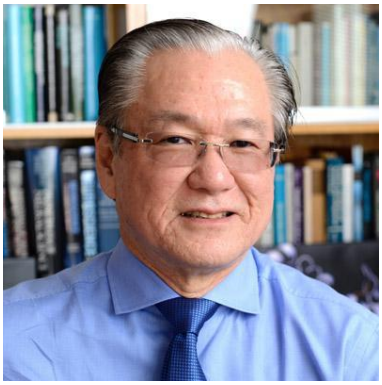
View Poster Session Map

Research Day Acknowledgements

Research Day is sponsored by the Office of Research. Thank you to Cecilia Hillard, PhD, and Susan Cohen, MD, for leading the planning team. Thanks to the following individuals for reviewing and judging our Poster Session presenters:

- Akiko Mammoto, MD, PhD, Assistant Professor, Pediatrics, Neonataology
- Anna Huppler, MD, Assistant Professor, Pediatrics, Infectious Diseases
- Antje Kroner-Milsch, MD, PhD, Assistant Professor, Neurosurgery
- Banani Banerjee, PhD, Assistant Professor, Medicine-GI
- Caitlin O'Meara, PhD, Assistant Professor, Physiology
- Debebe Gebremedhin, PhD, Associate Professor, Physiology
- Deepali Rathore, Postdoctoral Fellow, Center for Biomedical Mass Spectrometry Research, Office of Research
- Heather Toth, MD, Associate Professor, Medicine, General Internal Medicine, Hospitalist
- James Antczak, PhD, Assistant Director, Office of Technology Development, Office of Research
- Jenna Sarvaideo, DO, Assistant Professor, Medicine-Endocrinology
- Jennifer L. Brown, CCRP, Program Manager I, Neurology
- Jennifer Strande, MD, PhD, Associate Professor, Medicine, Cardiology
- John Meurer, MD, MBA, Professor, Institute for Health & Equity
- Kalpa Vithalani, PhD, Assistant Director, Office of Technology Development, Office of Research
- Kathleen Murkowski, Program Manager II, Pediatrics, Critical Care
- Katja Kovacic, MD, Assistant Professor, Pediatrics - GI
- Kelsey Porada, Clinical Research Coordinator, Pediatrics
- Kenneth Matthew Scaglione, PhD, Assistant Professor, Biochemistry
- Kevin P. Boggs, PhD, Office of Research
- Li-Shu Wang, PhD, Associate Professor, Medicine-Hematology & Oncology
- Melinda Dwinell, PhD, Associate Professor, Physiology
- Michael Flister, PhD, Assistant Professor, Physiology
- Nancy Dahms, PhD, Professor, Biochemistry
- Navdeep Gupta, MD, Assistant Professor, General Internal Medicine
- Oleg Palygin, PhD, Assistant Professor, Physiology
- Purushottam Laud, PhD, Professor, Institute for Health & Equity, Biostatistics
- Qing-song Liu, PhD, Associate Professor, Pharmacology
- Ranjan Dash, PhD, Professor, Biomedical Engineering
- Sadie Larsen, PhD, Assistant Professor, Psychiatry
- Srividya Kidambi, MD, Associate Professor, Medicine-Endocrinology
- Susan Taylor, MD, MPH, Associate Professor, Pediatrics, Anesthesiology
- Susan Cohen, MD, Assistant Professor, Pediatrics - Neonatology
- Tadanori Mammoto, MD, PhD, Assistant Professor, Radiology
- Tami Maier, PhD. Assistant Safety Officer, Finance & Administration, Environmental Health
- Tom Aufderheide, MD, Professor, Emergency Medicine
- Veronica Flood, MD, Associate Professor, Pediatrics – Hematology & Oncology
- W. Monty McKillop, PhD, Manager, GMP Vector Facility
- Xiao Chen, PhD, Assistant Professor, Medicine, Hematology & Oncology
- Yi-Wen Huang, PhD, Assistant Professor, Obstetrics and Gynecology
- Zeljko Bosnjak, PhD, Professor, Medicine-Endocrinology

About Keynote Speaker Dr. Joseph Takahashi



Joseph S. Takahashi is Chair of the Department of Neuroscience and an Investigator of the Howard Hughes Medical Institute at UT Southwestern Medical Center. He currently holds the Loyd B. Sands Distinguished Chair in Neuroscience. Before moving to UT Southwestern, Dr. Takahashi was the Walter and Mary Elizabeth Glass Professor in the Life Sciences at Northwestern University. During his 26-year tenure at Northwestern, he held appointments as professor in the Department of Neurobiology and Physiology on the Evanston campus and professor in the Department of Neurology at Northwestern University Medical School. In addition, he was also the director of the Center for Functional Genomics.

Dr. Takahashi received a BA in biology from Swarthmore College in 1974 and a PhD in neuroscience from the University of Oregon, Eugene, in 1981. For postdoctoral training, he was a pharmacology research associate at the National Institute of Mental Health from 1981-1983.

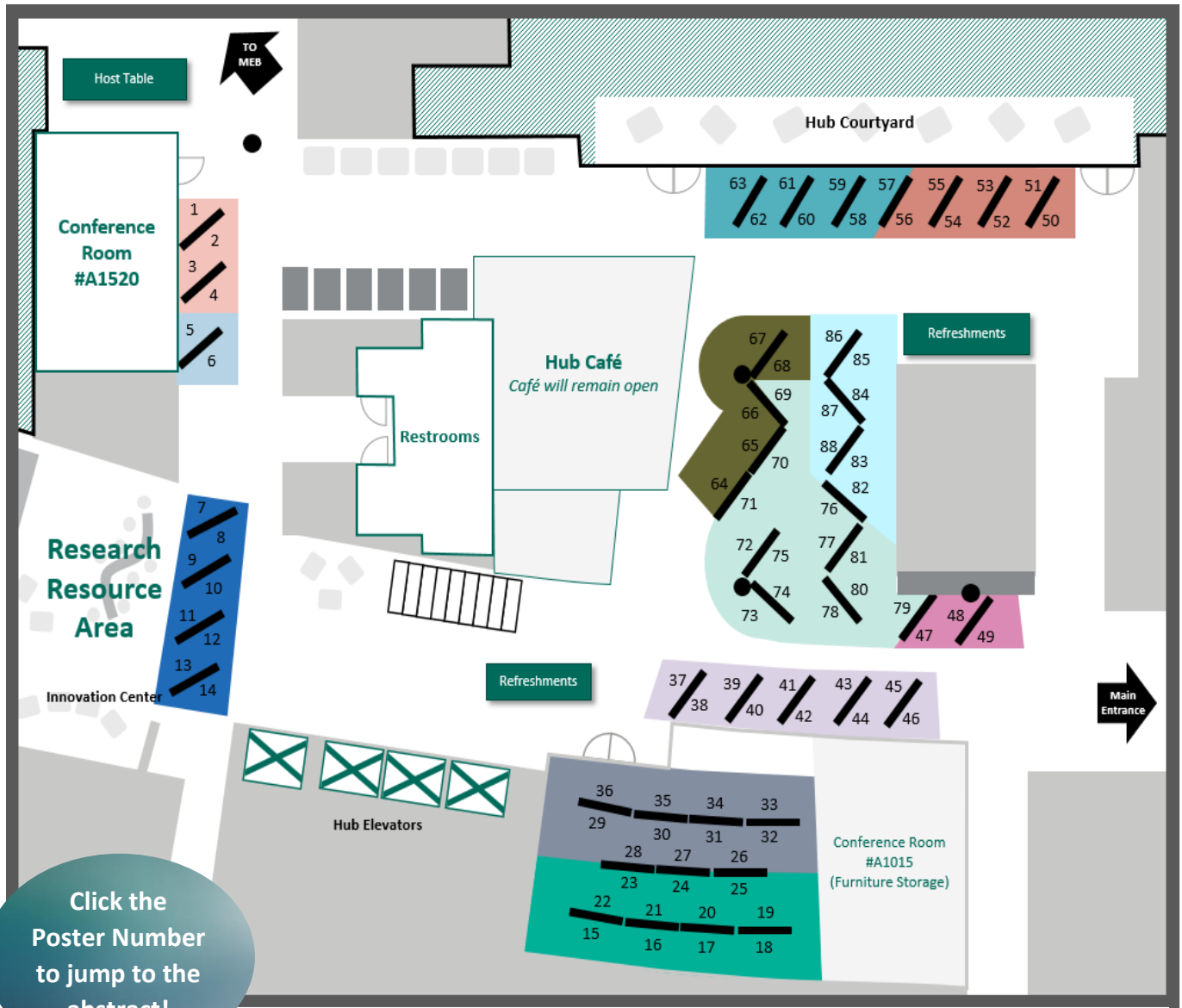
Dr. Takahashi has pioneered the use of forward genetics and positional cloning in the mouse as a tool for discovery of genes underlying neurobiology and behavior, and his discovery of the mouse and human clock genes led to a description of a conserved circadian clock mechanism in animals.

He is the author of more than 260 scientific publications and the recipient of many awards including the Honma Prize in Biological Rhythms Research, NSF Presidential Young Investigator Award, Searle Scholars Award, Bristol-Myers Squibb Unrestricted Grant in Neuroscience, and the C. U. Ariens Kappers Medal. He received the W. Alden Spencer Award in Neuroscience from Columbia University in 2001, was elected a Fellow of the American Academy of Arts and Sciences in 2000, a Member of the National Academy of Sciences in 2003 and a Member of the National Academy of Medicine in 2014.

Dr. Takahashi has served on a number of advisory committees for the National Institutes of Health, as well as scientific advisory boards for Eli Lilly and Company, Bristol-Myers Squibb Neuroscience Committee, the Genomics Research Institute for the Novartis Foundation, the Klingenstein Fund, the Searle Scholars Foundation, the McKnight Foundation, the Allen Institute for Brain Science, the Max Planck Institute for Biophysical Chemistry, and the Restless Legs Syndrome Foundation. He was also a co-founder of Hypnion, Inc., a biotech discovery company in Worcester, Mass., that investigated sleep/wake neurobiology and pharmaceuticals (now owned by Eli Lilly and Co.). He is a co-founder of ReSet Therapeutics, Inc., a biotech company that works on the role of clocks in metabolism.

He is on the Editorial Boards for *PNAS, eLife, J Biol Rhythms, Neurobiology of Sleep and Circadian Rhythms, Genes, Brain and Behavior*, and Section Head, Animal Genetics, Biology Reports Ltd., *Faculty of 1000*.

Poster Session Map



Track Color Code:

- Blood, Immunity & Infection
- Pulmonary
- Surgery, Ophthalmology, Otolaryngology & Orthopaedics
- Cancer
- Neuroscience
- Education
- Metabolism, Endocrine & Digestive
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3	Kavya Puchhalapalli	Medicine: Hematology and Oncology	Management and Outcomes of Venous Stents in Patients with Acute Lower-Limb Deep Vein Thrombosis	Support Staff
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72	Amy Nader	Neurosurgery	Acute Injury Characteristics Distinguish Different Subpopulations of Mild Traumatic Brain Injury (mTBI)	Support Staff
73	Elizabeth Rodriguez, RT(R) VI	Radiology	Sphenopalatine Nerve Block: Clinical Considerations and Safety and Efficacy	Support Staff
74	Joshua Pohlman	Radiology	Next generation mobile digital radiography: Can dose be reduced without sacrificing image quality in the neonatal intensive care unit?	Clinical Fellows & Residents
75	Brycen Bodell, MD	Radiology	Evaluating parenchymal enhancement characteristics utilizing a novel imaging software	Senior Faculty
76	Jacqueline Blank, MD	Surgery: Colorectal Surgery	Auricular Neurostimulation for Non-Pharmacologic Post-Operative Pain Control: A Randomized Controlled Trial	Clinical Fellows & Residents
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87	Lida A. Zeighami	Genomic Sciences & Precision Medicine Center: Bioinformatics Research and Development	Developing and Implementing a Robust and Thorough RNA-Seq Data Analysis and Deliverable Report	Support Staff
88	Wendy M Demos	Genomic Sciences & Precision Medicine Center	Applications and Methods for Interpretation of WGS and WES Data	Support Staff

Poster #	1
Abstract Title:	Reestablishing homeostasis in a spontaneous mouse model of ileocolitis
Presenter(s):	Christopher L DeCiantis, PhD ✉
Authors:	Christopher L DeCiantis, Jonathan C Jeschke, Christopher G Mayne, Jennifer Ziegelbauer, Selena Singh, Mariko Suchi, Nita H Salzman, and Calvin B Williams
Dept/Division:	Pediatrics: Rheumatology
Category:	Support Staff
Introductions:	We aim to establish treatments that will restore ileal homeostasis in a murine model of colitis, including treatment of disease and prevention of ileocolitis.
Methods:	We have developed a spontaneous model of ileocolitis designed to study the processes that promote homeostasis within the ileum. Our system uses a "Bigenic" approach that combines TCR transgene mice with another transgenic line expressing the cognate antigen in ileal crypts. Bigenic mice exhibit decreased nTreg production that predisposes them to developing a chronic ileocolitic inflammatory disease in the weeks after weaning. Half of Bigenic mice accumulate ileal-reactive Treg cells and fail to develop colitis. In the absence of IFNγ (*Ifng*$^{-/-}$), Bigenic mice are unable to establish this homeostatic state, resulting in a fully penetrant and acute colitis. We aimed to identify interventions capable of treating established colitis and restoring mucosal homeostasis in *Ifng*$^{-/-}$ Bigenic mice. We undertook studies where adoptive transfer of nTreg cells from healthy mice into *Ifng*$^{-/-}$ Bigenic mice was evaluated for prevention of and rescue from disease state. Further studies were performed where *Ifng*$^{-/-}$ Bigenic mice were started at weaning on a prophylactic treatment with ad libidum non-absorbable antibiotics in their drinking water and continued for three weeks. Additionally, *Ifng*$^{-/-}$ Bigenic mice were allowed to naturally progress into a disease state at which time the same antibiotic treatment was initiated, starting around 40 days of life, and continued for nine weeks.
Results:	We found both adoptive nTreg immunotherapy and ad libitum non-absorbable antibiotics were able to prevent ileocolitic disease when treatment was initiated at weaning. Similarly, both treatments were sufficient to reverse established disease among *Ifng*$^{-/-}$ Bigenic mice. However mice receiving nTreg cells were less likely to exhibit weight loss episodes following rescue. Interestingly, *Ifng*$^{-/-}$ Bigenic mice transiently treated with antibiotics at weaning did not subsequently manifest the acute ileocolic inflammatory disease or the degree of breakthrough weight loss observed in antibiotic-rescued *Ifng*$^{-/-}$Bigenic mice.
Conclusions:	Adoptive transfer of nTreg cells is sufficient to allow *Ifng*$^{-/-}$ Bigenic mice to internally establish mucosal homeostasis. Our findings indicate that manipulation of the microbiome, without directly acting on the host, can facilitate the establishment of mucosal homeostasis and resistance to spontaneous ileocolitic disease.
Reference 1:	Jeschke, J. C., et al. A model of TH17-associated ileal hyperplasia that requires both IL-17A and IFNγ to generate self-tolerance and prevent colitis. *Mucosal Immunology* **11**, 1127-1137 (2018) https://www.nature.com/articles/s41385-018-0023-6

Poster #	2
Abstract Title:	Infection rate of tunneled femoral noncuffed central venous catheters vs. peripherally inserted central catheters in neonates and infants: A single institutional experience
Presenter(s):	Christopher Peske, PA-C ✉
Authors:	Jonathan Lee MD, David Moe MD, Christopher Peske PA-C, Nghia-Jack Vo MD
Dept/Division:	Pediatrics: Pediatric Imaging
Category:	Clinical Fellows & Residents
Introductions:	Purpose: Feasibility and satisfactory outcomes of neonate and infant tunneled femoral noncuffed central venous catheters (CVCs) has been demonstrated in the literature. However, concerns exist regarding potential increased infection rates of femoral CVCs over traditional peripherally inserted central catheters (PICCs) due to relative proximity of femoral CVCs to the groin and diaper. This study's purpose is to compare the infection rate of image guided interventional radiology placed tunneled femoral CVCs to non image guided neonatal intensive care unit placed PICCs in a large series of neonates and infants at a single institution.
Methods:	Materials and Methods: A retrospective review was performed for all neonates and infants receiving a tunneled femoral noncuffed CVC by interventional radiology or a PICC by neonatal intensive care between 2012 and 2014. Individual infection rates were determined by the hospital team using central line-associated blood stream infection (CLASBI) criteria. Total catheter days, age of patient at catheter placement, catheter dwell time, reason for catheter placement, catheter size and CLABSI events were recorded.
Results:	Results: 204 patients received a tunneled femoral noncuffed CVC and 203 patients received a PICC. In the tunneled femoral noncuffed CVC cohort, 111 subjects were male and 92 subjects were female with the total number of catheter days at 4238, average age of CVC placement at 69.0 days, average dwelling time of 20.9 days, and total infection rate of 0.025. In the PICC cohort, 112 subjects were male and 92 subjects were female with the total number of catheter days at 4089, average age of PICC placement at 11.7 days, average dwelling time of 20.4 days, and total infection rate of .020. This equates to a CLABSI event in 1.18/1000 catheter days for interventional radiology placed tunneled femoral noncuffed CVC s versus 0.98/1000 catheter days for neonatal intensive care PICCs.
Conclusions:	Conclusion: The infection rates are nearly identical for tunneled femoral noncuffed central venous catheters and peripherally inserted central catheters in neonates and infants.

Poster #	3
Abstract Title:	Management and Outcomes of Venous Stents in Patients with Acute Lower-Limb Deep Vein Thrombosis
Presenter(s):	Kavya Puchhalapalli ✉
Authors:	Kavya Puchhalapalli, Lisa Baumann Kreuziger
Dept/Division:	Medicine: Hematology and Oncology
Category:	Support Staff
Introductions:	Anticoagulant therapy is a highly effective strategy to treat deep vein thrombosis (DVT). It is efficient in preventing acute thromboembolic complications but doesn't actively eliminate thrombus. Residual thrombus can cause further clot formation and may result in post-thrombotic syndrome (PTS). Hence, endovascular therapies are being explored to treat acute thromboreduction. Supplementary catheter-directed thrombolysis (CDT) involving localized delivery of thrombolytic agent, has been observed to be effective in decreasing PTS at 24-months in comparison to conventional anti-coagulation alone. Furthermore, venous stents have shown efficacy and are being increasingly used post-CDT, to improve venous patency and promote recanalization. Studies have not been completed to understand how patients should be treated after venous stent placement for acute venous thrombosis. We reviewed the Medical College of Wisconsin (MCW) experience as a part of an international registry of management and outcomes of stents in acute DVT patients.
Methods:	We retrospectively reviewed adult patients with venous stents inserted as part of acute lower-limb DVT management between 9/1/2016 and 8/31/2017 at Froedtert Hospital. The clinical records were obtained using the Cohort Discovery Tool (CDT) of the Froedtert Hospital/ MCW Clinical Data Warehouse (CDW). Patient records were selected by filtering for ICD-10 procedure codes for open/ percutaneous intravascular stent placement. For each record, various data variables were looked at including baseline clinical characteristics, type, dose and duration of antithrombotic management, characteristics of venous stents, and management post-stent insertion.
Results:	Of all the CDW patients records searched, 33 met the above-mentioned inclusion criteria. Of those, only 13(39%) had stents placed for acute DVT management. 20(61%) were excluded since they didn't meet the diagnosis criteria of lower-limb DVT; 9 were upper extremity DVTs, and 12 were patients with a diagnosis of DVT, but stents placed (cardiac, renal, etc.) for other conditions. Of the 13 included patients, median age was 38, mean age was 43, and 54% were female. Data from these records based on aforementioned variables, was input into the online international registry.
Conclusions:	Most venous stents at MCW are not placed for acute DVT. Due to the rarity of venous stent placement for this indication, the international registry can be utilized to understand the management and outcomes of patients after venous stent placement.
Reference 1:	Prandoni, Paolo, et al."Residual venous thrombosis as a predictive factor of recurrent venous thromboembolism."Ann Intern Med 137.12(2002):955-960.
Reference 2:	Enden, Tone, et al."Long-term outcome after additional catheter-directed thrombolysis versus standard treatment for acute iliofemoral deep vein thrombosis. "The Lancet 379.9810(2012):31-38.
Reference 3:	AbuRahma, Ali, et al."Iliofemoral deep vein thrombosis: conventional therapy versus lysis and percutaneous transluminal angioplasty and stenting. "Annals of surgery 233.6(2001):752.

Poster #	4
Abstract Title:	Altered neural calcium signaling in human iPSC-derived cortical organoids with cytomegalovirus infection
Presenter(s):	Scott Terhune ✉
Authors:	Samantha L. Sison, Amanda Johnson, Benjamin S. O'Brien, Scott S. Terhune, and Allison D. Ebert
Dept/Division:	Microbiology & Immunology
Category:	Senior Faculty
Introductions:	Human cytomegalovirus (HCMV) is a beta herpesvirus that upon infection during pregnancy can cause severe congenital birth defects including microcephaly, vision loss, and hearing loss. Currently, no approved treatment options exist for managing in utero infections. Our previous work showed that the antiviral compound maribavir (MBV) decreases HCMV infection in undifferentiated human induced pluripotent stem cell (iPSC) derived neural progenitor cells (NPCs) and allowed progression to early steps in differentiation. However, it remains to be determined whether MBV-treated NPCs can differentiate into functional glutamatergic neurons and astrocytes. Here we evaluated the impact of infection on calcium signaling using cultured NPCs as well as in three-dimensional iPSC-derived cortical organoids.
Methods:	iPSCs were cultured and differentiated toward NPCs and 3D cortical organoids using standard differentiation protocols. At various time points post-differentiation, HCMV expressing GFP was added to the cultures. MBV was added to some of the cultures at the time of infection to inhibit viral encapsidation and egress. Differentiation and cell survival was determined in vitro by immunocytochemistry and in organoid cryosections by immunofluorescence. Functional changes were quantified using live-cell ratiometric imaging measuring intracellular calcium changes following stimulation of purinergic and voltage-gated channels with ATP and KCl, respectively.
Results:	In the absence of infection, acutely plated NPC populations exhibited increasing percentages of ATP-responsive astrocytes and KCl-responsive neurons over time in culture consistent with maturation. Following infection using GFP-expressing HCMV, NPCs exhibited reduced baseline calcium levels and were unresponsive when evaluated 5 days post infection. In contrast, addition of MBV resulted in reduced numbers of GFP-positive cells, and the GFP-negative cells within the population exhibited more normal ATP- and KCl-responsive signaling. To extend these studies, we used early and late stage multicellular iPSC-derived cortical organoids. We first confirmed proper differentiation and laminar organization within uninfected organoids. Upon HCMV infection, we observed GFP-expressing cells within the tissues regardless of the developmental stage. MBV treatment reduced the numbers of GFP-expressing cells, and the GFP-negative cells exhibited more normal KCl-responsive signaling.
Conclusions:	Our studies demonstrate that HCMV infection significantly impairs neural function. Moreover, our data indicate that MBV-mediated inhibition of HCMV infection allows NPCs within a complex population to develop into functional neural tissues.

Poster #	5
Abstract Title:	Improving the Treatment of Pulmonary Exacerbations with Home IV Antibiotic Therapy
Presenter(s):	Nicholas Antos, MD ✉
Authors:	Nicholas Antos, MD, Nicole Brueck, APNP, Theresa Kump, Thomas Wade, Julie Noe, MD
Dept/Division:	Pediatrics: Pulmonary
Category:	Junior Faculty
Introductions:	Pulmonary exacerbations (PEx) are a substantial burden for CF patients and many do not recover lost lung function. Despite this, best practices are lacking for the length, type and location (hospital or home) of IV treatments. Recent analysis showed IV treatments in the hospital were more successful than those in the home, including in return to 90% of baseline FEV1 (Schechter 2017). Our previous quality improvement (QI) initiatives focused on hospital care and communication. As our Home IV Antibiotic Therapy (HIAT) use was increasing, we began a QI project to similarly improve our HIAT. Specific Aims include improving discharge planning, standardizing follow-up practices, and safe care administration.
Methods:	We evaluated our HIAT process, including initiation, planning, and discontinuation. As HIAT occurs outside of the healthcare system many care gaps exist, such as a lack of regular documentation and problems occurring away from aid. Multiple types of problems existed, with medical complications and central line issues being most common and labs errors identified as most avoidable. When to use HIAT was also not standardized or well defined, leading to confusion for the family and care team. To address these concerns, we designed a set process and leveraged the electronic health record to standardize our care/communication. The new process includes setting individualized criteria for HIAT use, including a specific FEV1 goal, minimum number of hospital days, and stable social situation/compliance. Follow up is now scheduled at 7 days for all, with lab tests generally coordinated. Charting templates, including a Home IV Road Map, were devised to allow consistent and accurate communication and monitoring.
Results:	After implementation our tools and process were quickly adopted, with 100% compliance by 6 months. As for safety, we now better monitor potential issues and have had no more errors with laboratory tests. As for efficacy, our average rate of return to ≥90% of baseline FEV1% by first follow-up visit was 87% before intervention and increased to 96% after intervention. All patients have successfully met this goal for >1 year, nearing special cause variation (G- and P-chart, limited by sample size). Interestingly, despite starting the project due increasing HIAT, we had a regular decrease with frequency essentially halving every year. Reasons for this are multiple, including increased awareness of advantages/disadvantages of hospital versus home, patient transitions, and precise selection of appropriate candidates. Most start the course in the hospital and transition to home. Overall, we feel our care quality and communication has improved with this process and tools.
Conclusions:	Exacerbation treatment is an essential part of CF care, with much uncertainty on best practices. Using set criteria, we have standardized our HIAT care plans and have had successful return to baseline FEV1, similar to our inpatient care. We have had a subsequent decrease in overall HIAT use, with multiple causes and temporally related to our project. Further work is needed to better define PEx treatment needs and our next steps include increased integration with home care companies and our adult program.
Acknowledgements:	Supported by a QI Grant from the CF foundation

Poster #	6
Abstract Title:	Is it really necessary to scan-check Computed Tomography Pulmonary Angiography (CTPA) study in evaluating Pulmonary Embolism?
Presenter(s):	Zachary Laste ✉
Authors:	Zachary Laste, Melissa Wein, Naveen Kulkarni, Dhiraj Baruah
Dept/Division:	Radiology: Cardiothoracic
Category:	Junior Faculty
Introductions:	Standard of our practice for CTPA is that a scan check is performed by a radiologist (mostly resident/fellow in training) This is to avoid patient recall due to unsatisfactory study Scan check interrupts clinical workflow & can be critical at times Technologist should know what is an adequate study Technologist should also know when to reinject/repeat
Methods:	Duration - October 2016 through January 2017 Inclusion criteria – all CTPA examination from the emergency department scanner type – GE Revolution scanner CTPA examinations are divided in two groups Group 1 (daytime) – studies performed from 7 am to 4.59 pm Group 2 (afterhours) – studies performed from 5 pm to 6.59 am Group 1 cases were scan checked by a resident radiologist Group 2 cases were not scan checked unless technologist decided that scan check is necessary Cases were retrospectively evaluated by 4 radiologists with experience reading chest CT Parameters evaluated - Recall Diagnostic quality (Optimum opacification and respiratory motion) Reason technologist requested to scan check in group 2
Results:	Technologist documented 268 cases from group 2 (afterhours) Out of 268, called for scan-check 82 cases Reasons for scan check in technologists note – Respiratory motion related artifacts – 39 (repeated in 12) Suboptimal contrast opacification – 21 (repeated in 10) Contrast extravasation/ IV access issue – 2 (both repeated) Resident wanted to scan check – 15 (none repeated) No reason – 5 (none repeated) No recall in either group How many studies would the retrospective reviewers have repeated? Group 1 (Daytime) – total 13 (5%) 4 cases with HU < 250 9 cases due to respiratory motion Group 2 (Afterhours) – total 21 (6%) 8 cases with HU < 250 13 cases due to respiratory motion
Conclusions:	This project shows importance of radiology technologists understanding of CTPA studies and how that can avoid unnecessary scan-check Limiting unnecessary scan checks will help avoid interruption of Radiologists' workflow
Reference 1:	Mountain D, Keijzers G, Chu K, Joseph A, Read C, Blecher G, Furyk J, Bharat C, Velusamy K, Munro A, Baker K, Kinnear F, Mukherjee A, Watkins G, Buntine P, Livesay G, Fatovich D. RESPECT-ED: Rates of Pulmonary Emboli (PE) and Sub Segmental PE with Modern ComputedTomographic Pulmonary Angiograms in Emergency Departments: A Multi-Center Observational Study Finds Significant Yield Variation, Uncorrelated with Use or Small PE Rates. PLoS One. 2016 Dec 5;11(12):e0166483. doi: 10.1371/journal.pone.0166483. eCollection 2016. Erratum in: PLoS One. 2017 Aug 29;12 (8):e0184219
Reference 2:	Wittram C. How I do it: CT pulmonary angiography. AJR Am J Roentgenol. 2007 May; 188 (5):1255-61
Reference 3:	Godwin JD, Webb WR, Gamsu G, Ovenfors CO. Computed tomography of pulmonary embolism. AJR 1980; 135:691-695

Poster #	7
Abstract Title:	A Single-Institution Review of 77 Patients Managed with Nephroureterectomy for Upper Tract Urothelial Carcinoma
Presenter(s):	Halle Foss ✉
Authors:	Halle Foss, BA; Garrett Berger, PharmD; Scott Johnson, MD; Peter Langenstroer, MD; William See, MD; Kenneth Jacobsohn, MD
Dept/Division:	Urology
Category:	Support Staff
Introductions:	Upper tract urothelial carcinoma (UTUC) makes up only 5-10% of all urothelial carcinomas. Unlike lower tract urothelial carcinoma, it is difficult to stage UTUC pre-operatively due to the inadequacy of biopsy in assessing depth of invasion. This study aims to report long-term outcomes for patients who underwent nephroureterectomy for UTUC at a single institution over a 16-year period.
Methods:	A retrospective chart review was completed for all patients who underwent nephroureterectomy at Froedtert Hospital from January 2000 through December 2016. Patients were excluded if they had metastatic disease at presentation, non-urothelial pathology, or insufficient medical records. Medical records were reviewed for demographic, operative, and follow-up information. Statistical analysis was performed with Stata 14.2.
Results:	A total of 91 patients were evaluated, 11 were excluded from analysis for non-urothelial pathology, 2 for evidence of metastasis at presentation, and 1 for insufficient medical records. Mean age was 70 +/- 10.1 years, and BMI was 29 +/- 5.4. 50 patients were male (65%). Median follow-up time was 37.8 months. Pre-operative biopsy was performed in 50 patients (65%), however this only yielded staging information in 6 (12%) as Ta, and 2 (4%) as T1. Of these 8 patients who had staging pre-operatively, 6 (75%) were upstaged after surgery. Final pathology was T0 in 1 (1.3%), Ta in 16 (20.8%), Tis in 5 (6.5%), T1 in 13 (16.9%), T2 in 9 (11.7%), T3 in 29 (37.7%), and T4 in 3 (3.9%) patients. Lymph node dissection was performed in 33 patients (42.9%), of which 4 (12.1%) were positive. The majority of cases were performed via a robotic approach (54%; n=42), with the remainder being laparoscopic (25%; n=19) or open (21%; n=16) procedures. Mean length-of-stay was 5.7 +/- 3.4 days. 30-day post-op complication rate was 58.4%. 11 patients (15%) received adjuvant chemotherapy. Over a median follow-up of 37.8 months, 39 patients (51%) developed recurrence or distant metastasis and 18 (27%) died of disease. Overall survival and recurrence-free survival was 90.1, 75.6%, and 52.4% and 60.5, 44.1 and 41.6% at 1, 3, and 5 years respectively.
Conclusions:	UTUC is an uncommon, but lethal disease, with nearly half of patients who underwent nephroureterectomy for UTUC dying within 5-years. Recurrence was also common, with over half of patients developing either local or distant recurrence within 5-years after surgery.

Poster #	8
Abstract Title:	Agglutination: Prevalence and Contributory Factors
Presenter(s):	Garrett K. Berger, PharmD ✉
Authors:	Garrett K. Berger, PharmD, Luriel Smith-Harrison, MD, Jay Sandlow, MD
Dept/Division:	Surgery: Urology
Category:	Support Staff
Introductions:	Agglutination is a finding noted in semen analyses (SAs) that often causes confusion as to its significance. While some have attributed agglutination to antisperm antibodies (ASAs), there are other causes as well, such as genital tract infection and ascorbic acid deficiency. Additionally, it is known that patients with ASAs often have risk factors such as a history of scrotal trauma or surgery. Therefore, we sought to determine the prevalence of agglutination in our patient population and correlate it with these risk factors, regardless of the presence/absence of ASAs.
Methods:	A retrospective study was conducted on the SAs of men seen at a single academic Reproductive Center between January 2017 and February 2018. In addition to the standard SA characteristics, additional gathered data points included: variability between agglutination tests, history of scrotal trauma, and history of scrotal surgery. Statistical analysis was performed using SPSS v24.
Results:	Of the 1095 charts identified, 133 (12.1%) patients experienced agglutination (61.7% scant, 21.8% moderate and 16.5% excessive). Of patients who underwent multiple SAs, 24 (12.2%) showed variability. Furthermore, patients who underwent scrotal surgery carried 3.4 times the risk for agglutination (X2 $p<.01$) and 5.5 times the risk for variability (X2 $p<.01$) as compared to those patients without a history significant for scrotal surgery. Trauma was seen in six (1.9%) patients and carried no statistical significance with respect to agglutination or variability (X2 $p=.75$, $p=.27$, respectively).
Conclusions:	Agglutination is a relatively common finding in men presenting to a reproductive clinic with little intra-patient variability. Scrotal surgery confers a higher risk of agglutination and variability. While the clinical significance of this has yet to be determined, the presence of agglutination may help discern patients with immunologic fertility factors.

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Poster #	9
Abstract Title:	Interaction between Streptococcus pneumoniae and Haemophilus influenzae: Mutualistic or Competitive Symbiotic Relationship?
Presenter(s):	Jacob Hawig ✉
Authors:	Jacob Hawig, Wenzhou Hong, Joseph E. Kerschner
Dept/Division:	Otolaryngology & Communication Sciences
Category:	Support Staff
Introductions:	With over 3 million cases of otitis media (OM) occurring annually in the United States, middle ear infections have profound impact on the public health caring system. The population most at risk for this infection are young children, as up to 95 percent of children experiencing at least one episode of ear infection by age 3. Streptococcus pneumoniae (Spn) and nontypeable Haemophilus influenzae (NTHi) are two of the main bacterial pathogens of OM. High rates of co-colonization and co-infection of Spn and NTHi have been evident in the upper respiratory tract and middle ear cavity of OM patients. Although Spn has competitive advantage by producing hydrogen peroxide to inhibit NTHi growth, co-infection with NTHi enhanced pneumococcal persistence and biofilm formation in vivo in chinchilla OM model. We hypothesize that NTHi can specifically enhance pneumococcal survival and this enhancement may be hindered because of the death of NTHi due to hydrogen peroxide produced by Spn. In order to test the hypothesis co-culturing experiments of Spn and NTHi were performed in this study.
Methods:	Co-cultures were performed by mixing with different initial cell densities of Spn and NTHi (cell rations were 1:1, 1:10 and 1:100, respectively) within different medium conditions. Cultures of sole species were set up as controls. Viable cells were counted by plating serially diluted cultures at 16, 24, 36 and 48-hour time points post the initiation of the culturing.
Results:	The enhancement of NTHi on Spn survival showed dose-dependent and time-dependent manners. The amounts of viable cell of solely cultured NTHi didn't fluctuate significantly from 16 to 48-hour time points. Solely cultured Spn died rapidly from 16-hour time point and no viable cell was counted after 36-hour time point. When co-cultured with NTHi, pneumococcal survival was enhanced but displayed different patterns in the cultures with different ratios of initial cell densities. Mixed with more Spn cells (1:1 ratio) killed NTHi cells quickly (before 16-hour time point) resulting in Spn death even there were more viable Spn cells at 24-hour time point compared to the sole culture. In the co-culture with less Spn cells (1:100 ratio), NTHi survived longer (more than 36 hours) and more viable Spn cells were counted at 48-hour time point. Absence of hemin and NAD which are required for NTHi growth in the medium, the enhancement on pneumococcal survival in the co-cultures was observed but impaired significantly compared to the co-cultures within medium supplemented with hemin and NAD.
Conclusions:	There is a dynamic but Spn-oriented interaction between Spn and NTHi in in vitro culture. Live NTHi cells can enhance pneumococcal survival but the enhancement could be hindered by the death of NTHi caused by Spn. Future study will be focused on the molecular mechanism regulating this inter-species interaction, which would help to develop novel effective method to control OM and other polymicrobial infections.

Poster #	10
Abstract Title:	Splitting Hairs and Challenging Guidelines: Defining the Role of Perioperative Antibiotics in Pediatric Appendicitis Patients
Presenter(s):	Kimberly K. Somers, PA-C, MPAS, BS, BA ✉
Authors:	Kimberly K Somers, PAC, Daniel Eastwood, MS, Ying Liu, PhD, Marjorie J. Arca, MD
Dept/Division:	Surgery: Pediatric Surgery
Category:	Support Staff
Introductions:	Antibiotics are an integral part of treatment of both acute and complicated appendicitis. We sought to determine if an association exists between surgical site infections (SSI) in patients with acute and complicated appendicitis and the timing of perioperative antibiotics.
Methods:	We performed single institution review utilizing a prospectively collected appendicitis database on all patients with acute (n=988) and complex appendicitis (n=561) from 1/1/2013 until 12/31/2017. Duration of intravenous antibiotics in complicated appendicitis was determined by clinical criteria (afebrile, non-tachycardia, and able to tolerate feeding). The primary outcome measure is development of surgical site infection (SSI) within 60 days of surgery.
Results:	For acute appendicitis (AA), SSI occurred in 2.5% of patients with no statistical significance (p=0.566) seen between those who received preoperative antibiotics within 60 minutes of incision (2.1%) versus greater than 60 minutes (3%). Patients who received post-operative antibiotics had 2.65% SSI compared to 1.4% of patients who did not receive post-operative antibiotics (p=0.718). For complicated appendicitis (CA), SSI occurred in 19.1% of patients with no statistical significance (p=0.739) between those who received preoperative antibiotics within 60 minutes of incision (19.6%) versus greater than 60 minutes (18.5%). A grid search for the optimal window of preoperative antibiotic yielded the time interval <;20 minutes or >;80 minutes prior to incision to have less SSI. Adjusting for age, patients given antibiotic in the 20-80 window had significantly fewer complications after discharge (OR=0.41, 95% CI 0.20, 0.84, p=0.0157).Two CA groupings emerged with respect to clinical response: (1) Early Responders (ER), who met discharge criteria in 6 days or less, and (2) Late Responders (LR) who met discharge criteria >;6 days. ER's SSI rates (8.8%) were statistically lower (49.3%, p<;0.001) and had less need for readmission compared to LR (4.0% versus 18.3%, p<;0.001). ER required a significantly shorter duration of IV antibiotics and length of stay as well as a much lower rate of postoperative infection and need for readmission compared to LR. In the ER group, we noted a higher rate of SSI in patients who received 1 (25%) or 2 (14%) days of IV compared to 3-6 days (average 8%). In logistic regression controlling for age at surgery, ER patients with oral antibiotics had lower odds of complication than patients discharged with no oral antibiotics (OR 0.40.5, 95% CI 0.185, 0.884; p=0.0233). In contrast, oral antibiotics did not protect patients in the LR group from having post-operative SSI.
Conclusions:	Preoperative antibiotics given within 60 minutes of incision did not confer an advantage against SSI in AA or CA. In AA, postoperative antibiotics did not protect against SSI. In CA, physiologic response to treatment should guide therapy.
Acknowledgements:	Melissa Lingongo, BS, CCRC, Michelle Knezevich, Brooke Pinar for reviewing operative notes on contamination findings.
Reference 1:	Rosenberger MH, Politano AD, Sawyer RG. The surgical care improvement project and prevention of post-operative infection, including surgical site infection. Surg Infect (Larchmt) 2011; 12(3):163-8.
Reference 2:	Mineci PC, Mahida JB, Lodwick DL, Sulkowski JP, et al. Effectiveness of patient choice in nonoperative vs surgical management of pediatric uncomplicated acute appendicitis. JAMA Surg 2016; 151(5):408-415.
Reference 3:	Coakley BA, Sussman ES, Wolfson TS, Bhagavath AS, Choi JJ, Ranasingh EN, Lynn ET, Divino CM. Postoperative antibiotics correlate with worse outcomes after appendectomy for nonperforated appendicitis. J Am Coll Surg 2011: 213(6): 778-83, PMID 21958510.

Poster #	11
Abstract Title:	Detection of pepsin in oral secretions of infants with and without laryngomalacia
Presenter(s):	Miles Klimara ✉
Authors:	Miles J. Klimara BA, Tina Samuels MS, Nikki Johnston PhD, Robert H. Chun MD, Michael E. McCormick MD
Dept/Division:	Otolaryngology & Communication Sciences
Category:	Support Staff
Introductions:	Laryngomalacia is a common cause of stridor associated with laryngopharyngeal reflux (LPR). Although pepsin in operative supraglottic lavage specimens has been associated with severe laryngomalacia, its presence in oral secretions of ambulatory patients with less severe disease is unknown. Prospective case-control study design comparing patients in an ambulatory setting under 2 years old with laryngomalacia to children without laryngomalacia.
Methods:	Children less than 2 years old with laryngomalacia diagnosed by flexible laryngoscopy and children without stridor were selected. Oral secretion samples were obtained in clinic from all subjects. Pepsin, IL-1β, and IL-8 enzyme-linked immunosorbent assay were performed.
Results:	Sixteen laryngomalacia and sixteen control patients were enrolled. Pepsin was detected more frequently in oral secretions of patients with laryngomalacia (13/16) than in controls (2/16; $p < 0.001$). Higher median pepsin was observed in laryngomalacia than control specimens ($p < 0.001$). Four patients with laryngomalacia developed symptoms requiring supraglottoplasty. All 4 had salivary specimens positive for pepsin, but there was no significant association between the presence or level of pepsin and severity of laryngomalacia or need for operative management. No significant associations were found in the levels or presence of salivary IL-1β or IL-8 and other measures such as the presence or level of pepsin, laryngomalacia vs. control group, or need for operative management.
Conclusions:	Pepsin in salivary specimens demonstrated an association with laryngomalacia, supporting the use of salivary pepsin as a noninvasive tool for future investigation of LPR in patients with laryngomalacia of varying degrees of severity.
Acknowledgements:	Aniko Szabo, PhD and Joy Liu, MS - Division of Biostatistics. Funding from Department of Otolaryngology.

Poster #	12
Abstract Title:	The Acceptance of Teleophthalmology in Community Health Settings in Milwaukee
Presenter(s):	Nathalie Abenoza, BA ✉
Authors:	Nathalie Abenoza, BA
Dept/Division:	Ophthalmology
Category:	Support Staff
Introductions:	According to the Wisconsin Department of Health Services, 8% of Wisconsin adults, or 356,000 adults, have diabetes and about 138,000 additional adults have diabetes and are not aware of it. To make matters worse, only about 50% of the diagnosed diabetics are getting the required yearly eye examination in the United States, resulting in preventable vision loss. Salud a la Vista (SALV) is a partnership between the Milwaukee Health Department, UCC, and various academic institutions throughout Milwaukee that bring retinal screenings to at risk communities with limited resources with the use of a mobile non-mydriatic retinal camera. SALV combines telemedicine and community-based screening to break down barriers that at-risk populations in Milwaukee face such as access to care, cost, insurance, and cultural and language barriers with hopes of improving eye screening rates. The purpose of this project is to assess the acceptance and attitudes of participants towards teleophthalmology in community health settings in Milwaukee.
Methods:	Satisfaction surveys were given to participants after completing the retinal screening process in either Spanish or English. 400 paper surveys were completed by the participants. The surveys were then input into an Excel spread sheet where each of the 8 multiple choice responses were analyzed. In addition, there were three free response questions that were input, and general themes and common responses were identified.
Results:	The SALV tele-eye health project had an overwhelmingly positive response and was very well received. Over 80% of the responses strongly agreed that they were comfortable during the session, that the location they received the screening was convenient, and that they would use telemedicine again. Most importantly, over 80% of the responses agreed that they would recommend this screening to their friends and families. About 70% reported that they liked seeing the image of their retina after their screening and 65% reported that telemedicine helped them get more involved with their health. About 50% of the participants who agreed to complete a survey strongly agreed that it helped having a bilingual/Spanish staff do the screening while about 25% were neutral. Concerns for privacy were addressed in the survey and 30% of the respondents were concerned about privacy where as 50% were not concerned at all.
Conclusions:	Teleophthalmology helps bring services that at-risk communities throughout Milwaukee may not have access to. The satisfaction surveys show that bringing retinal screenings to community centers in urban areas of Milwaukee with bilingual staff allows for participants to overcome barriers such as language and factors that limit access to care. The use of teleophthalmology in these community settings also gets the participants engaged, excited, and involved with their health, which may lead to improved eye screening rates and better health outcomes.

Poster #	13
Abstract Title:	"Familiarity" Trends of Successful Urology Residency Match Applicants
Presenter(s):	Samuel Engelsgjerd, BA; Melissa Wong, BS; Adam Koraym, BS ✉
Authors:	Samuel Engelsgjerd, BA; Melissa Wong, BS; Adam Koraym, BS; Jay I. Sandlow, MD; R. Corey O'Connor, MD
Dept/Division:	Urology
Category:	Clinical Fellows & Residents
Introductions:	The urology residency match is a highly competitive process. Each year over 450 senior medical students apply for approximately 300 available training positions. As a result, well-qualified students may go unmatched. We sought to determine if a training program's "familiarity" with an applicant played a role in the successful match into a urology residency.
Methods:	We analyzed data from successful allopathic urology residency applicants in the United States between 2015 and 2018. Information was collected from the American Association of Medical Colleges applications and UrologyMatch.com including each candidate's name, hometown, undergraduate institution, graduate program (if applicable), medical school, location of visiting sub-internships in urology and urology residency program.
Results:	Complete data were available for 920 of 1,197 applicants (77%). 221/920 (24%) successful students matched into their home urology training programs. 342/920 (37%) applicants rotated as visiting sub-interns prior to matching at their respective programs. 45/920 (5%) candidates matched into residency training programs in which they previous studied as undergraduate or graduate students. Finally, 76/920 (8%) applicants matched into programs within 150 miles of their recorded hometown. Overall, 684/920 (74%) successful urology match candidates met a minimum of one recorded metric.
Conclusions:	Program "familiarity" with students may play a major role in where urology candidates successfully match. Our study demonstrated nearly ¾ of urology residency applicants matched into either their home institutions, visiting sub-internship programs, site of previous undergraduate/graduate studies or training programs within 150 miles of their hometown.

Poster #	14
Abstract Title:	Sub-fertility and the Psychological Impact on Men
Presenter(s):	Pranav Dadhich, MD ✉
Authors:	Luriel Smith-Harrison MD, Abbey R. Kruper PsyD, Pranav Dadhich MD, Garrett K. Berger PharmD, Jay I. Sandlow MD
Dept/Division:	Urology
Category:	Clinical Fellows & Residents
Introductions:	With fertility concerns being present in 50% of couples, this study aims to quantify the psychologic impact of sub-fertility on men.
Methods:	This is a prospective population study utilizing a single questionnaire. All men being evaluated for sub-fertility at a single academic center were provided with a qualitative questionnaire. Using Likert scales, we were able to probe several psychologic and emotional domains. These domains included effect on mood, marital relationship, and sexual experience. Likert scales were used to better characterize the participants' abilities to cope with sub-fertility, along with desire for more resources. Data were analyzed using SPSS v24.
Results:	One hundred twenty-three men completed the questionnaire. Sixty-two of the 123 men (49%) reported a negative effect on mood. In addition, thirty (24%) reported a negative effect on their relationship, while 25% of men reported a negative impact on their sexual experience. While the majority of men felt that they were able to cope, nearly one-third (32%) of men had doubts about their ability to manage the emotional toll. Additionally, more than one-in-five men (22%) requested additional resources to address the emotional and behavioral effects of sub-fertility.
Conclusions:	Sub-fertility has a significant impact on the emotional and psychologic well-being of men who present at reproductive clinics. One in five men feel the need for additional resources or treatment to address their emotional concerns. While the medical management of these patients is paramount, the psychosocial ramifications must not be discounted.

Poster #	15
Abstract Title:	Molecular and Genetic markers in Appendiceal mucinous neoplasms - A systematic review
Presenter(s):	Andrew Stein ✉
Authors:	Andrew Stein, BS; T. Clark Gamblin, MD, MBA; Callisia Clarke, MD; Susan Tsai, MD; James Thomas, MD; Ben George, MD; Harveshp Mogal, MD
Dept/Division:	Surgery: Surgical Oncology
Category:	Research Support Staff
Introductions:	Significant advances have been made in the histologic classification of Appendiceal Mucinous Neoplasms (AMNs), however, the role of somatic alterations (SAs) is evolving. We performed a systematic review of the literature to identify putative SAs, representative of the histologic entities that comprise AMNs. Further, we sought to identify SAs that are associated with aggressive clinical phenotypes.
Methods:	We searched MEDLINE for studies on AMNs, including molecular markers or genomic alterations, published between 1990 and 2017. Based on available consensus guidelines, studies were grouped under low-grade and high-grade histological type for primary and metastatic tumors.
Results:	A total of 22 studies involving 970 tumor samples (primary and metastatic) were identified. PCR, Sanger and Next Generation Sequencing were the commonly used methods for DNA sequencing. Median age ranged between 49-71. Six studies involving 135 primary low-grade AMNs (including well differentiated adenocarcinoma) identified KRAS (71.1%) as the predominant SA. Five of these studies noted SAs in GNAS in 44.6% of 65 LAMNs. KRAS was identified in 74% of 11 studies with 187 low-grade PMP (pseudomyxoma peritonei). In eight of these studies, GNAS SAs were noted in 53% of 83 tumors. Five studies noted TP53 SAs in only 5.9% of 34 tumors. High-grade AMNs (mucinous adenocarcinomas NOS, moderate to poorly differentiated adenocarcinomas, adenocarcinoma with signet ring cells and Goblet cell carcinoids) demonstrated significantly lower SAs in KRAS (45.2% of 436 tumors in 10 studies) and GNAS (26.4% of 110 tumors in five studies) and higher SAs in TP53 (26.7% of 120 tumors in five studies). In high-grade PMP, SAs were noted in KRAS (70.5% of 122 tumors in eight studies), GNAS (41.3% of 46 tumors in six studies) and TP53 (44% of nine tumors in two studies). PIK3CA, ATM, APC, AKT1 and SMAD4 were other less frequent (<;15%), albeit potentially relevant mutations identified.
Conclusions:	While KRAS and GNAS are the predominantly identified SAs in primary and metastatic low-grade AMNs, they are less frequently noted in high-grade tumors. Conversely, TP53 is rare in low-grade but frequently altered in high-grade primary and metastatic AMNs. Although SAs may provide valuable insights into tumor heterogeneity and variability in tumor biology, larger studies utilizing clinically annotated genomic databases from multi-institutional consortiums may improve their identification and clinically applicability in the management of AMNs.

Poster #	16
Abstract Title:	The marine natural product manzamine-A inhibits cervical cancer by targeting the SIX-1 Protein
Presenter(s):	Dev Karan ✉
Authors:	Dev Karan, Seema Dubey, Lucia Pirisi, Alexis Nagel, Ivett Pina, Mark T Hamann
Dept/Division:	Pathology
Category:	Senior Faculty
Introductions:	Natural products remain an important source of drug leads covering unique chemical space and providing significant therapeutic value for the control of cancer and infectious diseases resistant to current drugs. In the present study, we investigated the anti-cancer activity of a natural product called manzamine-A (MA) from an Indo-Pacific sponge. This molecule is part of a unique group of alkaloids with diverse biological activities.
Methods:	Cervical cancer cell lines C33A, HeLa, SiHa, and CaSki, were obtained from the American Type Culture Collection. Anti-cancer activity of manzamine-A was performed using multiple cellular assays including: cell viability assay, cell proliferation, colony formation assay, cell-cycle analysis, apoptosis analysis, and western blot analysis for multiple target proteins.
Results:	Our data demonstrated the anti-proliferative effects of MA at relatively low and non-cytotoxic concentrations (up to 4 µM). Mechanistic investigations confirmed that MA blocked cell cycle progression in SiHa and CaSki cells at G1/S phase as compared to C33A and HeLa cells. In apoptotic assays, HeLa cells showed the highest sensitivity to MA as compared to other cell types (C33A, SiHa and CaSki). MA significantly regulated a number of cell cycle-related genes, including restoration of p21 and p53 activity. Interestingly, MA decreased the levels of the oncoprotein SIX1 (a homeodomain-containing transcription factor) which is associated with oncogenesis in cervical cancer. To further investigate structure-activity relationship (SAR) among the MA class with potential anti-cancer activity, molecular networking (MolN) analysis facilitated the efficient identification, de-replication, and assignment of structures from the manzamine class and revealed significant potential in the design of optimized molecules for the treatment of cervical cancer.
Conclusions:	These data suggest that this sponge-derived natural product class warrants further attention with regard to the design and development of novel MA analogs which may be efficacious for preventive and therapeutic treatment of cancer. In addition this study reveals the significance of protecting fragile marine ecosystems from climate change-induced loss of species diversity.

Poster #	17
Abstract Title:	The feasibility of creating a multi-biomarker panel to predict treatment response for pancreatic cancer
Presenter(s):	Haidy Nasief ✉
Authors:	Haidy Nasief, William Hall, Beth Erickson, X. Allen Li
Dept/Division:	Radiation Oncology
Category:	Clinical Fellows & Residents
Introductions:	Pancreatic cancer is one of the leading causes of cancer death in the United States. Detecting treatment response is a critical step in the treatment of pancreatic cancer. CT images are one of the treatment modalities that are used to monitor oncologic changes. Radiomics is the field that converts medical images into quantitative data. Change of radiomic features in longitudinal images, delta-radiomics, can be potentially used as an imaging bio-marker for treatment response. However, although delta-radiomic features (DRFs) have been associated with several clinical endpoints in a variety of applications and Radioimmunoassay test (RIA, CA19-9) has been used as a clinical biomarker for pancreatic cancer, the complex relationships of radiomics and clinical factors are largely unknown. This expletory study provides an attempt to uncover this relationship to improve patient specific outcomes and find DRFs that are correlated to the clinical biomarker (CA 19-9) and to tumor response.
Methods:	Daily CTs were acquired during routine CT-guided chemo-radiation therapy (CRT) for 15 patients with pancreatic head cancer and radioimmune assay (RIA, CA19-9) test results. Patients were divided into good- and poor- response groups based on their pathological responses. The pancreatic head was segmented using MIM software and inspected by another experienced researcher to ensure consistency. Changes of 73 radiomic features between fractions were extracted from the segmented regions on the daily CTs. The CA19-9 test results were acquired for each fraction for these patients. A regression model was built to examine the effect of combining CA 19-9 and DRFs on response. Concordance statistic was used to measure the effectiveness of the model. A value below 0.5 indicates a very poor model, 0.5 means that the model is no better than predicting an outcome than random chance, 0.7-0.8 indicate a good model, over 0.8 indicate a strong model, and 1 means that the model perfectly predicts tumor response.
Results:	The results show CA19-9 is correlated to the delta-radiomic features (Entropy and cluster tendency). Incorporating the clinical biomarker CA19-9 with delta radiomic features in our model increased the concordance statistic from 0.57 to 0.86 indicating a stronger model to predict treatment response.
Conclusions:	A multi-biomarker panel that uses delta radiomics and clinical biomarkers has the potential to lead to a faster discovery of tumor response, increase the prognostic value, and hence, lead to better patient specific outcomes.

Poster #	18
Abstract Title:	Surgical and oncological management of a case of desmoplastic small round cell tumor with liver metastasis in a pediatric patient
Presenter(s):	Jerry Xiao ✉
Authors:	Xiao J, Browning M, Turaga K, Whitehouse J, Lal D
Dept/Division:	Surgery: Pediatric Surgery
Category:	Research Support Staff
Introductions:	Desmoplastic small round cell tumor (DSRCT) is a rare sarcoma primarily affecting adolescents and young adults. Outcomes are poor with a 5-year overall survival of 15%-25%. This paper presents the case of an 8-year-old girl with progressive abdominal pain and distention. Imaging demonstrated a large diffuse abdominal pelvic peritoneal mass with metastasis to the liver. Open biopsy revealed diffuse peritoneal disease and a diagnosis of DSRCT. The patient was treated with neoadjuvant chemotherapy followed by cytoreductive surgery + hyperthermic intraperitoneal chemotherapy (HIPEC). She experienced intrabdominal disease recurrence shortly after cytoreductive surgery/HIPEC which was surgically resected, followed by whole abdomen radiation and autologous stem cell transplant.
Methods:	This case report was developed via review of the patient's medical chart including operative notes, imaging and pathology reports, and other medical data.
Results:	The patient is now over 5 years out from completing therapy and remains disease free.
Conclusions:	Previous papers describe liver metastasis and tumor recurrence after resection portending a dismal prognosis. Our patient demonstrates that multimodal chemotherapy, radiation and aggressive surgical resection with HIPEC can lead to long-term survival.
Reference 1:	Stiles, Z. E., Dickson, P. V, Glazer, E. S., Murphy, A. J., Davidoff, A. M., Behrman, S. W., … Deneve, J. L. (2018). Desmoplastic small round cell tumor: A nationwide study of a rare sarcoma. Journal of Surgical Oncology, (March). http://doi.org/10.1002/jso.25071
Reference 2:	Subbiah, V., Lamhamedi-Cherradi, S.-E., Cuglievan, B., Menegaz, B. A., Camacho, P., Huh, W., … Ludwig, J. (2018). Multimodality Treatment of Desmoplastic small round cell tumor: Chemotherapy and Complete Cytoreductive Surgery Improve Patient Survival. http://doi.org/10.1158/1078-0432.CCR-18-0202
Reference 3:	Hayes-Jordan, A. A., Coakley, B. A., Green, H. L., Xiao, L., Fournier, K. F., Herzog, C. E., … Surg, A. (2018). Desmoplastic Small Round Cell Tumor Treated with Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy: Results of a Phase 2 Trial. Oncol, 25, 872–877. http://doi.org/10.1245/s10434-018-6333-9

Poster #	19
Abstract Title:	Pathological characteristics and outcomes of patients with endometrial cancer and isolated tumor cells (ITC) or micrometastases (MM) identified with sentinel lymph node mapping
Presenter(s):	Justin Harold ✉
Authors:	Justin Harold, Denise Uyar, Erin Bishop, Melodee Nugent, Pippa Simpson, William Bradley
Dept/Division:	Obstetrics & Gynecology
Category:	Clinical Fellows & Residents
Introductions:	The objective was to evaluate pathologic correlates and clinical outcomes of patients with isolated tumors cells (ITC) and micrometastases (MM) identified after sentinel lymph node (SLN) mapping with indocyanine green in the treatment of endometrial cancer. Management of patients with this pathology is unclear as there is minimal data on whether detection of ITC or MM pathology should result in upstaging of cancer. It is unclear whether this pathology influences disease-free and overall survival.
Methods:	Women who underwent SLN mapping from November 2013 to April 2017 were identified and clinical/pathologic data collected. Those with ITC or MM on final pathology were reviewed for clinical outcomes and pathological factors and compared to those without ITC or MM. Median follow-up (in months) was reported as the time from surgery to the patient's last visit with a healthcare provider. When present, ITC pathology did not result in upstaging of cancer; patients with micrometastases were upstaged to IIIC.
Results:	There were 12 patients identified with ITC, MM, or both in either their SLN (9 patients) and/or pelvic and para-aortic specimens (3 patients). The histology was endometrioid in 7 patients (58%), with 5 FIGO Grade I tumors and 2 FIGO Grade 2. There were 5 patients with serous carcinoma (42%). Patients with ITC/MM were more likely than those without to have lymphovascular space invasion (LVSI) (P=0.015) and >50% myometrial invasion of their tumor (75% vs. 34%, P=0.007). Stage ≥IIIC was present in 50% of patients with ITC/MM versus 6% of patients without ITC/MM (P=0.003). Histology and FIGO grade were not statistically different between patients with and without ITC/MM. Median follow-up for patients with SLN ITC/MM was 7.5 months (4-35 months). There was 1 death from intercurrent disease, and 1 recurrence in a patient with IIIC1 serous carcinoma after treatment with adjuvant whole pelvic radiation therapy and chemotherapy. Three patients with ITC were not treated with adjuvant therapy; all were free of recurrence at last follow-up (6-7 months). One patient with endometrioid histology had ITC positive SLN but no pelvic or para-aortic nodes to evaluate. Adjuvant whole pelvic radiation therapy was given based on myometrial invasion >50%, and there was no evidence of recurrence at last follow-up (4 months).
Conclusions:	In this small group of patients with ITC and/or MM identified in their SLN specimens, myometrial invasion and LVSI were higher. Appropriate management of patients with ITC and/or MM should be evaluated in a multi-institutional prospective trial to further evaluate outcomes and the appropriate therapy.
Reference 1:	Isolated tumor cells identified by sentinel lymph node mapping in endometrial cancer: Does adjuvant treatment matter? Plante, M et al. Gynecol Oncol. 2017 Aug;146(2):240-246. doi: 10.1016/j.ygyno.2017.05.024. Epub 2017 May 31.

Poster #	20
Abstract Title:	Nuclear-Independent Telomerase Activity Restores Microvascular Dysfunction Induced by Neoadjuvant Chemotherapy in Breast Cancer Patients
Presenter(s):	L.E. Norwood Toro, PhD ✉
Authors:	L.E. Norwood Toro, J. Linn, J. Hockenberry, A. Kong, and A. M. Beyer
Dept/Division:	Medicine: Cardiology
Category:	Research Support Staff
Introductions:	The adverse impacts of chemotherapy (CT) on the cardiovascular (CV) system, even years after its cessation, are well documented. Due to its association with tumor growth, TERT, the catalytic subunit of telomerase, is an established target of CT. The effects of CT drugs on the tumor vasculature are well studied; however, little evidence exists on the effects of CT on the host microcirculation. Microvascular (MV) dysfunction is a known early indicator of numerous CV disease phenotypes, including heart failure. The goal of this study was to evaluate the prolonged consequences of previous CT treatment on the human MV, and whether TERT activation can reverse the CT-induced dysfunction.
Methods:	MV function was tested using isolated vessel preparation from breast cancer patients. Endothelial dependent dilation to flow (FMD) and smooth muscle mediated dilation (papaverine), were evaluated in freshly isolated adipose or coronary MV ± doxorubicin (Dox). Adipose vessels from cancer patients with and without previous CT were assessed one month after cessation of therapy.
Results:	Ex vivo treatment with Dox reduced endothelial mediated dilation by 90% in both coronary and adipose MV. In vessels from patients with neoadjuvant CT, FMD was severely decreased. Using a novel decoy peptide (nucXTERT) that blocks TERT nuclear translocation, the effects of neoadjuvant CT on endothelial function were reversed. The telomerase inhibitor BIBR 1532 specifically blocked the effect of nucXTERT. Papaverine-induced dilation was not affected by neoadjuvant CT.
Conclusions:	MV dysfunction is reduced after previous exposure to Dox either acutely (ex vivo) or after prior CT (in vivo). TERT activation restores physiological FMD. Our studies show for the first time the effect of Dox on human MV function and the effect of TERT activation in reversing CT damage. These studies provide the groundwork for ways to prevent adverse CV side effects from CT without affecting cancer cell lethality.
Acknowledgements:	This work was supported by NIH R01 HL133029, We Care Foundation Grant; MCW-Cardiovascular Center Pre-PPG grant, Advancing a Healthier Wisconsin - Redox Biology Grant.

Poster #	21
Abstract Title:	The Association between Medication Prescription Synchronization and Adherence to Oral Adjuvant Breast Cancer Endocrine Therapy
Presenter(s):	Nicole Fergestrom ✉
Authors:	Nicole Fergestrom, Purushottam Laud, Liliana Pezzin, Aaron Winn, Ann Nattinger, Joan Neuner
Dept/Division:	Center for Advancing Population Science
Category:	Research Support Staff
Introductions:	One-third to one-half of patients prescribed adjuvant endocrine therapy with tamoxifen or an aromatase inhibitor either discontinue early or skip a substantial number of pills. Research to improve this has been disappointing. We investigated whether poor pharmacy synchronization of medication fills is an unrecognized barrier to adherence.
Methods:	A cohort of women aged 66-90 years old with Stage 0-3 hormone receptor-positive breast cancer were identified from the Surveillance, Epidemiology and End Result (SEER)-Medicare claims-linked cancer registry. Women with Medicare pharmacy claims documenting at least one endocrine therapy prescription fill and at least one other medication fill were identified, and the 3-month synchronization of their medication fills was calculated as the quotient of the number of pharmacy visits and the number of filled medications subtracted from 1. Since there was strong correlation between synchronization and number of medications, synchronization quartiles were stratified by number of medications. Quartiles were assigned within each of the 3 number of medication groups. Logistic regression was used to assess the association between synchronization stratified by the number of medications and adherence to endocrine therapy (defined as medication possession ratio >80%) over the subsequent year.
Results:	The study cohort included 3,212 women treated with endocrine therapy for breast cancer. Over 31% were age 70 or younger, and 38.0% had stage 2 or 3 disease. During the three months after the first endocrine therapy prescription, the mean number of unique medications was 7.0 (S.D. 3.8) and the mean number of pharmacy visits was 8.6 S.D. 4.7) for a mean synchronization of 0.3 ((S.D. 0.2). In an adjusted model, compared with the highest synchronization, those in the lowest synchronization group were less likely to be adherent (Odds Ratio 0.67 (95% CI 0.54, 0.84)) as well as compared to the second-highest group (0.78 (0.63, 0.96)). Neither age nor race/ethnicity were associated with adherence, and results were unchanged with inclusion of information about duration of fills (30 vs 90 days).
Conclusions:	Prescription fill synchronization is strongly associated with adherence to endocrine therapy. Research into interventions to improve adherence should include prescription synchronization and other health systems barriers.

Poster #	22
Abstract Title:	Development of α-CD30 Bispecific Antibody Immunotherapy for Hodgkin Lymphoma
Presenter(s):	Robyn A. A. Oldham ✉
Authors:	Oldham, Robyn AA; Faber, Mary L; Thakur, Archana; Lum, Lawrence G; Medin, Jeffrey A
Dept/Division:	Pediatrics
Category:	Research Support Staff
Introductions:	Although Hodgkin Lymphoma (HL) is highly treatable, 15-25% of patients have refractory disease or relapse. Chemotherapy resistant disease is challenging to treat: novel therapeutic strategies are needed for this subset of patients. One recent approach has been to target CD30 for HL immunotherapy. Brentuximab vedotin, an Î±-CD30 antibody-drug conjugate (ADC), is already FDA approved. The efficacy of antibody therapy is based on target, epitope, and affinity. One of our objectives is to develop novel anti-CD30 antibodies with varying binding properties. We then plan to generate anti-CD30/anti-CD3 bispecific antibodies (bi-mAbs) and CARs for clinical development. Bispecific CD30/CD3 antibodies provide conceptual advantages over naive antibody therapies by possibly increasing effectiveness and by reducing potential side effects associated with using conjugated cytotoxic compounds in ADC therapy.
Methods:	We generated fifteen anti-human CD30 hybridoma cell lines through the immunization of mice with purified recombinant huCD30-GST protein. Five hybridomas were selected for further analyses. All candidates showed specific binding to CD30 by flow cytometry and ELISAs, and were characterized by both DNA and protein sequencing. Our purified CD30 antibodies were then heteroconjugated with anti-huCD3 antibodies for in vitro/in vivo analyses. Our conjugated antibodies bind both tumor cells and T cells. Subsequent in vitro assessments will test their ability to trigger target cell death. For in vivo studies, CD30 bi-mAbs will be administered to C57BL/6 mice, or pre-incubated with human T cells and administered to NRG mice bearing eGFP/luciferase-expressing huCD30+ lymphoma grafts. In vivo treatment efficacy will be monitored by overall mouse survival and tumor growth/regression, tracked by bioluminescent imaging.
Results:	Characterization studies showed that 4 of our antibodies bound to a similar CD30 epitope, while a 5th bound to a separate site. Both epitopes are distinct from that bound by Brentuximab vedotin, however. Characterization of antibody affinity and analyses of the biological and cytotoxic effects of each antibody is underway.
Conclusions:	We have developed antibodies that target unique CD30 epitopes and allow us to prepare bispecific CD30/CD3 antibodies. The addition of anti-CD3, will potentially enhance immune response to the tumor. Ultimately, we aim to test our optimized bi-mAb in clinical trials, with the goal of improving survival for HL patients presenting with relapsed and refractory disease.

REFERENCE POSTER

(Abstract Retracted)

Poster #	24
Abstract Title:	Comparing the Costs of Metastatic Neuroendocrine Tumor Treatments
Presenter(s):	S. B. White, MD, MS, FSIR ✉
Authors:	W. S. Rilling, MD, FSIR
Dept/Division:	Radiology
Category:	Senior Faculty
Introductions:	To understand typical multi-modality treatment regimens for metastatic neuroendocrine tumors (mNETs) and their relative associated costs.
Methods:	This is an IRB approved single center retrospective study evaluating adult patients treated for mNETs between 5/1994-6/2016. Demographics, date of diagnosis, location of primary tumor, date of liver metastasis, pathological grade, and surgical history were extracted. Liver directed therapy (LDT) dates and types were collected. Treatment duration, cycles, and reason for discontinuation was collected for all systemic therapies. Treatment related toxicities were recorded using the CTCAE v4.0. The hospital billing system was queried to identify standard costs of LDTs, hormonal, and intravenous (IV) therapies. Oral drug costs were obtained from the hospital pharmacy order acquisition system.
Results:	A total of 161 hepatic mNET patients were identified; 83 males and 78 females with mean age of 57. 91 patients underwent a total of 264 LDTs (mean LDTs per patient 2.9±2.1), which included: cTACE (n=148), DEB-TACE (n=15), TARE (n=84), and TAE (n=7). Patients in the LDT group also received adjuvant systemic therapies. The following were the most common hormonal, IV, and oral agents, respectively: octreotide (n=77) and lanreotide (n=8); etoposide (n=10), carboplatin (n=7), and cisplatin (n=5); and capecitabine (cape) (n=28), temozolomide (tem) (n=27), verolimus (n=24) and sunitinib (n=17). LDT patients' systemic therapy durations were: octreotide 38.6 (SEM=3.3), lanreotide 5.7 (SEM=0.5), cisplatin/etoposide 4.7 (SEM=0.7), carboplatin/etoposide 3.4 (SEM=1.3), cape/tem 8.2 (SEM=2.2), everolimus 5.2 (SEM=1.3), and sunitinib 5.1 (SEM=1.6) months. 71 patients received systemic therapy only. The following were the most common hormonal, IV, and oral therapies, respectively: octreotide (n=56) and lanreotide (n=5); etoposide (n=18), carboplatin (n=12), and cisplatin (n=6); and cape (n=18), tem (n=19), everolimus (n=11), and sunitinib (n=7). These patients' systemic therapy durations were: octreotide 30.7 (SEM=3.5), lanreotide 4.6 (SEM=1.6), carboplatin/etoposide 2.9 (SEM=0.8), isplatin/etoposide 2.1 (SEM=0.7), cape/tem 4.3 (SEM=0.9), everolimus 10.7 (SEM=2.0), and sunitinib 3.9 (SEM=1.3) months. Octreotide was the most common therapy and used as a baseline. Compared to 6 months of octreotide, each LDT, and 6 months of IV and oral chemotherapy was 0.8x ± 0.5, 1.63x ± 0.11, and 1.48x ± 1.95 the cost respectively
Conclusions:	Although a single session of LDT may incur higher costs, prolonged systemic regimens surpass LDT costs.

Poster #	25
Abstract Title:	Liver-directed therapy(LDT) for metastatic renal cell carcinoma(mRCC): Single center experience
Presenter(s):	Timothy Zellmer ✉
Authors:	Timothy Zellmer, William Lea, MD
Dept/Division:	Radiology
Category:	Support Staff
Introductions:	Liver metastases arising from RCC are common and signify a poor prognosis. Given the negative impact of liver metastases on overall survival (OS) and quality of life, it is reasonable to consider therapies directly targeting these lesions in select patients. Little is known about how minimally invasive LDT affects outcomes in patients with mRCC.
Methods:	Nine patients with mRCC underwent LDT for liver-dominant or liver-only metastatic disease between 2005 and 2015. Retrospective chart review was performed under an IRB protocol to identify patient and disease characteristics, imaging response, and time to next systemic treatment, OS and toxicities. Patients were seen in clinic at one month post-LDT to monitor for toxicities. Imaging was obtained within 2 months prior to treatment and at 3 and 6 months following LDT.
Results:	Each patient underwent a median of 2.3 procedures. A total of 18 transarterial chemoembolizations (TACE) and 5 yttrium-90 radioembolizations were performed. 2 patients had metastatic disease confined to the liver, and 7 had liver-dominant disease. 7 had multifocal disease involving <25% of the liver, and 2 had multifocal disease involving >25% of the liver. 8/9 patients received prior systemic therapies, receiving a median of 3 (0-4) distinct treatments. 4/9 patients were undergoing systemic therapy at the time of LDT, 1 patient declined further treatment, and the median time to initiation of the next systemic therapy in the remaining patients was 3 months (range 2-4 months). Median OS from first line systemic therapy was 39 months, 95% CI [25.9-53.3], and the median OS from the first LDT was 22 months (from 5-45 months). Follow-up imaging post-LDT showed PR or SD in 88% of cases at 3 months and 44% of cases at 6 months. At one month post-procedure, 8/9 patients maintained performance status, and only one patient experienced CTCAE grade 3-4 toxicity
Conclusions:	The median OS in RCC patients with liver disease and systemic therapy alone is 14.3 months. The improved median OS of 39 months with LDT in our unmatched and heavily pretreated cohort suggests a role for LDT. LDT is generally well tolerated and should be considered for patients with liver-dominant mRCC with good performance status.

Poster #	26
Abstract Title:	Comparison and Analysis of U.S. State-Level Concussion Legislation to Find a Model Policy
Presenter(s):	Adam M. Wuensch ✉
Authors:	Adam M. Wuensch, Lindsay D. Nelson
Dept/Division:	Neurosurgery
Category:	Research Support Staff
Introductions:	In the context of youth contact sports in the United States (U.S.), there has been increased awareness of the physiological effects of concussion and fear about the potential for "second impact syndrome." Consequently, legislation has been passed in all 50 U.S. States and the District of Columbia (D.C.), in an aim to increase awareness of concussion risks, improve management, and prevent repeat injury within the window of cerebral vulnerability. While the laws display a great public health response, little attention has been paid to examining how different states have operationalized their concussion laws. Comparing state legislation might reveal themes, identify areas for improvement, and lead to refinement of state laws to improve protection and coverage of youth athletes.
Methods:	Our primary objective was to code and compare original state concussion legislation and current amendments of the 50 U.S. states and D.C. A secondary objective was to quantify associations between different policy decisions and state demographic characteristics to determine the degree to which policies could be explained by state characteristics (e.g. population, resource availability) or instead may be based on more idiosyncratic factors.
Results:	Review of legislation disclosed that some policies were virtually universal across states, including: requiring a signed annual information sheet, requiring athletes to be removed from competition immediately following symptom onset, and requiring signed authorization to return to play by appropriate healthcare professionals. Conversely, other policies were more infrequent and operationalized with more variability across states including: coach training, coverage of private school districts, healthcare providers approved for management of concussion, and the decision making capacity granted to school districts and state athletic associations. Analysis of policy and demographic variables largely yielded no significant associations between variables. However, states that enacted legislation earlier tended to allow schools flexibility in deciding their own return-to-play protocols (phi = 30, p=.032) and punish coaches for not following protocols (phi = .29, p=.042). Similarly, states that had more frequent coach training intervals tended to also require yearly signed information sheets (phi = .28, p=.048) and set return-to-play protocols at the state level (phi = .31, p=.026). Policy features were uncorrelated with state demographics, including population density, state gross domestic product, and number of active doctors.
Conclusions:	Overall, while there is substantial variability in how states have defined their laws around youth concussion, most are following the core guidelines set by the Centers for Disease Control and National Federation of State High School Associations. Further research to determine the degree to which these laws are adhered to by different athlete groups and to establish their influence on concussion management and outcomes would be valuable for informing how to use policy more effectively in the future to improve the clinical care of youth athletes.

Poster #	27
Abstract Title:	Aberrant GATA6 expression induces senescent-like phenotypes in iPSC-derived astrocytes
Presenter(s):	Allison Ebert ✉
Authors:	Samantha L. Sison, Madeline R. Brunner, Benjamin S. O'Brien, Ann DeLaForest, Michele A. Battle, Allison D. Ebert
Dept/Division:	Cell Biology, Neurobiology & Anatomy
Category:	Senior Faculty
Introductions:	Spinal muscular atrophy (SMA), a leading genetic cause of infant mortality, is characterized by loss of motor neurons in the spinal cord, skeletal muscle atrophy, and death due to a substantial reduction in SMN protein. We have previously found that SMN deficient astrocytes exhibit significant morphological and functional abnormalities that contribute to motor neuron demise in SMA, but the underlying mechanisms are unclear. Recently, the transcription factor GATA6 was identified as a downstream target of SMN and shown to be aberrantly upregulated in SMA. However, its role in disease pathology is unknown. Here we investigated whether increased GATA6 expression contributes to astrocyte malfunction.
Methods:	To test for the adoption of cellular senescence in SMA, we generated astrocytes from induced pluripotent stem cells (iPSCs) from SMA patients and healthy individuals. Astrocytes were analyzed by qRT-PCR, immunocytochemistry, and fluorescence assays to quantify morphological alterations, levels of GATA6, Pai1, p53, and senescence-associated beta-galactosidase activity.
Results:	We have previously found that GATA6 is upregulated in SMA iPSC-derived astrocytes compared to control astrocytes. We confirmed these data and show that GATA6 is not normally expressed in healthy human brain in adolescent, middle aged, and elderly individuals. We next aimed to determine what role increased GATA6 expression could be playing in SMA astrocytes. A related GATA transcription factor, GATA4, has been shown to be involved in regulating cellular senescence, so we assessed if excess GATA6 can also induce a senescence-like phenotype. We have previously shown that SMA iPSC-derived astrocytes have increased production of microRNA 146a, which is specifically expressed in senescent cells. Therefore, we tested for expression of additional markers of cellular senescence and found that SMA iPSC-derived astrocytes exhibited increased expression of markers associated with the senescence associated secretory phenotype, but not DNA damage. We next asked if exogenous GATA6 expression could induce a cellular senescence-like phenotype in control astrocytes. We transiently transfected control iPSC-derived astrocytes with a GATA6 expression plasmid and found an increase in the number of beta-galactosidase positive astrocytes compared to untransfected conditions. Additionally, we saw an increase in the number of cells containing vacuoles, a phenotype consistent with senescence. Together, these data suggest that aberrant GATA6 expression induces cells to adopt a senescent-like phenotype in which the secretory and morphological properties are altered, which may help explain how SMN deficient astrocytes contribute to motor neuron loss in SMA.
Conclusions:	GATA6 is a known downstream target of SMN and its expression has been previously shown to be correlated with disease severity. Here, we have identified a potential consequence of GATA6 upregulation in SMA astrocytes that may help explain the mechanisms contributing to astrocyte-mediated motor neuron loss. As such, future studies will investigate whether reducing GATA6 expression in astrocytes is therapeutically beneficial target.
Acknowledgements:	We thank Steve Duncan (MUSC) for the GATA6 plasmids. This work is supported by CureSMA and NIH/NINDS R21NS102911-01A1

Poster #	28
Abstract Title:	Measuring the Acute Effects on Sleep After Sport-Related Concussion Using Self-Report and Actigraph Measures
Presenter(s):	Anna Klotz ✉
Authors:	Anna Klotz, Daniel L. Huber, Ciaran Considine, Michael A. McCrea, and Lindsay D. Nelson
Dept/Division:	Neurosurgery
Category:	Research Support Staff
Introductions:	Sleep disturbances following a sport-related concussion (SRC) can occur in up to 70% of athletes and have been proposed to be important contributors to SRC recovery and persistent symptoms. However, the acute effects on sleep after SRC are poorly understood. Furthermore, self-report measures of sleep might be unreliable and better reflect mood symptoms (i.e., depression) than sleep. Actigraphs, on the other hand, may offer significant advantages over self-report measures due to their objective nature and the availability of detailed sleep-related metrics. The aim of this study was to estimate the acute effects of SRC on sleep using both self-report and actigraph measures.
Methods:	Participants were recruited from Project Head-to¬-Head II, a large, prospective study of SRC that enrolled high school and collegiate football players between the 2015-2017 football seasons. Athletes who were followed after SRC or after selection as a matched teammate control were eligible for the sleep-monitoring substudy. We enrolled contact controls (N=26) and athletes with SRC (N=58) at 24-48 hours postinjury and provided them with a commercial activity tracker and a mobile application that delivered an abbreviated set of sleep questions daily (with questions adapted from the Pittsburgh Sleep Quality Index). Participants provided daily sleep data for two weeks. Cross-sectional comparisons between SRC and contact controls were computed to establish the effects of SRC on sleep. Sleep metrics were correlated between the actigraph and mobile survey data.
Results:	Self-reported sleep efficiency was decreased in participants with SRC compared to contact controls within two days postinjury and rapidly normalized thereafter. Actigraph recordings of sleep efficiency showed no significant group differences. Total amount of sleep (as measured through either mode of assessment) was not affected by SRC. Mobile survey measures were slightly to moderately correlated to actigraph measures.
Conclusions:	There is a difference in information gathered between self-report and objective sleep measures. While there appear to be subjective impairments in sleep efficiency after SRC, the transient nature of this effect makes it important to measure sleep in a detailed manner (i.e., through daily ratings).

Poster #	30
Abstract Title:	Dorsal root ganglionic field stimulation selectively blocks nociceptive sensory afferents
Presenter(s):	Bin Pan ✉
Authors:	Bin Pan, Dongman Chao, Quinn Hogan
Dept/Division:	Anesthesiology: Research
Category:	Junior Faculty
Introductions:	Dorsal root ganglion field stimulation (GFS) has been shown to be effective in relieving clinical pain associated with nerve injury and neuropathic pain in nerve injury animal models. However, its mechanism has not been explored.
Methods:	In vivo single unit recording from fibers teased from the 4th lumbar dorsal root were employed. Fiber types (Aβ, Aδ, C) were defined by conduction velocity.
Results:	Action potentials (APs) generated by GFS (20Hz) in C-type units progressively vanished within 20 seconds, whereas block of GFS-induced Aβ activity persisted, while Aδ showed intermediate stability. Activity generated peripherally by electrical stimulation of the sciatic nerve and punctate mechanical stimulation of the receptive field (glabrous skin) was likewise promptly blocked (within 20 s) by GFS, with a preferential blockade of AP trains in C-type units, whereas Aβ and Aδ units were minimally affected. After tibial nerve injury, punctate mechanical stimulus (von Frey) threshold was reduced from 29.4 +/- 5.48 gram (n=10) to 2.71 +/- 0.45 gram (n=7), which was reversed to 14.29 +/- 2.98 gram (n=7) during GFS.
Conclusions:	These results suggest that GFS produces use-dependent blocking of afferent AP trains, possibly by inducing enhanced filtering of APs at the sensory neuron T-junction.
Acknowledgements:	Supported by NIH grant 1R01NS103812

Poster #	31
Abstract Title:	Effects of Blast Mild Traumatic Brain Injury in Preclinical Models of Cognitive Function and Addiction Liability
Presenter(s):	Chris Olsen ✉
Authors:	Matthew J Muelbl, Megan Slaker, Natalie N Nawarawong, Clay Gerndt, Alok Shah, Matthew Budde, Brian Stemper, Christopher M Olsen
Dept/Division:	Pharmacology & Toxicology
Category:	Senior Faculty
Introductions:	- Each year, an estimated 1.7 million Americans sustain a TBI in a civilian setting. - Mild TBI (mTBI) accounts for 75% of all brain injuries and causes a host of neuropsychological sequelae, including cognitive impairments. - Our previous data has found that blast mTBI (bTBI) results in microstructural damage in the medial prefrontal cortex (mPFC), an area also vulnerable in human brain injury. - Cognitive flexibility and working memory are impaired by disruption of mPFC activity. - Drug seeking is modulated by mPFC. - There is no consensus as to whether the elevated rates of substance abuse reported in individuals with mild TBI have a neurological component.
Methods:	Rats were exposed to either blast overpressure (450 kPa, 80 kPa*ms) or sham conditions. In experiment one, rats were trained in a series of cognitive tasks to assess learning ability, cognitive flexibility, and working memory. In experiment two, rats were trained to self-administer intravenous oxycodone and underwent drug seeking tests where drug was replaced with saline.
Results:	In experiment one, injured rats were impaired in acquiring the visual discrimination task, but not other tests of cognitive flexibility or working memory. Injured rats showed a high degree of variability in acquisition of visual discrimination, with approximately half of them falling within the range of sham-treated rats. In experiment two, injured rats had lower self-administration of oxycodone, but higher levels of drug seeking following abstinence. Furthermore, the linear association between drug intake and seeking observed in sham-treated rats was abolished in repeated blast-treated rats.
Conclusions:	The results indicate that a single blast exposure is sufficient to impair learning of a visual discrimination rule in a subset of animals approximately one month following injury. These results are consistent with human studies that find substantial variability in persistent cognitive effects following mild traumatic brain injury. The results are also consistent with elevated rates of substance abuse following mild traumatic brain injury and suggest that there is a neurological component to this phenomenon.
Acknowledgements:	National Institute on Drug Abuse, Advancing a Healthier Wisconsin

Poster #	32
Abstract Title:	How Should TBI Symptoms Be Assessed? Comparing Traditional Self-Report Instruments to a Novel Structured Interview
Presenter(s):	Georgia Ristow ✉
Authors:	Georgia L. Ristow, Amy M. Nader, Hannah Bartels, Alexa Wild, Robyn E. Furger, Terri A. deRoon-Cassini, & Lindsay D. Nelson
Dept/Division:	Neurosurgery
Category:	Research Support Staff
Introductions:	Symptom measures are important in the study and treatment of traumatic brain injury (TBI). Self-report questionnaires are commonly used to assess TBI symptoms but can be prone to various threats to validity (e.g., response bias). Structured interviews are considered the gold standard method for assessing psychiatric conditions and TBI-related disability and may yield more valid estimates of TBI symptoms than self-report measures.
Methods:	In this pilot study, we developed and tested the novel Structured Interview of TBI Symptoms (SITS) which was administered to a sample of patients with TBI (N = 54) recruited prospectively from a level I trauma center and assessed at 3 months postinjury. Analyses established relationships between ratings on the SITS and two commonly used self-report TBI symptom scales—the Rivermead Postconcussion Symptom Questionnaire (RPQ) and the Sport Concussion Assessment Tool 5 (SCAT5). The Minnesota Multiphasic Personality Inventory-2 Restructured Form (MMPI-2-RF) was used to evaluate the influence of acquiescence, a form of response bias, on all three measures.
Results:	Symptom severity scores on the SITS correlated highly with both RPQ (r = .94) and SCAT5 (r = .83) total scores. Additionally, the SCAT5 was the only measure that showed significant correlations with acquiescence (r = .32).
Conclusions:	Although the high correlation of the SITS and RPQ implies that total scores on these measures are essentially interchangeable, the SITS yields additional information not available through traditional self-report instruments, including a larger pool of items and more detailed information about patients' pre-injury and polytrauma-related symptoms. These findings imply that self-report questionnaires provide a reasonably valid method for assessing TBI symptoms but that the RPQ may be more accurate than the SCAT5 in the civilian TBI population. Additionally, the SITS appears to provide a valid assessment of TBI symptoms and yields additional information that may be valuable in clinical and research settings. A larger-scale study is warranted to refine the SITS and to establish how the additional information available in this measure can help advance translational TBI research.
Acknowledgements:	This projected was funded by the Center for Patient Care and Outcomes Research (now known as CAPS), Medical College of Wisconsin

Poster #	33
Abstract Title:	Characterizing the Role of IL-12p40 and Hemorrhage in Spinal Cord Injured Mice
Presenter(s):	Jose Rosas ✉
Authors:	Jose Rosas, Brandy Aperi, Kyle Stehlik, Antje Kroner
Dept/Division:	Microbiology & Immunology
Category:	Research Support Staff
Introductions:	Traumatic spinal cord injury (SCI) is a relatively frequent event which imposes a massive burden on the health, quality of life and socioeconomic situation of affected persons and their families. The National Spinal Cord Injury Statistic Center (NSCISC) reported in 2018 that approximately 17,700 new cases occur each year and an estimated 282,000 people in the U.S. live with spinal cord injuries. Tissue damage during SCI occurs in two phases: primary and secondary damage. Primary damage is caused by the initial trauma that disrupts the structural integrity of the spinal cord resulting in tissue damage and cell death. Inflammation and hemorrhage are two secondary damage processes that promote subsequent tissue damage. Various cell types contribute to inflammation after SCI, including microglia and macrophages, which phagocytose cellular debris, including red blood cells at the injury site. Uptake of blood breakdown products and iron results in a pro-inflammatory phenotype of macrophages which release pro-inflammatory cytokines such as TNF, IL-12, IL-23 and IL-1 beta. IL-12 and IL-23 are two key cytokines that share the IL-12p40 subunit and modulate the innate and adaptive immune response
Methods:	We are using a contusion model of SCI in C57BL/6 mice, IL-12p40 knockout mice (deficient for IL-12 and IL-23) and IL-23p19 knockout mice (deficient only in IL-23). A laminectomy is performed at T11 and a contusion is induced with the Infinite Horizon Impactor device. Mice are assessed behaviorally, using a specialized scoring system, the Basso Mouse Score (BMS), ladder walk and an automated treadmill system to detect locomotor recovery, and a hot plate test to monitor sensory recovery. Expression levels of mRNA were measured by QPCR on SCI tissue homogenate taken from the injury site using the deltadeltaCt method. Results were confirmed by Western blot on SCI tissue homogenate and immunostaining on PFA perfused fixed tissue. Hemorrhage in the injured spinal cord was measured by MRI and amounts were verified by measuring hemoglobin in the tissue using the QuantiChrom Hemoglobin Assay Kit. Using QPCR, immunofluorescence and Western blot, we can show an upregulation of IL-12p40, IL-23p19 and the receptors at various time points after injury.
Results:	As expected, higher amounts of hemoglobin are present in injured tissue compared to uninjured SCI tissue, which will be correlated to hemorrhage volumes measured by MRI. Furthermore, IL-12p40 KO mice show improved recovery after SCI compared to wildtype mice, while recovery in IL-23p19 knockout mice is not different from wildtype mice.
Conclusions:	Our data indicate that factors from the IL-12 family are modulated after SCI and contribute to the lesion development after SCI. Genetically inhibiting IL-12p40 resulted in better locomotor recovery, which could be attributed to either IL-12 alone or the combination with IL-23. The absence of IL-23 alone was not beneficial after SCI.
Acknowledgements:	Milwaukee VA Medical Center, Wings for Life Foundation, Matthew Budde PhD Lab

Poster #	34
Abstract Title:	Resting-state functional connectivity after concussion is associated with clinical recovery
Presenter(s):	Mayank Kaushal ✉
Authors:	Mayank Kaushal, Lezlie Y. España, Andrew S. Nencka, Yang Wang, Lindsay D. Nelson, Michael A. McCrea, Timothy B. Meier
Dept/Division:	Neurosurgery
Category:	Research Support Staff
Introductions:	There is mounting evidence supporting the notion that physiological effects following sport-related concussion (SRC) are prolonged in relation to clinical recovery. To address this, we evaluated changes to resting-state functional connectivity (rs-FC) of the whole-brain network following SRC. In addition, we explored physiological effects of SRC in subgroups with different temporal recovery profiles to determine if observed rs-FC alterations are present in all concussed athletes or only in those reporting delayed symptom recovery following concussion.
Methods:	Following approval from an institutional review board, high school and collegiate football athletes were enrolled during preseason and participated in this study between July 2015 and May 2017. Athletes that suffered SRC (N=62) were assessed across the acute (within 48 hours) and sub-acute (days 8, 15, and 45) phases post-injury. Matched football athletes without concussion served as controls (N=60) and participated in similar visits. Each athlete provided demographic and health history information and completed a battery of questionnaires and neuropsychological tests during the preseason. The clinical assessment battery was repeated at each follow-up visit while injury and recovery information (e.g., number of days symptomatic) was collected in concussed athletes. Multi-band resting-state fMRI was used to assess whole-brain rs-FC at each visit using network-based statistic and average nodal strength from regions of interest defined using pre-determined whole-brain parcellation templates.
Results:	Concussed athletes had elevated symptoms, psychological distress, and oculomotor, balance, and memory deficits at 48 hours post-concussion relative to controls, with diminished but significant elevations in balance, symptom, and psychological impairments at 8 days post-concussion. Both rs-FC analysis revealed that concussed athletes demonstrated a global increase in rs-FC at 8 days post-concussion relative to controls that was independent of analysis method and whole-brain parcellation scheme adopted. There were no rs-FC differences at the 48-hour, 15-day, or 45-day visits. Further analysis revealed the group effect at the 8-day visit was driven by the large minority of concussed athletes still symptomatic at their visit; asymptomatic concussed athletes did not differ from controls.
Conclusions:	The present study is the largest study to prospectively evaluate the effects of SRC on whole-brain rs-FC over multiple time points during the acute and sub-acute phase. Current findings suggest that whole-brain rs-FC alterations following SRC are delayed in onset but associated with the presence of self-reported symptoms.

Poster #	35
Abstract Title:	Comparison of Pre-Operative Diffusion Tensor Imaging, T2 Signal Intensity versus Combined T2 Signal Intensity and Diffusion Tensor Imaging in a Large Series of Cervical Spondylotic Myelopathy Patients for Assessment of Disease Severity and Prognostication of Recovery
Presenter(s):	Saman Shabani ✉
Authors:	Saman Shabani, Mayank Kaushal, Matthew Budde, Shekar Kurpad
Dept/Division:	Neurosurgery
Category:	Clinical Fellows & Residents
Introductions:	Cervical spondylotic myelopathy (CSM) is a common cause of spinal cord dysfunction. Recently it has been shown diffusion tensor imaging (DTI) might be a better biomarker compared to T2 signal intensity (T2SI) on magnetic resonance imaging (MRI) for CSM. However, there has not been any study to our knowledge to assess the DTI, T2SI, and combination of T2SI and DTI in same set of patient population to determine disease severity and recovery.
Methods:	A prospective analysis of 55 patients with preoperative DTI was done. Presence or absence of T2SI at the level of maximum compression (LMC) was determined. Normalized T2SI (NT2SI) regardless of presence or absence of T2SI at LMC was determined by calculating T2SI at LMC/T2SI at level of foramen magnum. LMC NT2SI, +/- T2SI, and fractional anisotropy (FA) were obtained and correlated to preop mJOA and mJOA at 3, 6, 12, 24 months. Regression analysis and independent t-tests were used for analysis of the data.
Results:	There was a significant correlation between preop mJOA and LMC FA (P=0.048). There were no significant correlations between preop mJOA and presence of T2SI. With regard to ˆ†mJOA, significant relationships were discovered with LMC FA at 12 months (p <; 0.05); on the contrary, there were no significant relationships associated with NT2SI or presence of T2SI. Combining NT2SI or presence of T2SI to LMC FA in multivariate linear regression analysis also did not improve the predictive value significantly, compared to using LMC FA alone.
Conclusions:	In this larger prospective study of CSM patients, FA at LMC shows to be a better biomarker for determining the disease severity, and both short and long-term outcomes compared to T2SI at LMC. Additionally, combined FA with T2SI or NT2SI did not have superiority compared to FA alone in these subgroups of patients.

Poster #	36
Abstract Title:	A time course analysis of cell components and electrophysiological properties in 3D cerebral organoids derived from human induced pluripotent stem cells
Presenter(s):	Xiaowen Bai & Sarah Logan ✉
Authors:	Sarah Logan, Yasheng Yan, Xiaojie Liu, Lai-kang Yu, Congshan Jiang, Thiago Arzua, Zeljko Bosnjak, Qing-song Liu, Xiaowen Bai
Dept/Division:	Cell Biology, Neurobiology & Anatomy
Category:	Senior Faculty
Introductions:	Neurodevelopmental disease modeling has long been a challenge for scientists, primarily due to limitations of animal models and the lack of an appropriate in vitro human model resembling the developing brain. The recently established three dimensional (3D) human cerebral organoids using induced pluripotent stem cells (iPSCs) by Dr. Jurgen Knoblich's lab has revolutionized the availability of human models for experimental studies in vitro. However, little is known about the evolution over time of cell components and important neuronal electrophysiological parameters in iPSC-derived neurons.
Methods:	Through a combination of qRT-PCR and immunostaining, we analyzed the expression of pluripotency, developmental, and ion channel markers over time as iPSCs differentiated to cerebral organoids, from day 0 to day 60 after the initiation of neuronal differentiation. Additionally, we investigated the formation of synapses through electron microscopy, and used whole-cell patch clamping to assess the electrical and chemical channel activity within the neural network.
Results:	The results showed that cerebral organoids developed progressively in culture dishes. Over time, the expression of pluripotent and neural stem cell markers was reduced, with an increase in neuron, astrocyte, oligodendrocyte, and ion channel markers as the cerebral organoids matured. The electrophysiological data revealed that neurons within cerebral organoids displayed spontaneous action potentials, and contained functional glutamatergic (AMPA and NMDA) and gamma-Aminobutyric acid (GABA)-ergic currents within formed synapses.
Conclusions:	Collectively, in comparison with previous 2D neural in vitro models, cerebral organoids more accurately reproduce neurodevelopmental characteristics of the in vivo human brain. Our findings of the emergence of different neural lineages throughout cerebral organoid maturation, combined with network connectivity and electrophysiological profile, provide additional evidence of translational relevance. Thus, the cerebral organoid model is promising for use in studies on human neurodevelopment, modeling neurodevelopmental diseases (e.g., autism), and application in personalized medicine.
Acknowledgements:	This work was supported by grant R01 GM112696 from the National Institutes of Health (to X. Bai).
Reference 1:	Lancaster MA, Renner M, Martin CA, Wenzel D, Bicknell LS, Hurles ME, Homfray T, Penninger JM, Jackson AP and Knoblich JA. Cerebral organoids model human brain development and microcephaly. Nature. 2013;501:373-9.

Poster #	37
Abstract Title:	Serving up Peds Soup: Podcasting for Resident Education
Presenter(s):	James McCarthy, MD ✉
Authors:	James McCarthy, MD; Kelsey Porada, MA
Dept/Division:	Pediatrics: Hospital Medicine
Category:	Junior Faculty
Introductions:	Podcasts, audio or video files that can be downloaded or streamed on smartphones and other media players, are increasingly used as a resource in all areas of education. However, there are relatively few pediatrics-specific podcasts geared toward resident education. This study aimed to develop a podcast, titled Peds Soup, focused on core topics for pediatric residents and to evaluate resident attitudes toward the podcast as an educational tool.
Methods:	All 91 residents in the Medical College of Wisconsin Pediatrics, Internal Medicine-Pediatrics, Pediatrics-Neurology, and Pediatrics-Anesthesia Residency programs were given instructions on how to access the Peds Soup podcast at a housestaff meeting and/or through email. Anonymous surveys were distributed via email at one and three month intervals after the project launch and included yes/no, five-point Likert scale, and free response questions to assess listening patterns and residents' perceptions of the podcast. All residents were able to access the podcast whether or not they participated in the survey. Additionally, the podcast hosting site provided anonymous statistics to track both total and episode-specific downloads as well as information on the geographic location of downloads.
Results:	Twenty-four residents responded to the first survey (S1) and 21 responded to the second (S2). Among those who had listened to the Peds Soup podcast, the majority of respondents agreed or strongly agreed that the podcast helped them learn new information (18/18 S1, 18/19 S2), reinforce information they had already learned (18/18 S1, 19/19 S2), review important information for pediatric boards (16/18 S1, 17/19 S2), apply knowledge to clinical cases (17/18 S1, 19/19 S2), and find time to study (16/18 S1, 18/19 S2). In both surveys, 100% of respondents agreed or strongly agreed that they would continue listening to the Peds Soup podcast and would recommend it to others as a tool for studying pediatrics. To date, the 20 episodes Peds Soup have been downloaded a total of 6,915 times across 48 states and 59 countries. Download statistics also show a consistent increase in the number of downloads per episode, both in Wisconsin and worldwide.
Conclusions:	This study shows that residents view the Peds Soup podcast as a valuable learning tool that helps them find time to study. The results also suggest potential for future growth given residents' plans to continue listening to Peds Soup, their willingness to recommend it to others, and the steady increase in downloads despite the podcast not being actively promoted outside the study group. Podcast-based learning has the potential to be a worthwhile addition to medical school and residency curricula.

Poster #	38
Abstract Title:	Mentoring in community engagement: Developing the next leaders of community engaged research
Presenter(s):	Jessica De Santis ✉
Authors:	Jessica L. De Santis, Sarah P. O'Connor, Zeno Franco, David A. Nelson, & Syed M. Ahmed
Dept/Division:	Community Engagement
Category:	Research Support Staff
Introductions:	Community Engaged Research (CEnR) leads policy change and action through community partnership, is relevant to the community, reduces health disparities, and improves trust between academics and the community. CEnR is an important factor to ensuring research is relevant to the health needs of those being served; however, most researchers have no experience in CEnR in graduate study programs. We propose mentoring will provide researchers with the knowledge to be engaged in and leaders for CEnR. The purpose of this study was to implement mentoring for CEnR as a method for developing the next leaders for CE.
Methods:	Mentoring was approached through the new mindset on mentoring model. Three mentors and eight mentees representing six MCW departments and institutes, a regional campus, and a non-MCW institution tracked their progress using a rubric, needs assessment, and program survey. Mentees and mentors met individually as needed; mentees also engaged in peer coaching with cohort members monthly.
Results:	Professional growth from mentees in the program included a first-time publication, a prestigious Robert Wood Johnson Foundation award, a CE Pathway program for medical students, and explicit expression of self-confidence in leading CE scholarship institutional change.
Conclusions:	The program has expanded in its second year to include six mentors and 13 mentees. It is the hope of this study that the program be a model for all institutions looking to develop leaders for CE.

Poster #	39
Abstract Title:	Quality Improvement in Interventional Radiology: Techniques to Improve Patient Satisfaction Scores
Presenter(s):	Janet Ste. Marie, BSN ✉
Authors:	KL Welch, RT(R) VI
Dept/Division:	Radiology
Category:	Research Support Staff
Introductions:	Managing a patient's peri-procedural pain is vital to a positive patient experience in Interventional Radiology (IR). Patient satisfaction scores are one way to track this. At our institution, patient satisfaction (Avatar Solutions, Chicago, IL) scores from 2012 to 2013 were found to be below our goal in pain management. The purpose of this study was to implement strategies to increase our pain-related patient satisfaction scores.
Methods:	This project was part of a quality improvement project, and therefore exempt by the Institutional Review Board. Four new processes were implemented to increase pain-related patient satisfaction scores. First, Lidocaine Hydrochloride buffered with 8.4% Sodium Bicarbonate was utilized for local anesthesia for all procedures. Second, scripting cards (Fig. B) which reflected the survey language were given to providers. In addition, signs were posted in all pre-procedural rooms asking patients to report pain they were experiencing. Finally, patient discharge instructions were updated to include survey-specific language regarding post-procedure pain management. Between initial patient satisfaction scores in July 2013 and March 2014, patients were anonymously surveyed and asked the following questions: "My request for pain control was responded to quickly" and "I was taught how my pain would be managed".
Results:	Customer Satisfaction scores improved by 8.46% (82.69% to 91.15%) and 7.09% (80.88% to 87.97%) for the two questions, which translated into an increase to our division's Top Box Score Customer Service Score.
Conclusions:	Incorporating buffered local anesthetic, specific language, signage, and updating discharge instructions into our practice have proven effective at increasing our patient satisfaction scores in regard to pain management.

Poster #	40
Abstract Title:	Best time for high fidelity? How do you know?
Presenter(s):	David Pugh ✉
Authors:	David Pugh; Jutta Novalija
Dept/Division:	Anesthesiology
Category:	Senior Faculty
Introductions:	Many Anesthesiologists are unsure about the best management of patients with implanted devices as there is little standardization between manufacturers. High fidelity simulation scenarios allow the learner to practice the management of common problems related to IEDs encountered in the OR during surgery. However, it is unclear when is the best time to implement a curriculum focused on the management of IEDs during Anesthesia resident training. We implemented the same high-fidelity simulation scenario at different levels of training to our anesthesia residents to identify the best time to use high fidelity simulation in their learning process.
Methods:	To assess the ability to anticipate problems during surgery with a patient who has an implanted pacemaker we created a high-fidelity simulation case and ran it for our first, second and third year residents. The trainees were individually assessed by an observer using a checklist and debriefing was done in groups of three using the experiences to highlight different thought processes. The performance on the checklist and management decisions were compared between the three levels of training to establish when the residents had sufficient knowledge and experience to apply in the simulation scenario.
Results:	The first-year residents had a significant knowledge gap, which prohibited them from anticipating complications and applying important treatment options. While more senior residents asked for a magnet and placed it during the scenario, only less than 35% of junior residents were able to treat bradycardia and hypotension related to the inhibition of pacemaker by placing a magnet over the device. More junior residents were also more inclined to call for an electrophysiology (EP) consult as they ran out of ideas early on. This serves as a sign of lack of experience and knowledge to work through the problem. The majority of residents was unable to verbalize what the expectation was from the EP consult and what they wanted the service to do for their patient during the surgery.
Conclusions:	High fidelity simulation is an expensive teaching modality and while it is useful to address knowledge gaps, likely not the best choice for learners early in their training. The simulation scenario focused on pacemaker management was helpful but likely not the best teaching tool during the first year of Anesthesia training due to a large knowledge gap at this stage of training. More senior residents in their 2nd and 3rd year of training had enough knowledge base and clinical experience to apply appropriate treatment options during the scenario and benefited most from the debriefing to understand differences in management between learners and choices in different environments and clinical situations.
Reference 1:	Zendejas B, Cook DA, Farley DR Teaching first or Teaching Last: Does the Timing Matter in Simulation -Based Surgical Scenarios? Journal of Surgical education. 2010;67(6):433-438
Reference 2:	Maddry JK, Varney SM, Sessions D, et al. A Comparison of Simulation-Based Education Versus Lecture-Based Instruction for Toxicology Training in Emergency Medicine Residents. Journal of Medical Toxicology. 2014;10(4):364-368

Poster #	41
Abstract Title:	The Development of a Nurse Externship Program in Interventional Radiology
Presenter(s):	Debra Barnes, BS, RT(R) CV ✉
Authors:	Debra Barnes, BS, RT(R) CV
Dept/Division:	Radiology
Category:	Research Support Staff
Introductions:	Recruitment and retention for specialty care nurses is challenging. It can often take months to find qualified candidates to train. There is a national nursing shortage that is expected to continue. With the current aging population and baby boomers reaching retirement, there will be an increased need for replacement nurses. In addition, adequate staffing is noted as concerning in the employee survey question for nurses on the Froedtert Staff Engagement Survey. Our goal for the program was to expose these nursing students to experiences that would spark interest in working in the Heart & Vascular areas on their future career. In this program, the extern is able to evaluate their level of interest in the Heart & Vascular specialties in a structured learning environment. They are exposed to and gain experience in critical care and assessment skills that could contribute to their career decision after graduation.
Methods:	Leadership at Froedtert & MCW Heart & Vascular Service Line recognized the unique learning opportunity that the Heart & Vascular specialties offer and supported the creation of a Nurse Externship at Froedtert Memorial Lutheran Hospital (FMLH).
Results:	The program was developed by managers, lead staff and educators from Interventional Radiology (IR) Cardiovascular Intensive Care Unit (CVICU) and the Cardiac Catheterization Laboratory (CCL). This ten week, full time, paid program, includes one week for hospital orientation, two weeks in IR, two weeks in CCL, two weeks in in PAR and three weeks in CVICU. The program is offered from the end of May through the beginning of August, during the summer break in most nursing programs. The externs are hired as optional part time employees and intended to be released from the position after the program. Interviews are conducted and externs are chosen based on evaluation of the educational transcripts, three letters of recommendation and a letter written by the candidate detailing their interest in the program. Department educators provide department orientation, tours, review of floor routine, shift routine, how report works and workflow specifics of each shift. Assigned clinical RN preceptors work one on one with the externs, sharing the patient load. The nurse preceptor remains accountable for the patient with the extern assisting in patient care activities. Clinical experience is designed to meet the externs learning needs. The externs are provided with a Competency Outcome Performance Assessment Tool (COPA) which tracks the procedures and experiences the student has obtained. The preceptor updates the COPA with the extern on a weekly basis. In addition, a weekly evaluation is completed by the preceptors and discussed with the externs, offering suggestions for areas of improvement, constructive and positive feedback, and encouraging best practice. Offering clinical experience in both PAR and procedure areas provides exposure for nursing students that may not have otherwise be afforded to them in their respective nursing programs. Clinical experience in CVICU offers opportunities to mature critical thinking skills, experience in caring for critical patients and helps the extern develop confidence in basic and complex patient care assessment and skills. Employment upon graduation to specialty department is limited to nurses with critical care experience; however, fellowship programs are available at FMLH in the Intensive Care Units geared toward new nursing graduates. Having this experience exposes them to the critical care environment.
Conclusions:	Upon completion of the program, interviews were conducted by the managers and lead staff with both externs. Both externs found the program to be highly valuable to their nursing development and had great interest in working in critical care at FMLH. Some of the comments were: "Helped build bedside manner."; "Was allowed to practice my skills, make connections to those things I was taught in school and make personal connections."; and "I wish the experience was longer." This program gave them a unique experience and perspective of what the patient experiences in interventional areas outside of the ICU. Both externs applied for the critical care fellowship program and both were hired into it, one in the CVICU and one in the Medical Intensive Care Unit (MICU). Development of a nurse externship program creates a unique educational opportunity for nursing students, exposing them to nursing opportunities in the Heart & Vascular specialties. The experience gained by the nurse extern fosters personal interest and an understanding of the employment options offered at Froedtert & MCW Heart & Vascular Service Line upon graduation. One of our program goals is that the experience of the nurse extern in the interventional space may encourage this future professional pathway for some of the nurse externs.

Poster #	42
Abstract Title:	Do you know it when you see it? - Creating curriculum to meet new board exam requirements
Presenter(s):	Jutta Novalija & Stylianos Voulgarelis ✉
Authors:	Jutta Novalija; Stylianos Voulgarelis
Dept/Division:	Anesthesiology
Category:	Senior Faculty
Introductions:	Teaching of cardiac ultrasound as part of point of care ultrasound POCUS) skills is an increasing priority during anesthesia residency training, but the degree of transesophageal echo (TEE) teaching is highly variable between training programs (1). In our residency program the interest in more TEE teaching has been well established and TEE knowledge has also become a part of the American Board of Anesthesia OSCE APPLIED exam stations (2). Residents are exposed to TEE teaching of knowledge and skills throughout their residency training, however it remained unclear, if there was a need to change the curriculum to adequately prepare the graduating residents to pass the OSCE task stations related to TEE. To address this question, we surveyed the CA3 class in their last couple of months about their confidence to obtain TEE views and make the diagnosis of common clinical scenarios.
Methods:	Based on the published content outline by the ABA about the task stations during the APPLIED exam we developed a focused intervention in small groups to review the knowledge and expectations for the TEE task station and review the TEE skills to obtain the 11 basic views (3) using a TEE simulator. Resident's confidence in TEE and TTE acquisition and interpretation of images was assessed at baseline and after the training session.
Results:	Overall the short intervention significantly increased the resident's ability to obtain and interpret the basic TEE views. When our residents were asked to name the views as published in the 2013 consensus statement by the SCA (1) without specific pre-learning, the majority of the residents was able to choose the correct name of the view from a list as published in the ABA content outline. On the other hand, when they were asked to write down the name of the view from memory, only the 4-chamber view was correctly identified over 90% of the time. The ME bicaval view reached a successful active recall in more than 60% of the time, which likely reflects the very distinct look of this view and naming, which appears to be easier to be recalled than other views. The other 9 views had an accuracy of less than 40% when tested for active recall.
Conclusions:	We showed feasibility and effect of a focused intervention to teach basic TEE knowledge and skills and prepare for the OSCE stations of the APPLIED board exam. Using blended methods to identify knowledge gaps and enhance the application of learned content by using hands on skills on a simulation task trainer, third year anesthesia residents increased their ability to interpret and perform a basic TEE exam. Based on the feedback future teaching can be tailored even closer address the views, which the residents had more difficulty to distinguish by name and relevance.
Reference 1:	Mitchell JD, Matyal R Teaching Transesophageal Echocardiography in Education in Aensthesia: How to Deliver the Best Learning Experience, Ed Bowe EA, Schell RM, DiLorenzo AN. Cambridge University Press (June 30 2018).
Reference 2:	http://www.theaba.org/PDFs/APPLIED-Exam/APPLIED-OSCE-ContentOutline
Reference 3:	Reeves ST, Finley AC, Skubas NJ et al Perioperative Transesophageal Echocardiography Examination: A Consensus Statement of the American Society of echocardiography and the society of Cardiovascular Anesthesiologists. J Am Soc Echocardiogr 2013;26:443-56

Poster #	43
Abstract Title:	Advanced Technologist Levels for Interventional Radiology Demonstrate a Strong Correlation to Positive Staff Engagement
Presenter(s):	Julie Aguilar, BSN, RN, RCIS ✉
Authors:	Julie Aguilar, BSN, RN, RCIS
Dept/Division:	Radiology
Category:	Research Support Staff
Introductions:	Historically, the interventional Technologists at Froedtert & MCW had one opportunity for career advancement as a Lead Technologist. This sole leadership role does not recognize or reward the technologists that are held to very high standards of proficiency. The complexity of procedures at the Froedtert campus is becoming more difficult, requiring the IR technologists to be not only proficient, but to excel at managing complex technologies, products and procedures. There was no way to recognize the staff for the additional responsibilities that they were required to take on. During regular rounding with management, the staff expressed concern with overall pay and job satisfaction as related to recognition. This was also a concern identified from the technologists on the annual staff engagement survey. The survey results were generally low in areas involving pay, recognition and overall job satisfaction. Comparisons of questions from 2016 to 2017 show significant improvement in several areas that could be contributed to the initiation of the technologist levels.
Methods:	Senior management recognized the level of expectation and complexity of the technologist role at Froedtert & MCW and sought to reward the technologist staff with an opportunity for advancement. A tiered system was created by leadership to recognize the technologists for their advanced application skill sets. As part of this tiered approach, all of the current technologists were moved to a new technologist level 1 job description that Included competency In all job requirements and successful Vascular interventional (Vi} certification within one year. As part of this step, a market analysis was completed for wages and adjustments were made. A program was then created to allow for staff to submit a portfolio to advance to a technologist level 2 or 3. As part of this program, the IR physicians requested to mentor the technologists related to their professional growth. These portfolios were then reviewed by a panel of management and physicians to determine the level of advancement for promotion and salary increase. The expectation is that these portfolios will be updated annually and reviewed at each performance evaluation for assessment of continued engagement and competency.
Results:	A significant improvement was identified in some key questions from the 2016 to 2017 surveys that strongly correlate to the technologist level program. The survey allows for staff to choose six answers: Strongly Agree, Agree, Neutral, Disagree, Strongly Disagree or N/A. The first question that we found had significant improvement was: "My pay is fair compared to other healthcare employers in this area." In 2016, the question had 44% negative responses (Disagree or Strongly Disagree}, 22% Neutral and 33% positive (Agree or Strongly Agree}. In 2017, the same question had zero percent negative responses, 8% neutral and 92% positive (Agree or Strongly Agree}. This was a 78% increase in positive responses. After this program, this concern was no longer shared with leadership during staff rounding discussion.
Conclusions:	Recruitment and retention can be a challenge for technologists in IR. One of the questions in the staff engagement survey says: "I would stay with this organization if offered a similar job elsewhere." In 2016, 22% answered this question negatively, 17% were neutral and 61% were positive. This program increased positively by 31% in 2017, bringing the positive responses to 80%. Furthermore, when technologist job opportunities were previously posted, it could be months and months with no qualified candidates. With a recent job posting, there are 6 qualified candidates to interview for one opening. This is definitely a shift in positive recruitment efforts. Recognition is an important factor when insuring satisfaction. In 2016, there was a 78% positive response to the question "I am satisfied with the recognition I receive for doing a good job." This increased by 13% in 2017 to 88% overall positive. Additionally in 2017, 100% of the technologists answered positive to "Overall, I am a satisfied employee" and 100% to the question "My work is meaningful." There is an Action Planning Readiness score that indicates to the leader how receptive the staff is to working on those things that need improvement. The technologists scored 92% positive in this area. There are a number of questions that measure the overall engagement of the staff. The technologists increased this score by .30 to 4.59 (Scale 1-5). There is a series of power item questions that help to determine the overall staff engagement and likelihood that they will stay with the organization. One hundred percent of the technologist scored in a Tier 1 for these questions. This is the highest level in the survey. A tiered technologist level system has created an opportunity for career growth and professional advancement within the specialty. This program has resulted in increased staff engagement by the technologists as measured by the annual staff engagement survey in areas of pay, recruitment, retention and recognition. This supports our original vision for this program to provide corccr development opportunities and promote recruitment and retention in the profession.

Poster #	44
Abstract Title:	Consulting experiences during postdoctoral training do not alter scientific productivity
Presenter(s):	Julie E. Tetzlaff ✉
Authors:	Julie E. Tetzlaff
Dept/Division:	Pathology: Pediatric Pathology
Category:	Junior Faculty
Introductions:	Postdocs and graduate students of the biomedical sciences are increasingly considering careers outside of academia. Often, training beyond, or outside the scope of, a 'traditional academic' postdoc is required. We addressed this need by establishing the business consulting group PICO (Postdoc Industry Consultants). PICO provides participants with business experience, training, soft skill development and networking opportunities all of which make them more marketable for a career in industry, or a variety of other career types. PICO participants complete consulting projects with local companies. These consulting projects are limited to approximately 5 hours of work per week and are conducted outside of normal business hours, when possible. Participation in PICO (or similar internship or externship opportunities) can be viewed as a distraction, or interference, from the trainee's primary responsibility; their scientific research. Understandably, the trainee's principal investigator (PI) may view participation in internships and externships as a distraction or interference to scientific productivity.
Methods:	To address this issue, we conducted a survey to quantify postdoc productivity based on traditional scientific metrics of productivity such as, number of manuscripts published, conferences attended and grants submitted.
Results:	We found that postdocs who participated in PICO were just as productive, compared to a group of postdoc controls who did not participate in PICO. We also surveyed PICO PIs to acquire their thoughts regarding any effects PICO may have had on the postdocs in their laboratory. Overall, PIs and postdocs reported that they felt PICO would have a positive contribution on the trainee's career and professional development. Notably, there was disagreement between PICO postdocs and their PIs regarding the level of distraction PICO imposed on laboratory work.
Conclusions:	Overall, these results are encouraging and indicate that a postdoc's training can include internship participation without interfering with scientific productivity, but they also illustrate a critical need to acknowledge any concerns PIs may have regarding postdoc internship training and productivity.
Acknowledgements:	We thank the MCW faculty and postdocs who generously took the time to participate in this survey. The development of this program would not have been possible without generous funding from the Burroughs Wellcome Fund (Career Guidance for Trainees grant). The networking events described were supported by the National Center for Advancing Translational Sciences, National Institutes of Health, Award Number UL1TR001436. The content is solely the responsibility of the author(s) and does not necessarily represent the official views of the NIH. We gratefully acknowledge Ms. Paris Eason (Senior Administrative Assistant, Medical College of Wisconsin) for her assistance in designing and distributing the surveys. And Dr. Aniko Szabo, PhD (Associate Professor, Division of Biostatisticians, Institute for Health and Society, Medical College of Wisconsin) for her excellent statistical guidance.

Poster #	45
Abstract Title:	Current State of Palliative Care Training in Interventional Radiology Fellowship: A Survey of Recent IR Trainees
Presenter(s):	S. B. White, MD, MS, FSIR ✉
Authors:	S. M. Tutton, MD, FSIR
Dept/Division:	Radiology
Category:	Senior Faculty
Introductions:	Palliative care is a requisite skill in the care of patients living with oncologic disease. Interventional Radiologists have assumed a more direct role in the management of oncology patients as the scope and efficacy of treatment has improved, however it is unclear whether palliative training as a component of IR fellowship has kept pace. We sought to understand how training in palliative care is structured within current Interventional Radiology fellowships and whether this training is sufficient to prepare trainees to deal with this patient population
Methods:	An online survey was sent to all former fellows-in-training registered by the Society for Interventional Radiology between 2012 and 2016. The survey consisted of 66 questions over 7 sections which covered fellowship training and experiences, attitudes, and preparation in the context of palliative care as well as respondent characteristics. All survey responses were anonymous. 74 survey responses were received over a one-month period from 1,066 invitations (7% response rate). Survey methods and questions were reviewed and approved by the Institutional Review Board at the Medical College of Wisconsin.
Results:	Most respondents report some experience in discussing goals of management with critically ill patients and/or family (98%) and changing goals of care from curative to palliative (85%) during fellowship, however far fewer report direct observation (57% and 48%) or critical feedback (51% and 54%) from attending physicians. Formal teaching in the management of post-procedural complications was high (8.0/10) but the amount of teaching related to management of patients at end of life and communicating end-of-life goals with patients was comparatively low (5.0/10 and 3.2/10, respectively). Further, the quality of such teaching was rated poorly (2.5/10). Respondents report an average level of preparation in caring for patients at the end of life (6.3/10, standard deviation 1.9), however relatively few received explicit teaching in telling a patient that they are dying (9%), determining when to refer patients to hospice (17%), or discussing cessation of anti-neoplastic therapy with patients (21%).
Conclusions:	IR trainees are often called on to provide end-of-life care, however formal training in palliative care is lacking during fellowship. Self-reported scores in preparation for dealing with patients at the end of life indicate an opportunity for improvement, particularly in the areas of attending observation and feedback

Poster #	46
Abstract Title:	Optimizing medical student learning experiences on hospital medicine teams-a qualitative study
Presenter(s):	Yogita Segon, Riley Westein, Sun Young Jeong, Michael Gehring ✉
Authors:	Yogita Segon, Riley Westein, Sun Young Jeong, Michael Gehring
Dept/Division:	Medicine: General Internal Medicine
Category:	Junior Faculty
Introductions:	Background: As the landscape of healthcare is changing, hospitalists are progressively at the fore front of medical training as educators both for students and residents. There is some literature suggesting that hospitalists are rated favorably by both house staff and medical students as better clinical educators on inpatient internal medicine rotation as compared to traditional non-hospitalist faculty. There is a lack of substantial data to assess impact of hospitalists on measurable knowledge and skills outcomes of medical students. Few studies have raised concerns about possible negative impacts on autonomy and decision making of learners, less bedside teaching exposure and a decrease in subspecialty exposure at resident level but such impact on medical student education is an uncharted territory. My pilot study focused on the educational experience of medical students and hospitalists on hospitalist rotations. I determined areas of improvement on both sides and identified major challenges faced by hospitalists in optimizing the learning experience for medical students. Objectives: 1.To compare the overall educational experiences of medical students on hospitalist teams and house staff teams. 2.To determine possible areas of improvement on hospitalist teams to provide more effective teaching to medical students 3.To determine the major challenges that hospitalists face in providing a better educational experience to medical students on hospitalist teams Research Question: What are medical students' and hospitalist faculty's perspective on improving quality educational experience on medicine inpatient hospitalist service?
Methods:	This qualitative pilot project involved one-on-one interviews with third year medical students and hospitalist physicians.
Results:	Multiple themes emerged from these interviews. Student interviews generated themes around the ideal structure and content of rounds. In addition, student perceptions around the impact of attending and team-based variability on learning experiences were elucidated. The hospitalist attendings interviewed opined on barriers to providing a better learning experience for students. In addition, several learner and rotation based changes to optimize student experience were suggested by the hospitalists.
Conclusions:	Data collected so far suggests that students appreciate variability in different attending's style of working and teaching and are willing to adapt as long as expectations are discussed beforehand. They really value dynamic feedback. The hospitalist attendings perceived high patient census as the biggest barrier to providing better learning experience for students. Changes recommended by them included more proactive involvement of students in the logistics of patient care and a desire for a set of recommended best practices to optimize learning experiences on hospitalist teams.

Poster #	47
Abstract Title:	Characterization of immunogenic epitopes of α-galactosidase A in patients affected by Fabry disease under enzyme replacement therapy
Presenter(s):	Simone Scalia ✉
Authors:	Simone Scalia, Ju Huang, Murtaza S. Nagree, Mary Faber, Suzanne Ducett, Gabrielle Geddes, Jeffrey A. Medin
Dept/Division:	Pediatrics
Category:	Clinical Fellows & Residents
Introductions:	Fabry disease is a multi-systemic lysosomal storage disorder caused by a reduction or absence in activity of ?-galactosidase A (?-gal A). This reduction in activity causes the storage of globotriaosylceramide and related species in lysosomes, triggering a cascade of cellular events that determine disease pathology. The treatment of choice for Fabry disease is enzyme replacement therapy (ERT), which can halt disease progression and improve quality of life for patients. However, immune responses against the therapy have been observed in many patients and may be correlated with decreased efficacy of the treatment. It may therefore be beneficial to study this immune response and how it may correlate to the >800 known mutations and/or various presentations. Our first aim is to characterize the immune reactivity of ?-gal A in Fabry patients treated with ERT.
Methods:	Antibody titers were determined in plasma samples from 54 Fabry patients that were being treated with ERT using a modified ELISA in which wild-type ?-gal A was used to capture patient anti-?-gal A IgG antibodies. These were detected in serial dilutions of the plasma, and titers determined by considering the highest dilution at which antibody was still detectable. We are now determining which specific epitopes of ?-gal A these antibodies react to using PEPperMAP technology.
Results:	14/54 (38.6%) patients had high IgG titers, matching numbers from work by others. PEPperMAP analyses identified the most reactive epitopes of ?-gal A in some samples, and we are extending our analyses to study patterns of immunogenicity among our high IgG cohort.
Conclusions:	A consistent number of patients have an immune response against the standard-of-care treatment for Fabry disease, ERT, reducing its efficacy. Our results confirmed this, and have shown a trend towards preference for specific reactive epitopes of ?-gal A which we will verify in additional patients. From these data we may determine mutations or patient pathology that are more likely to have an immune response; this information can be used for preventative medicine.
Acknowledgements:	The authors would like to thank the patients, their families, and their physicians for participating in this study. The authors also would like to thank past and present members of the Medin lab for technical support and advice.
Reference 1:	Colomba P, Scalia S, Cammarata G, Zizzo C, Francofonte D, Savica V, Alessandro R, Iemolo F, Duro G. Fabry disease, a complex pathology not easy to diagnose. Cardiogenetics, 2015 Vol.5 No.1, doi: 10.4081/cardiogenetics. 2015.5612.
Reference 2:	Deegan PB. Fabry disease, enzyme replacement therapy and the significance of antibody responses. J Inherit Metab Dis. 2012 Mar;35(2):227-43.

Poster #	48
Abstract Title:	An In Vivo Enrichment Platform to Enhance Hematopoietic Cell-Directed Gene Therapy
Presenter(s):	Murtaza S. Nagree ✉
Authors:	Murtaza S. Nagree; Mary L. Faber; Everett Tate; Ju Huang; Mark A. Schroeder; John F. DiPersio; Jeffrey A. Medin
Dept/Division:	Pediatrics: Hematology and Oncology
Category:	Research Support Staff
Introductions:	Hematopoietic stem cell (HSC) transplantation following viral modification of autologous product is being investigated as therapy for multiple inherited disorders. As one example, our FACTs team (FAbry disease Clinical research and Therapeutics) is investigating the safety of ex vivo lentiviral (LV) modification and infusion of patient HSCs to achieve long-term correction of Fabry disease (clinicaltrials.gov: NCT02800070). After engraftment, leukocytes differentiating from the genetically modified HSCs can secrete Î±-galactosidase A (Î±-gal A) and uncorrected bystander cells can take it up. This may lead to systemic enzymatic correction and substrate reduction in many tissues. Treatments such as these may benefit from a directed method to enrich for genetically modified cells after transplant. Such enrichment may lead to an increase in therapeutic cargo delivery. Enriching a mature compartment of modified hematopoietic cells rather than HSCs may be sufficient to elicit a therapeutic benefit in many settings. Targeting mature cells may also allow finer control and reversibility of enrichment with less potential side-effects.
Methods:	T cell and B cell proliferation and maturation are inhibited by mycophenolic acid (MPA). The pro-drug mycophenolate mofetil (MMF) is routinely used in the clinic as an orally administered immunosuppressant with few serious side-effects. The target of this drug, inosine-5'-monophosphate dehydrogenase 2 (IMPDH2), can be conferred with resistance by mutating two amino acids (T333I and S335Y; IMPDH2IY). We have constructed dual-promoter LV vectors that engineer expression of IMPDH2IY and other transgenes of interest. We have been optimizing our enrichment platform using Î±-gal A as the model transgene.
Results:	In an in vitro model, we have shown an 8-fold increase in vector copy number (VCN) after exposure of transduced cells to MPA. Enrichment also increased cellular and secreted Î±-gal A activity by 8-fold and 13-fold, respectively. We then engineered luciferase expression in our cell model (Luc+). We xenografted Luc+ cells in NOD/rag/gamma (NRG) mice to determined appropriate cell dosage and to track location and timing of engraftment. Next, we will xenograft cells expressing IMPDH2IY and administer MMF to optimize enrichment conditions. We have also initiated work with ex vivo-transduced syngeneic bone marrow transplants (BMT) in Fabry mice. Preliminary data from these studies suggest that the vector and this enrichment schema have no adverse effects on hematopoiesis or the health of mice.
Conclusions:	We hope to apply optimized MMF conditions from our xenograft model to our BMT model to examine any benefits of our enrichment platform. We anticipate that our strategy will have utility in many other inherited disorders treatable with HSC-directed gene therapy.

Poster #	49
Abstract Title:	Understanding acid ceramidase mutations and their interactions with glycosphingolipid pathways
Presenter(s):	Carissa Ahrenhoerster ✉
Authors:	C. Ahrenhoerster, M. Nagree, JA Medin
Dept/Division:	Pediatrics
Category:	Research Support Staff
Introductions:	Acid ceramidase (ASAH1;ACDase) is an enzyme that catabolizes the sphingolipid ceramide (85305-88-0) into sphingosine and a free fatty acid. Alterations in acid ceramidase expression or activity may be associated with complex diseases including numerous cancers(1). Our lab has developed and studied a model of acid ceramidase deficiency(2) that, in humans, leads to a lysosomal storage disorder (LSD) called Farber disease (228000). This model has a missense mutation (P361R) and accumulates ceramide in many organs and has perturbed hematopoiesis, splenomegaly and hepatomegaly, which cumulatively lead to animal mortality by 9-11 weeks of age. However, the mechanism behind these perturbations and the exact cause of death are unclear.
Methods:	To further elucidate the function of ACDase we created a mouse line with a mutation (T41A) that is associated with Spinal Muscular Atrophy with Progressive Myoclonic Epilepsy (SMA-PME; 159950) in humans, a disease with very different pathology compared to Farber disease, including muscle loss, and seizures in childhood(3). In addition to studying a different mutation, we would like to address the source of pathologically accumulated ceramide. We hypothesize that majority of accumulated ceramide in our P361R model is produced by catabolic breakdown of complex glycosphingolipids. Two families of GSLs, the globosides and gangliosides, are formed from a common precursor glucosylceramide. We have previously shown that introduction of a mutant copy of glucocerebrosidase (GCase) can double the lifespan of P361R mice. We are now probing the contribution of globosides by introducing a mutation in alpha-galactosidase A (GLA;GALA). GALA catabolizes the least complex globoside, globotriaosylceramide.
Results:	Unlike P361R mice, T41A mice live past a year and half and are generally healthy and fertile. No effect on mendelian ratios is observed. Preliminary data suggest no obvious signs of muscle atrophy even in older mice. However, a two-fold increase in total ceramide levels has been observed in the plasma of these mice compared to littermate wild-type controls, suggesting there may be some underlying pathology. We are currently validating these results and tracking ceramide levels with age and physical stress.
Conclusions:	These data may provide targets for substrate reduction in acid ceramidase deficiencies, and may be a gateway to understanding biochemical events that lead to pathological ceramide turnover in complex diseases.
Reference 1:	Frohbergh, M., He, X. & Schuchman, E. (2015). The molecular medicine of acid ceramidase. Biological Chemistry, 396(6-7), pp. 759-765. Retrieved 9 Jul. 2018, from doi:10.1515/hsz-2014-0290
Reference 2:	Alayoubi, A. M., Wang, J. C. M., Au, B. C. Y., Carpentier, S., Garcia, V., Dworski, S., "¦ Medin, J. A. (2013). Systemic ceramide accumulation leads to severe and varied pathological consequences. EMBO Molecular Medicine, 5(6), 827-842. http://doi.org/10.1002/emmm.201202301
Reference 3:	Zhou, J., Tawk, M., Tiziano, F. D., Veillet, J., Bayes, M., Nolent, F., "¦ Melki, J. (2012). Spinal Muscular Atrophy Associated with Progressive Myoclonic Epilepsy Is Caused by Mutations in ASAH1. American Journal of Human Genetics, 91(1), 5-14. http://doi.org/10.1016/j.ajhg.2012.05.001

Poster #	50
Abstract Title:	Mitochondrial fission proteins mediate vascular endothelial dysfunction in T2DM and acute experimental hyperglycemia conditions
Presenter(s):	Jingli Wang ✉
Authors:	Jingli Wang, Sudhi Tyagi, Venkata Puppala, Rong Ying, Mamatha Kakarla, Amberly Branum, Katharine Lippert, Elise Nelton, R. Blake Hill, and Michael E. Widlansky
Dept/Division:	Medicine: Cardiology
Category:	Research Support Staff
Introductions:	Dynamin-related protein 1 (Drp1), a mitochondrial fission-driving protein, reverses mitochondrial and endothelial dysfunction due to low glucose conditions and in arterioles from humans with diabetes (DM). However, Drp1 has multiple docking proteins that facilitate its fission activity. Fis1 appears to be an important Drp1-docking protein under pathological conditions. Drp1 and Fis1's roles in regulating endothelium-dependent vasodilation and nitric oxide (NO) bioavailability in human vessels exposed to high glucose and Fis1's role in patients with DM remains unknown.
Methods:	Human gluteal adipose arterioles were dissected and mounted in a perfusion chamber connected with a video microscopy. Vessels were either intralumenal perfused with 20 nM of siFis1 or siDrp1 or scrambled control siRNA for 24 hours. Following incubation, vessels were exposed to a 6 hours hyperglycemic challenge (HG, 33 mM), Endothelium-dependent vasodilation was tested with increasing concentrations of acetylcholine [Ach (10-10 - 10-5 M)]. NO production from some of these vessels were determined by testing DAF-2 DA fluorescent intensity in absence or presence of L-Name. Addition vessels were treated with Drp1-Fis1 interaction inhibitor P-110 and underwent similar testing.
Results:	In DM arterioles and in HG-treated vessels, siFis1, siDrp1 and P110-TAT reversed impaired Ach-induced vasodilation compared with scrambled siRNA or control. (n = 5, p <; 0.001). Suppressed NO production in HG treated vessels could be restored by siFis1 (58.9 ± 17.4 vs. 20.2 ± 5.5 A.U., n = 9, p <; 0.05). L-NAME blocked this rescue.
Conclusions:	Interruption of the interaction between Fis1 and Drp1 proteins reverse DM and HG-associated endothelial dysfunction and may be a promising therapeutic target to improve DM vascular outcomes.

Poster #	51
Abstract Title:	Pulmonary Pressure Waveform Monitoring Non-inferior to Contrast Venography in Cryoballoon Ablation
Presenter(s):	Katie Cohen, Sudhi Tyagi ✉
Authors:	Katie Cohen, Ridhima Kapoor, Sudhi Tyagi, Marcie Berger
Dept/Division:	Medicine: Cardiology
Category:	Clinical Fellows & Residents
Introductions:	Atrial fibrillation treated with cryoballoon ablation relies on pulmonary contrast venography (CV) to confirm vein occlusion prior to delivery of ablative therapy. Pulmonary pressure waveform (PWM) monitoring offers an alternative, contrast-free, method of assessing pulmonary vein occlusion. Prior studies have not compared the procedural differences and outcomes following application of these two techniques.
Methods:	Subjects who underwent cryoballoon ablation for atrial fibrillation after pulmonary vein isolation with either PWM (n=18) or CV (n=18) between 1/1/2016 and 1/31/2018 were included in this study. Baseline demographic information, procedural and outcomes data following a 3-month blanking period were collected for all subjects.
Results:	The average age of the PWM cohort was 62.2 +/- 9.0 years compared to 63.9±+/- 5.9 years for the CV group (p=0.50). Cryoballoon ablation procedures were performed entirely without contrast in the PWM group while the CV group received on average 49.6 +/-15mg of contrast (p<;0.001). Creatinine did not change significantly pre to 24-hours post-procedure within either cohort (Table 1). The CV cohort received a significantly higher number of cryoballoon applications (8.8 +/- 1.5 vs 6.8 +/- 1.9, p<;0.001) leading to increased procedural duration (3.88 +/- 0.51 vs 3.28 +/- 0.62 hours, p=0.008). At 6 months post-procedure, 2 subjects in the CV group suffered recurrent atrial fibrillation while all subjects in the PWM group remained recurrence free (p=0.467).
Conclusions:	Pressure waveform monitoring introduces a novel, non-inferior method to demonstrate pulmonary vein occlusion prior to cryoballoon ablation procedures. This technique may expand the utility of cryoballoon ablation to patients with renal impairment and contrast allergy.

Poster #	52
Abstract Title:	Fis1 Knockdown Rescues Vascular Monolayer Integrity and Reduces Vascular Inflammation Under Dysglycemic Conditions
Presenter(s):	Mamatha Kakarla ✉
Authors:	Mamatha Kakarla, David Trykall, Jingli Wang, Sudhi Tyagi, Rong Ying, Megan Harwig, John Egner, Blake Hill and Michael Widlansky
Dept/Division:	Medicine
Category:	Research Support Staff
Introductions:	Abnormal glucose levels as seen in diabetes (DM) result in endothelial dysfunction characterized in part by increased vascular endothelial inflammation and increased permeability between endothelial cells. Emerging data suggest the abnormal vascular phenotype in dysglycemia is due to excessive mitochondrial superoxide production driven by mitochondrial fission. DM patients express increased Fis1, an outer mitochondrial membrane protein involved in fission, in their endothelial cells.
Methods:	Under normoglycemic (5 mM) and dysglycemic conditions (2 mM and 30 mM glucose), mRNA transcripts of inflammatory markers in immortalized human microvascular endothelial cells (HMEC-1) were measured Fis1 knockouts (KO, CRISPR/Cas9) and control HMEC-1 cells (normal 5mM). Tight junction dynamics in Fis1 siRNA HMEC-1 knockdown monolayers and scrambled control monolayers were assessed under normal and low glucose (2mM) conditions by transendothelial electrical resistance.
Results:	Under dysglycemic conditions, mRNA transcripts for anti-inflammatory markers (TANK, MAD3, NFKBIE) were elevated in HMEC-1 Fis1 KOs compared to normal glucose HMEC-1 (n =6, p<;0.05). Fis1 siRNA HMEC-1 monolayers exhibited higher resistance compared to scrambled siRNA under normal (n=4, p<;0.0001) and low glucose conditions (Figure, n=5, p<;0.0001).
Conclusions:	Reducing Fis1 expression promotes endothelial health by reducing endothelial inflammation and permeability of the endothelium that is usually seen under dysglycemic conditions. These data suggest therapies to reduce the activity or levels of Fis1 may be a promising target for the reduction of vascular disease in DM patients.

Poster #	53
Abstract Title:	Sphingolipids Influence the Mediator of Flow Induced Dilation: Role of Neutral Ceramidase
Presenter(s):	Mary Schulz ✉
Authors:	Mary Schulz, David Gutterman, and Julie Freed
Dept/Division:	Anesthesiology
Category:	Research Support Staff
Introductions:	Flow-induced dilation (FID) is a critical physiological mechanism to maintain tissue perfusion which relies on the formation and release of vasoactive compounds. We have previously shown that ceramide, a sphingolipid known to be elevated in plasma of patients with cardiovascular disease, can initiate a transition in FID mediator from NO to H_2O_2 in healthy arterioles.1 We hypothesized that manipulation of the sphingolipid pathway to favor ceramide formation would promote H_2O_2-dependent FID, whereas forcing the pathway towards S1P, a sphingolipid with opposing effects, would restore NO-dependent FID.
Methods:	Small arterioles (100-200µm) were dissected from surgically discarded human adipose tissue. Healthy arterioles were incubated overnight (~16-20hrs) with the neutral ceramidase (NCdase) inhibitor, ceranib-1 (10µM). Arterioles from patients with CAD were treated overnight (~16-20hrs) with adiponectin, (2µg/mL) a known NCdase activator,2 the adiponectin receptor agonist AdipoRON (5 µM), a NCdase adenovirus, or sphingosine-1-phosphate (S1P) (1µM). Following constriction with endothelin-1, changes in internal diameter in response to increases in flow (0 to 100 cmH_2O pressure gradient) were recorded using video microscopy. Changes in internal diameter were also recorded in the presence of the nitric oxide synthase inhibitor L-NAME (100µM) or the H_2O_2 scavenger PEG-catalase (500 U/mL).
Results:	L-NAME did not affect FID in healthy arterioles pre-treated with the NCdase inhibitor, Ceranib-1 (83.6%±4.1 of maximal dilator capacity, n=7) compared to vehicle-treated control (76.9%±5.0, n=10), however dilation was abolished in the presence of PEG-Catalase (500 Units/ml) (1.9%±4.9, n=7, $p<0.01$, one-way ANOVA). In arterioles collected from CAD patients, L-NAME significantly impaired the vasodilatory response to flow in S1P (0.3%±2.0%, n=8), adiponectin (18.6% ± 9.0%, n=6), AdipoRON (33.0% ± 11.0%, n=6) and NCdase adenovirus-treated vessels (35.3% ± 13.5%, n=5) compared to vehicle treated control (69.4% ± 7.7%, n=6), whereas PEG-Catalase had no effect.
Conclusions:	NO-dependent FID can be restored by shifting the sphingolipid balance away from ceramide by inhibiting ceramide formation, increasing expression of NCdase, or by administration of S1P, adiponectin, or the adiponectin receptor agonist, AdipoRON. These data support the conclusion that sphingolipids have a tremendous influence on the mediator of FID and NCdase likely has a key role in determining the mechanism by which microvessels vasodilate in response to flow.
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Reference 2:	Wang Y, Wang X, Lau WB, Yuan Y, Booth D, Li JJ, Scalia R, Preston K, Gao E, Koch W, Ma XL. Adiponectin inhibits tumor necrosis factor-alpha-induced vascular inflammatory response via caveolin-mediated ceramidase recruitment and activation. Circulation research. 2014;114:792-805

Poster #	54
Abstract Title:	CRISPR/Cas9-mediated genome editing in patient-derived iPSC-cardiomyocytes recapitulate an MYH6-R443P phenotype in a HLHS family
Presenter(s):	Min-Su Kim ✉
Authors:	Min-Su Kim, Aron Geurts, John Lough, Michael Mitchell, Aoy Tomita-Mitchell
Dept/Division:	Surgery
Category:	Research Support Staff
Introductions:	Hypoplastic Left Heart Syndrome (HLHS) is a clinically and anatomically severe form of Congenital Heart Disease (CHD). Although prior studies suggest that HLHS has a complex genetic inheritance, its etiology remains largely unknown. We previously demonstrated that rare variants in the α-myosin heavy chain (*MYH6*) gene are significantly enriched in HLHS ($p<1x10^{-5}$, observed in 10.5% or 20/190 HLHS subjects). Analysis of clinical outcomes showed that survival without cardiac transplant was reduced in HLHS subjects with *MYH6* variants ($p=6x10^{-3}$) as compared to those without MYH6 variants. Transcriptome and protein expression analyses from cardiac tissue revealed differential expression of cardiac contractility genes, notably upregulation of the β-myosin heavy chain (*MYH7*) gene in subjects with *MYH6* variants. Visualizing α-actinin in atria showed intrinsic disrupted sarcomere structure in HLHS patients with *MYH6* variants. We observed that patient-specific induced pluripotent stem cells (iPSCs) were defective in cardiomyogenic differentiation in vitro. Additionally, sarcomere structure in cardiomyocytes derived from iPSCs produced from a family trio (unaffected mother-affected father-patient) carrying a variant in *MYH6* (*MYH6*-R443P) was dysmorphic.
Methods:	We introduced the *MYH6*-R443P variant into iPSCs derived from the unaffected parent using CRISPR/Cas9 technology. The gene edited cell lines were differentiated into cardiomyocytes and immunostained with α-actinin.
Results:	We observed that the *MYH6*-R443P phenotype in HLHS-iPSCs was recapitulated; specifically, gene-edited heterozygous and homozygous lines were displayed defective cardiomyogenic differentiation, and, sarcomere structure was dysmorphic.
Conclusions:	We conclude that the etiology of *MYH6*-associated HLHS may be informed utilizing iPSCs.

Poster #	55
Abstract Title:	Endothelial cilia regulate cerebral-vascular development
Presenter(s):	Shahram Eisa-Beygi ✉
Authors:	Shahram Eisa-Beygi, Suzan El-Rass, Huseyin C. Yalcin, Shubhangi Prabhudesai, Fatiha Benslimane, Mahmoud Khatib Ali Abdelrasool, Zain Zaki Salim Zakaria, Patricia E. Burrows, Ramani Ramchandran
Dept/Division:	Radiology
Category:	Junior Faculty
Introductions:	The primary cilium is a flow-sensitive organelle and in blood vessels, cilia project into the vascular lumen and function as mechanical sensors of blood flow. However, the involvement of cilia during flow-independent vascular morphogenesis events remains unknown. Recent animal studies reveal that endothelial cilia are crucial for cerebral vascular integrity. However, the distribution pattern of endothelial cilia during the processes of cranial vascular assembly, patterning and maturation remains unknown
Methods:	We employed transgenic lines, confocal microscopy, genetic loss-of-function models and aberrant shear stress levels to elucidate the spatio-temporal and functional profile of endothelial cilia to brain vascula development.
Results:	We report that primary cilia are enriched in nascent cranial vessels that assemble via vasculogenesis and in later-forming angiogenic hindbrain capillaries. Cilia emerge prior to onset of circulation in the primitive vascular plexus, and are enriched around the boundaries of intravascular spaces in angiogenic sprouts. Larval and juvenile brain vessels harbor cilia, mainly at sites of high curvature, vessel bifurcation points and in vessels undergoing remodeling. Finally, we show that loss of cilia-associated proteins increases susceptibility to vascular rupture and hemorrhage in developing brain
Conclusions:	These findings suggest that endothelial cilia are required for both flow-independent and flow-mediated aspects of cerebral-vascular morphogenesis.

Poster #	56
Abstract Title:	Serum Mitochondrial Peptide Levels Correlate with Vascular Health
Presenter(s):	Sudhi Tyagi ✉
Authors:	Sudhi Tyagi, Mamatha Kakarla, Jingli Wang, Amberly Branum, Venkata Puppala, Michael Widlansky
Dept/Division:	Medicine: Cardiology
Category:	Clinical Fellows & Residents
Introductions:	Cardiovascular (CV) risk factors result in mitochondrial membrane hyperpolarization and increased mitochondrial reactive oxygen species (mtROS) that activate pathways resulting in impaired endothelial function. Inner mitochondrial membrane proteins uncoupling protein-2 (UCP2) and prohibitin-1 (PHB1) can favorably impact mtROS and mitochondrial membrane potential (MMP). Whether these proteins could be leveraged as systemic biomarkers to detect impaired endothelial function in humans with diabetes remains unknown. We tested the hypothesis that diabetes-induced vascular dysfunction correlates with decreased mitochondrial peptide levels in serum.
Methods:	Non-diabetic and type 2 diabetic (T2DM) subjects were recruited for studies including a brachial flow mediated dilation (FMD) assessment and venous blood sampling. T2DM subjects with FMD <; 5.6% and non-T2DM subjects FMD ‰¥ 5.6% were included for analyses. ELISA was performed to measure serum concentrations of PHB1 and UCP2. Mitochondrial membrane potential was measured from isolated leukocytes using JC-1.
Results:	Non-T2DM subjects (n=52) with average age 45.4±9.0 years and FMD 7.43±1.70 % along with T2DM subjects (n=52) with average age 56.2±7.9 years and FMD 3.23±1.38 % participated in this study. T2DM subjects with MMP ‰¤ -180 mV had decreased circulating UCP2 levels (2.88±2.84 ng/mL) compared to non-diabetics with MMP >; -180 mV (5.11±3.52 ng/mL) (p=0.014). Within T2DM subjects, there was trend toward a decrease in circulating UCP2 concentration in those with MMP ‰¤ -180 mV (p=0.08). PHB1 levels were not significantly different between diabetics and non-diabetics (13.68 ± 6.05 vs 13.71 ± 5.12 ng/mL, p=0.98).
Conclusions:	Reduced circulating UCP2 levels appear associated with impaired endothelial function and MMP hyperpolarization in T2DM humans. Further work in larger dataset is necessary to determine the utility of UCP2 as a biomarker for endothelial health in DM.

Poster #	57
Abstract Title:	Increasing Mammography Uptake through Academic-Community Partnerships in Ethnic Minority Communities
Presenter(s):	Emmanuel Tavares; Amrita Rao ✉
Authors:	Emmanuel Tavares; Amrita Rao; Melissa DeNomie; Arman Tahir; Fauzia Qureshi; Sailaja Kamaraju MD
Dept/Division:	Medicine: Hematology and Oncology
Category:	Research Support Staff
Introductions:	While Caucasian women have a higher incidence of breast cancer, women of color are shown to have a higher mortality. Delay in diagnosis and treatment has been attributed to factors such as decreased knowledge and reduced access. Community Based Academic Partnerships (CBAPs) appear to be an effective method of collaborating with communities to promote cancer awareness and screening efforts. Milwaukee is a city with high racial segregation with social and health disparities, as well as a high influx of both refugees and immigrants in recent years. Newly immigrated women have a lower utilization of screening practices. While immigrant populations in Milwaukee have not yet been specifically studied, it can be theorized that these women will also be less likely to adhere to screening practices.
Methods:	Partnerships were formed with ethnic and religious minority communities in Milwaukee. Breast cancer education workshops were conducted over 2 years at trusted community sites. Surveys were administered at the workshop to quantify breast cancer knowledge, demographic data, and perceived barriers to breast health care. We partnered with the Columbia St. Mary's Mobile Mammography unit to provide free screening mammograms to qualified women. Interviews were conducted with individuals representing 3 communities that participated in the workshops. Interviews focused on community leader assessment of workshop effectiveness, goals, and sustainability.
Results:	493 women from immigrant and refugee communities attended a breast health workshop. 374 participants fully completed the surveys. 188 women (‰¥40 years old) reported no prior mammogram in the past 2-5 years. 60% of these women were insured and 40% were uninsured. After attending the workshop, mammogram uptake was 100% among insured women and 80% in uninsured women. Finances, language, and access to screening were heavily endorsed barriers to screening. Women were satisfied by the workshop, with 73% rating as highly informative. Utilization of an ethnic group's native language was noted as a major strength in breast health education. Recruitment of participants was a significant challenge faced by all of the community sites. Positive impact on attendees centered on increased exposure and improved knowledge base of the participants. Cultural factors cited as barriers were education, sensitivity of the topic, fear, and confidentiality.
Conclusions:	Our CBAP offered culturally tailored breast health education and access to screening via a mobile mammography unit. Workshops were well attended, highly rated and resulted in increased uptake of screening mammography, as shown through workshop surveys and reaffirmed through interviews with community leaders. These small group interviews proved to be an important tool for further delving into the barriers to breast healthcare. Discussions also touched on the relationship of women with medicine, and relationship dynamics among partners, families and communities that make women more or less likely to seek breast health care.
Acknowledgements:	Susan G Komen
Reference 1:	Gorin S, JE H, Cheng B, SJ S. Delays in breast cancer diagnosis and treatment by racial/ethnic group. Arch Intern Med. 2006;166(20):2244-2252. http://dx.doi.org/10.1001/archinte.166.20.2244.
Reference 2:	Teal R, Moore AA, Long DG, Vines AI, Leeman J. A community-academic partnership to plan and implement an evidence-based lay health advisor program for promoting breast cancer screening. J Health Care Poor Underserved. 2012;23(2 Suppl):109-120. doi:10.1353/hpu.2012.0076
Reference 3:	Rapkin BD, Massie MJ, Jansky EJ, Lounsbury DW, Murphy PD, Powell S. Developing a partnership model for cancer screening with community-based organizations: the ACCESS breast cancer education and outreach project. Am J Community Psychol. 2006;38(3-4):153-164. doi:10.1007/s10464-006-9071-2

Poster #	58
Abstract Title:	Financial barriers for pharmacy-based immunization services
Presenter(s):	Inez Pabian, BS ✉
Authors:	Karen J. MacKinnon, BPharm, R.Ph., Sarah Sorum, PharmD, Erica Martin, BS, Mary Hayney, PharmD, MPH, Samantha Lewiston, BS, Inez Pabian, BS
Dept/Division:	School of Pharmacy
Category:	Research Support Staff
Introductions:	Background: Pharmacy-based immunization services play an important role in making vaccines available to the public and preventing disease. However, these services have not been fully implemented because barriers in the healthcare reimbursement environment exist. Objective: To determine the barriers related to vaccine reimbursement identified by pharmacists.
Methods:	A survey regarding potential barriers to full provision of immunization services in related to reimbursement for vaccine administration was distributed to the pharmacist membership of the Pharmacy Society of Wisconsin in July 2017.
Results:	Twenty-seven responses were received. Survey results show 59% of respondents identify the time the pharmacist spends preparing and administering the vaccination may not be reimbursed as the largest barrier to vaccine provision. Respondents also identified variability when submitting claims for different vaccines or to different payers (56%), inability for their pharmacy to submit vaccine claims for all types of vaccines (44%), patients receiving incorrect information from their insurance provider about which vaccines are covered (41%), and inability to receive reimbursement for supplies (41%) as additional barriers. Administering vaccines too infrequently to have an efficient process in place for submitting claims and the time it takes to submit a claim were not considered barriers by any of the survey respondents.
Conclusions:	Numerous barriers to reimbursement of pharmacist-provided vaccines must be removed which could increase access to and administration of vaccines, therefore reducing the prevalence of vaccine-preventable diseases. The Pharmacy Society of Wisconsin, through the Wisconsin Pharmacy Foundation and funded by the Advancing a Healthier Wisconsin Endowment, aims to address these barriers through implementation of a statewide protocol, improving patient engagement, revising trainings, and convening financial stakeholders.

Poster #	59
Abstract Title:	Community conversations: A multiple-method approach to addressing cancer disparities
Presenter(s):	Lauren Matthews, MPH ✉
Authors:	Lauren Matthews, MPH; Magdalisse Henderson; Marques Hogans Sr., MPH; Kathleen Jensik, MSW; Liana Woodley; Vanica Guignard; Staci Young, PhD; Kirsten Beyer, PhD, MPH, MS; Melinda Stolley, PhD
Dept/Division:	Cancer Center
Category:	Research Support Staff
Introductions:	Background: Cancer disparities are a significant public health issue. Identifying underserved areas with high disparities and engaging communities will inform relevant efforts to reduce disparities. Purpose: To identify geographic areas in Southeastern Wisconsin with high cancer incidence and mortality; and to understand African Americans' (AA) perceptions and experiences of cancer disparities.
Methods:	Methods. Adaptive spatial filtering, a disease mapping method, was used to estimate spatial patterns of cancer incidence, late stage incidence, and mortality for breast, colorectal, lung and prostate cancer. We also conducted semi-structured focus group with AA women and men living in Milwaukee. Groups were stratified by gender and cancer diagnosis (breast or prostate). Inductive content analysis was used to examine perceptions of existing cancer disparities and how they can be addressed.
Results:	Results. Maps highlighted areas of significant disparities in Milwaukee zip codes representing predominantly African-American neighborhoods. Nine focus groups were conducted with 79 AA men and women (mean age 51 years). Themes related to reasons for disparities included: decrease in community investment, food deserts, medical mistrust, lack of AA health professionals, cancer myths, and fear. Potential solutions included: community-based cancer education, greater workforce diversity achieved through pipeline programming, better access to healthy foods and strategies to improve communication and build trust between patients and their doctors.
Conclusions:	Discussion. Future research interventions and programming should seek innovative strategies to build cancer awareness and education and improve access to trusted quality care.

Poster #	60
Abstract Title:	How to Measure Quality Healthcare: Critiques and Recommendations from Primary Care Providers and Community Members on Quality Measures.
Presenter(s):	Mai See Thao ✉
Authors:	Thao MS, Dhore N, Kaigama CN, Ogawa L, Ortega LM, Pattock A, Pergament S, Satin D, Scandrett M, Soto I, Soto M, Svedberg B, Yang M, Culhane-Pera K.
Dept/Division:	Family and Community Medicine
Category:	Junior Faculty
Introductions:	The Minnesota legislature directed the Minnesota Department of Health to develop a new framework of quality healthcare measure to implement pay-for-performance (P4P), in an effort to decrease cost and improve quality. Primary care providers (PCP) and community leaders were recruited to assess their experiences and critiques of quality healthcare, quality metrics, and impact of P4P on health equity.
Methods:	Community-based action research methods were employed. Qualitative interviews was conducted with 14 PCPs (4 individual interviews and 3 focus groups) who had worked at both safety net and non-safety net primary care clinics in Minneapolis-St Paul MN USA metropolitan area. Four-hour listening sessions were held with 21 community leaders who are from 7 ethnically diverse urban communities.
Results:	For PCPs, current quality measures are 1) influenced more by patients and clinic systems than by clinicians; 2) are not the same as measuring quality healthcare; 3) are not how patients and clinicians define quality in healthcare; and 4) are embedded in historical social inequities. For community leaders, ideal quality healthcare has 1) respectful trusting relationships; 2) identifies and addresses historical trauma, structural racism, and social-structural determinants of health; 3) has structures and processes that support health equity; 4) prioritizes culturally responsive mental health, health promotion, and patient education; and 5) promotes access to care, with patient-centered integrated healthcare and system navigation. Together, leaders and PCPs think that P4P reinforces an inequitable healthcare system and should be replaced by patient-centered metrics within a broader patient-centric system that reaches for health equity.
Conclusions:	Community leaders and PCPs have similar perspectives about quality health care and the role of quality measures, and they are against a P4P system that could decrease health equity and increase health disparities. Community leaders and PCPs have valuable relevant perspectives for the legislative policy-setting process.
Acknowledgements:	Mo Mike and Misty Blue

Poster #	61
Abstract Title:	Use of Predictive Modeling to Identify the Factors Associated with the Timing and Patient Outcomes of Clinical Ethics Consultation
Presenter(s):	Mary E. Homan, MA, MSHCE, DrPH ✉
Authors:	Mary E. Homan, MA, MSHCE, DrPH
Dept/Division:	Institute for Health & Equity: Center for Bioethics and Medical Humanities
Category:	Junior Faculty
Introductions:	This study assessed how predisposing characteristics (male, African American, Hispanic race, age over 65 years), enabling factors (Medicaid, living will, health care proxy), need condition (decisional capacity), and health behaviors (late ethics consultation) were statistically associated with two adverse patient outcomes of excess length of stay and low realization rate.
Methods:	I employed the Gelberg-Andersen Behavioral Model for Vulnerable Populations to predict the two adverse patient outcomes. I hypothesized that a delay of ethics consultation (after first two days) H1 increased the odds of an excess LOS and H2 increased the odds of a low realization rate. I conducted statistical analysis of adverse patient outcomes using descriptive statistics and logistic regression modeling. The source population included all patients who received an ethics consultation between 2013 and 2016 (n = 495) at six hospitals. Inclusion criteria were: inpatients, GMLOS of at least two days, and age at least 18 years. This resulted in a study population of 372 cases.
Results:	The odds of an excess length of stay were six times greater for the late consult group than the early consult group (OR = 5.98; 95% CI [3.73, 9.61]). For patients who survived to discharge, the odds of an excess length of stay were almost five times greater for the late consult group (OR = 4.87; 95% CI [2.48, 9.56]). For patients who expired or went onto hospice, the odds of an excess length of stay were ten times greater for the late consult group than the early consult group (OR = 10.33; 95% CI [4.81, 22.21]). The odds of a low realization rate for the late consult group were three times greater than the early consult group (OR = 2.99, 95% CI [1.87, 4.79]). The odds of a low realization rate were two times greater for those who survived to discharge in the late consult group than those who survived to discharge in the early consult group (OR = 2.20; 95% CI [1.14, 4.62]). For patients who expired or were discharged to hospice, the odds of a low realization rate among the late consult group were four times greater than patients with an early consult who expired (OR = 4.45; 95% CI [2.17, 9.12]). There was an average net margin savings among Medicare patients who received early consultation of $14,191.74 per case.
Conclusions:	Ethics consultations can help reduce length of stay when performed early in a patient's hospitalization. Data from this study can inform best practices on what to look for when a patient is admitted to a hospital, how to identify barriers in the provision of quality care, and to prepare for labor and resource-intensive cases. These findings provide opportunities for shared savings among patients, payors, and providers.

Poster #	62
Abstract Title:	I'm Too Sexy For My... Taking A Sexual History In The Hospital Setting To Capitalize On A Missed Opportunity
Presenter(s):	Vanessa McFadden MD PhD ✉
Authors:	Vanessa McFadden MD PhD, Alyssa Stephany MD, Anna Schmitz MD, Sonia Mehta MD, Kelsey Porada MA, Michelle Pickett MD
Dept/Division:	Pediatrics: Hospital Medicine
Category:	Junior Faculty
Introductions:	Half of all new sexually transmitted infections occur among 15-24 year olds and 1 in 4 adolescent females has had an STI. Adolescents are known to have poor access to reproductive health care. Hospitalized adolescents are a captive audience, yet reproductive healthcare is not often discussed during hospitalization as preliminary research, from our institution, demonstrated only 55% of hospitalized adolescents had any documentation of sexual history, with males, patients admitted directly to the intensive care unit (ICU), and those hospitalized for non-ingestion complaints, with even less documentation. The objective of this study was to increase the percentage of documented sexual history for adolescents aged 13 years old and older hospitalized on the hospital medicine service.
Methods:	This is a prospective study from 5/1/17 to 12/31/17 at a stand-alone academic children's hospital, with baseline data from 5/1/17 to 7/30/17 and post intervention data from 11/20/17 to 12/31/17. Interventions consisted of: resident education including evidence-based reasons for taking a sexual history in hospitalized adolescents and presentation of current institutional practice habits, and development of electronic health record template to facilitate intervention implementation workflow. Data collected included patient demographics and sexual history defined as any documentation of sexual history within the entire hospital encounter. Subgroups analyzed were males, patients admitted directly to the intensive care unit (ICU) then transferred to the acute care unit, and those hospitalized for non-ingestion complaints. Data was analyzed using descriptive statistics and unpaired T tests to determine changes in sexual history documentation post intervention.
Results:	150 patients were included in the baseline data and 51 patients in the post-intervention. Overall, documentation of sexual history significantly increased from 55% to 75%, p=0.02. Documentation in males increased from 36% to 53%, p=0.22, and for patients initially admitted to the ICU then transferred to the acute care unit increased from 14% to 33%, p=0.36, but both were not significant. Documentation for non-ingestion complaints significantly increased from 48% to 73%, p<0.01.
Conclusions:	Following brief interventions, overall sexual history documentation increased during our study period, yet there continues to be a need for further improvement, especially for males and patients initially cared for in the ICU setting but ultimately discharged from the hospital medicine service. Hospitalizations are an important opportunity to improve overall adolescent health given this population's known poor access to reproductive healthcare. Beyond improving sexual history documentation, further research is needed to assess if this effort translates to enhanced provision of reproductive healthcare services.

Poster #	63
Abstract Title:	Fostering Partnerships for Health through a Community Engaged Research (CEnR) Seed Grant Program
Presenter(s):	Zeno Franco, PhD; Sarah P. O'Connor, MS ✉
Authors:	Zeno Franco, PhD; Sarah P. O'Connor, MS; Trina Van Schyndel, MS; David A. Nelson, PhD, MS; & Syed M. Ahmed, MD, DrPH
Dept/Division:	Office of Community Engagement
Category:	Research Support Staff
Introductions:	The Office of the Associate Provost & Senior Associate Dean for Community Engagement at the Medical College of Wisconsin (MCW) houses the Community Engagement (CE) Core. The CE Core aims to more fully integrate MCW's CE mission throughout the campus and the community to impact health equity and health disparities across the state of Wisconsin. The implementation of a Community Engaged Research (CEnR) Seed Grant Program is one of several key strategies employed to accomplish this goal. The CEnR Seed Grant Program seeks to support community-academic teams conducting CEnR projects in Wisconsin. Research teams include co-principle investigators—one who is a MCW faculty member and one who is a representative from a Wisconsin-based community organization. As a partly-matched program, the CEnR Seed Grant Program also seeks to leverage funding from and build partnerships with interested MCW centers, institutes, and campuses. Finally, through these campus partnerships, the program seeks to support awardees' efforts to obtain additional extramural research funding to further benefit Wisconsin communities.
Methods:	The CE Core, in collaboration with MCW centers, institutes, and campuses, initiated five CEnR Seed Grant Program application cycles between 2016 to 2018. Documents from the application and selection process for each of these five cycles provided administrative data on the co-principle investigators, their partnerships, and the CEnR research projects themselves.
Results:	Four out of the five CEnR Seed Grant Program cycles invited applications focused on health issues across the state of Wisconsin, and the remaining cycle focused on health issues in the Green Bay and Central Wisconsin regions of Wisconsin. Across these five cycles, the CE Core, in collaboration with MCW centers, institutes, and campuses, awarded eight seed grants—three Cancer focused, two Cardiovascular focused, one Translational focused, and two focused on health issues in the Central Wisconsin and Green Bay regions of Wisconsin. Joint funding across these five cycles came from the CE Core and three MCW partner centers and institutes—the Cancer Center, the Cardiovascular Center, and the Clinical and Translational Science Institute of Southeast Wisconsin.
Conclusions:	In looking at data gathered through application and selection documents from each of these five CEnR Seed Grant Program cycles, observable outcomes include the following: number of new MCW partnerships promoting CEnR, number of community organizations receiving first-time funding for research, number of unique community partners receiving CEnR Seed Grant Program funding, and number of unique zip codes in which CEnR research is taking place. Future research may examine outcomes related to awardees' efforts to obtain additional extramural research funding to further benefit Wisconsin communities.
Acknowledgements:	The Community Engagement Core Implementation Initiative is funded by the Advancing a Healthier Wisconsin Research and Education Program (AHW REP).

Poster #	64
Abstract Title:	Withaferin A induced macrophage polarization in association with inflammasome activation: Implications to target tumor microenvironment
Presenter(s):	Brice Ayissi Owona ✉
Authors:	Brice Ayissi Owona, Seema Dubey and Dev Karan
Dept/Division:	Pathology
Category:	Research Support Staff
Introductions:	Macrophage plasticity and polarization is a well-established phenomenon associated with inflammation and its associated diseases including cancer. However, the status of inflammasome complex proteins, a key regulator of inflammation, remains uncharacterized in the polarized macrophages. In this study, we used a natural product withaferin A (WFA) to determine its effect on macrophage polarization using monocyte-derived THP-1 cells.
Methods:	Following the standard method of cytokine-induced polarization, M1 (pro-inflammatory) and M2 (anti-inflammatory) macrophages, treatment of M2 macrophages with WFA induces M1-like characteristics. Macrophages without cytokine treatment (M0 macrophages) served as control. The polarization plasticity of macrophages was validated using RT-PCR and qPCR for M1 (CXCL10, IL12) and M2 (CCL20 and CCL5) markers. On the other hand, the colocalization of NLRP3, ASC and AIM2 proteins was studied in M0, M1, M2 and M2W macrophages by immunofluorescence.
Results:	Interestingly, analysis of AIM2, NLRP3, and NLRP6 inflammasome in M1 type macrophages and the WFA treatment of polarized M2 macrophages showed increased gene expression levels of AIM2 and NLRP6 while NLRP3 remains unchanged. Furthermore, immunofluorescence assay showed increased level of AIM2 and NRLP6 inflammasome proteins in WFA treated THP-1 cells. These data indicate that WFA promotes polarization of M2 anti-inflammatory macrophages toward M1-like phenotype associated with increased levels of AIM2 and NLRP6 inflammasome proteins.
Conclusions:	This observation may represent a new concept of inflammasome proteins in macrophage polarization modulating inflammation and warrant further investigation. Since inflammation plays a key role in the initiation of tumor growth and development, targeting inflammasome complex may help in manipulating the tumor microenvironment to further improve treatment strategy.

Poster #	65
Abstract Title:	Production and Characterization of PDL1 Mutants
Presenter(s):	Kemi Adeyanju ✉
Authors:	Kemi Adeyanju, Blake Hill and Jeffrey Medin
Dept/Division:	Pediatrics: Hematology and Oncology
Category:	Research Support Staff
Introductions:	Activation of a naÃ¯ve T cell requires two distinct signals, one from the interaction of antigen with the T cell receptor (TCR) and the other from costimulatory molecules expressed on antigen presenting cells. The balance of an immune response is maintained by the series of costimulatory or coinhibitory receptors that promulgate positive or negative signals respectively. Receptors delivering coinhibitory signals function as immune checkpoints and are important regulators of immune tolerance and autoimmunity. One such coinhibitory axis is programmed cell death (PD-1) and its ligand programmed death ligand-1 (PDL1). Signaling through this pathway has also been implicated in the development of regulatory T cells (Treg). Regulatory T cells mediate peripheral tolerance by suppressing autoreactive T cells that could otherwise play a key role in the pathogenesis in a number of autoimmune diseases.
Methods:	To determine if PDL1 proteins with higher binding affinity to PD-1 would better promote the development of Treg, we used rational design and computer modeling to predict sites on the PDL1 molecule that might favor sustained PD-1 ligation. This resulted in the identification of seven point mutations to the PDL1 molecule that were distributed into the mutants PDL1A, PDL1B, PDL1C and PDL1D.
Results:	DNA encoding PDL1A-D with a C-terminal 6xHis tag were synthesized, cloned into pcDNA3.4 and the cloning was confirmed by enzymatic digest and sequence analysis. We then used the Expi293 mammalian expression system to produce the recombinant mutant proteins PDL1A-D and purified them by affinity chromatography on a Ni-NTA column. Signaling by PDL1A-D after PD-1 ligation will be assessed via western blot to determine which mutant has a higher affinity to PD-1 compared to the wild-type protein.
Conclusions:	The binding affinity between the PDL1 mutants and PD-1 will also be evaluated with the use of surface plasmon resonance. Finally, the PDL1 mutants will be assessed for their ability to generate Treg.

Poster #	66
Abstract Title:	Age-dependent changes in cell size control endothelial cell growth through YAP1
Presenter(s):	Megan Muyleart ✉
Authors:	Megan Muyleart, Tadanori Mammoto, Akiko Mammoto
Dept/Division:	Pediatrics
Category:	Research Support Staff
Introductions:	Age-dependent impairment of lung regeneration and repair contributes to the pathogenesis of aging-associated chronic lung diseases (CLD). Angiogenesis—the formation of new blood capillaries- plays a key role in lung regeneration and is impaired in aging animals. Thus, in order to develop more efficient therapies for aging-associated CLD, we need to understand the mechanisms by which aging impairs angiogenesis in the lung. In addition to soluble growth factors, biophysical factors modulate angiogenic gene expression and regulate endothelial cell (EC) behaviors and function. We have reported that changes in cell size and geometry control EC growth. It is known that cell size increases during aging in various tissues. However, the effects of age-dependent increases in EC size on impairment of angiogenesis in the aged lung and the underlying mechanism have not been explored before. The mechanosensitive transcriptional co-activator, Yes-associated protein (YAP1), senses various mechanical forces (e.g., cell size, stiffness, flow) and controls angiogenesis and organ regeneration. Deregulation of YAP1 is involved in cellular senescence and contributes to the pathogenesis of CLD. We hypothesize that age-dependent increases in EC size may suppress EC proliferation in the aged mouse lung through aberrant YAP1 signaling.
Methods:	We culture young vs. aged mouse lung ECs on fibronectin-coated single-cell sized islands of different sizes, and analyze the effects of EC size on YAP1 activity, cytoskeletal structure, and cell proliferation, apoptosis, and senescence. We also manipulate YAP1 expression/activity in young vs. aged mouse lung ECs cultured on fibronectin-coated islands of different sizes to determine whether cell size controls EC growth through YAP1.
Results:	Pulmonary ECs in aged mice (24 months (24M) old) are significantly larger than those in young mice (2M old). The levels of YAP1 decrease and EC proliferation is inhibited in ECs isolated from aged mouse lungs. When we culture aged lung ECs on single-cell sized fibronectin-coated large islands of size comparable to aged mouse lung EC, YAP1 is excluded from the nucleus and EC proliferation is attenuated, while reduction of the aged EC size increases the YAP1 activity and restores EC proliferation.
Conclusions:	Age-dependent increases in EC size impair aged EC proliferation through YAP1 signaling. Since most current therapies for CLD, which focus mainly on the chemical signaling pathways, are not highly successful, modulation of mechanical signaling reveals significant clinical relevance to treat aging-associated CLD.
Reference 1:	Mammoto, A. and Mammoto, T et al. Nature 457, 1103-1108 (2009).
Reference 2:	Mammoto, A. Muyleart., M. Kadlec, A. Gutterman, D. Mammoto, T. Microvascular Research 119, 73-83 (2018).
Reference 3:	Mammoto, T., Jiang, E., Jiang, A. & Mammoto, A. American journal of respiratory cell and molecular biology 49, 1009-1018 (2013).

Poster #	67
Abstract Title:	Novel roles for GATA4 in defining the squamocolumnar junction in the GI tract: Implications for Barrett's esophagus
Presenter(s):	Michele A. Battle ✉
Authors:	Delaforest, Ann, Thompson, Cayla, Kohlnhofer, B, Stavniichuk, R, Wojta, K, Pulakanti, K, Rao, S, Battle, MA
Dept/Division:	Cell Biology, Neurobiology & Anatomy
Category:	Senior Faculty
Introductions:	Reactivation of pathways used during development to pattern tissue fate and function can play a role in disease. Our work explores the idea that abnormal re-activation of the developmentally important transcription factor GATA4 in the stratified epithelium of the esophagus contributes to the pathology of Barrett's esophagus (BE), a premalignant metaplasia preceding esophageal adenocarcinoma (EAC). Our previous studies identified GATA4 as an essential regionalizing factor within the small intestinal epithelium. GATA4 is also differentially expressed at the squamocolumnar junction, where it is present within the columnar epithelium of the glandular stomach but is absent from the stratified epithelium of the esophagus/forestomach. In BE, this boundary is disrupted, and the esophageal stratified epithelium is replaced by columnar epithelium. The lack of GATA4 in normal esophageal epithelium and its presence in BE metaplasia along with the observation that the GATA4 gene is frequently amplified and expressed in EAC suggest a role for GATA4 in BE/EAC pathogenesis. We hypothesize that exclusion of GATA4 from esophageal/forestomach epithelium during development is essential to establish a normal squamocolumnar junction.
Methods:	To test this hypothesis, we used Gata4 conditional knockout and knock-in mice with Sonic Hedgehog Cre to eliminate GATA4 in the columnar epithelium of the mouse hindstomach or to induce GATA4 in the stratified epithelium of mouse forestomach during development. We examined phenotypes in conditional mutants by histochemistry, immunohistochemistry, and RNA-Seq. We used ChIP-Seq to map the GATA4 binding profile in normal mouse hindstomach epithelium and combined GATA4 binding data with gene expression data from mutants to identify high-confidence GATA4 direct targets.
Results:	We found that GATA4-deficient hindstomach epithelium was stratified rather than columnar, resembling the epithelium of the forestomach/esophagus. Conversely, GATA4-expressing forestomach contained columnar epithelium whereas control forestomach consisted solely of stratified epithelium. RNA-Seq revealed alterations in the transcriptomes of GATA4 mutants. The transcriptome of hindstomach epithelium lacking GATA4 shifted toward that of forestomach epithelium, and the transcriptome of forestomach epithelium expressing GATA4 shifted toward that of hindstomach epithelium. We found a network of esophageal and gastric transcription factors to have altered expression in GATA4 conditional mutants. One key altered factor was p63, a master regulator of stratified squamous epithelial development. Importantly, many transcripts associated with human BE were similarly mis-regulated in GATA4 conditional mutants.
Conclusions:	Together, these data support the hypothesis that GATA4 has an essential role in squamocolumnar junction development. Our data suggest that GATA4 promotes columnar over stratified squamous epithelial development at the squamocolumnar junction by regulating expression of a transcription factor network, including GATA4-mediated repression of the stratified epithelial cell master regulator p63. Finally, altered expression of many BE-associated genes in GATA4 mutants further links GATA4 transcription factor function to human BE.
Acknowledgements:	We thank Rhonda Souza, Baylor, Scott and White Research Institute, Dallas, TX.

Poster #	68
Abstract Title:	Interaction of membrane proteins AT1R and MAS1 using computational methods
Presenter(s):	Nikita R. Dsouza ✉
Authors:	Nikita R. Dsouza, Eric C. Exner, Andrew S. Greene, Michael T. Zimmermann
Dept/Division:	Genomic Sciences & Precision Medicine Center: Bioinformatics R&D
Category:	Research Support Staff
Introductions:	Angiotensin II receptor 1 (AT1R) is a part of the renin-angiotensin system (RAS) that binds angiotensin II to stimulate chemical signals essential for regulating blood pressure via the balance among body fluids and salts. Another RAS effector peptide, Ang-(1-7), plays a protective role in the cardiovascular system through its interaction with the G-protein coupled receptor, MAS1. Studies suggest AT1R forms a membrane-bound complex with MAS1 when Ang-(1-7) is bound, but no experimental structures exist to investigate this interaction.
Methods:	We studied the heterodimerization of AT1R and MAS1 using computational methods in order to predict the most likely interaction surface. We generated 3D model structures for the individual membrane proteins AT1R and MAS1 for both human and rat protein sequences, using homology modeling. Using Rosetta and custom scripting, we docked the two proteins including contributions of the membrane environment. The human and rat models were docked independently and the results compared between species. Geometric, energetic, and cluster-based analysis were used to assess candidate poses.
Results:	Top scoring poses contained highly favorable features that were consistent with experimentally determined membrane protein complexes including a leucine zipper and flanking salt bridges. The helices that interacted with each other were the same in the representative poses obtained from the minimum interface energy and median RMSD. We identified the same helix interaction between the rat AT1R and MAS1, and human. The structure of MAS1 was evaluated to explain the slight shift in the interaction of poses obtained from the interface energy, total energy and RMSD median in both human and rat proteins.
Conclusions:	We have predicted a likely heterodimerization pose of two membrane proteins using computational methods. We are currently exploring experimental validation, but our model informs the design of an experimental system that will reduce the cost and increase the efficiency of future studies.
Reference 1:	Hoffmann BR, Stodola TJ, Wagner JR, et al. Mechanisms of Mas1 Receptor-Mediated Signaling in the Vascular Endothelium. Arterioscler Thromb Vasc Biol. 2017;37(3):433-445.

Poster #	69
Abstract Title:	Molecular Modeling and Simulations to Discern the Consequences of Rare Genetic Variants
Presenter(s):	Michael T. Zimmermann ✉
Authors:	Michael T. Zimmermann, Nikita R. Dsouza, Donald G. Basel, Eric W. Klee, Raul Urrutia
Dept/Division:	Genomic Sciences & Precision Medicine Center: Bioinformatics R&D
Category:	Junior Faculty
Introductions:	Demand is increasing for DNA-based diagnoses for individual patients who present with phenotypes indicative of rare diseases, but for whom routine genetic testing failed to yield a diagnosis. Clinical application of DNA-based testing using high-throughput technologies has led to the identification of a large number of novel variants, many of which lack prior clinical evidence, making their implications for the patient uncertain. For this reason, they are categorized as Variants of Uncertain Significance (VUSs).
Methods:	Computational tools for simulating the atomic-level effects of variants on protein structure and dynamics are well established, but have not achieved systematic use in clinical settings. We are applying molecular modeling and simulation to generate specific hypotheses for the molecular effects of VUSs identified during the course of clinical genomics sequencing. Detailed in silico analyses represent an additional level of information for the interpretation of VUSs—information that is overlooked by current clinical guidelines. Because the dynamics of each protein differ from one another, we generate protein-specific metrics for quantifying how variants affect the protein. Additionally, our process leverages multiple established disease variants as well as polymorphisms as comparators for determining the significance and consistency of VUS-associated effects.
Results:	Here we present our process for molecular modeling and specific examples for VUSs identified through next-generation sequencing of clinical cases presenting with undiagnosed diseases. Functional validation using in vitro assays confirmed the effects predicted by modeling.
Conclusions:	We believe molecular modeling will become an increasingly important component in the process of interpreting the effects of human genetic variation.
Reference 1:	Zimmermann MT, Urrutia R, Oliver GR, et al. Molecular modeling and molecular dynamic simulation of the effects of variants in the TGFBR2 kinase domain as a paradigm for interpretation of variants obtained by next generation sequencing. PLoS One. 2017;12(2):e0170822.
Reference 2:	Zimmermann MT, Urrutia R, Cousin MA, et al. Assessing Human Genetic Variations in Glucose Transporter SLC2A10 and Their Role in Altering Structural and Functional Properties. Frontiers in Genetics. Accepted. doi: 10.3389/fgene.2018.00276.
Reference 3:	Paquin A, Ye D, Tester DJ, Kapplinger JD, Zimmermann MT, Ackerman MJ. Even pore-localizing missense variants at highly conserved sites in KCNQ1-encoded Kv7.1 channels may have wild-type function and not cause type 1 long QT syndrome: Do not rely solely on the genetic test company's interpretation. HeartRhythm Case Rep. 2018;4(2):37-44.

Poster #	70
Abstract Title:	Use of Over-The-Counter Medication in the Management of High School and Collegiate Sport Related Concussion
Presenter(s):	Alexa Wild ✉
Authors:	Alexa Wild, Ryan Dunn, Amy Nader, Michael A. McCrea
Dept/Division:	Neurosurgery
Category:	Research Support Staff
Introductions:	Sport-related concussion (SRC) is highly prevalent in contact and collision sports, with common sequelae of persistent headaches, fatigue, irritability, insomnia, and difficulties with concentration and memory. Symptom resolution after a SRC is crucial for facilitating a successful recovery and return to play. Current position statements have made recommendations regarding medication use for symptomatic management after SRC1, but little research has investigated medication use in the athletic population. Our study investigated the frequency of over-the-counter medication (OTC) use after SRC, including types of OTC medications used and factors that influence OTC use after SRC.
Methods:	Project Head-to-Head is a prospective study enrolling Southeast Wisconsin high school and collegiate athletes (2,867) during the 2012-2017 sports seasons. Athletes were enrolled in the study during preseason baseline assessments. Concussed athletes completed serial post-injury assessments (<;6 and 24-48 hours; 8, 15 and 45 days) after SRC, along with a group of matched athlete control without concussion.
Results:	Out of the 284 athletes who completed serial assessments after a SRC, 43.5% used OTC specifically to treat SRC symptoms. Of the athletes that used OTC to treat symptoms, 44.8% used acetaminophen, 38.5% used nonsteroidal anti-inflammatory drugs (i.e., Advil, Motrin, ibuprofen, Aleve) and 10.8% used other OTC (i.e., Aspirin, Excedrin, etc.). Chi-square test for independence showed using OTC after a SRC was significantly associated with previously using OTC use at baseline (χ^2 (1) = 4.16, p=.041) and the athlete's institution (χ^2 (12) = 25.01, p =.015). There was no obvious indication that an OTC user had greater severity of injury (i.e., loss of consciousness, amnesia, or sideline Sport Concussion Assessment Tool 3 (SCAT) symptom severity score) (p's>;.05) compared to non-users. Independent t-test analysis revealed athletes that used OTC after SRC had higher Brief Symptom Inventory-18 (BSI-18) somatization scores acutely (p=.006), reported more severe headache and pressure in head (p's<;.017) SCAT symptoms at the 48hr time point, and had significantly higher ratings on SCAT of sensitivity to light or noise, feeling slowed down, feeling in a fog and fatigue 8 days' post-injury (p's<;.05).
Conclusions:	Current recommendations advise against the use of nonsteroidal anti-inflammatory drugs following SRC, yet our data revealed that over a third of athletes using OTC medications for SRC symptoms report taking a nonsteroidal anti-inflammatory drug. This study indicated that whether an athlete uses OTC after a SRC is less likely related to the injury itself, but is more likely related to individual (e.g., pre-injury OTC medication use habits) and environmental factors (e.g., institution or care provider). These findings highlight the importance of disseminating information regarding OTC recommendations in the management of a SRC to not only healthcare providers (athletic trainers, physicians, etc.), but to the athletes themselves and the parents of athletes.
Reference 1:	Brogolio, S P., Cantu, R.C., Gioia G. A., Guskiewicz K. M., Kutcher J., Palm M., & Valovich McLeod T. C. (2014). National Athletic Trainers' Association Position Statement: Management of Sport Concussion. Journal of Athletic Training, 49, 245-265. doi: 10.4085/1062-6050-49.1.07

Poster #	71
Abstract Title:	The Impact of Exercise on Women Who Experienced Intimate Partner Violence
Presenter(s):	Samantha Below ✉
Authors:	Samantha Below, M3
Dept/Division:	Neurosurgery
Category:	Research Support Staff
Introductions:	Intimate partner violence (IPV) is a growing problem in the United States. Research found individuals who experience IPV may become psychologically disturbed, which correlated with an increased risk of chronic disease and disability. Inversely, positive thoughts and wellness activities are correlated with improved health.
Methods:	Women residing at a domestic violence shelter participated in a weekly wellness program and were instructed to complete a Rand-36 Short Form Health Survey (SF-36) before and after completing each walk or run for a minimum of 20 minutes for 1-10 weeks on their own time. In conjunction to this, weekly discussion groups were held with a focus on mental health
Results:	Over three months, 23 women were enrolled in the program. The scores for all participants in all health areas were averaged and categorized as pre, or post intervention. They were then compared to the Rand average and standard deviation. In all areas, the participants had lower health scores than the Rand Medical Outcomes Study population. Post scores were higher than the pre-survey scores in all areas, but no statistical difference was found when using a paired t-test.
Conclusions:	Most participants expressed a desire to be more active, healthier and lose weight. The quality of the data assessing the effectiveness of the intervention may be compromised by subjects self-reporting exercise. Due to the independent nature of the project, there is an increased compromise to the quality of the data in assessing the effectiveness of the intervention. However, the participants expressed that the program added value to their lives.
Reference 1:	Leedy, M. G. (2000). Commitment to distance running: Coping mechanism or addiction? Journal of Sport Behavior, 23, 255-270.
Reference 2:	Hays, K. (1999). Working it out: Using exercise in psychotherapy. Washington, DC: American Psychological Association
Reference 3:	Biddle, S. J. H., & Mutrie, N. (2001). Psychology of physical activity: Determinants, well-being, and interventions. New York: Routledge.

Poster #	72
Abstract Title:	Acute Injury Characteristics Distinguish Different Subpopulations of Mild Traumatic Brain Injury (mTBI)
Presenter(s):	Amy Nader ✉
Authors:	Nader, A. M., Tetzlaff, J. E., McCrea, M. A., & Nelson, L. D.
Dept/Division:	Neurosurgery
Category:	Research Support Staff
Introductions:	Mild traumatic brain injury (mTBI) is typically defined based on crude clinical signs and symptoms that are imperfect markers of brain injury. Consequently, patients with mTBI diagnoses vary substantially in injury severity and outcomes. Understanding how to stratify mTBI patients into subgroups with distinct injury pathophysiology and prognoses will inform translational research aimed at identifying mTBI biomarkers as well as the development of precision medicine clinical trials. The objective of this study was to explore the degree to which there are subtypes of mTBI, discernable on the basis of traditional acute injury characteristics, which show distinct relationships with other proxies of injury severity and outcome. In particular, we hypothesized that patients with different levels of evidence for loss of consciousness (LOC; Witnessed, Suspected, No) would manifest different relationships with various subjective and objective markers of mTBI severity.
Methods:	We analyzed data from two recent prospective studies in which we enrolled patients with mTBI from either a level I trauma center emergency department (ED; N = 98) or an inpatient trauma unit (N = 75). We evaluated patients on average 2 days postinjury and followed them up to 90 days postinjury. Analyses focused on comparing Witnessed, Suspected, and No LOC groups within each sample on available medical record variables and clinical assessment measures.
Results:	Both samples yielded evidence of important differences between Witnessed and Suspected LOC groups, although specific findings differed across samples. For example, in the ED cohort, the Witnessed LOC group showed more acute and persistent neurocognitive impairment as well as more prolonged symptom duration as compared the Suspected and No LOC groups. In the inpatient cohort, participants with Suspected LOC had more significant acute mTBI symptoms and showed a trend toward lower rates of acute intracranial findings on clinical head CT as compared to both Witnessed and No LOC groups.
Conclusions:	The findings imply that there are meaningful differences in clinical characteristics and perhaps injury biomarkers in patients with these different types of LOC. *How* acute injury characteristics, which form the basis of mTBI diagnoses, should be defined and assessed is an under-researched topic that deserves more attention in future work.

Poster #	73
Abstract Title:	Sphenopalatine Nerve Block: Clinical Considerations and Safety and Efficacy
Presenter(s):	Elizabeth Rodriguez, RT(R) VI ✉
Authors:	Elizabeth Rodriguez, RT(R) VI
Dept/Division:	Radiology
Category:	Research Support Staff
Introductions:	In the United States, 13% of adults (37 million people) suffer from migraines. Of those, 30% of sufferers report that migraines result in a severe disability. The national headache foundation estimates that migraines cost the US more than $20 billion, when accounting for medical expenses, missed work and decreased productivity from sufferers. Small studies have demonstrated that sphenopalatine ganglion (SPG) blocks are effective at treating migraines. Not completely understood is the exact mechanism of chronic migraines. There are multiple theories that typically revolve around stimulation of the Superior Salivatory Nucleus (SSN). Parasympathetic outflow from the SPG is triggered from the SSN leading to vasodilation of cranial blood vessels which secrete inflammatory mediators to meningeal nocioceptors. Trigeminoautonomic reflex - afferent trigeminal sensory neurons from meningeal vessels project through the thalamus to the pons. The neurons in the pons reflexively stimulate the SSN which increases parasympathetic output from the SPG, otic, and carotid ganglia via the facial nerve. Autonomic dysfunction from SPG can present as lacrimation, nausea, emesis, nasal congestion, rhinorrhea, forehead/facial sweating, conjunctival injection, salivation, diarrhea, and polyuria.
Methods:	A retrospective review of all patients undergoing SPG blocks at our institution from May to November of 2017 were included in the IRB approved study. Patient demographics, diagnosis and indication for procedures, number of SPG blocks, time interval between blocks, initial and follow up MIDAS and HIT-6 scores and subjective improvement in their headaches and peri- and post procedural complications were collected. Data was also collected on insurance reimbursement for this procedure. Patients whose insurance denied coverage and did not proceed with therapy, were excluded from the analysis. Descriptive statistical analysis was performed.
Results:	To date, 20 patients were treated with SPG blocks at our institution. The patient population consisted of 3 males and 17 females. The ages of the patients treated ranged from 11 years old to 76 years old. All patients were treated on a minimum of two separate dates, some patients were treated as many as eight times. Subjectively, all patients getting more than a single treatment had clinical improvement in their symptoms, which ranged from complete resolution of headaches to decreased pain/intensity and/or increased interval between headaches. Only 2 minor complications were noted in the 2o patients. One patient developed a self resolving nose bleed, and one developed vertigo, that resolved with treatment with an anti-histamine
Conclusions:	Based on current studies, SPG blockade is a safe and effective treatment for chronic headaches such as cluster headaches, migraines, tension headaches, and other trigeminal autonomic cephalalgias, with minimal associated complications

Poster #	74
Abstract Title:	Next generation mobile digital radiography: Can dose be reduced without sacrificing image quality in the neonatal intensive care unit?
Presenter(s):	Joshua Pohlman ✉
Authors:	Pohlman JR, Moe DC, and Vo JN.
Dept/Division:	Radiology
Category:	Clinical Fellows & Residents
Introductions:	Introduction of a new mobile digital radiography technology may allow for improved image quality while decreasing radiation dose. The purpose of this study is to compare a next-generation mobile x-ray system to current technology amongst a frequently examined homogeneous patient population. One such patient population, who are also most sensitive to the effects of ionizing radiation, are infants within the neonatal intensive care unit (NICU). During an infant's stay within the NICU, daily portable chest radiographs are often acquired. This frequency of exams allows for a crossover case-controlled comparative image quality assessment between current and next-generation mobile x-ray systems at equivalent and reduced dose settings.
Methods:	Between 4/6/2017 and 8/25/2017 both a next generation (GE Optima XR240amx, GE Healthcare, Chicago IL) and a present technology (Carestream DRX-Revolution, Carestream Health, Rochester NY) mobile digital radiographic systems were used concurrently in the NICU. Two cohorts of 36 patients, who underwent chest radiography from both systems during a single NICU stay, were retrospectively formed for equivalent and next-generation radiation reduced dose radiographs. Time between control radiographs was minimized for each patient. The resulting 144 radiographs were graded by two blinded radiologists on a 4-point scale (non-diagnostic, below-average, average, excellent) during a systematic review. Quality values from the 4 cohorts were compared using Student's t-test. Additionally, radiation dose values (kVp, mAs, and dose-area product (DAP)) were collected for each radiograph and analyzed.
Results:	At equivalent dose, although the next generation system tended to have superior quality ratings, there was no significant difference between the two x-ray systems (average DAP of 7.5 vs. 9.4 mGy-cm2, p-value = 0.261; average quality rating of 2.26 vs. 2.06, p-value = 0.058; next generation and current technology systems respectively). Moreover, after radiation dose was reduced on the next generation system there remained no significant difference in image quality between systems (average DAP of 4.7 vs. 7.3 mGy-cm2, p-value = 0.004; average quality rating of 1.99 vs. 2.09, p-value = 0.225; next generation and current technology respectively).
Conclusions:	Compared to current technology, a next-generation mobile digital radiographic system allows for radiation dose reduction while maintaining image quality in NICU radiographs. This finding suggests the new technology will increase the margin of safety for a vulnerable patient population.

Poster #	75
Abstract Title:	Evaluating parenchymal enhancement characteristics utilizing a novel imaging software
Presenter(s):	Brycen Bodell, MD ✉
Authors:	E.J. Hohenwalter, MD, FSIR
Dept/Division:	Radiology
Category:	Senior Faculty
Introductions:	Final catheter position for therapeutic agent delivery in Liver Directed Therapy (LDT) relies heavily on 2D digital subtraction angiography (DSA) and is subjective. This feasibility study utilizes a prototype Siemens software package to evaluate parenchymal enhancement characteristics on 2D DSA by subtracting vasculature and evaluating the underlying contrast time curve information.
Methods:	Retrospective analysis of DSA was performed on 19 patients previously enrolled in an IRB approved study. Angiograms of patients who underwent DEB-TACE were reviewed. Images were acquired at a standard frame rate of 3 frames per second. The prototype software package was installed on a standalone research workstation with deidentified images. The software algorithm used a band pass filter to suppress vascular structures and a gain multiplier to enhance the underlying parenchyma enhancement in each image. The resulting contrast time curves for each pixel in a 2D DSA series were evaluated for: Time to peak (TTP), time to half peak (THP), time to half washout (THW), time of arrival (TOA), area under the curve (AUC) and wash-in rate (WIR). Resulting images displayed the values in a color wash, compressing the underlying functional information of the complete 2D DSA run into a single color image. The color images were evaluated by a group of board certified interventional radiologists.
Results:	Of the 19 enrolled patients, six datasets were excluded due to breathing motion image quality degradation. The remaining thirteen datasets were evaluated for information gain for the six processing modes. TTP, THP showed to be to affected by contrast density fluctuation between systole and diastole resulting in noisy color images which yielded limited additional information. Evaluation of THW was limited in the available datasets. Evaluation showed that for reliable results additional frames until near complete wash-out of the contrast need to be acquired. TOA was robust and allowed assessment of contrast blockages or stenotic areas. AUC demonstrates the final distribution of contrast and the potential distribution of treatment agent. WIR highlighted further differences in contrast uptake, with regions of increased vascular supply filling faster than those with less tumor and/or less tumor vascularity.
Conclusions:	Using this post-processing software, additional information can be derived that cannot easily be gained by simple review of 2D DSA data alone. Initial evaluation showed considerable potential for area under the curve and wash-in rate showing the most information gain to the reviewer panel on potential distribution of treatment agent. Next efforts will focus on optimizing the 2D DSA acquisition sequence and contrast injection, evaluating further functional parameters and patient motion compensation.

Poster #	76
Abstract Title:	Auricular Neurostimulation for Non-Pharmacologic Post-Operative Pain Control: A Randomized Controlled Trial
Presenter(s):	Jacqueline Blank, MD ✉
Authors:	Jacqueline J Blank MD, Ying Liu PhD, Ziyan Yin MS, Christina M Spofford MD PhD, Timothy J Ridolfi MD, Kirk A Ludwig MD, Mary F Otterson MD MS, Carrie Y Peterson MD MS
Dept/Division:	Surgery: Colorectal Surgery
Category:	Clinical Fellows & Residents
Introductions:	Opioid medications are the cornerstone of postoperative pain control, but they have negative physiologic and psychologic effects. Additionally, the opioid epidemic implores surgeons to utilize non-pharmacologic methods of pain control. The objective of this study was to determine whether an auricular neurostimulation device may be used as an adjunct to pain control after elective colorectal surgery. We hypothesize that the use of an auricular neurostimulation device will decrease postoperative narcotic consumption.
Methods:	This placebo-controlled trial included opioid-naÃ¯ve adult patients who underwent elective bowel resection one of two academic institutions between December 2016 and April 2018. Patients were followed for 30 days postoperatively. Observers and participants were blinded to device activity. Active and inactive devices were randomized and placed on the right ear prior to surgery, and remained in place for five days. All patients received the same postoperative pain regimen. The primary outcome was total narcotic consumption; secondary outcomes included pain, nausea, and anxiety scores, return of bowel function, complications, 30-day readmission rates, and use of narcotics at 2 weeks and 30 days postoperatively.
Results:	Of 209 patients assessed for eligibility, 152 were excluded, 5 patients withdrew, and data from 52 patients was analyzed. The average age was 58.6 years and 30 patients (55.8%) were male; baseline characteristics were similar between groups. Overall analysis did not demonstrate an advantage for active neurostimulation devices. Subgroup analyses demonstrated a benefit for patients with open laparotomy incisions (29.0 +/- 1.70 vs 84.95 +/- 27.22 oral morphine equivalents [OME] per day for active vs inactive devices, p=0.0278), as well as for older patients (27.08 +/- 19.55 vs 66.80 +/- 30.56, 69.80 +/- 47.40 vs 103.92 +/- 58.80, and 94.82 +/- 44.88 vs 100.87 +/- 53.01 OME/day for patients >;70 years, 60-70 years, and 50-60 years, respectively; p=0.01092). There were no differences in total pain scores, anxiety scores, nor the proportions of patients who experienced postoperative nausea.
Conclusions:	For older patients and those with larger abdominal incisions, auricular neurostimulation may be useful to decrease narcotic consumption, and these subgroups warrant additional research to quantify the effect of neurostimulation. Further investigation is necessary to determine long-term effects of the auricular neurostimulation device on narcotic use after surgery.

Poster #	77
Abstract Title:	Outcomes Following Thoracic Endovascular Aortic Repair for Acute Aortic Syndromes
Presenter(s):	Parag J. Patel MD, MS, FSIR ✉
Authors:	Parag J. Patel MD, MS, FSIR
Dept/Division:	Radiology
Category:	Senior Faculty
Introductions:	Thoracic aortic endografts were initially indicated for and most studied in the treatment of thoracic aortic aneurysms followed by traumatic aortic transection. However, there has been increasing use of thoracic aortic endografts in acute aortic syndromes, including aortic dissection, penetrating atherosclerotic ulcer, and intramural hematomas. Over the last 5 years, in our tertiary care institution with a large volume of thoracic endovascular aortic repair (TEVAR), more endovascular repairs have been performed for acute aortic syndrome than for aneurysm. This study examines the outcomes of TEVAR in this patient population
Methods:	An IRB approved HIPAA compliant retrospective review of all patients undergoing TEVAR for acute aortic syndrome with complicating features (contained rupture, persistent pain, aneurysmal degeneration, malperfusion, or progression despite medical management) from September 2012 through November 2017 were reviewed. Pre-procedure cross-sectional imaging, type and size of endograft used, and post-procedure outcomes, including clinical outcomes and follow up imaging results, were reviewed. Specifically, imaging was assessed for aortic remodeling. Positive aortic remodeling was defined as a thrombosed false lumen, increased true lumen, and absence of aneurysmal degeneration within the treated segment, as assessed on imaging follow up prior to any additional intervention. Negative aortic remodeling was defined as increase in size of a patent false lumen or aneurysmal degeneration within the treated segment.
Results:	34 patients ranging in age from 30-88 years (mean 61) underwent TEVAR for acute aortic syndrome between September 2012 and November 2017 (Table 1). Follow up duration ranged from 0-60 months (mean 9 months). Of the 34 patients, 9 (26%) required additional intervention, 4/9 (44%) endovascular and 5/9 (56%) open surgical intervention. Twenty-five (74%) demonstrated positive aortic remodeling on follow up imaging, 6 (18%) had negative aortic remodeling, and 6 (18%) demonstrated an endoleak. Three (9%) patients developed spinal ischemia with permanent lower extremity weakness and 2 (6%) suffered a cerebrovascular accident. There were 4 (12%) deaths: 1 within 24 hours due to multi-organ failure and 3 >;30 days after the procedure, of unrelated causes (Table 2). All 3 of the patients with postoperative retrograde aortic dissection had an intramural hematoma component on their initial CT; the degree of graft oversizing was less than 15% for all 3 (ranged from 0-13%). Two of the 3 patients with postoperative spinal cord ischemia had a final aortic coverage length of >;300 mm, though 2 other patients had a final aortic coverage length of >;300 mm and did not develop spinal cord ischemia.
Conclusions:	TEVAR is a safe and effective option for the treatment of acute aortic syndrome, with the majority showing positive aortic remodeling on follow up imaging. The overall morbidity is lower than that seen with open aortic repair and the rate of spinal cord ischemia is similar to that seen in other studies looking at both endovascular and open repair

Poster #	78
Abstract Title:	Whole exome sequencing in developmental ocular disorders confirms genetic heterogeneity and unexpected findings
Presenter(s):	Linda M. Reis ✉
Authors:	Linda M. Reis, Eric Weh, Sarah DeBehnke, Rebecca C. Tyler, University of Washington Center for Mendelian Genomics, Elena V. Semina
Dept/Division:	Pediatrics: Developmental Biology
Category:	Research Support Staff
Introductions:	Developmental ocular disorders encompass a broad range of ocular conditions which are typically present at birth, including anophthalmia/microphthalmia, coloboma, Axenfeld-Rieger anomaly, Peters anomaly, aniridia, congenital glaucoma, and congenital cataract. A large number of genes have been implicated in these conditions but the proportion of developmental ocular disorders which can be explained by mutations in known genes is not clear.
Methods:	We performed whole exome sequencing on a cohort of 48 probands with developmental ocular disorders and family members when available (34 families); probands were sorted by primary diagnosis of cataract (14), anterior segment dysgenesis (18), microphthalmia, anophthalmia, coloboma (10), or optic nerve phenotypes (6). Exome data was reviewed for mutations in known ocular genes and trio analysis for novel genes is ongoing.
Results:	Causative variants were identified in 12 families including two probands with dual genetic diagnoses (PAX6/45,XO and PDE4D/GJA3), six cases with expanded ocular phenotypes associated with known genes (HNRNPK, KERA, RARB, SOX2, SOX11, and SHH), one case of a dominant genetic etiology despite a presumed recessive family history (PAX6), one case which confirms a newly reported phenotype of cataract and premature ovarian failure (TRNT1), and two cases fully consistent with previous reports (CRYAA and LTBP2). Additional candidate variants and variants of interest were identified including three cases with NF1 and unilateral developmental ocular disorders with NF1 disruption identified. The affected gene was unique to each family with the exception of PAX6, confirming the genetic heterogeneity of developmental ocular conditions.
Conclusions:	The affected gene was unique to each family with the exception of PAX6, confirming the genetic heterogeneity of developmental ocular conditions. The frequency of dual diagnosis and unexpected findings emphasizes the importance of unbiased analysis of whole exome data.

Poster #	79
Abstract Title:	Does Accessing Chest Ports During Inpatient Hospitalization Increase Risk of Catheter Based Infection?
Presenter(s):	Jenny Riesenberg ✉
Authors:	S. B. White, MD, MS, FSIR
Dept/Division:	Radiology
Category:	Support Staff
Introductions:	Since its advent in 1982, chest ports (CP) have become the standard of care for administering chemotherapy to cancer patients. It has been shown that placing chest ports during an inpatient hospitalization portends an increased risk of infection. Because cancer patients can become neutropenic, these infections can be devastating and lead to a delay in chemotherapy and result in open draining wounds further delaying care. Though placement of CPs on inpatients leads to higher rates of infections, there is no data to suggest if accessing an already implanted CP on inpatients confers an increased risk of infection. Therefore, this study aims to evaluate the infection rate of patients who have their CPs accessed in the inpatient setting.
Methods:	Using our QA/QI database, we determined a cohort of patient with CPs. We then stratified the patients into two groups, group 1: those admitted to the hospital and had their CPs accessed during their hospitalizations and group 2: those that were hospitalized and did not have their CPs accessed. Patient records were reviewed to obtain post procedural infections (cellulitis, blood stream infections, port pocket infections defined by positive blood cultures, positive tip cultures, or pus/cellulitis at the site of CP insertion). Using the patients in group 1, we split them into two groups: patients treated by ward nurses and patients treated by specialized trained nurses or venous access team members by looking at their patient records. Once the patients were divided into their groups, we compared infection rates when attempting to access the CP.
Results:	Of the 100 patients analyzed, 66 had their CP accessed during an inpatient hospitalization. The general ward nurses accessed 60 of those CPs, resulting in 6 total infections, while the VAT members accessed 6 CPs with no complications. The 34 patients who did not have their CP accessed as inpatients did not develop any infections.
Conclusions:	Preliminary data suggests infection rates are increased when CPs are accessed during inpatient hospitalization. It remains to be seen if there is a significant correlation for higher rates of infections with ward nurses accessing the CP compared to VAT members.

Poster #	80
Abstract Title:	Heart Rate Variability Biofeedback in Pain Management
Presenter(s):	Rebecca Anderson & Sarah Endrizzi ✉
Authors:	Anderson, R., Wilson,,A., & Endrizzi, S.
Dept/Division:	Anesthesiology: Pain Management
Category:	Senior Faculty
Introductions:	Millions of Americans suffer from chronic pain. Treatment costs are in the billions and some patients still do not find relief. Current effectiveness research shows positive results for biofeedback training as an intervention for headache and other types of chronic pain.
Methods:	The present retrospective, archival study used patient information (N=72) collected during a heart rate variability biofeedback training program to assess treatment effectiveness among patients who experience chronic pain. More specifically, the study was designed to examine six research questions focused on patient-reported levels of pain and distress, as well as catastrophizing, depression, anxiety, and somatization. It was hypothesized that after three sessions of biofeedback, the patient scores on these six variables would decrease.
Results:	A significant reduction in self-reported pain and distress was found immediately after the biofeedback session, however, pain and distress scores generally returned to the pre-session baseline by the beginning of the next biofeedback session and the reductions in pain and distress were not maintained between sessions revealing a "sawtooth" pattern. On average, patients reported a decrease of more than one point on a 0 to 10 rating scale when rating their pain after the biofeedback training intervention (1.21 for Session 1; 1.63 Session 2; and 1.50 for Session 3). There was a slightly greater reduction in distress ratings than pain ratings after each session of biofeedback (i.e., distress ratings decreased an average of 1.75 after Session 1, 1.67 after Session 2, and 1.74 after Session 3). Of the four symptom measures (catastrophizing, depression, anxiety, and somatization), a statistically significant reduction was found only in the case of catastrophizing scores. When comparing Session 1 and Session 3 catastrophizing, the scores decreased 3.14 points on average (SD = 7.63), t (69) = 3.45, p = .001.
Conclusions:	This finding strengthens the existing research literature that highlights the importance of targeting physical and psychological symptoms when developing a comprehensive pain management plan. Additionally, benefits can be achieved with an inexpensive treatment and no negative side effects.
Reference 1:	Hallman, D. M., Olsson, E. G., von Scheele, B., Melin, L., & Lyskov, E. (2011). Effects of Heart
Reference 2:	Institute of Medicine of the National Academies Report (2011). Relieving Pain in America: A
Reference 3:	Nestoriuc, Y., Martin, A., & Andrasik, F. (2008a). Biofeedback treatment for headache

Poster #	81
Abstract Title:	The role of inflammatory biomarkers in youth with co-occurring chronic pain and obesity
Presenter(s):	Keri R. Hainsworth, PhD ✉
Authors:	Keri Hainsworth, PhD; Pippa Simpson, PhD; Hershel Raff, PhD; Mitchell Grayson, MD; Ratka Galijot; Steven Weisman
Dept/Division:	Anesthesiology: Clinical Anesthesiology
Category:	Senior Faculty
Introductions:	Cytokine levels are associated with debilitating chronic pain conditions that share obesity as a risk factor (e.g. osteoarthritis and migraines), although their mechanistic connections are not clear. Additionally, pro-inflammatory cytokine levels are correlated with anxiety and depression, both common in pediatric chronic pain. We hypothesized that differences in pain and functional disability in youth with co-morbid chronic pain and obesity may be associated with a cytokine imbalance (i.e. increased pro-inflammatory cytokines and decreased anti-inflammatory cytokines). The current study examined relationships between body weight and pain status, serum biomarker concentrations, and measures of physical and emotional functioning.
Methods:	The study included 128 adolescents (Mean 15.3 ± 1.6 (SD) years; 58% female; 84% Caucasian) classified into 4 groups: healthy controls (n=32), chronic pain alone (n=30), obesity alone (n=36), and chronic pain + obesity (CPO; n=30). Validated measures of pain, functional disability, anxiety and depression were completed. Serum biomarkers included C-reactive protein (CRP), TNF-alpha, adiponectin, leptin, and IL-6.
Results:	Serum CRP, leptin and the leptin/adiponectin ratio were significantly greater (p values = .004 - .01) in females with CPO compared to any other group, including those with obesity alone. Additionally, CRP, leptin, and IL-6 were positively correlated with pain intensity and functional disability for the CPO group alone (r values = .39 - .87, p values <; .001 - <; .05).
Conclusions:	The results of this study suggest that cytokine concentrations are differentially affected by the co-occurrence of chronic pain and obesity, as compared with the effects associated with either condition alone. The synergistic augmentation of pro-inflammatory cytokines may underlie the co-occurrence of chronic pain and obesity, particularly in female patients.

Poster #	82
Abstract Title:	Simple Protocol For Standard Peptide Cleanup (SP2): A Robust Peptide Cleanup Method For Mass Spectrometry Using Carboxylate-Coated Magnetic Beads
Presenter(s):	Michael Pereckas ✉
Authors:	Michael Pereckas, Matthew Waas, Rachel A. Jones Lipinski, Rebekah L. Gundry
Dept/Division:	Office of Research: Center for Biomedical Mass Spectrometry Research
Category:	Research Support Staff
Introductions:	Sample preparation for proteomic analysis often involves reagents or consumables that interfere with the analysis of the samples by mass spectrometry. Detergents and chaotropes included for solubilization or digestion of proteins, as well as polymeric contaminants introduced by molecular weight cutoff filters and by beads used in sample enrichment strategies, can strongly interfere with LC-MS/MS signal and be detrimental to instrumentation. Reverse-phase solid-phase extraction methods, while effective at removing salts, are largely ineffective at removing polymers and detergents that are retained on reverse-phase material and co-eluted, and even concentrated, with peptides of interest. Using an orthogonal retention mechanism on carboxylate-coated beads enables the removal of both classes of contaminants, and permits elution directly into MS-friendly mobile phase.
Methods:	A fluorometric peptide assay was used to evaluate sample recovery of a tryptic digest cleaned by adsorption onto GE Healthcare Life Sciences Sera-Mag carboxylate-modified magnetic beads. Titrations of bead and peptide amounts were used to characterize the relationship between bead:sample ratio and recovery. A range of modifications were evaluated including binding time, temperature, starting concentration, number of washes, wash volumes, elution time, elution volume, elution solution, and mixing. LC-MS/MS was used to evaluate recovery across a range of hydrophobicities using a peptide standard mix and to demonstrate the performance on samples of varied complexity. A liquid handling system (epMotion 5073m, Eppendorf) was used to automate the procedure.
Results:	Highest recovery was obtained when a peptide:bead ratio of 50-100 was used. Trituration after addition of acetonitrile is critical for maximum recovery. The protocol is tolerant of other variables and is rapid and efficient whether the sample is fully aqueous or has high organic solvent content, and repeated washing or washing in large volumes of acetonitrile do not cause increased losses.
Conclusions:	The method is robust and insensitive to variation in time, temperature, peptide concentration, mixing technique, and extent of washing. SP2 can be equally applied phosphopeptides and glycopeptides as well as unmodified peptides. Especially in core facility settings where source of material may vary - SP2 serves as a useful catch-all to remove known and unexpected contaminants.
Acknowledgements:	This work was supported in part by the National Institutes of Health [R01-HL126785 and R01-HL134010 to RLG; F31-HL140914 to MW].
Reference 1:	Hughes CS, Sophia F, Gareld DA, Furlong EF, Steinmetz LM, Krijgsveld J, Ultrasensitive proteome analysis using paramagnetic bead technology. Mol Sys Bio, 2014. 10(10)
Reference 2:	Moggridge S, Sorensen PH, Morin GB, Hughes CS, Extending the compatibility of the SP3 paramagnetic bead processing approach for proteomics. J Prot Res, 2018, 17(4), 1730-1740

Poster #	83
Abstract Title:	Relative quantitation of proteoforms released by mechanical stimulation of mouse skin using complementary top down mass spectrometry analysis workflows
Presenter(s):	Theodore R. Keppel, PhD ✉
Authors:	Francie Moehring, Matthew Waas, Theodore R. Keppel, Deepali Rathore, Ashley M. Cowie, Cheryl L. Stucky, Rebekah L. Gundry
Dept/Division:	Office of Research: Center for Biomedical Mass Spectrometry Research
Category:	Research Support Staff
Introductions:	Mechanotransduction encompasses the processes through which mechanical stimuli are converted into electrochemical signals to enable us to sense our surrounding environment through touch. While the molecular and cellular mechanisms underlying touch transduction are not yet well-defined, previous studies suggest that epidermal cells, 95% of which are keratinocytes, release biomolecular factors, including lipids, peptides, proteins, and oligosaccharides, to activate or modulate cutaneous sensory neuron terminals. Such biomolecules may be analyzed via the collection of secreted material following mechanical stimulation of glabrous skin from naive mice. The goal of this study is to identify soluble protein proteoforms that may act as mediators of skin cell-sensory neuron communication.
Methods:	Dissected adult male mice (n = 6) glabrous hind paw skin sections were placed into wells containing physiological buffer. Skin sections were repeatedly mechanically stimulated for 1 minute or left unstimulated for equal duration. Buffer solution was removed and the assayed protein concentration was normalized within stimulation condition per mouse prior to injection onto nanoLC-MS. Mass spectrometry data were acquired on a Q-Exactive MS in-line with a Dionex Ultimate 3000 RSLCnano system (Thermo) and PicoChip Source (New Objective). Data were analyzed using ProSight PD 1.1 (Proteinaceous) as a plug-in node within Proteome Discoverer 2.2 (Thermo) and BioPharma Finder version 2.0 (Thermo). Proteoform identifications were matched with protein feature quantitation to relatively quantify differences between stimulated and unstimulated samples.
Results:	Using ProSight PD 1.1 platform, 47 proteoforms were identified in the comparison of stimulated vs. unstimulated secretion buffers in a minimum of three mice of either condition. A total of 30 of these identified proteoforms match ≥99% sequence coverage from the UniProt mouse proteome database, showing limited proteolytic activity in sample processing. Using BioPharma Finder, a component detection method was used to identify protein mass spectral features and merge their respective charge state data. The sum of intensities of a component's charge states was used for comparing that component's abundance across samples with an ANOVA analysis used for determining statistical significance. Of the identified proteoforms, seven proteoforms were identified either exclusively or with significantly greater abundance in the stimulated group. Additionally, seven proteoforms were identified with greater abundance in the unstimulated control group.
Conclusions:	Overall, 47 proteoforms were identified, 90% of which are annotated as extracellular or extracellular exosome-related in UniProt, showing the utility of this workflow for identifying secreted proteins with few contaminants (e.g. albumin, hemoglobin). The scope of analysis can broaden to include lipid, small molecule and metabolite analyses using orthogonal sample preparation and MS instrumentation.
Acknowledgements:	We thank Drs. Ioanna Ntai, Richard LeDuc, Joseph Greer, Paul Thomas, Phil Compton, and Ryan Fellers at Northwestern University for guidance regarding top down data collection and analysis. Special thanks to Tara Schroeder and David Horn at Thermo Fisher Scientific for assistance with BioPharma Finder.

Poster #	84
Abstract Title:	Precision Assessment of Heterogeneity in Human Pluripotent Stem Cell-derived Cardiomyocyte Cultures Using Cardiac Troponin I
Presenter(s):	Weerasekera, R. ✉
Authors:	Weerasekera, R., Waas, M., Gundry, R. L.
Dept/Division:	Biochemistry
Category:	Research Support Staff
Introductions:	Human pluripotent stem cell-derived cardiomyocytes (hPSC-CM) have the potential to be a relevant and high throughput model system for both drug discovery and cardiotoxicity testing. The use of hPSC-CM for these applications is currently limited by the inability to identify and select homogeneous populations of functionally defined hPSC-CMs from heterogeneous cultures.
Methods:	In order to assess heterogeneity of cultures, flow cytometry is used to quantify the percentage of cells which express cardiomyocyte-specific proteins.
Results:	We use several commercially available TNNI3 antibody clones and three sample preparation techniques to validate TNNI3 antibodies for use with flow cytometry in the assessment of heterogeneity of hPSC-CM cultures.
Conclusions:	Preliminary results demonstrate a differential susceptibility of antibody clone's flow cytometry signal to fixation conditions.

Poster #	85
Abstract Title:	Dosages of chronic medications taken from EMR can predict effectiveness of tramadol
Presenter(s):	William Gross ✉
Authors:	Gross, William L, Crouch, Samantha L, Woehlck, Harvey J
Dept/Division:	Anesthesiology
Category:	Junior Faculty
Introductions:	The volume of data in the modern electronic medical record (EMR) has enabled new levels of analyses previously impossible to perform. In this retrospective study, we extracted chronic medication dosage information from an EMR in order to predict the effectiveness of tramadol as an analgesic agent within an inpatient population. Since tramadol is a prodrug that is activated by the liver enzyme CYP2D6, its potency is greatly affected by common CYP2D6 polymorphisms1. The CYP2D6 enzyme system also metabolizes many other commonly used drugs, making their effectiveness and tolerability variable. We hypothesized that patients who had polymorphisms in their CYP2D6 enzymes would have characteristic patterns of chronic medication dosages, which could then be utilized to predict analgesic response to tramadol.
Methods:	Data from Froedtert Hospital was searched using the MCW CTSI's de-identified Honest Broker Tool. Selection criteria included inpatients who received tramadol during their hospitalization, were previously prescribed other medications metabolized by CYP2D6, and did not have a diagnosis of chronic pain. This resulted in a cohort of 4968 patients. Tramadol was considered effective if a different opiate medication was not prescribed within 3 days following tramadol administration. The dosages of the predictor drugs were defined as the dosages of the last outpatient prescription before being prescribed tramadol. Predicted drug dosages were entered into a logistic regression model to predict tramadol effectiveness. To account for non-linear interactions among combinations of drugs, drug dosages were also entered into a simple perceptron neural network, using split-data verification.
Results:	Analyzing each predictor drug individually revealed several sets that were significantly associated with tramadol effectiveness. The most significant effects were seen in the beta blocker metoprolol (OR 0.997, p = 0.002), with similar trends seen with carvedilol (OR 0.987, p = 0.089) and propranolol (OR 0.993, p = 0.062). Several antidepressants also had strong correlations with tramadol success, including bupropion (OR 1.003, p = 0.018), paroxetine (OR 1.015, p = 0.031), with a similar trend for citalopram (OR 1.011, p = 0.091). The combined model predicted tramadol effectiveness correctly with 60% accuracy.
Conclusions:	Using readily available data from the EMR, we were able to build a simple model that was effective at predicting a clinically relevant data point. In the future, utilizing an expanded data set and more complex models, we may be able to develop full phenotypes by examining prior chronic medication response. This would allow us to individualize medical decisions based on the predicted response of each patient, limiting patient exposure to ineffective medication and inadequate pain management.
Reference 1:	1. Wang, G., Zhang, H., He, F., Xiang, M. (2006) Effect of the CYP2D6*10 C188T polymorphism on postoperative tramadol analgesia in a Chinese population. Eur J Clin Pharmacol 62: 927. http://doi.org/10.1007/s00228-006-0191-2

Poster #	86
Abstract Title:	Reduced Representation Bisulfite Sequencing analysis pipeline - An experience
Presenter(s):	Jenica Abrudan ✉
Authors:	Jenica L. Abrudan, Lida A. Zeighami , Wendy Demos, Michael Zimmermann
Dept/Division:	Genomic Sciences & Precision Medicine Center
Category:	Research Support Staff
Introductions:	Gene expression can be regulated at both genetic and epigenetic levels. Epigenetics is the study of inheritable phenotypic changes not encoded in the genome. One efficient technique for studying genome-wide methylation levels is Reduced Representation Bisulfite Sequencing (RRBS).
Methods:	We used existing programs to develop a RRBS analysis pipeline for identifying and analyzing differentially methylated regions from raw sequences.
Results:	We developed an analysis pipeline to identify differentially methylated regions from raw sequence files and provide a set of data visualizations, statistical comparison, and knowledge-based annotations, to facilitate their interpretation. This pipeline will be used by GSPMC research as a standardized, modular, efficient, and reproducible process that minimizes the number of human input steps. 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. We considered Bismark [1] and BSMAP [2]. We and others report similar performance between these two aligners, but there is greater community support for Bismark. This support consists of more downstream analysis packages (CpG calling, DMR finding). Bismark, however, has been shown to introduce a point of bias in the data by only considering the potential CpG sites present in the original reference genome and would not call a CpG site created de-novo by an individual’s specific genomic variants. The DMRfinder [3] suite fills this gap, can call CpG sites including those that are de-novo in a sample, and is compatible with Bismark output. Data generated in these prior steps will be used to assess differentially methylated regions (DMRs) and those regions will be annotated for their functional effects using well-established reference resources for gene function and cellular processes. In studies with more than one group of treatments or conditions, we will assess pairwise differences as well as across-group differences at each DMR. Functional associations between these two methods will be compared and contrasted. Finally, we generate a standardized report containing sequence and experiment quality metrics, a list of raw and annotated DMRs as well as gene/pathway enrichment analysis results.
Conclusions:	We have developed and will continue to improve, a standardized RRBS workflow in order to provide an efficient, robust, and thorough analysis service.
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:	Xi, Y. and W. Li, BSMAP: whole genome bisulfite sequence MAPping program. BMC Bioinformatics, 2009. 10: p. 232.
Reference 3:	Gaspar, J.M. and R.P. Hart, DMRfinder: efficiently identifying differentially methylated regions from MethylC-seq data. BMC Bioinformatics, 2017. 18(1): p. 528.

Poster #	87
Abstract Title:	Developing and Implementing a Robust and Thorough RNA-Seq Data Analysis and Deliverable Report
Presenter(s):	Lida A. Zeighami ✉
Authors:	Lida A. Zeighami, Jenica L. Abrudan, wendy Demos, Michael Zimmermann
Dept/Division:	Genomic Sciences & Precision Medicine Center: Bioinformatics R&D
Category:	Research Support Staff
Introductions:	RNA-Seq is a technique to quantify gene expression and thereby study transcriptomic differences between biologic conditions. We will broadly divide RNA-Seq analysis into two parts: Experimental and Computational (bioinformatics). Experimental methods and their quality control (QC) are critical foundational steps. Thus, we have developed a robust system for monitoring sample and experimental quality throughout our process. The experimental output is raw nucleotide sequences in FASTQ (or FASTA) format. Computational or bioinformatics analyses begin from these data. There are different softwares and pipelines available to analyze raw data and generate feature (gene/exon/transcript) quantification, identify differentially expressed genes, discover novel transcripts, annotate functions affected, call expressed variants, and detect gene fusions. Finally, functional analysis and data visualization facilitate interpretation of these quantified features.
Methods:	To process RNA-Seq data, we evaluated the strengths and limitations of algorithms supporting two different needs - a rapid service with short turn-around and a more throughout standard service. In “rapid” service, we apply Kallisto [1] which does not need to align reads to the reference genome, instead counting unique sequence tags within each transcript. This process provides a fast method to generate results, but more limited in applications. In standard service, we apply MAP-RSeq pipeline [2], which is designed around standard sequence aligners such as STAR and Bowtie and includes many quality control, quality assurance, and robustness checks.
Results:	Both services feed into our statistical assessments to find which genes are changing their expression in association with treatment or other conditions. We have developed a tool to generate an interactive and comprehensive web-based report to deliver these results, along with QC metrics, and presented in accessible ways. This report includes summary of experiments/samples, sequencing metrics, pre-alignment/alignment quality assessment, Gene/Exon counts (raw and normalized value), Differential expression analysis (using two different approaches, Pairwise and GLM) and visualization such as PCA plot, Venn diagram, Volcano plot, HeatMap and DE-PCA plot. Delivering the results in a web format has many advantages including interactive and publication-quality plots leveraging open-source standards. Interactive plots facilitate data exploration and thereby interpretation.
Conclusions:	We have developed two different workflows and a common analysis and reporting strategy, to support delivery of rapid service when needed, and standard robust service for routine research needs.
Reference 1:	Bray NL, Pimentel H, Melsted P, Pachter L. Near-optimal probabilistic RNA-seq quantification. Nature biotechnology. 2016;34(5):525-527.
Reference 2:	Kalari, K.R., et al., MAP-RSeq: Mayo Analysis Pipeline for RNA sequencing. BMC Bioinformatics, 2014. 15(1): p. 224.

Poster #	88
Abstract Title:	Applications and Methods for Interpretation of WGS and WES Data
Presenter(s):	Wendy M Demos ✉
Authors:	Wendy M Demos M.S., Lida Zeighami M.S., Jenica Abrudan Ph.D., Stefano Rosati B.S., Michael Zimmermann Ph.D.
Dept/Division:	Genomic Sciences & Precision Medicine Center: Bioinformatics R&D
Category:	Research Support Staff
Introductions:	The widespread use of Whole Genome Sequencing (WGS) and Whole Exome Sequencing (WES) for clinical practice and research discovery creates demand for efficient and effective workflows to support a diversity of applications including clinical diagnoses, understanding mechanisms of human disease, and genetic predisposition. In clinical practice today, WGS and WES give a prospective diagnostic rate ranging from 25-41% 1, 2. Workflows for clinical diagnostics require validations and are subject for regulations as defined by the ACMG Clinical Laboratory Standards for Next-Generation Sequencing, CAP, CLIA, and the FDA. These validations are rigorous and time consuming. Thus, efficient systems to manage data and knowledge annotations are critical. Additionally, workflows must be customized to each clinical test offering. In today's era of Precision Medicine, flexibility is needed as genomics-based guidelines are developed for each disease area. Additional flexibility is required for supporting research. If the same (or similar) systems can support both research and clinical operations, additional efficiencies will be made.
Methods:	Utilizing the Biological Reference Repository (BioR) 3 we have developed a customizable workflow to assist in annotation and interpretation of variants found via WES and WGS for research discovery. BioR stores annotation data in catalog format. The package allows for the creation of specific annotation resource catalogs as well as the use of catalogs created from widely utilized databases that include population frequency, pharmocogenomic, phenotypic, and other genomic information. Input data are compiled in a variant call format (vcf) text file and include Structural variations (SV), single nucleotide variations (SNV), and insertions and deletions (Indels). Appropriate programmatic filters are applied to narrow down the variants of interest found in the cohort or single sample vcf. We have created a customized report that gives quality metric information in regard to input data as well as variants of potential interest and cohort frequency.
Results:	We have developed a flexible annotation and interpretation workflow for the analysis of research WGS and WES data that not only is suited for single but also cohort analysis. In addition to clinically relevant annotations, additional data most relevant to the scope of the research study can be appended to support additional discovery. This flexibility supports an integrated annotation approach to both clinical and researcher applications, increasing efficiency, standardization, and data interpretability.
Reference 1:	Daoud H, Luco SM, Li R, et al. Next-generation sequencing for diagnosis of rare diseases in the neonatal intensive care unit. CMAJ. 2016;188:E254-E260.
Reference 2:	Lionel AC, Costain G, Marshall CR. Improved diagnostic yield compared with targeted gene sequencing panels suggests a role for whole-genome sequencing as a first-tier genetic test. Genetics in Medicine. 2018;20:435-443.
Reference 3:	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.

MCW Research Overview: Funding

Research Grant Awards Over $1M: September 2017 – August 2018

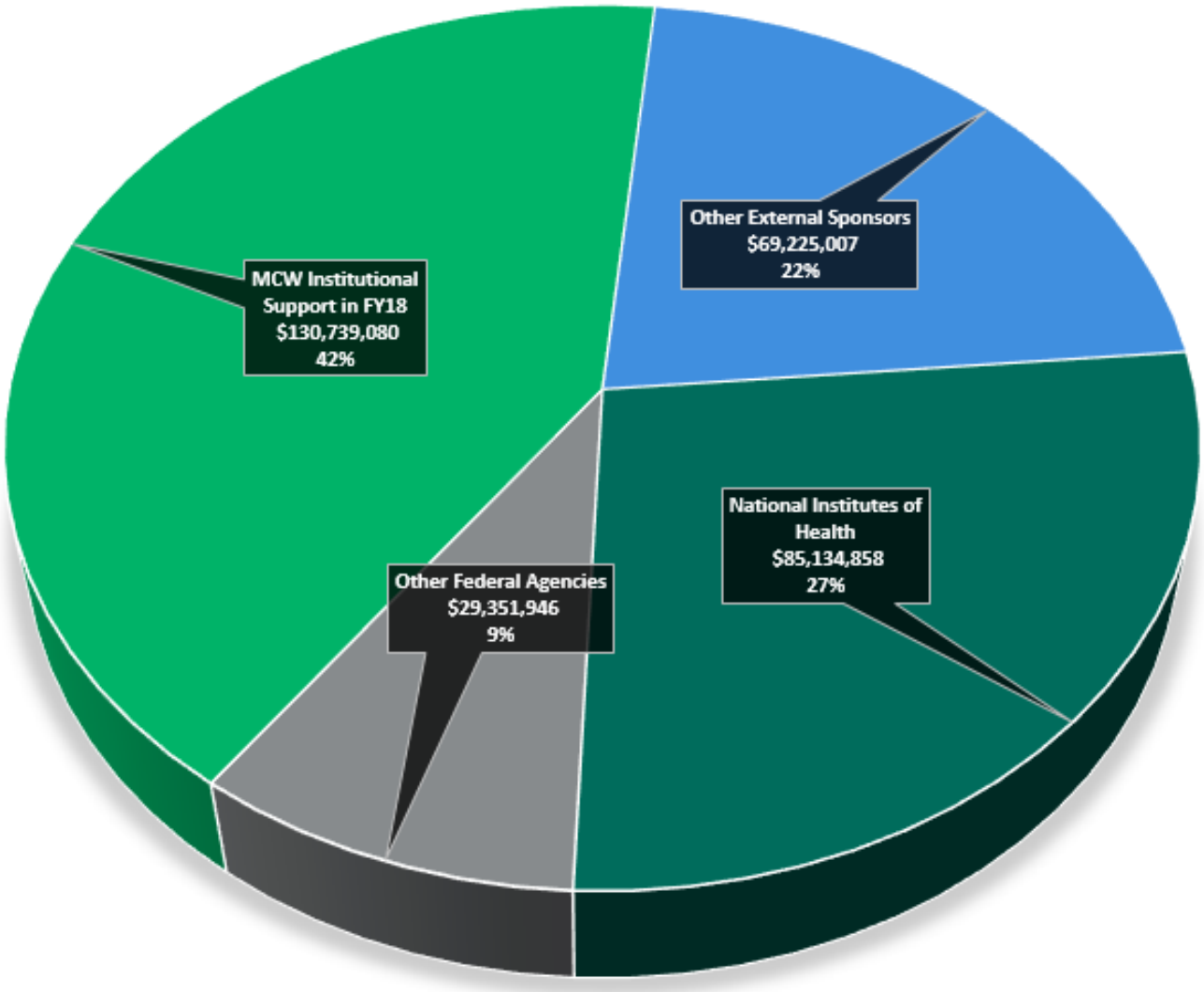
Principal Investigator	Project	Sponsor	Total*
Dara Frank Jimmy Feix	Type III effector-cofactor dynamics within the cellular environment	National Institute of Allergy and Infectious Disease (R01)	$2.2M
Joseph Carroll	Assessing Photoreceptor Structure and Function in Normal and Diseased Retinae	National Eye Institute (R01)	$2.0M
Jeffrey Kelly Yuri Amirkhanian	Increasing PrEP Use in High-Risk Social Networks of African American MSM in Underserved Low-Uptake Cities	National Institute of Nursing Research (R01)	$3.4M
Quinn Hogan	Harnessing T-junction filtering; bidirectional control of sensory neuron impulse traffic	National Institute of Neurological Disorders & Stroke (R01)	$2.3M
Frank Pintar	Crash Injury Research and Engineering Network (CIREN) Motor Vehicle Occupant Enrollment	Department of Transportation	$1.6M
Leonard Egede	COME ALIVE MILWAUKEE: Community Empowerment And Lifestyle Intervention for Ethnic Minorities	Advancing a Healthier Wisconsin Endowment	$2.8M
Timothy Meier	The role of neuroactive kynurenine metabolites in the chronic sequelae of concussion and contact sport exposure	National Institute of Neurological Disorders & Stroke (R01)	$1.8M
Douglas Rizzo Mary Horowitz Mei-Jie Zhang	Stem Cell Therapeutic Outcomes Database (SCTOD)	Department of Health and Human Services	$22.6M
Meetha Medhora	Mechanism of radiation induced endovascular injury and mitigation via the Notch-Dll4 pathway	National Institute of Allergy and Infectious Disease (U01)	$2.6M
David Mattson Allen Cowley Aron Geurts Mingyu Liang Alexander Staruschenko	Renal Mechanisms in Blood Pressure Control	National Heart, Lung, and Blood Institute (P01)	$9.3M
John Imig	Novel Therapy of Kidney Disease	Falk Medical Research Trust	$1.0M
Ming You	Pancreas Cancer Research Program	Advancing a Healthier Wisconsin Endowment	$7.2M
Mary Horowitz	A Data Resource for Analyzing Blood and Marrow Transplants	National Cancer Institute (U24)	$1.1M
Julia Dickson-Gomez	Effects of State Laws to Reduce Opioid Diversion on Transitions to Injection Drug Use and HIV/HCV Transmission	National Institute on Drug Abuse (R01)	$2.9M
Hubert Forster	Integrated Physiology Training: Molecule to Organism	National Heart, Lung, and Blood Institute (T32)	$1.4M
Jennifer Walsh	Longitudinal Predictors of PrEP Use and Adherence Among Young Black MSM	National Institute of Mental Health (R01)	$1.2M
Marcello Bonini	Biophysical forces and pancreatic cancer phenotypic specification	Advancing a Healthier Wisconsin Endowment	$1.0M
Brian-Fred Fitzsimmons	Cognitive Neuroscience Research Program	Advancing a Healthier Wisconsin Endowment	$2.0M
Allen Cowley David Mattson	Mechanisms of renal immune cell infiltration in salt-sensitive hypertension	National Heart, Lung, and Blood Institute (R01)	$2.5M

Principal Investigator	Project	Sponsor	Total*
Brian Volkman	Sulfotyrosine-guided discovery of small molecule chemokine inhibitors	National Institute of General Medical Sciences (R01)	$1.2M
Raul Urrutia	Precision Medicine of Pancreatic Cancer	Advancing a Healthier Wisconsin Endowment	$1.9M
Girija Konduri	AMP Kinase regulation in persistent pulmonary hypertension of the newborn	National Heart, Lung, and Blood Institute (R01)	$1.5M
Melinda Stolley	Men Moving Forward: A Lifestyle Intervention for African American Prostate Cancer Survivors	National Cancer Institute (R01)	$3.2M
Ming You Li Lily Wang	Chemoimmunoprevention of EGFR-Driven Non-Small Cell Lung Cancer	National Cancer Institute (R01)	$3.2M
Matthew Dellinger	Gigiigooinaan (Our Fish): A New Advisory to Promote Anishinaabe Health and Wellness	National Institute of Environmental Health Sciences (R01)	$1.3M
Janette Strasburger	Fetal Electrophysiologic Abnormalities in High-risk Pregnancies Associated with Fetal Demise	National Heart, Lung, and Blood Institute (R01)	$2.5M
Michael Widlansky Mary Eapen	Stimulating Access to Research in Residency (StARR)	National Heart, Lung, and Blood Institute (R38)	$1.0M
Ulrich Broeckel	Characterization and Genetics of KI toxicity in iPSC-derived cardiomyocytes	National Heart, Lung, and Blood Institute (R01)	$3.0M
Mary Sorci-Thomas Daisy Sahoo	SR-BI and PCPE2: Novel partners in bi-directional cholesterol transport	National Heart, Lung, and Blood Institute (R01)	$2.8M
Joseph Carroll	Characterization of Existing and Newly Developed Models of Usher Syndrome	Foundation for Fighting Blindness	$1.1M
Melinda Dwinell	Hybrid Rat Diversity Program	NIH Office of the Director (R24)	$3.1M
Scott Terhune Allison Ebert	Cytomegalovirus manipulation of functional cortical tissue development	National Institute of Allergy and Infectious Disease (R01)	$1.5M
Cecilia Hillard	Developing Innovative, Translational Research Programs in Clinically Relevant Neurological Disorders	Advancing a Healthier Wisconsin Endowment	$3.0M
Marcelo Bonini	MnSOD Acetylation Promotes Cancer Stem Cell Phenotypes in Breast Cancer	National Cancer Institute (R01)	$1.8M
Brian Smith	Discovering and Exploiting Selectivity within Tandem Bromodomains	National Institute of General Medical Sciences (R35)	$1.9M
Amy Drendel	The Effect of Emergency Department and After-Emergency Department Analgesic Treatment on Pediatric Long Bone Fracture Outcomes	National Institute on Minority Health and Health Disparities (R01)	$2.9M
Amanda Brandow	Investigating the role of the microbiome and inflammation in acute and chronic pain in patients with sickle cell disease	National Heart, Lung, and Blood Institute (R01)	$3.7M
David Brousseau Julie Panepinto	Implementation of evidence based care for the acute treatment of sickle cell disease pain	National Heart, Lung, and Blood Institute (U01)	$1.1M
Jyoti Sengupta Banani Banerjee	Neuromolecular Mechanisms of Chronic Pelvic Pain in Neonatally-induced Cystitis	National Institute of Diabetes and Digestive and Kidney Diseases (R01)	$2.4M
Jeffrey Binder	Concept Representation in the Human Brain	National Institute on Deafness and Other Communication Disorders (R01)	$3.0M

*Projected Cumulative Awards rounded to the nearest hundred-thousand

MCW Overall Research Funding FY18

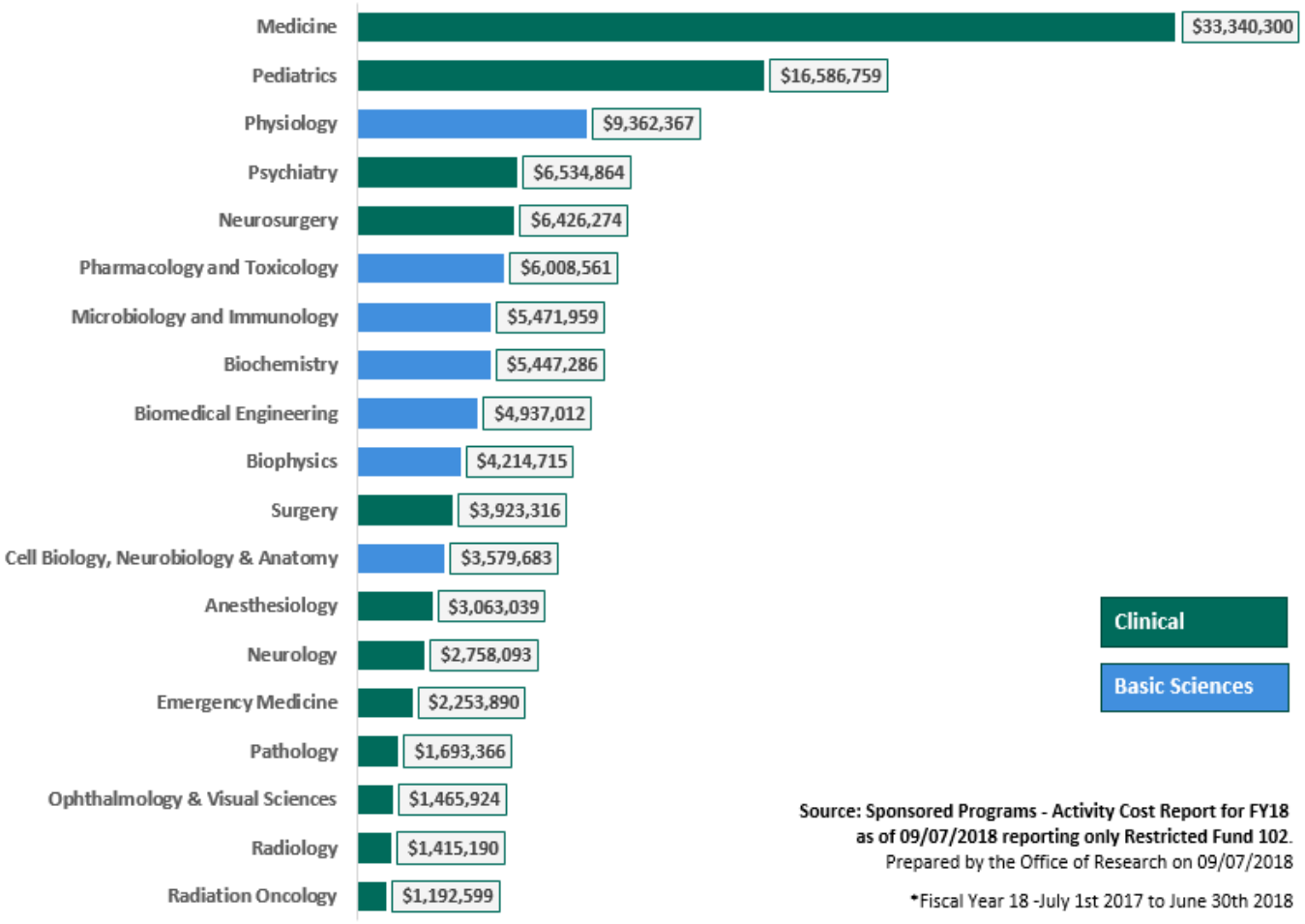
FY18 was July 1st 2017 to June 30th 2018



$314.5M in Total Costs. Expended in Research, Teaching, Training and Related Purposes in FY18 which lead to improve patient care and health outcomes.

Source: Business Information "Grants Cube" as of 9/7/2018
Prepared by the Office of Research on 9/7/2018

MCW FY18* Total Awards for Research
Top 20 Departments

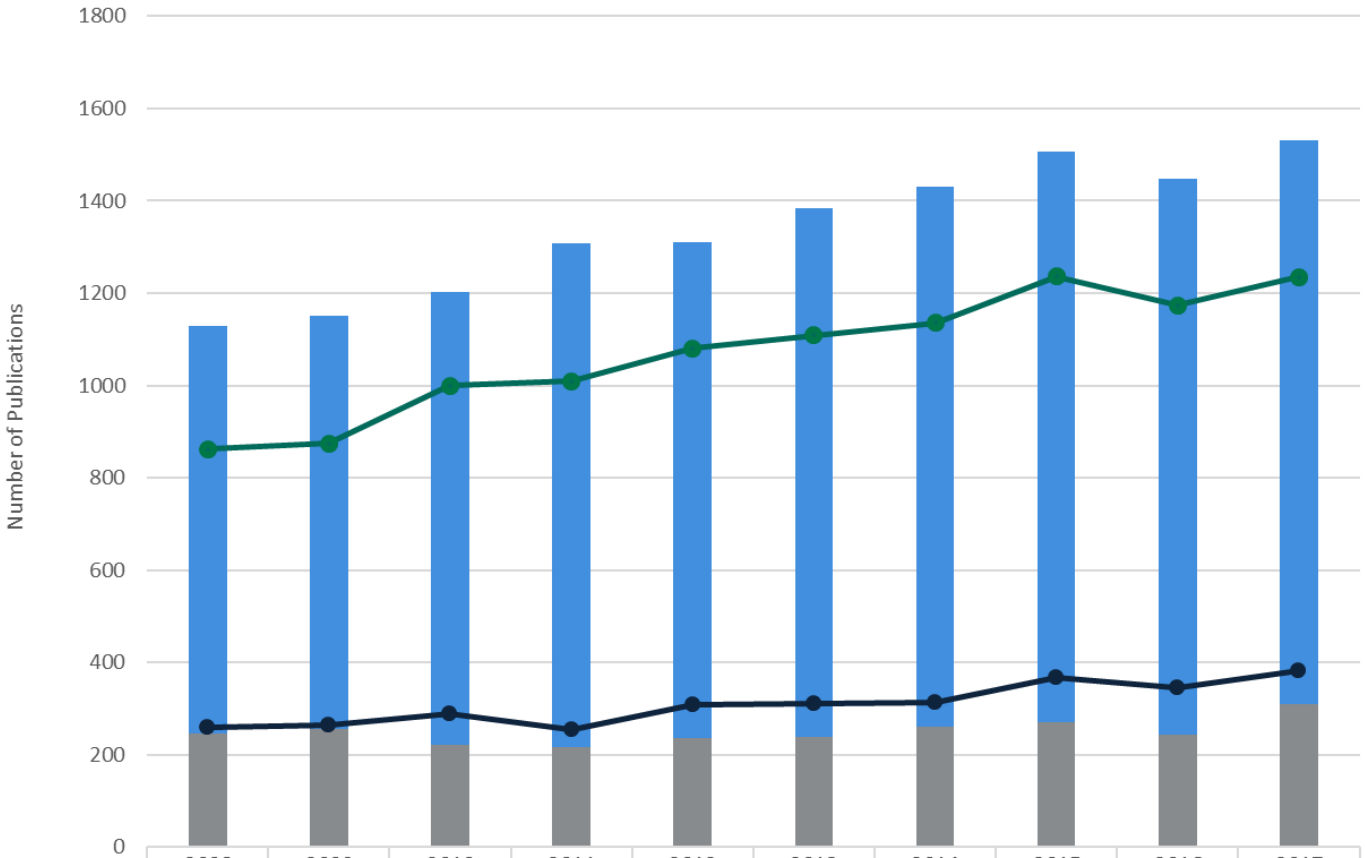


Source: Sponsored Programs - Activity Cost Report for FY18 as of 09/07/2018 reporting only Restricted Fund 102.
Prepared by the Office of Research on 09/07/2018

*Fiscal Year 18 -July 1st 2017 to June 30th 2018

MCW Research Overview: Publications

MCW Total Annual Publications with Impact Factor (IF)



	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
≥ Median IF	882	895	981	1093	1076	1147	1170	1237	1204	1221
< Median IF	246	256	221	216	235	238	260	270	244	311
Top Qrt IF	603	611	710	754	772	799	823	868	827	854
IF > 5.0	259	264	289	255	308	310	313	368	346	381

Source: MCW Libraries analysis based on Thomson Reuters Journal Citation Reports

High Impact Publications: 2017-2018

The following articles were published between 2017 and 2018 by MCW authors in a journal with a 2017 impact factor or 20 or greater. (MCW authors' names are in bold.)

1. Avidan MS, Maybrier HR, Ben Abdallah A, Jacobsohn E, Vlisides PE, Pryor KO, Veselis RA, Grocott HP, Emmert DA, Rogers EM, Downey RJ, Yulico H, Noh G, Lee YH, Waszynski CM, Arya VK, **Pagel PS, Hudetz JA**, Muench MR, Fritz BA, Waberski W, Inouye SK, Mashour GA, PODCAST Res Grp. Intraoperative ketamine for prevention of postoperative delirium or pain after major surgery in older adults: an international, multicentre, double-blind, randomised clinical trial. *Lancet*. 2017;390:267-275.

2. Bashey A, **Zhang M**, McCurdy SR, **St Martin A, Argall T**, Anasetti C, Ciurea SO, Fasan O, Gaballa S, **Hamadani M**, Munshi P, Al Malki MM, Nakamura R, O'Donnell PV, Perales M, Raj K, Romee R, Rowley S, Rocha V, Salit RB, Solh M, Soiffer RJ, Fuchs EJ, **Eapen M**. Mobilized Peripheral Blood Stem Cells Versus Unstimulated Bone Marrow As a Graft Source for T-Cell-Replete Haploidentical Donor Transplantation Using Post-Transplant Cyclophosphamide. *Journal of Clinical Oncology*. 2017;35:3002-+.

3. Berlowitz DR, Foy CG, Kazis LE, Bolin LP, Conroy MB, Fitzpatrick P, Gure TR, Kimmel PL, Kirchner K, Morisky DE, Newman J, Olney C, Oparil S, Pajewski NM, Powell J, Ramsey T, Simmons DL, Snyder J, Supiano MA, Weiner DE, **Whittle J**, SPRINT Res Grp. Effect of Intensive Blood-Pressure Treatment on Patient-Reported Outcomes. *N Engl J Med*. 2017;377:733-744.

4. Bress AP, Bellows BK, King JB, Hess R, Beddhu S, Zhang Z, Berlowitz DR, Conroy MB, Fine L, Oparil S, Morisky DE, Kazis LE, Ruiz-Negron N, Powell J, Tamariz L, **Whittle J**, Wright JT, Jr., Supiano MA, Cheung AK, Weintraub WS, Moran AE, SPRINT Res Grp. Cost-Effectiveness of Intensive versus Standard Blood-Pressure Control. *N Engl J Med*. 2017;377:745-755.

5. Campbell BB, Light N, Fabrizio D, Zatzman M, Fuligni F, de Borja R, Davidson S, Edwards M, Elvin JA, Hodel KP, Zahurancik WJ, Suo Z, Lipman T, Wimmer K, Kratz CP, Bowers DC, Laetsch TW, Dunn GP, Johanns TM, Grimmer MR, Smirnov IV, Larouche V, Samuel D, Bronsema A, Osborn M, Stearns D, Raman P, Cole KA, Storm PB, Yalon M, Opocher E, Mason G, Thomas GA, Sabel M, **George B**, Ziegler DS, Lindhorst S, Issai VM, Constantini S, Toledano H, Elhasid R, Farah R, Dvir R, Dirks P, Huang A, Galati MA, Chung J, Ramaswamy V, Irwin MS, Aronson M, Durno C, Taylor MD, Rechavi G, Maris JM, Bouffet E, Hawkins C, Costello JF, Meyn MS, Pursell ZF, Malkin D, Tabori U, Shlien A. Comprehensive Analysis of Hypermutation in Human Cancer. *Cell*. 2017;171:1042-+.

6. Chen S, Dykes JC, McElhinney DB, Gajarski RJ, Shin AY, Hollander SA, Everitt ME, Price JF, Thiagarajan RR, **Kindel SJ**, Rossano JW, Kaufman BD, May LJ, Pruitt E, Rosenthal DN, Almond CS. Haemodynamic profiles of children with end-stage heart failure. *Eur Heart J*. 2017;38:2900-2909.

7. Demark-Wahnefried W, Schmitz KH, Alfano CM, Bail JR, Goodwin PJ, Thomson CA, Bradley DW, Courneya KS, Befort CA, Denlinger CS, Ligibel JA, Dietz WH, **Stolley MR**, Irwin ML, Bamman MM, Apovian CM, Pinto BM, Wolin KY, Ballard RM, Dannenberg AJ, Eakin EG, Longjohn MM, Raffa SD, Adams-Campbell LL, Buzaglo JS, Nass SJ, Massetti GM, Balogh EP, Kraft ES, Parekh AK, Sanghavi DM, Morris GS, Basen-Engquist K. Weight Management and Physical Activity Throughout the Cancer Care Continuum. *Ca-a Cancer Journal for Clinicians*. 2018;68:64-89.

8. **Derse AR**. Health Care Professionals and Law Enforcement. *N Engl J Med*. 2017;377:2515-2517.

9. Fakhry C, Zhang Q, Nguyen-Tan PF, Rosenthal DI, Weber RS, Lambert L, Trotti,Andy M.,,III, Barrett WL, Thorstad WL, Jones CU, Yom SS, **Wong SJ**, Ridge JA, Rao SSD, Bonner JA, Vigneault E, Raben D, Kudrimoti MR, Harris J, Le Q, Gillison ML. Development and Validation of Nomograms Predictive of Overall and Progression-Free Survival in Patients With Oropharyngeal Cancer. *Journal of Clinical Oncology*. 2017;35:4057-+.

10. Hingorani SR, Zheng L, Bullock AJ, Seery TE, Harris WP, Sigal DS, Braiteh F, **Ritch PS**, Zalupski MM, Bahary N, Oberstein PE, Wang-Gillam A, Wu W, Chondros D, Jiang P, Khelifa S, Pu J, Aldrich C, Hendifar AE. HALO 202: Randomized Phase II

Study of PEGPH20 Plus Nab- Paclitaxel/Gemcitabine Versus Nab- Paclitaxel/Gemcitabine in Patients With Untreated, Metastatic Pancreatic Ductal Adenocarcinoma. *Journal of Clinical Oncology*. 2018;36:359-+.

11. **Hogan WJ, Shaker R**. In Memoriam-Konrad H. Soergel, MD, 1929-2017. *Gastroenterology*. 2017;153:1172-1173.

12. Landsburg DJ, Falkiewicz MK, Maly J, Blum KA, Howlett C, Feldman T, Mato AR, Hill BT, Li S, Medeiros LJ, Torka P, Hernandez-Ilizaliturri F, Reddy NM, **Singavi A, Fenske TS**, Chavez JC, Kaplan JB, Behdad A, Petrich AM, Bast MA, Vose JM, Olszewski AJ, Costa C, Lansigan F, Gerson JN, Barta SK, Calzada O, Cohen JB, Lue JK, Amengual JE, Rivera X, Persky DO, Peace DJ, Nathan S, Cassaday RD. Outcomes of Patients With Double-Hit Lymphoma Who Achieve First Complete Remission. *Journal of Clinical Oncology*. 2017;35:2260-+.

13. Liu X, Yagi H, Saeed S, Bais AS, Gabriel GC, Chen Z, Peterson KA, Li Y, Schwartz MC, Reynolds WT, Saydmohammed M, Gibbs B, Wu Y, Devine W, Chatterjee B, Klena NT, Kostka D, Bentley KLdM, Ganapathiraju MK, Dexheimer P, Leatherbury L, Khalifa O, Bhagat A, Zahid M, Pu W, Watkins S, Grossfeld P, Murray SA, Porter GA, Jr., Tsang M, Martin LJ, **Benson DW**, Aronow BJ, Lo CW. The complex genetics of hypoplastic left heart syndrome. *Nat Genet*. 2017;49:1152-+.

14. Marigorta UM, Denson LA, Hyams JS, Mondal K, Prince J, Walters TD, Griffiths A, **Noe JD**, Crandall WV, Rosh JR, Mack DR, Kellermayer R, Heyman MB, Baker SS, Stephens MC, Baldassano RN, Markowitz JF, Kim M, Dubinsky MC, Cho J, Aronow BJ, Kugathasan S, Gibson G. Transcriptional risk scores link GWAS to eQTLs and predict complications in Crohn's disease. *Nat Genet*. 2017;49:1517-+.

15. Mast AE, **Murphy EL**. The price of blood is measured in iron. *Lancet*. 2017;390:2331-2333.

16. Saver JL, Carroll JD, Thaler DE, Smalling RW, MacDonald LA, **Marks DS**, Tirschwell DL, RESPECT Investigators. Long-Term Outcomes of Patent Foramen Ovale Closure or Medical Therapy after Stroke. *N Engl J Med*. 2017;377:1022-1032.

17. Sekeres MA, Othus M, List AF, Odenike O, Stone RM, Gore SD, Litzow MR, Buckstein R, Fang M, Roulston D, Bloomfield CD, Moseley A, Nazha A, Zhang Y, Velasco MR, Gaur R, **Atallah E**, Attar EC, Cook EK, Cull AH, Rauh MJ, Appelbaum FR, Erba HP. Randomized Phase II Study of Azacitidine Alone or in Combination With Lenalidomide or With Vorinostat in Higher-Risk Myelodysplastic Syndromes and Chronic Myelomonocytic Leukemia: North American Intergroup Study SWOG S1117. *Journal of Clinical Oncology*. 2017;35:2745-+.

18. Shroyer AL, Hattler B, Wagner TH, Collins JF, Baltz JH, Quin JA, **Almassi GH**, Kozora E, Bakaeen F, Cleveland JC, Jr., Bishawi M, Grover FL, Vet Affairs ROOBY-FS Grp. Five-Year Outcomes after On-Pump and Off-Pump Coronary-Artery Bypass. *N Engl J Med*. 2017;377:623-632.

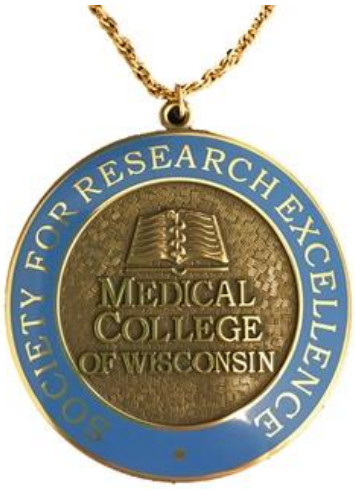
19. Smilowitz NR, **Gupta N**, Guo Y, Berger JS, Bangalore S. Perioperative acute myocardial infarction associated with non-cardiac surgery. *Eur Heart J*. 2017;38:2409-2417.

20. **Stolley M**, Sheean P, Gerber B, Arroyo C, Schiffer L, **Banerjee A, Visotcky A**, Fantuzzi G, Strahan D, **Matthews L**, Dakers R, Carridine-Andrews C, Seligman K, Springfield S, Odoms-Young A, Hong S, Hoskins K, Kaklamani V, Sharp L. Efficacy of a Weight Loss Intervention for African American Breast Cancer Survivors. *Journal of Clinical Oncology*. 2017;35:2820-+.

21. Sullivan KM, Goldmuntz EA, Keyes-Elstein L, McSweeney PA, Pinckney A, Welch B, Mayes MD, Nash RA, Crofford LJ, Eggleston B, Castina S, Griffith LM, Goldstein JS, Wallace D, Craciunescu O, Khanna D, Folz RJ, Goldin J, Clair EWS, Seibold JR, Phillips K, Mineishi S, Simms RW, Ballen K, Wener MH, Georges GE, Heimfeld S, Hosing C, Forman S, Kafaja S, Silver RM, Griffing L, Storek J, LeClercq S, Brasington R, **Csuka ME**, Bredeson C, **Keever-Taylor C**, Domsic RT, Kahaleh MB, Medsger T, Furst DE, SCOT Study Investigators. Myeloablative Autologous Stem-Cell Transplantation for Severe Scleroderma. *N Engl J Med*. 2018;378:35-47.

22. **Zielonka J, Joseph J**, Sikora A, Hardy M, Ouari O, **Vasquez-Vivar J**, **Cheng G,** Lopez M, **Kalyanaraman B.** Mitochondria-Targeted Triphenylphosphonium-Based Compounds: Syntheses, Mechanisms of Action, and Therapeutic and Diagnostic Applications. *Chem Rev*. 2017;117:10043-10120.

Society for Research Excellence



The Office of Research is pleased to host the MCW Society for Research Excellence, a new collective of select MCW faculty with a demonstrated commitment to discovery, mentorship, leadership, and advancement in research.

Mission: To foster, promote and recognize excellence across MCW in all types of research and discovery.

Members of the SRE are characterized by such experience as:

- Sustained research leadership leading to high impact discoveries or findings
- History of serving as an effective mentor for trainees and/or junior faculty
- National recognition for research, such as high visibility publications, national or international leadership roles, and/or receipt of awards
- MCW full time or full professional effort appointment for at least 5 years

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Joseph J. Carroll, PhD
Ophthalmology

About the Office of Research

Our Mission: The Office of Research is an integrated resource for facilitating scientific discovery through administrative support of investigators, education and training, and ensuring regulatory compliance.

What do we do?

Our department is comprised of 9 specialized units that oversee research. Virtually every MCW researcher interacts with our office in some way...

- Wet and dry lab space assignments
- Grant submission and management
- Human and animal research safety and compliance
- Formalized regulatory and safety approvals
- Electronic research systems training and maintenance
- Data and literary resource access
- Intellectual property guidance and assurance

We continuously look for new ways to improve the research experience! You can contact a member of our administrative team via email: research@mcw.edu.

Office of Research Leadership

Ann B. Nattinger, MD, MPH, MACP
Associate Provost for Research
Senior Associate Dean for Research, School of Medicine
Professor of Medicine
Lady Riders Professor of Breast Cancer Research

Dr. Ann Nattinger stepped into the role of Senior Associate Provost for Research in October 2015. Prior to this appointment, Dr. Nattinger served as Division Chief of General Internal Medicine for 15 years. A major proponent of research in academic medicine, in 2001 Dr. Nattinger also founded the Center for Patient Care and Outcomes Research (now known as CAPS) and served as Center Director for 16 years.

Dr. Nattinger is a nationally recognized cancer health services researcher, focusing on breast cancer treatment, survivorship and outcomes. Her research has been funded by the National Institutes of Health, the Department of Defense and the American Cancer Society. She has authored or co-authored more than 170 scientific papers, abstracts and book chapters. Among Dr. Nattinger's many accomplishments, she received the esteemed designation as a "Master" of medicine from the American College of Physicians. Additionally, Dr. Nattinger received the Distinguished Service Award in 2012, MCW's highest faculty and staff honor.

Cecilia J. Hillard, PhD
Associate Dean for Research
Professor of Pharmacology and Toxicology
Director, Neurosciences Research Center

Dr. Cecilia Hillard was named Associate Dean for Research in November 2015 after serving eight months as co-Interim Senior Associate Dean for Research. Outside of these leadership roles in the Office of Research, Dr. Hillard has served as director of the Neuroscience Research Center since its inception in 2010. She was also Inaugural Director of the Neuroscience Graduate Training Program from 1996-2010.

As a highly active researcher, Dr. Hillard's laboratory is primarily focused on the pharmacology and biochemistry of the cannabinoids and endocannabinoids. Her significant bibliography and frequent invitations to present attest to her reputation as a leader in her field. Dr. Hillard is an MCW graduate and a true advocate for the Basic Sciences. Frequently named an Outstanding Medical Student Teacher, Dr. Hillard takes an active role in training and mentorship, receiving MCW's highest honor, the Distinguished Service Award, in 2011.

Marja T. Nevalainen, MD, PhD
Assistant Dean for Research
Professor of Pathology
Associate Director of Education, Cancer Center

Dr. Nevalainen is an internationally recognized prostate cancer researcher. Her work has been funded by the NIH's National Cancer Institute, the Department of Defense, the American Cancer Society, and several industry sponsors. Many patents and licensing agreements have been developed in the Nevalainen Lab. She is frequently invited to speak to international audiences, including the Gordon Conferences, the Endocrine Society and the European Association of Urological Research. Her work has appeared in the Journal of Clinical Oncology, Journal of Clinical Investigation, Clinical Cancer Research, Nature Urology, Cancer Research and Molecular Cancer Therapeutics, and she has been a long time Senior Editor for Elsevier's Journal of Biochemistry and Cell Biology, and Editorial Board Member for the American Journal of Pathology and The Prostate. A passionate educator, Dr. Nevalainen has mentored dozens of students and is an important leader in the MCW Cancer Center's education programs. Dr. Nevalainen has served in a number of grant review panels including NCI, American Cancer Society and DOD Prostate Cancer Integration Panel over multiple years.

Lisa R. Henk, MS
Chief Administrator for Research Operations

Lisa Henk joined the Office of Research leadership team in January, 2016 as Chief Administrator for Research Operations. Prior to this appointment, Lisa served a dual role as Administrator for the Department of Pharmacology and Toxicology and the Neurosciences Research Center for four years. She also served as Interim Business Administrator for the Human and Molecular Genetics Center for much of 2015. Since 2008, Lisa has been an important leader in Basic Science Administration at MCW.

In her role as Chief Administrator, Lisa provides operational leadership for Office of Research functions. She works closely with each of the department's nine units to facilitate development, enhance efficiency, and provide the best possible experience for researchers and staff. Lisa maintains a focus on both the immediate needs and long-term objectives of MCW research.

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April A. Haverty, MPE, JD
Director
Grants & Contracts Office

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Director, MCW Libraries

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Joseph D. Thulin, DVM, MS, DACLAM
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Associate Professor

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Sandra L. Jensen, MS, RLATG, CPIA
Institutional Animal Care & Use Committee Office and Safety Committees Manager

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Todd Senglaub, MHP
Radiation Safety Officer

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All of Us Research Program

The future of health begins with you JoinAllofUs.org

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Froedtert & Medical College of Wisconsin

BloodCenter of Wisconsin™ PART OF VERSITI

A Member of *All of Us* Wisconsin

What is Precision Medicine?

Precision medicine is health care that is based on you as an individual. It takes into account factors like where you live, what you do, and your family health history. Precision medicine's goal is to be able to tell people the best ways to stay healthy.

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All of Us is part of the Precision Medicine Initiative. It will gather information from many people to help researchers learn how to fit the right treatments to the right people.

We hope that one million or more people will join *All of Us*. We are asking people from all over the United States to join *All of Us* so that our research reflects the diversity of our country. People who join will give us information about their health, habits, and what it's like where they live. By looking for patterns, researchers may learn more about what affects people's health.

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Blood Research Institute

From its beginning in 1947, BloodCenter of Wisconsin (BCW), part of Versiti, has supported basic, translational, and clinical research to advance patient care. Research at BCW 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). The BRI was constructed in 1991 and expanded in 2006 to a total of 87,000 sq ft. The BRI is home to 33 investigators and more than 120 research staff, including fellows, graduate students, technologists, and administrative personnel. Total extramural funding for research in 2017 was $15.2 million, including a Training Grant in Transfusion Medicine, currently in its 38th year, which provides stipends for outstanding postdoctoral fellows engaged in NIH-funded research and a Program Project Grant from the National Institutes of Health, currently in year 10, looking at the molecular and clinical biology of von Willebrand Disease.

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, BloodCenter research in Immunobiology focused on understanding the mechanisms involved in antibody/antigen recognition. BloodCenter investigators played an important role in the first allogeneic bone marrow transplant 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 NK 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. A newly funded Translational GlycOmics K12 Program, part of the National Career Development Consortium for Excellence in Glycosciences will train 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 9 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.

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. Over 34,000 square feet of space is dedicated to the center's laboratories, 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 140 CVC members from 26 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 cardiovascular scientists, 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
Microvesicle
Prevention
Redox Biology & Medicine

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 Northwestern Mutual Professor in Cardiology, 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. Moreover, as a green center, the CVC is also guided by an external scientific advisory board, internal scientific advisory board, institutional leadership, and a CVC advisory board.

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. Last year, the CVC was awarded a $1.6 million postdoctoral training grant from the National Heart, Lung, and Blood Institute, one of only six postdoctoral training programs on campus.

The CVC offers its primary members and their trainees access to core facilities including microscopy, imaging, other core equipment, free biostatistical support, a quarterly newsletter, conference rooms for meetings and presentations, eligibility for CVC grant awards, and promotion and sponsorship of the CVC Seminar Series and the Lunch and Learn Seminar Series, which are held on an almost weekly basis during the regular school year in the CVC's main conference room on the fourth floor of the HRC.

Last year, the members of the CVC were awarded more than $43.5 million in total funding, with $21.3 million being funded by the National Heart, Lung, and Blood Institute of the National Institutes of Health. More than 50 trainees were mentored and 460 scientific articles were published in peer-reviewed journals.

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

Center for Advancing Population Science

The Center for Advancing Population Science (CAPS) (formerly Patient Care and Outcomes Research (PCOR)) is proud to support the MCW Research Day. CAPS mission is to develop, test, and implement innovative strategies that transform healthcare and optimize quality, value, and cost. CAPS is comprised of a diverse group of investigators, supported by dedicated staff, with a wide range of clinical backgrounds and areas of research expertise. CAPS Investigators are focused on becoming a global leader in healthcare transformation through innovative research to improve the health of diverse populations and geographic regions. Center faculty range in backgrounds of clinical training including internal medicine, surgical disciplines, pediatrics, physical medicine and rehabilitation, emergency medicine and hematology-oncology, as well as economics, epidemiology, human factors, and biostatistics. The research approaches used are broad and include survey methods, secondary analysis of existing large databases, and the design and implementation of interventions to improve the delivery of health care. With an interdisciplinary perspective, we can design studies that will translate innovative research to care that makes a difference in patients' lives. In addition to implementing innovative research projects, CAPS faculty are dedicated to mentoring medical students, residents, graduate, undergraduate and high school students to foster the next generation of health services researchers and innovators.

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 the awareness of 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**, particularly related to breast cancer therapy and survivorship issues;
- **Cancer outcomes**, 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;
- **Fertility issues,** including decision-making by patients seeking care for fertility problems and the expansion and validation of a sexual function measure,
- **Use of the electronic medical record (EMR),** especially as it relates to communication between the doctor and patient, and;
- **Measurement of patient-reported outcomes**, including health-related quality of life, with applications in both research and clinical care.

For more information about CAPS, please visit: https://www.mcw.edu/Center-for-Advancing-Population-Science-CAPS.htm

Center for AIDS Intervention Research (CAIR)

The Center for AIDS Intervention Research (CAIR) in the Department of Psychiatry and Behavioral Medicine was first established in 1994 and has successfully competed for renewed funding since then. CAIR began its 25th year in 2018 as an NIMH-supported P30 Center. Jeffrey A. Kelly, Ph.D., Professor of Psychiatry and Behavioral Medicine, is CAIR'S Director.

CAIR's mission is to conceptualize, conduct, and scientifically evaluate the effectiveness of new intervention strategies to prevent HIV infection in populations vulnerable to the disease. CAIR's research also develops improved strategies to promote health and alleviate adverse mental health consequences among persons living with HIV. CAIR is committed to disseminating its findings both to the scientific community and to public health providers so they benefit from Center research.

CAIR's approach to achieving this mission 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 HIV prevention methods. CAIR is the only NIMH-supported HIV behavioral research Center located between the nation's east and west coasts. CAIR is a resource to investigators, institutions, and service providers from across the broad midsection of the country. The Center is also a scientific field leader at both national and international levels. Within the framework of its thematic mission on intervention research and emerging from intensive Center-wide priority-setting, the following specific aims guide CAIR's research:

(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 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-related disparities through research that identifies and responds to the needs of racial and ethnic minority populations with greatest HIV incidence and disease burden;
(5) As the only NIMH AIDS Research Center (ARC) located in the center of the United States, to develop, evaluate, and lead in the implementation of high-impact HIV prevention and to serve as a resource to health departments, providers, researchers, and community constituencies in mid-sized and underserved cities across the broad midsection of the country.

Center leadership includes:

Jeffrey A. Kelly, Ph.D.— Center Director; Interim Director, Intervention and Dissemination Core
Dr. Kelly has devoted his attention almost exclusively to HIV/AIDS behavioral research since the mid-1980s within the areas of HIV prevention interventions, interventions to reduce adverse health consequences among infected persons, and the transfer of HIV prevention research advances to AIDS service providers. He has evaluated interventions carried out at the level of individuals, groups, social networks, and communities with a variety of vulnerable populations. His present work develops and evaluates interventions to improve treatment linkage, retention, and adherence among HIV+ persons, and PrEP use and risk behavior reduction among high-risk uninfected persons.

Julia Dickson-Gomez, Ph.D.— Director, Qualitative Core and Co-Director, Dissemination and Implementation Science Core (DISC)
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.

Yuri A. Amirkhanian, Ph.D.—Director, International Core
Dr. Amirkhanian carries out research evaluating HIV prevention interventions that rely on existing social structures of high-risk communities in Eastern Europe and the U.S. He has studied social network prevention approaches with Roma (Gypsy) ethnic minorities, men who have sex with men, immigrants, and persons living with HIV infection. Dr. Amirkhanian's work also identifies mechanisms accounting for how interventions produce their effects and why effects vary within the same population. His interests include methods to transfer research findings to service providers, as well as network-level interventions to reach and then engage HIV+ persons to enter medical care.

Carol L. Galletly, J.D., Ph.D.—Director, Developmental Core
Dr. Galletly is an attorney and social scientist whose research applies empirical methods to guide the development of sound law and policy on critical issues at the intersection of individual behavior and the public health. Her research is multimodal, making use of quantitative and qualitative analytic methods and findings. She addresses topics including sexual health, HIV seropositive status disclosure, stigma, and the assessment of structural-level HIV prevention interventions. Currently, Dr. Galletly is examining the influence of US immigration-related laws and policies on utilization of healthcare and resources related to HIV infection, alcohol and drug use disorders, intimate partner violence, and reduced HIV testing.

Timothy L. McAuliffe, Ph.D.—Director Quantitative Core
Dr. McAuliffe is a biostatistician with particular experience in the evaluation of HIV prevention intervention outcomes. His research at CAIR focuses on the reliability and validity of self-reported risk behavior, and the development and evaluation of novel HIV risk and medication adherence assessment strategies, including the use of electronic diaries for reporting activity and associated events. His expertise has led to the development of analytical strategies in HIV prevention trials involving community and social network randomization.

Jennifer L. Walsh, Ph.D. —Co-Director, Dissemination and Implementation Science Core (DISC)
Dr. Walsh is a developmental psychologist whose primary research interests are HIV prevention, sexual health promotion, and the application of advanced statistical methods to health behavior data. Her current project uses integrative data analysis to combine data from four randomized controlled trials of HIV prevention interventions independently conducted at STI clinics to better understand factors promoting intervention success. Dr. Walsh's other research interests include pre-exposure prophylaxis (PrEP), sexual health and risk among adolescents and emerging adults, and the impact of socioeconomic disadvantage and neighborhood factors on diverse health behaviors.

Karen M. Opgenorth, M.S.—Director—Administration Core
Responsible for the Center's day-to-day management and budgetary functions, Ms. Opgenorth has been with the Center since its inception. She leads the administrative team supporting investigator research, implementation of research projects, and ensuring that Center operations maintain compliance with funder and institutional policies.

Additional faculty at CAIR includes:

Michelle R. Broaddus, Ph.D., Associate Professor
Dr. Broaddus's interests in HIV and STI prevention are guided by the influence of gender roles and communication technologies, condom negotiation, and contexts of sexual risk among high-risk youth and adolescents. Additional interests include linkage and retention in care among people living with HIV who are at risk of falling out of care, and community-based systems change for improved behavioral health across Wisconsin.

Laura R. Glasman, Ph.D., Assistant Professor
Dr. Glasman's research explores the interaction of the structural, network and motivational influences on HIV-related behaviors among Latino immigrants to the USA. She also conducts research on multilevel approaches to promote sexual health and access to services among Latino American women who use substances. Dr. Glasman has a strong interest in applying meta-analytical methods to understand behavior change in different contexts and populations, and she has conducted meta-analytic studies to determine how people form attitudes that influence their HIV-related behaviors.

Steven A. John, Ph.D., MPH, Assistant Professor
Dr. John's research studies factors that can increase use of pre-exposure prophylaxis (PrEP) among high-risk uninfected men who have sex with men (MSM) who are not presently PrEP users. His research has shown that HIV self-testing accompanied by home-based PrEP services has the potential to increase PrEP uptake among men with barriers to clinic-based care and that men in steady but nonmonogamous relationships are willing to persude their partners to initiate PrEP.

Andrew E. Petroll, M.D., M.S., Associate Professor
Dr. Petroll is an infectious disease specialist with a focus on the care of HIV-positive patients. His research interests include how patients' risk behaviors for HIV transmission are addressed in clinical settings, how patient-physician interactions affect the disclosure and discussion of HIV risk behaviors, and how patient and physician characteristics influence such discussions. He is also studying the effectiveness of interventions aimed at improving discussions about HIV risk behavior and about HIV pre-exposure prophylaxis between health care providers. In addition, he is evaluating factors that affect receipt of medical care for HIV and antiretroviral medication adherence among older, rural-dwelling individuals living with HIV.

Katherine G. Quinn, Ph.D., Assistant Professor
Dr. Quinn's research examines the role of social and structural drivers of HIV among racial and sexual minorities. She uses intersectionality to examine various identities and stigmas including racism, homonegativity, HIV stigma, medical mistrust, and poverty. Additionally, she has interest in examining poverty, inequity, housing stability, and homelessness among people living with and at risk for HIV.

Sergey S. Tarima, Ph.D., Associate Professor
Dr. Tarima is a biostatistician with expertise in clinical trial design, statistical methodology, and applied data analysis. His research interests in statistical methodology include the use of findings of prior literature to improve the precision of statistical estimators, regression analyses and quantile regression for investigating the predictors of quantiles at longer tails of skewed data, and sample size reestimation in the presence of multiple nuisance parameters. He also employs techniques for estimation of missing, censored, and partially grouped data, as well as survey data analysis.

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, glycans, metabolites, and small molecules. With more than 50 established project workflows to choose from, as well as highly customized analyses, we work together with investigators in a flexible and collaborative model, to apply the most advance methods available in an individualized approach. We also provide significant support for grant applications. We can assist with preparation of the research plan sections pertaining to mass spectrometry, as well as provide a letter of support, budget information, and facilities & resources documentation. 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, examples of projects we undertake.

MEDICAL COLLEGE OF WISCONSIN

Center for Biomedical Mass Spectrometry Research

All projects begin with a consultation with MS Center experts. To schedule your free consultation, please visit our website!

Center for Healthy Communities and Research

(Department of Family and Community Medicine)

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 $4.3M and $2.8M respectively) 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.

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 4 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, a 7.0T GE Healthcare MR950 located in the MRI annex, 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
- GE Healthcare Discovery MR950 7T 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 at the Medical College of Wisconsin is a newly established Center whose mission is to advance research in immunological disease mechanisms and translate those findings into the development therapeutic strategies that are applied in the clinic.

Specifically, the Center for Immunology combines expertise in basic and clinical immunology to:

- integrate immunological resources around emerging needs in clinical care that will constitute the personalized healthcare of tomorrow.
- coordinate immunological research investment capacity and strengthen communication between scientists, physicians and our community.

The comprehensive new 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.

Achieving these goals will enable Center for Immunology clinicians, research scientists, students, and staff to collaboratively discover novel diseases, 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.

Translational research programs within the new Center for Immunology are:

- Innate Immunology
- Adaptive Immunology
- Immuno-Genomics & Proteomics
- Immuno-Oncology & Therapy

Educational programs within the Center for Immunology include seminars, mini-symposia, journal clubs, work-in-progress research forum, graduate courses, fellowships, patient educational material, and community outreach materials.

Faculty, scientists, and students interested in membership of the Center for Immunology should contact Connie Siegel (csiegel@mcw.edu) for a list of benefits and an application.

If you are interested in learning more about the Center for Immunology or working with Center investigators please contact Michael Dwinell, PhD, Center Director at mdwinell@mcw.edu

The 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. 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 >400 centers across the globe, a clinical database containing information on >475,000 patients, and a biospecimen repository containing >140,000 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 >10 prospective studies ongoing. Since inception, the organization has published >1,200 articles and chapters in scientific publications. In 2017, the CIBMTR generated 82 publications and presented 71 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 complication of HCT therapy. They utilize the CIBMTR's clinical database to answer clinically important questions in a timely manner.
- **Clinical Trials**. The CIBMTR supports prospective research to evaluate new transplant and cellular therapies. The Blood and Marrow Transplant Clinical Trials Network (BMT CTN) conducts multicenter Phase II and III national trials while the Resource for Clinical Investigations in Blood and Marrow Transplantation supports Phase I and II trials that bridge the gap between single-center studies and the larger trials of the BMT CTN.
- **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 conducts research in health disparities, health policy, and system capacity issues. Current studies focus on costs and cost-effectiveness, insurance coverage, individualized care plans, post-transplant care, and informed consent.
- **Bioinformatics**. The CIBMTR provides expertise in, and conducts research on, translational and operational bioinformatics. Recent endeavors include analyzing next generation sequencing typing data and investigating the role of genetic ancestry in finding a match.
- **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 and, worldwide, any HCTs performed with products procured through the Program. The goal is to make blood and marrow transplants available to all who need them and to increase the safety and effectiveness of HCT.

Center for Microbiome Research

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.

MEDICAL COLLEGE OF WISCONSIN
Center for Microbiome Research

Services and Programs Offered

- Consultation: Study & Experimental Design, Funding Applications
- Microbiota-targeted Sample Collection & Processing
- Gnotobiotic Core Facility: Axenic and gnotobiotic rodent colonies, husbandry & experiments
- Bioinformatics & Biostatistics
- Gnotobiotic Isolators, MoBio Powerlyzer, FreezerPro Biorepository Mgmt Software
- Invited Speaker Seminar Series and Journal Club
- Pilot Experiment RFA

Contact Us:

Nita Salzman, MD, PhD
Center Director
msalzman@mcw.edu | (414) 955-4244

Mary Holtz, PhD
Program Manager
mlholtz@mcw.edu | (414) 955-5467

MACC Fund Research Center, 5th Floor, #5029; Email for an appointment
https://www.mcw.edu/Center-for-Microbiome-Research.htm

Center for Neurotrauma Research

(Department of Neurosurgery)

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

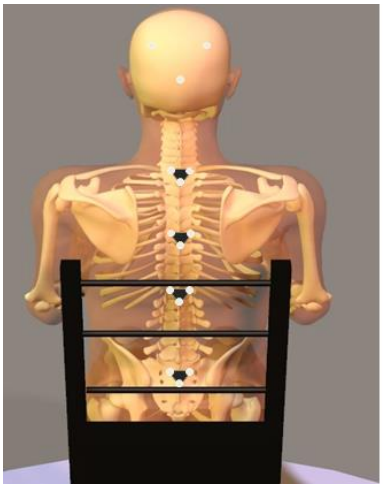
Traumatic Brain Injury (TBI) is a significant public health problem with national estimates of TBI in the United States range anywhere from 1.4 million to 4 million brain injuries per year, depending on the study and methods used to define and include cases. About 75% of TBIs that occur each year are 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.

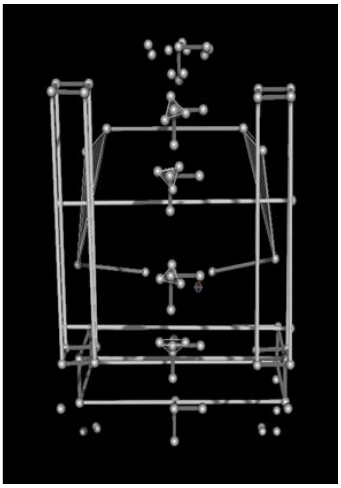
Head and Spine Biomechanics

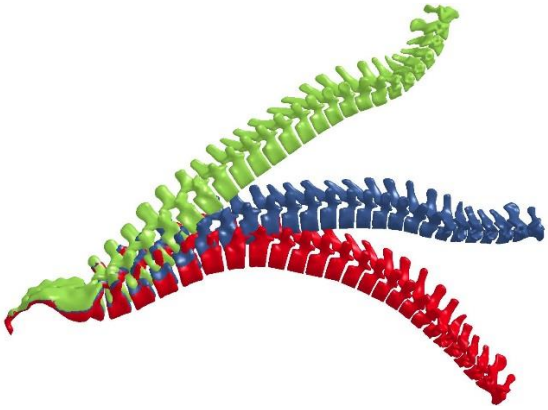
One of the longest running research programs in the Department of Neurosurgery has focused on head and spine biomechanics, with emphasis on trauma and disease. This research area brings together engineering scientists specializing in biomechanics and neurosurgeons to determine how the spine and the head-neck 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.

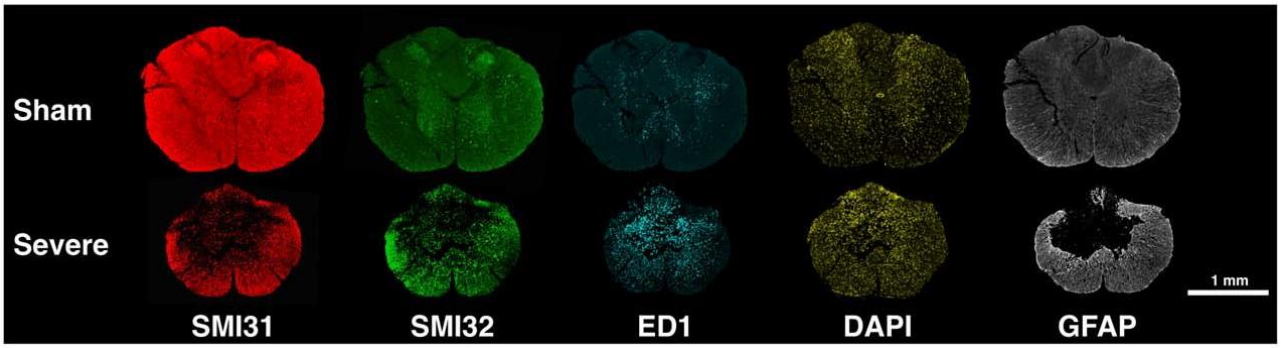
Patient Specific Modeling

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 CoSMM is a research center in the Department of Physiology at the Medical College of Wisconsin. The mission of the CoSMM is to develop and apply systems molecular approaches to improve the understanding and treatment of human disease.

The primary function of the CoSMM is to serve as an **intellectual incubator** for research and project development. The current areas of focus at the CoSMM are **regulatory RNA, epigenomics and related translational research**.

The CoSMM currently has 24 member laboratories led by faculty with primary or secondary appointments in the Department of Physiology. CoSMM members lead more than $3M (annual total costs) of extramurally funded research specifically in the areas of regulatory RNA, epigenomics and related translational research.

CoSMM members **collaborate with more than 10 institutes, departments or divisions** at MCW in studies related to CoSMM's areas of focus, sharing our expertise with investigators across MCW.

CoSMM members have published dozens of studies on regulatory RNA, epigenomics and related translational research. Several examples of notable publications in CoSMM's areas of focus since 2017 are listed below (CoSMM member faculty shown in bold font).

1. **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.* 2018 Jul 13. [Epub ahead of print]
2. Sun X, Han Y, Zhou L, Chen E, Lu B, Liu Y, Pan X, **Cowley AW Jr**, **Liang M**, Wu Q, Lu Y, **Liu P**. A comprehensive evaluation of alignment software for reduced representation bisulfite sequencing data. *Bioinformatics*. 2018 Mar 22. [Epub ahead of print]
3. 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*. 2018 Mar; 10(3): e8046.
4. Chuppa S, **Liang M**, **Liu P**, Liu Y, Casati M, **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 Int*. 2018 Feb; 93(2): 375-389.
5. Baker MA, Davis SJ, **Liu P**, Pan X, Williams AM, Iczkowski KA, Gallagher ST, Bishop K, Regner KR, Liu Y, **Liang M**. Tissue-Specific MicroRNA Expression Patterns in Four Types of Kidney Disease. *J Am Soc Nephrol*. 2017. Oct; 28(10): 2985-2992.
6. **Mattson DL**, **Liang M**. Hypertension: From GWAS to functional genomics-based precision medicine. *Nat Rev Nephrol*. 2017 Apr; 13(4): 195-196.
7. Mitzelfelt KA, McDermott-Roe C, Grzybowski MN, Marquez M, Kuo CT, Riedel M, Lai S, Choi MJ, Kolander KD, Helbling D, Dimmock DP, Battle MA, Jou CJ, Tristani-Firouzi M, Verbsky JW, **Benjamin IJ**, **Geurts AM**. Efficient Precision Genome Editing in iPSCs via Genetic Co-targeting with Selection. *Stem Cell Reports*. 2017 Mar 14; 8(3): 491-499.

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 infrastructure. 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. In 2017, investigators were involved in nearly 1,000 active clinical research studies, and pediatric researchers had nearly $24 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
- Grants Development Office

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

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
- Vascular Biology & Hematology
- Patient-Centered Research.

Examples of research awards for ongoing CRI investigations include:

- Ulrich Broeckel, MD, professor of Pediatrics at the Medical College of Wisconsin and a research unit leader of the CRI was awarded a $2.5 million dollar NIH grant entitled "Genetics of Cardiomyocyte and Cardiac Matrix Interaction"
- Martin Hessner, PhD, professor of pediatrics at the Medical College of Wisconsin and a research unit leader of the CRI was awarded a $1 million dollar grant from the Juvenile Diabetes Research Foundation entitled "Prediction of Post-onset Partial Remission Duration in New Onset Type 1 Diabetes"
- Michael E. Mitchell, MD, associate professor of cardiothoracic surgery at Medical College of Wisconsin has been awarded a $3.3 million, 5-year grant from the NIH to complete a multi-center study of a new method to monitor pediatric heart transplant recipients for transplant rejection.
- Julie Panepinto, MD MSPH, professor of Pediatrics at the Medical College of Wisconsin and research unit leader of the CRI received a $2.7 million dollar NIH grant "Midwest Child Patient Reported Outcomes Consortium"
- Nita Salzman MD, PhD, professor of Pediatrics at the Medical College of Wisconsin and research unit leader of the CRI received a $2.0 million dollar NIH award entitled "Intestinal Enterococcal Dynamics; Modeling Host-Commensal and Host-Pathogen Interactions"
- Elena Semina, PhD, professor of Pediatrics at the Medical College of Wisconsin and CRI investigator was awarded a $2.0 million dollar NIH grant "MAB21L Family in Human Ocular Disease and Development"

Children's Research Institute researchers have also received recent funding from several national foundations including American Diabetes Association, American Cancer Society, American Heart Association, Cystic Fibrosis Foundation, Lillian Goldman Charitable Trust and the W.M. Keck Foundation.

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 CTSI CTO is a central resource towards implementation of clinical studies and trials. The CTO operates at MCW, CHW and the VA and can provide fully trained study coordinators, assistance with IND/IDE applications, study monitoring and audit, OnCore implementation, IRB navigation and submissions and patient recruitment and services.
- 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/

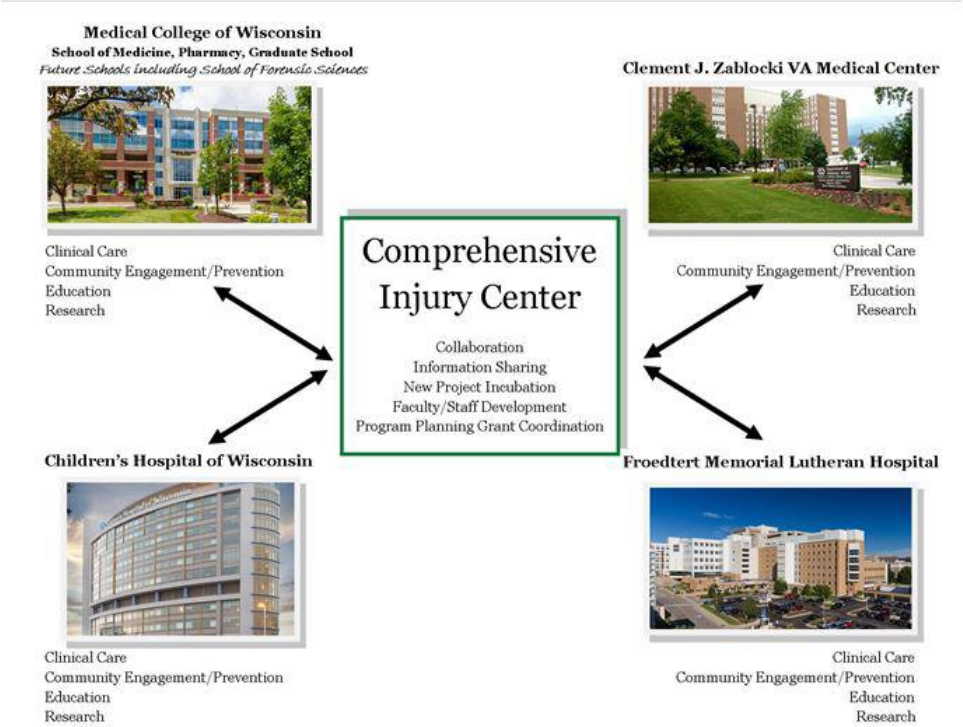
Comprehensive Injury Center

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 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
- Strengthen injury prevention and control practice by engaging our **community** through strong partnerships that facilitate, translate, and disseminate evidence-based programs and policies.

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.



Drug Discovery Center

The primary focus of the Drug Discovery Center is to facilitate and accelerate drug discovery and the translation of new basic discoveries in to therapies to improve human health. Research expertise at 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.

- Discovery to Clinic
- Collaborations
- Funding opportunity guidance
- Non-GLP PK and Tox studies
- Small Molecule modification & design
- CMC and Process development

Center's Signature Program

MEDICAL COLLEGE OF WISCONSIN | THERAPEUTIC ACCELERATOR PROGRAM

One step at a time in Multistep process

Mission: To facilitate and accelerate therapeutics & drug discovery by translation of ne basic discoveries into therapies.

TAP's Services:

- Providing internal project based funding opportunities
- Facilitating collaborations (internal & external)
- Independent scientific review and guidance
- I.P. disclosure assistance
- Project execution

For more information or discussion contact:

Dr. Ranjit Verma, rverma@mcw.edu, (414) 955 -5743
Dr. John Imig, jdimig@mcw.edu, (414) 955 -4834

Free Radical Research Center

Established by Dr. Balaraman Kalyanaraman in 2000 as part of the Department of Biophysics at MCW, the goal of the Free Radical Research Center (FRRC) is to provide intellectual and analytical support to MCW basic scientists and clinical researchers in free radical measurements by electron paramagnetic resonance (EPR) and other techniques. The FRRC is a spin-off from the National Biomedical EPR Center supported by the National Institutes of Health (NIH) Research Resource. It is unique because it combines both EPR and magnetic resonance imaging (MRI) methods. EPR is the only physical technique that can detect unambiguously free radicals in biological systems.

The FRRC is a well-recognized research resource, both nationally and internationally, with state-of-the-art EPR facilities, fluorescence, and HPLC techniques. The FRRC promotes and stimulates free radical research at MCW by developing and sharing comprehensive knowledge about various aspects of free radical reactions and antioxidants and by facilitating collaborations between basic and clinical researchers. In addition, the FRRC helps MCW researchers engaged in free radical and nitric-oxide-related research acquire NIH and other extramural funding.

The FRRC develops the capability of noninvasive fluorescence and MRI of physiological fluctuations in tissues and organs during oxidative stress. One major research focus of the FRRC is the development of high-throughput methodology for monitoring reactive oxygen and nitrogen species (ROS, RNS) in biological systems and application of those methods for screening of potential anti-inflammatory drugs.

The FRRC is composed of faculty members from various departments within MCW (including Anesthesiology, Biochemistry, Biophysics, Cancer Center, Medicine, Ophthalmology, Pharmacology & Toxicology, Physiology, Radiation Oncology, and Surgery), who have established collaborations with investigators from both national and international colleges, universities, and organizations.

The FRRC occupies a 2,000 SF space in the MCW Translational & Biomedical Research Center with a dedicated space for chemicals, an HPLC lab, an analytical lab, a sample preparation room (equipped with an analytical evaporator), a dark room, a cell culture room (equipped with an automatic cell counter and a Nikon microscope with digital imaging), and an organic chemistry room. The FRRC houses a variety of instruments, details of which can be found at www.mcw.edu/FRRC/FacilitiesandResources.htm. The resources and facilities of the FRRC have been utilized in numerous grants and program project grants over the past decade, and more than 100 research publications have cited the FRRC facility.

Examples of recent papers from the FRRC members on the development of new assays for ROS and RNS and on the role of redox signaling in cancer biology include (1-7).

1. Cheng G, Zielonka M, Dranka B, Kumar SN, Myers CR, Bennett B*, et al.* Detection of mitochondria-generated reactive oxygen species in cells using multiple probes and methods: Potentials, pitfalls, and the future. J Biol Chem **2018**;293:10363-80
2. Hardy M, Zielonka J, Karoui H, Sikora A, Michalski R, Podsiadly R*, et al.* Detection and Characterization of Reactive Oxygen and Nitrogen Species in Biological Systems by Monitoring Species-Specific Products. Antioxid Redox Signal **2018**;28:1416-32
3. Kalyanaraman B, Cheng G, Hardy M, Ouari O, Bennett B, Zielonka J. Teaching the basics of reactive oxygen species and their relevance to cancer biology: Mitochondrial reactive oxygen species detection, redox signaling, and targeted therapies. Redox Biol **2018**;15:347-62
4. Kalyanaraman B, Cheng G, Hardy M, Ouari O, Lopez M, Joseph J*, et al.* A review of the basics of mitochondrial bioenergetics, metabolism, and related signaling pathways in cancer cells: Therapeutic targeting of tumor mitochondria with lipophilic cationic compounds. Redox Biol **2018**;14:316-27

5. Pan J, Lee Y, Cheng G, Zielonka J, Zhang Q, Bajzikova M*, et al.* Mitochondria-Targeted Honokiol Confers a Striking Inhibitory Effect on Lung Cancer via Inhibiting Complex I Activity. iScience **2018**;3:192-207
6. Zielonka J, Hardy M, Michalski R, Sikora A, Zielonka M, Cheng G*, et al.* Recent Developments in the Probes and Assays for Measurement of the Activity of NADPH Oxidases. Cell Biochem Biophys **2017**;75:335-49
7. Zielonka J, Kalyanaraman B. Small-molecule luminescent probes for the detection of cellular oxidizing and nitrating species. Free radical biology & medicine **2018**

For more information, contact Jacek Zielonka, PhD, research director (955-4789 or jzielonk@mcw.edu) or visit the FRCC website (www.mcw.edu/FRRC.htm).

Genomic Sciences & Precision Medicine Center

The Genomic Sciences and Precision Medicine Center (GSPMC) is a full service, comprehensive reference laboratory offering some of the most advanced assays on the market today. We offer a broad range of research assays and services to assist in your research Initiatives from nucleic acid extraction to comprehensive data analytic solutions for basic, translational, and clinical research as well as functional validation of disease-associated genomic variants.

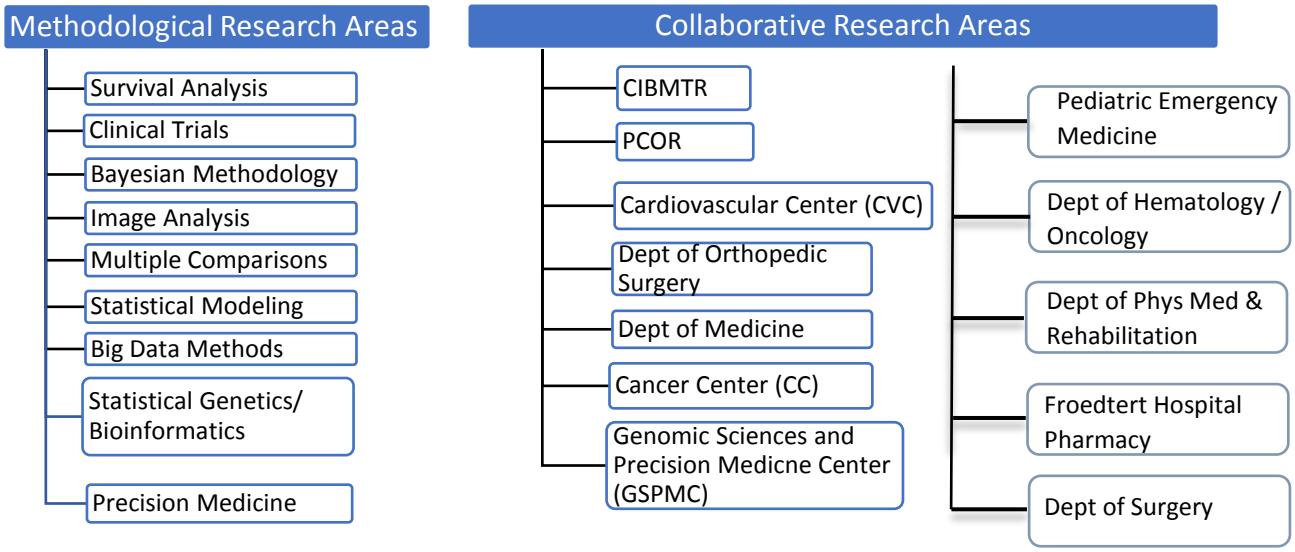
The GSPMC basic and clinical scientists lead the efforts at the Medical College of Wisconsin to provide quality precision medicine and health care by enabling researchers and clinicians to use genome sequence to understand disease, improve diagnosis and advance the treatment of our patients. We offer whole exome and genome sequencing, additional sequencing including RNA-Seq, ChIP-Seq and RRBS; robust data analysis and validation for precision diagnostics and therapeutics in pediatric and adult patients.

Currently, the GSPMC Sequencing Core deploys an Illumina NovaSeq 6000, three Illumina HiSeq 2500s, one Illumina MiSeq, and one ABI3730xl sequencer. We will soon be adding the second-generation Pacific Biosciences sequencer – the Sequel – to the arsenal, which will allow us to use extremely long sequencing reads (10-20kB) at the genome level to answer questions pertaining to structural variants, translocation events, and repeat disorders.

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

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 five faculty members, four postdoctoral fellows and twelve staff members. 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
Dr. Cassidy concentrates much of her research on pediatric trauma. She directs the Epidemiology Data Resource Center. Dr. Cassidy partners with many researches across MCW and assists with sampling, survey design, and registry development.

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.

Mallory O'Brien, MS, PhD
Dr. Mallory O'Brien is the 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 to develop opioid overdose reviews and sexual assault reviews.

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 active member 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 chemicals (NIH R21 11765725), GLNARCH outreach, and adapting mobile technology to improve environmental health literacy. He was recently award an R01 through NIEHS entitled "Gigiigooinaan (Our Fish): A New Advisory to Promote Anishinaabe Health and Wellness"

Community Health Division Research

Active project funding sources and titles

- AHW REDIRECT (Research on Early childhood Development by Improving Resilience and EQuiTy)
- AHW Cross-Cutting Cancer Initiative.
- NIDDK/CDC. Effect of ACA Medicaid expansion on diabetes.
- HWPP. Healthier children through a shared service network supporting ASQ screening and early intervention.
- HWPP. Born learning: Portage County community collaboration for optimal child development.

- CRI. Radiation induced heart disease population study.
- Milwaukee Succeeds/Betty Brinn Children's Museum. Evaluation of VROOM use by child cares, health and social service agencies, and parents.

Recent publications

- Azam, Jackson, Knudson, Meurer, Tarima. Use of secondary clinical data for research related to diabetes self-management education. *Research Social Admin Pharmacy* 2017.
- Azam, Young, Meurer, Nelson, Asan, Flynn, Knudson. Cultural and social challenges of diabetes self-management education through the voices of physicians. *WI Med J* 2018.
- May, Byonanebye, Meurer. Ethics of population health management: collapsing the traditional boundary between patient care and public health. *Population Health Management* 2017.
- Olson, Svoboda-Newman, Gardner-Volle, McNally, Fabian, Maurana. More than a conversation: the power of bringing scientists and community together to change perceptions about cancer. *J Cancer Education*. 2018.
- Sparapani, Tarima, Jackson, Rein, Meurer. Nonparametric recurrent events analysis with BART and an application to the hospital admissions of patients with diabetes. *Biostatistics* 2018.
- Tarima, Tarassenko, Rein, Sparapani, Meurer. Signs of residuals for testing coefficients in quantile regression. *Statistics and Simulation* 2018.

Recent national and state presentations

- Meurer, Coughlin, Hardy. Data infrastructure to inform early childhood developmental care systems. *Strive Together Convening.*
- Meurer, Coughlin, Jepson, Inman, Falduto, Hardy, Schmidt, Young, Cassidy. Statewide work to improve the early childhood developmental care system. *American Academy of Pediatrics* and *North American Primary Care Research Group.*
- Olson, Stolley, Millon-Underwood, Cawthra, Beyer, Fraser, Ignace, Pinsoneault, Salazar, Walker, Williams, Lucey, Maurana. An integrative approach to identify biological and socioeconomic contributors to cancer incidence and mortality. *Wisconsin Public Health Association.*
- Olson, Kamaraju, DeNomie, Stolley. Development of a comprehensive, immersive reality-based health tool to engage women in breast health education. *Military Health Systems Research Symposium.*
- Olson, Stolley, Millon-Underwood, Cawthra, Beyer, Fraser, Ignace, Pinsoneault, Salazar, Walker, Williams, Lucey, Maurana. An integrative approach to identify biological and socioeconomic contributors to cancer incidence and mortality. *Experimental Biology.*
- Olson, Taylor, Sparapani, Lenarczyk, Baker. A combined basic science and population science approach demonstrating the potential for simvastatin to mitigate cardiovascular disease after lower hemi body radiotherapy. *American Heart Association 2017 Scientific Sessions.*

Education programs

- MPH online degree and certificate programs
- HRSA T32 Primary Care Research Fellowship

Primary faculty members

- John Meurer, MD, MBA, professor and director of the Institute for Health & Equity
- Jess Olson, PhD, MPH, assistant professor
- Greer Jordan, PhD, assistant professor and MCW Chief Diversity and Inclusion Officer

National Biomedical EPR Center

The National Biomedical Electron Paramagnetic Resonance (EPR) Center at MCW is one of the largest EPR facilities in the nation. It is supported by a P41 research resource award by the National Institutes of Health (NIH) National Institute of Biomedical Imaging and Bioengineering (NIBIB).

The research conducted within the EPR Center includes both technological innovation and application of new techniques to biological problems. The main areas of research are free radicals, spin labeling, metal complexes, and metallo proteins. Inquiries on the use of the EPR Center are welcome. Spectrometers are available for S-, X-, L-, Q- , and W-band EPR, many with ENDOR, ELDOR, saturation-transfer, saturation-recovery, and multiquantum capabilities.

Collaborative Projects

- **Frequency Modulation ST EPR Studies of Macromolecular Dynamics at W-band. Albert H. Beth, Department of Molecular Physiology and Biophysics, Vanderbilt University.** The overall aims of this collaborative study are to determine the advantages of microwave frequency modulation for saturation transfer EPR (ST-EPR) studies of macromolecular dynamics at W-band. This project will combine the expertise of the National Biomedical ESR Center in design and construction of this novel new technology with the long-standing interest of the Beth laboratory in studies of very slow rotational dynamics of proteins and their macromolecular assemblies including advanced analyses of experimental data in terms of anisotropic rotational diffusion and constrained rotational diffusion. W-band is predicted to be superior to lower frequencies (e.g., X-band)^ for these demanding applications. The specific aims that will be addressed are: (1) to document the sensitivity of fm-ST-EPR at W-band to the global isotropic rotational diffusion of a well characterized model protein in solution as a function of modulation frequency; and (2) to extend this work to detailed characterization of the constrained anisotropic rotational diffusion of a transmembrane protein, the anion exchange protein, in the human erythrocyte membrane.
- **Applications of Information Geometry to the Analysis of NARS Spectroscopy. Keith A. Earle, Department of Physics, University of Albany (SUNY).** The specific objective of this collaboration is to use advanced statistical techniques and recent results from communication theory in order to fully characterize spin-spin interactions in the presence of coherent noise over a wide variety of conditions. This collaboration has direct applications for optimizing experimental parameters and in the analysis of dipolar distances up to 40A using the instrumental capability being further developed in TR&D Project 2. Collaborative Project 2. Specific Aims Specific Aim 1.1. Survey the parameter space and characterize an informative signal representation of non-adiabatic rapid sweep (NARS) experiments for use in determining interspin distances upwards of 40 A.Specific Aim 1.2. Assess the effects of various signal-processing filter techniques using an information metric as a way to quantify the influence of filtering on the parameter estimation problem.
- **Native Structure of Potassium Channels. Adrian Gross, Rosalind Franklin University of Medicine and Science, North Chicago, IL** We intend to measure distances between nitroxide spin labels at room temperature in the 20-30 A range. Two types of potassium channel samples will be studied: (1) Single mutants where the interspin distance is generated by the symmetry of the channel, and (2) double mutants where the interspin distance corresponds to a non-symmetry-related spin pair. Both sample types are routinely generated and studied in the laboratory.

- **High Pressure Q-Band NARS. Wayne L. Hubbell, Department of Ophthalmology and Chemistry and Biochemistry, University of California, Los Angeles** The aim of this project is to determine structural constraints on low-lying excited ("invisible") states of spin-labeled proteins populated by pressure.
- **Distance Measurements by L-Band NARS. Eric J. Hustedt, Department of Molecular Physiology and Biophysics, Vanderbilt University** The specific objectives of this project center on the use of the L-band NARS technology®® recently developed at the National Biomedical EPR Center at MCW to measure long range (>20 A) distance distributions in spin-labeled protein samples. The overall goal is to develop an understanding of how temperature and solvent conditions affect the measured distance distributions. It is anticipated that this work will have a major impact on our knowledge of how commonly used experimental conditions influence the results obtained. Specific Aim 1. Using either T4L or the CDB3 dimer, compare distance distribution measurements at cryogenic temperatures using DEER with those obtained at much higher temperatures using L-band NARS. Experiments will be designed to test how temperature effects the distance distributions obtained by changing the distributions of spin-label side-chain rotamers and protein conformers.Specific Aim 2. Using either T4L or the CDB3 dimer, investigate how different cryoprotectants and viscosity enhancing agents influence the distance distribution measurements made by L-band NARS.
- **Intermediate Distance Determinations in the Lipid A Transporter MsbA. Candice S. Klug and James S. Hyde, Department of Biophysics, Medical College of Wisconsin.** The specific objective of this collaboration is to obtain spin-spin distance information at physiologically relevant temperatures (i.e., noncryogenic) in a range not possible by other instrumental techniques (18-28 A) using a novel approach to an instrumental capability (L-band) being further developed in TR&D Project 2.Specific Aim 1. Compare the structural organization of MsbA A270T at its permissive and restrictive temperatures using L-band EPR distance determination. Specific Aim 2. Quantitate the population of the MsbA A270T homodimer in the closed and open conformations.
- **Role of RPE Melanosomes in Oxidative Stress in Vitro: Effects of Age-Related Modifications on Antioxidant and Pro-Oxidant Properties of the Pigment Granules. Tadeusz Sarna, Department of Biophysics, Jagiellonian University, Krakow, Poland.** The main goal of this project is to investigate physicochemical properties of human retinal pigment epithelium (RPE) melanosomes with aging using melanin free radical centers as intrinsic molecular probes of this important biological pigment and the proposed new approach to high frequency EPR spectroscopy. It is expected that this novel application of the segmental microwave frequency sweep from non-adiabatic to adiabatic FID and spin echo Fourier transform EPR at W-band to characterize motional and spectroscopic properties of melanin will provide us with unique information about key chemical and physical changes of the pigment granules induced in the human RPE by aging, which may reduce their protective capacity. Specific Aim 1. Verify the postulate that aging is accompanied by oxidative modifications of human RPE melanosomes that change spectroscopic parameters of the melanin radicals in a consistent way, pure absorption and dispersion spectra of RPE pigment granules from single donors of different age and of experimentally photoaged porcine RPE melanosomes will be obtained, and selected spectral features of the EPR signals will be employed to characterize early and late age-related changes of the pigment granules. Specific Aim 2. Test the hypothesis that chemical changes of RPE melanosomes occurring with aging differentially affect different parts and constituents of the pigment granules. D-band EPR spectra of melanosomes from donors of different age and from photobleached porcine RPE will be used in an attempt to spectrally resolve melanin free radical centers that exhibit significant overlap of their EPR spectra at W-band. Specific Aim 3. Test the hypothesis that aging of human RPE melanosomes and photoaging of porcine pigment granules modify the accessibility of melanin free radical centers to molecular oxygen, solvent molecules and various chemical agents affecting their reactivity. We will apply the developed method of segmental adiabatic sweeps of the microwave frequency at W-band to probe the distribution of phase memory times across the spectrum of melanin radicals in RPE melanosomes from donors of different age and in photobleached porcine melansomes. Specific Aim 4. Test the hypothesis that age-related changes of RPE melanosomes affect their morphology and nano-mechanical properties such as rigidity and porosity that could alter antioxidant and photoprotective properties of the granules. We will carry out passage experiments at the interface between the ARP and non-adiabatic conditions to measure very slow rotational diffusion of melanin radicals in RPE melansomes from donors of different ages and in partially photobleached porcine RPE pigment granules.

- **Structural Basis for SNARE-Mediate Membrane Fusion. Yeon-Kyun Shin, Department of Biochemistry, Biophysics & Molecular Biology, Iowa State University.** There is compelling evidence that the soluble N-ethylmaleimide-sensitive factor attachment protein receptor (SNARE) TMDs play an essential role in promoting the fusion pore opening. We hypothesize that the interaction between target membrane (t-) and vesicle associated (v)-SNARE TMDs drives the fusion pore opening. Alternatively, it is possible that the heterodimeric TMD is shaped in such a way that it could stabilize the fusion pore. Specific Aim 1. Investigate the heterotypic interaction between SNARE transmembrane domains (TMDs) using site-directed spin-labeling (SDSL) EPR. We will determine the structure and the membrane topology of V- and t-SNARE TMD heterodimer using SDSL EPR spectroscopy to investigate the structural basis effusion pore opening.
- **Enhanced Discrimination of Cholesterol Bilayer Domains in Model and Biological Membranes by Modification of the Electrostatic Surface Potential of the Membrane. Witold K. Subczynski, Department of Biophysics, Medical College of Wisconsin.** The specific objective of this collaboration is to develop a new EPR spin-labeling approach for investigation of phase-separated domains in lipid bilayers. Specifically, we will characterize the formation of cholesterol bilayer domains (CBD) in model membranes and in intact fiber cell plasma membranes of the human eye lens. A new instrumental capability at L-band, which is being further developed in TR&D Projects 1 and 2 (namely, the extremely narrow central line of EPR spectra of spin labels as well as a short spin-lattice relaxation time), will allow increased sensitivity for the discrimination of domains at a higher rate of lipid exchange. These high exchange rates "mix" results from coexisting domains. Specific Aim 1. Compare effects of water-soluble relaxation agents, neutral NiEDDA and negatively charged CrOx, on EPR spectra (linewidth, line intensity, and spin-lattice relaxation time) of CSL and T-PC in POPC/POPS membranes as a function of membrane surface potential. Specific Aim 2. Use optimized conditions as described in Aim 1 to investigate the formation of cholesterol bilayer domains (CBD) and evaluate the cholesterol solubility limit in POPC/POPS membranes. Specific Aim 3. Use approaches developed in Specific Aims 1 and 2 to determine the cholesterol concentration at which the CBD is formed in membranes made of from the major phospholipids of the lens fiber cell plasma membrane.
- **In Vivo Surface Chemistry with Applications in Measuring Ionizing Radiation Dose in Human Finger and Toenails. Steven G. Swarts, University of Florida-Gainesville.** The specific objective of this collaboration is to advance in vivo oximetry measurements in a subcutaneous tumor model in rats using a non-adiabatic rapid sweep (NARS) spectroscopy detection scheme. This collaboration utilizes the Center's previous research of NARS bridges and the proposed TR&D Project 1 to translate NARS technology to Dartmouth's established in vivo L-band (1.2 GHz) oximetry station. Specific Aim 1.Optimize instrumentation and data collection parameters for in vivo NARS oximetry. Specific Aim 2. Apply and assess in vivo NARS oximetry in a subcutaneous tumor model in rats with implantable biocompatible oxygen reporters and resonators.

Neuroscience Research Center

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

We envision that:

1. 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. The NRC scientists engage in science that is driven by questions whose answers have strong potential to "move the needle" with respect to our scientific understanding and eventual improvement of human health. NRC scientists use innovative approaches and techniques.
3. NRC scientists engage in collaborative research projects that bring scientists with complementary expertise and interests together that promote collegiality, sharing of data and ideas, and raise the quality of research of all participants in a manner that potentiates success.
4. The NRC scientists have access to high quality support staff, seed funds, equipment and expertise to carry out their research.

We are working towards achieving this vision with a combination of approaches. We host seminars, data sharing events, research in progress, symposia all with the goal of providing MCW faculty, students, staff and fellows with information. It is our intent that these events increase collaborations among NRC members and others in the MCW research community. The NRC has hosted meetings of the Milwaukee Area Society for Neuroscience, which includes nearly 150 neuroscientists, to provide an even larger range of collaborative opportunities.

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.

Please visit our website at https://www.mcw.edu/Neuroscience-Research-Center.htm for information about upcoming events and a list of the recent publications of NRC faculty.

If you are interested in joining the NRC, please send an email to Wesley Hoffmann (whoffmann@mcw.edu). She will make sure that you receive our weekly newsletter so that you can attend our events.

If you are interested in learning more about the NRC, please contact Cecilia Hillard, NRC Director at chillard@mcw.edu.

Research Computing Center

The Research Computing Center (RCC) provides the infrastructure and campus-wide access to resources required for high performance computing computationally intensive biomedical research. This includes shared hardware and research-specific software which is supported by MCW and research grants. RCC services and operations will be governed by representatives of the MCW Faculty in partnership with RCC leadership.

Spotlight on Science: A XNAT Image Repository for Research
Andrew Nencka, PhD
Assistant Professor of Biophysics

An array of servers provided by the Research Computing Center has allowed us, for the first time, to offer an integrated research imaging database, in parallel to the PACS used in the clinic, to researchers here at MCW. A diverse number of researchers in southeastern Wisconsin utilize the research dedicated magnetic resonance imaging systems on campus, and a growing number of studies are launching with the clinical systems housed with our campus partners. The XNAT installation offers a centralized destination to which we can push research images from the MRIs. Further subject and experimental metadata can also reside in the XNAT with those images. The project-based organization of the XNAT allows users to restrict access to sensitive imaging data. A gateway server allows us to transfer data to off-site collaborators through an interactive web application while maintaining the security of the MCW network and ensuring security for the transferred images.

Andrew Nencka, PhDThe framework underlying the XNAT allows us to deploy standardized image processing pipelines to automatically run on images which enter the database. Although best practices exist for image processing, implementing processing pipelines is non-trivial. Expert collaboration is required to attain high quality results in imaging studies because of this. With custom processing pipelines deployed in XNAT researchers can be assured that a tested, standardized processing pipeline is appropriately applied to their data. Further, such pipelines can be run in automated ways, allowing researchers to spend more time interpreting the experimental results rather than getting the data into an appropriate format. Additionally, this allows imaging collaborators to easily deploy their processing pipelines to multiple collaborative partners. This capability is highly valuable to researchers who wish to perform research _with_ the imaging technology rather than _on_ the technology, and offers a sizable efficiency improvement.

Experimental imaging protocols often include the collection of vast amounts of data which are currently of little diagnostic use in the clinic. Pushing such data into the clinical PACS can cause significant challenges in the clinical work flow. However, it is important in some imaging studies that data are made available to radiologists on the study team to perform screenings for incidental findings or adverse events. The XNAT architecture is deployed so that subsets of images in experimental protocols that have diagnostic value are forwarded to the PACS for reviews by radiologists, while using the clinical tools with which they are accustomed to working and avoiding the burden of excess research images in the PACS.

Some studies on campus include multi-center imaging. Such imaging, taking place across the country, requires a central repository to collate and store the imaging data. The XNAT gateway deployment offers an outward facing web application for external sites to upload study data. That data is then pulled into the main XNAT deployment on campus for organization, processing, and piping to PACS for clinical reads. Thus, the XNAT installation enables MCW to serve as an image data hub for large-scale, multi-institutional studies.

The Advantages of the RCC Service

The previous workflow for imaging included individual labs transporting physical media to and from the MRIs for data transfer, or network pushes to individual lab servers. This diversity in workflow between studies presented a challenge in the efficient operation of research MRI because scanner operators would need to verify transfer means, potentially mount drives, and manually implement data copying procedures. Because the XNAT acts as a PACS, it is set up as a target on the research imaging systems so that an imaging exam can now be pushed into the database with a single button click on the system.

With individual labs responsible for the storage and processing of their data, each lab requires significant computational and storage computing resources. Typical labs house servers with tens of terabytes of disk space for the imaging data. Significant unused disk space is deployed across those dozens of systems across campus. Consolidation of storage into the RCC Isilon array offers a level of efficiency impossible on the scale of individual lab servers. Further, individual lab servers are expensive and require non-trivial system administration if they are to run securely and efficiently. Labs are essentially required include members who have become capable system administrators to manage such systems. However, without formal training or knowledge of best practices, such lab members spend a disproportionate amount of time managing the systems rather than working on the scientific problems which they are best suited to address. Paired with this ad hoc organization, data for projects in a lab may be spread across numerous drives on several computers. Finally, there is a high level of variance in system administration expertise across labs. This leads to questions in the quality or existence of backups of data. There have been instances where irreplaceable data have been lost due to the failure of a single hard drive. Delegating the storage system management to the people running the RCC offers several increases in efficiency:

1) The lab expense of purchasing a server is transferred into a relatively low fee for storage use.
2) The wasted free disk space across dozens of servers is consolidated into usable space on a shared array.
3) Expert systems administrators efficiently manage systems in the RCC, freeing lab members to practice science.
4) Data backup and disaster recovery plans are in place, well vetted, and practiced.
5) Data organization is automated through the image database.

The physical presence of the XNAT servers in a secure data center gives them access to the RCC computational resources, as well. Several processing steps in functional neuroimaging studies include algorithms that take up to twelve hours on single imaging sessions. In even moderately sized studies with 20-50 subjects, each with multiple imaging sessions, it is not uncommon that a hundred imaging sessions must run through the processing pipeline. The need for over a thousand hours of processor time for the study slows labs down with the limited computational resources in their labs. It is not reasonable for such labs to purchase large computational resources because the bolus usage equates to an underpowered system when needed and an excessively large system for the majority of time. The shared resource of the computational hardware in the RCC offers an opportunity to run batch processing on imaging data stored in the XNAT in parallel across the group of subjects in a study. This architecture allows individual labs access to the high power computational resources that they occasionally require, while spreading the availability of those resources across all labs using the XNAT. Although this MPI job scheduling has not yet been deployed on the XNAT, it is built into the XNAT architecture and will be deployed moving forward.

Services

High Performance Computing Platforms
Manage open source scientific applications on several HPC platforms:

- A 552 Core Linux MPI cluster
- A 3 Terabyte RAM 40 Core Large Memory Linux server
- Four Graphical Processing Unit Servers with Three Nvidia K40 (2880 cores) each
- Four Graphical Processing Unit Servers with Four Nvidia K80 (4992 cores) each
- MATLAB Distributed Computing Cluster with 256 workers
- Three 48-core 384GB SMP Linux Servers

Example software used includes Gromacs, NAMD, VMD, R, Bioconductor, Matlab, Bowtie2, Cufflinks, Hmmr, Tophat, Schrodinger Small Molecule Suite, Samtools, and FreeSurfer. These are a representative sample of programs and not an exhaustive list of what is supported.

High Performance Storage
Provide large short term storage for analyses:

- Isilon Storage pool over 1 PB with seven I/O nodes
- Isilon Replication pool with 280TB with three I/O nodes
- Tape Library with four LTO 6 (6.25 TB) drives for archiving

The Storage pool and the HPC Systems are connected by a dedicated 10Gb LAN for maximum throughput.

Archival Storage
To provide long-term research data storage:

- 1.2 PB on three redundant storage nodes
- Snapshot capabilities
- Dedicated archiving LTO-6 tape drive

Software Licensing and Management
The RCC manages the license and license servers for ChemDraw, DNASTAR Lasergene, EndNote, GraphPad Prism, Ingenuity IPA, LabArchives, Matlab, PyMOL, SAS, SPSS, and X-Win32. Software licenses are offered at a significant discount.

Research Server Management
The RCC will configure, install, manage and operate servers for Research Cores within the Office of Research. The RCC provides and manages dbGaP servers.

Grant Submission Assistance
RCC will assist in evaluation of resources and processes needed to comply with data security requirements and provide boilerplate language to describe existing resources. It can also assist in identifying existing MCW resources that could be used for research efforts and design efficient solutions for research problems when needed.

Electronic Laboratory Notebook
The RCC supports the management of research data including an electronic laboratory solution by LabArchives.

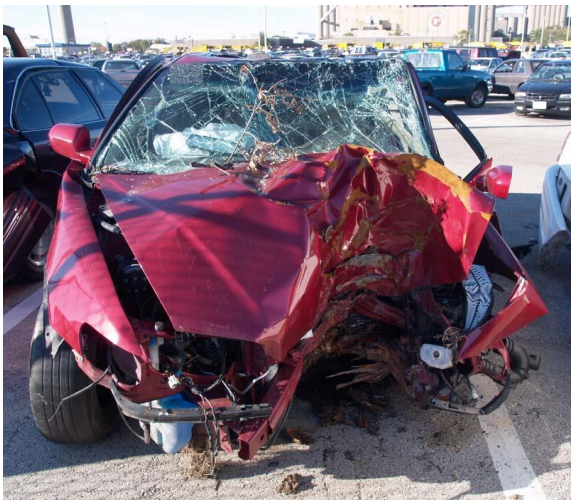
Research Application Training and Seminars
RCC sponsors on campus vendor training seminars for selected research applications.

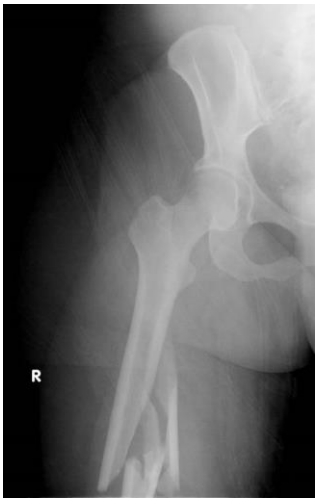
Crash Injury Research Engineering Network

MCW Neurosurgery

DEPARTMENT OF BIOMEDICAL ENGINEERING
MARQUETTE UNIVERSITY AND MEDICAL COLLEGE OF WISCONSIN

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

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 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.

For more information contact:

Nancy Dahms, PhD
(414) 955-4698 | ndahms@mcw.edu

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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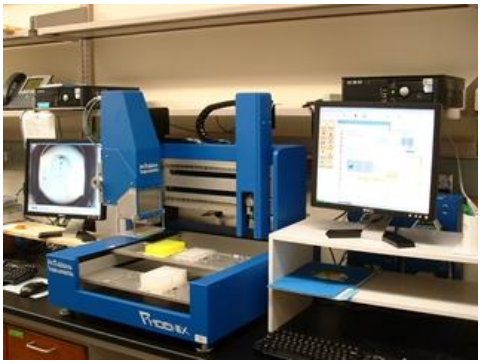
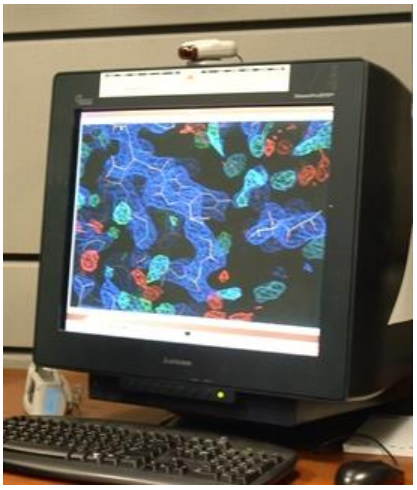
Macromolecular X-Ray Crystallography Facility

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

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

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.

The X-ray facility is located on the second floor of the Translational Biomedical Research Center (TBRC). The facility houses an X-ray diffraction system consisting of a Rigaku R-AXIS IV++ image plate detector system and MicroMax 007 generator equipped with Osmic confocal mirrors and an X-treme crystal cryocooler. The crystallization system includes a Hamilton STAR for solution making and a Phoenix equipped with a CrysCam for nanoliter crystallization and visualization. A fully automatic crystal incubator/imager (crystallization hotel) will soon be added to enhance throughput capacity.

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.

Jianhua Fu, PhD
jfu@mcw.edu | (414) 955-5849

Jung-Ja Kim, PhD
jjkim@mcw.edu | (414) 955-8479

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

Biomedical Engineering

DEPARTMENT OF BIOMEDICAL ENGINEERING

MARQUETTE UNIVERSITY

MEDICAL COLLEGE OF WISCONSIN

The Joint Biomedical Engineering Department (Joint Department) between Marquette University and the Medical College of Wisconsin 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 medical needs.

Clinical Collaborations
Help us to apply our newly developed technologies and discoveries so they can be used in clinical decision making. Clinical collaborators include:

- Blood Center of Wisconsin
- Otolaryngology-MCW
- Radiology-MCW
- Ophthalmology-MCW
- Physical Medicine and Rehabilitation-MCW
- Neurology-MCW
- Neurosurgery-MCW
- Herma Heart Center & the Pediatric Genetics Groups at Children's Hospital of WI
- VA Medical Center

Imaging
Departmental research groups develop imaging systems or applications that cover many different modalities such as

- CT
- Micro CT
- SPECT
- Fluoroscopy
- MRI and fMRI

Applications include imaging brain function and lung cellular activity

Analytics, Informatics & Software Engineering
Biomedical engineers work at the interface between computer and software engineering and the biomedical computational sciences. They conduct computational research, innovation and visualization in the areas of genomics, other areas of molecular sciences, and neuroscience

Crash Injury & Research Engineering Network
Real-world crashes are investigated to further the following objectives:

- Reconstruct and understand causation
- Improve prognosis and treatment for crash trauma patients
- Reduce time of recovery and treatment costs

- Disseminate data to industry, regulatory, and public agencies
- Develop strategies to reduce fatalities and injuries in automobile crashes
- Provide information to improve public infrastructure

Neurosystems & Neurorehabilitation
These research groups focus on the brain, nervous system, and motor control. They study aspects of neuroscience and neuromuscular control as they relate to normal function and in conditions like stroke rehabilitation and multiple sclerosis

Orthopaedics & Orthopaedic Rehabilitation
Researchers in this area study human motion and musculoskeletal physiology as it relates to human health and disease**.** They also perform clinical research in the areas of orthopaedic surgery and physical medicine and rehabilitation using biomedical engineering analysis methods, modeling, and instrumentation. This area also includes innovative prosthetic design and analysis to reduce crashes, develop and disseminate safety messages to the public, and train health care providers in vehicular safety and associated care.

Computational Biology & Systems Biology
Biomedical engineering specializes in understanding complex, interacting systems using the tools of Systems Biology. Integrating protein and metabolic function from molecule to the whole person involves many sophisticated models of how biological systems work and how computational science can be used to better understand them. Systems Biology incorporates computational models of huge networks of proteins, molecules, and genes to identify how they work together and allows our faculty and students to work in a broad array of new and exciting areas. Our faculty use a systems approach to study cardiovascular, pulmonary, neurological and skeletal biological diseases.

Cardiovascular & Pulmonary
Investigators in this area use high performance computing and modeling, as well as imaging to study the mechanical and physiological aspects of vascular and respiratory function to fight:

- Heart disease
- Hypertension
- Diabetes
- acute lung injury

Medical Device Innovation
Medical devices are at the heart of biomedical engineering. Innovations from our faculty and students have ranged from instruments to computer algorithms. Our group works closely with physicians and research scientists to translate ideas into devices.

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 the Medical College of Wisconsin and Marquette University.

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), redox, and magnetic resonance (MR) physics and brain imaging.

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 (a national P41 Research Resource supported by the NIH/NIBIB) is the most extensive EPR facility in the nation. 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 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 in 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 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 neurological and psychiatric disorders (e.g., early disease detection, precision disease prevention, prediction of disease development, and assessment of treatment efficacy in 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 and clinical settings. The Magnetic Resonance Imaging track places emphasis on MRI and MRS (magnetic resonance

spectroscopy); fMRI of the human brain is an active research area (neuroscience, contrast mechanisms, 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 Free Radical Research Center, National Biomedical EPR Center, Redox and Bioenergetics Shared Resource, and Redox Biology Program.

More Information

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

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.

In 2018, we are delighted to welcome 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 exoY 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 is an area of particular interest. 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. Other faculty address the role of the immune system in combating cancer, a novel immune checkpoint protein known as “Vista”.

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.

Immunology Program

The 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. As an integral part of the Department of Microbiology & Immunology, the Immunology Program is composed of research laboratories focused on the immunological aspects of autoimmunity, infectious disease, allergy, immunodeficiency and cancer. Graduate research training in immunology is offered through the Microbiology, Immunology and Molecular Genetics 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 Molecular Genetics, Blood Research Institute and the Children’s Research Institute seminar series. Now in its 12th year, the Immunology Group hosts an annual Immunology Symposium and Retreat. The 2018 Immunology Symposium will be held in the Fall of 2018. The Symposium highlights external speakers and is well attended by immunologists throughout southeast Wisconsin. The Retreat, which occurs the day prior to the Symposium, consists of faculty and selected trainee presentations, a poster session and

opportunities for social networking followed by a poster session. Participation is campus wide with presentations by graduate students and post-doctoral clinical fellows.

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).

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 her 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: Her long-term objective is to understand the interplay between host and bacterial factors that lead to life-threatening infections with P. aeruginosa. We have focused on the relationship between expression of toxins injected by the type III system and Pseudomonas pathogenesis in acute infection models. The local as well as the systemic delivery of toxins emphasize the pathogenic potential of the bacterium. Our hypothesis is that delivery of the type III toxins inhibits the uptake and destruction of P. aeruginosa during the initial stages of colonization, allowing multiplication past the point of resolution by innate immune mechanisms in compromised hosts. The outcome of infection is then determined by the extent of injury or compromised state of the host, the expression patterns of the various toxins, proteases and other destructive enzymes, and the host response.

Jack Gorski, PhD: He 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: We are 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 immunoevasive 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.

Christopher Kristich, PhD: He 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.

Mark McNally, PhD: His 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.

Vera Tarakanova, PhD: Her 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: His 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: His research focuses on identifying and functionally characterizing signaling pathways that control B cell development from hematopoietic stem cells (HSCs) and B cell function. His research employs multiple cutting-edge approaches, including targeted gene disruption, transgenic, bone marrow transplantation and high-throughput DNA/RNA sequencing technologies.

Li Lily Wang, PhD: Research in the Wang lab focuses on immune regulation mediated by the immune-checkpoint proteins, such as VISTA. We apply preclinical tumor models to investigate the mechanisms whereby VISTA controls the anti-tumor immunity, and design innovative immunotherapeutic strategies for cancer treatment.

Tom Zahrt, PhD: His 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 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 26 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.

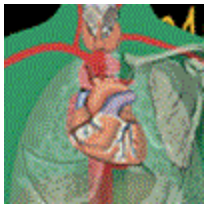
Physiology

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 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 of other basic science and clinical departments. The department is tightly integrated with several Research Centers on the MCW campus: the Cardiovascular Center, Human and Molecular Genetics Center, Center of Systems Molecular Medicine, and Neuroscience Research Center. We are also closely aligned with the recently established 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 recently established the Master's in Medical Physiology (MMP) Program to help 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 evolved from an original Program Project grant to 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).

Main areas of research in the Department of Physiology currently include:



Cardiovascular Physiology. This research is aimed at understanding fundamental principles of cardiovascular regulation and disease using a wide range of scientific techniques. The Department is working to understand fundamental principles of cardiovascular regulation and disease through a variety of diverse, yet related areas. The research is highly collaborative and spans the areas of molecular and cellular biology, genetics, proteomics, technology development and microcirculatory experiments. The major goals of this research are to understand alterations that occur in the vasculature and microvasculature in response to various stresses such as hypertension, high salt diet, and exercise. Our studies have focused on the mechanisms of blood vessel growth and regression, as well as on control of blood flow to tissues such as skeletal muscle and brain, and alterations in vessel reactivity. These measurements include gene and protein expression, receptor numbers, oxygen transport, local blood flow, and microvascular density to assess the ability of the cardiovascular microcirculatory network to meet the needs of the tissue.

Some of the departmental research programs are centered on characterizing the cellular and molecular mechanisms of muscle cell contraction, particularly arteriole muscle, and modifying these mechanisms by endothelial factors, neurotransmitters, and endogenous vasoactive agents. Intracellular electrophysiological recordings from muscle cells within intact arterial segments are done utilizing standard glass microelectrodes to study these phenomena. Cultured vascular muscle and endothelial cells are studied by voltage and patch-clamp techniques for analysis of ionic events. These techniques are being used to determine the mechanisms of the altered response of arterioles and small resistance arteries to changes in oxygen availability in hypertension. Another of our major goals is to identify the mechanisms by which a high salt diet leads to impaired vascular function, even in the absence of an elevation in blood pressure.

The department also has an interest in determining factors that can either protect the brain against ischemic damage or enhance recovery following a cerebrovascular accident. Certain hormones and pharmaceutical agents have been shown to

enhance brain capillary growth and also to reduce the extent of infarction resulting from exposure of the brain to ischemia. Research efforts are underway to elucidate the mechanisms of the capillary growth and investigate the relationship between increased vessel density and protection from stroke.

One of the best examples of cardiovascular research in the department of Physiology is supported by the American Heart Association Hypertension Center. MCW's center represents one of the four centers in the nation that form the American Heart Association Strategically Focused Hypertension Research Network (PI – Dr. Mingyu Liang). The center consists of basic, clinical, and population science projects led by Dr. David Mattson, Dr. Srividya Kidambi, and Dr. Theodore Kotchen, working with Dr. Cowley, Dr. Pengyuan Liu, and other investigators. The three projects are collectively testing the hypothesis that lifestyle factors and gene-environment interactions cause genome-wide changes in DNA methylation, which contribute to the development of hypertension and can be used as predictive or diagnostic markers of hypertension and related diseases.

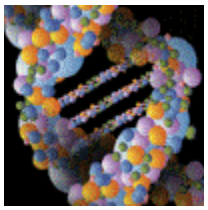
Renal Physiology. How do kidney function and blood flow work to regulate blood pressure? We use every approach from in vivo to in vitro to the genetic analysis of hypertension to understand this major health issue in this area. Renal physiology research in the Department of Physiology is primarily focused on the importance of renal blood flow and renal function in the regulation of arterial blood pressure.

Our studies have found that reductions of medullary blood flow result in excess retention of sodium and water, which leads to hypertension. Further work is now directed toward understanding the mechanisms that normally control renal medullary blood flow and how alterations in these pathways can lead to hypertension. In other departmental research, particular emphasis is placed on the paracrine, autocrine, and hormonal regulation of renal tubular and vascular function. Several years ago, research efforts were directed at the deleterious role of infiltrating immune cells in the kidney in the development of salt-sensitive hypertension and renal disease. Additionally, we are interested in the normal and pathophysiological regulation of ion channels in the kidney, and how it contributes to electrolyte balance; these studies are of high importance as ion channel function along the nephron is key to the control of blood pressure and often plays an important role in the development of such diseases as diabetes and hypertension. Studies utilize in vitro measurements of mRNA, protein, enzymatic activity, enzyme kinetics, ion channels activity, and cell signaling, as well as in vivo measurements of hormone levels, blood flow, blood pressure, and other indices of renal/cardiovascular function in anesthetized and conscious rats and mice. Experimental models widely used at the Department include various inbred and genetically manipulated rodent strains.

Respiratory Physiology. Respiratory physiology research in the Department of Physiology is focused on understanding the neural mechanisms involved in the control of breathing at various stages of maturity and in response to various environmental and physical stressors.

Maturation of the ventilatory control system takes place following birth, although the factors that influence this maturation remain under investigation. Studies use different animal models to gain insight into the time-course of normal development of the ventilatory control system, as well as the effect of environmental and genetic influences on these changes during development. Animal models have been used to determine whether a critical window of development exists in the ventilatory control system that has been proposed as a part of a triple-risk model of Sudden Infant Death Syndrome. In addition, the interaction of plasticity and genetic influences is being studied using inbred strains of rats exposed to perinatal hyperoxia. In combination, these studies are aimed at understanding how the ventilatory control system matures under both normal and stressed conditions.

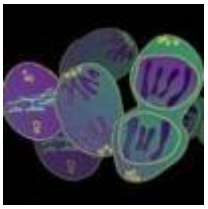
Other research is concerned with mechanisms regulating breathing in the adult. Breathing, respiratory muscle activity, heart rate and arterial blood pressure are continuously measured in all studies, which are completed in awake or asleep states. These studies provide insights into mechanisms of respiratory rhythm and pattern generation and intracranial chemoreception during normal conditions, during exercise, or when O_2 and CO_2 levels change in the brain. All these studies relate to disease conditions of central and obstructive sleep apnea, congenital central alveolar hypoventilation, and traumatic brainstem injury.



Physiological Genetics and Genomics. Research in the field of genetics and genomics focuses on the analysis of complex and common disorders and their underlying genetic basis using animal and human studies. Investigators in the Department use animal models, consomic and congenic rat strains, knock-out and transgenic rats and mice) or human studies combined with linkage analysis, single nucleotide polymorphism (SNP)-based association studies, and functional genomic analyses using transgenic rat and mouse models, microarray expression profiling, and siRNA to understand the mechanisms by which mutations affect organ function and integrity and ultimately lead to common disorders. Main areas of research interests in the area of genetics and genomics include:

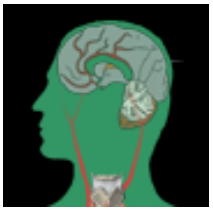
- Genetic and Genomic Technologies and Applications. The department is widely recognized as a leader in the development of genetic and genomic technologies and the application of these technologies to study hypertension and other disorders.
- Genetic & Physiological Basis of Salt-Sensitive Hypertension. This program focuses on advancing our understanding of the complex regulation and interplay of a set of genes which are responsible for salt-induced hypertension, renal injury, and vascularity/angiogenesis of the microcirculation in the salt-sensitive (SS) rat.
- Advanced Genetic Engineering Technology Development. Innovative rat genome editing technologies, some of which have been developed by our faculty, are being applied to generate multiple gene targeted rat models nominated by the scientific community in an NIH supported R24 program led by Drs. Melinda Dwinell and Aron Geurts. The Resource provides phenotypic characterization, cryopreserved sperm from each line, along with a tissue and primary culture bank for each strain, as well as distribution of all the animals and reagents to the community.
- Genetic Analysis of Respiratory Disorders. Studies in the department use different animal models to gain insight into the time-course of normal development of the ventilatory control system, as well as the effect of environmental and genetic influences on these changes during development.
- microRNA and Epigenomics. The microRNA and epigenomic research in the department is concentrated in the Center of Systems Molecular Medicine (CoSMM) founded and directed by Dr. Mingyu Liang.
- Cardiorenal Syndrome. Studies led by Dr. Alison Kriegel are examining the role of microRNAs in the development of cardiovascular disease in a model of chronic kidney disease.

Metabolism. Current work in our department focuses mainly on the physiological and hormonal regulation of glucose homeostasis and adiposity. Our main emphasis is on the study of metabolic alterations in obesity and diabetes. Research combines the molecular analysis of target tissues using microarray technology and proteomics with detailed analysis of metabolites and organismal function in cellular model systems, animal models and human biopsy samples. Additional efforts are aimed at elucidating the roles of neuropeptide Y and other hormonal regulators in basic metabolic processes of obesity, diabetes and hypertension.



Data from some of these studies are being used to build a multi-scale computational model of molecular energetics and mechanics. This model will help us understand the pathophysiology of the progression of substrate imbalances (hyperglycemia and dislipidemia), insulin resistance and the onset of type II diabetes in the metabolic syndrome, a common human disorder that includes obesity, diabetes, dyslipidemia, and hypertension.

Molecular & Cellular Physiology. The investigation of molecular and cellular functions is of paramount importance for understanding basic cellular and organismal physiological processes. Only this complete and detailed understanding will allow for effective analysis of disease states, and provide the basis for development of targeted pharmacological intervention. Research in the Department focuses primarily on understanding basic signaling and ion transport systems that regulate vascular function, contractility, and vascular growth in a variety of cellular environments. Commonly used experimental approaches include patch clamp analysis of ion channel currents, measurement of brain cerebral blood flow using laser-Doppler flowmetry, biochemical assay of lipid metabolites, reactive oxygen species, protein kinases and protein phosphatases, intracellular electrophysiological recording from muscle cells within intact arterial segments utilizing standard glass microelectrodes, television microscopy, oxygen microelectrodes, and other basic molecular approaches to characterize proteins and cellular mediators involved in these cellular mechanisms.



Neurophysiology. How does the brain and neural system control breathing at various stages of maturity and in response to environmental and physical stressors? Neurophysiology research in the Department of Physiology at MCW is closely linked to respiratory physiology research. It is centered on understanding the neural mechanisms involved in the control of breathing at various stages of maturity and in response to various environmental and physical stressors. Other projects focus on stroke and the reduction of the neural deficits resulting from it. Dr. Matthew Hodges' Lab, for instance, studies the effects of brain depletion of tryptophan hydroxylase, and as a result, brain depletion of 5-HT. The goal is to understand how these abnormalities, which are found in SIDS, affect physiological systems necessary for sustaining life, like breathing and body temperature control, and how additional environmental (increased heat) and other (inflammation) stressors affect these systems.

Computational Biology and Bioinformatics. This research direction provides an essential computational component to many of the areas in the field of physiology. For instance, genetics and genomics research investigating complex disease makes particularly widespread use of bioinformatics for such things as creating software to analyze and visualize SNPs and genetic variation, data management tools for association studies, data management software for scientific literature, visualization tools for genomic data, algorithms for comparative mapping, proteomics data management software, for comparative proteomics, and more.

One of the novel applications of computation in the Physiology department at MCW is the mathematics software that is being used to develop computational models of the transport and biochemical reaction of metabolites and other substances. Modeling the properties of such complex systems allows otherwise untestable hypotheses to be evaluated in silico (computer model) and their conclusions transferred to an in vivo (animal) experiment for further verification.

More traditional computational tools such as databases, websites and software applications are being built and used by a number of projects to capture, store and analyze experimental data. The demands of the projects are such that extensive use is made of high-powered hardware and multi-node clusters to provide the storage and raw processing power required to handle the large quantities of data being processed.

Selected publications from the Department of Physiology:

- Breaking the Cycle: Estrous Variation Does Not Require Increased Sample Size in the Study of Female Rats. Dayton A, Exner EC, Bukowy JD, Stodola TJ, Kurth T, Skelton M, Greene AS, Cowley AW Jr. Hypertension. 2016. 68(5):1139-1144
- Evidence of the Importance of Nox4 in Production of Hypertension in Dahl Salt-Sensitive Rats.Cowley AW Jr, Yang C, Zheleznova NN, Staruschenko A, Kurth T, Rein L, Kumar V, Sadovnikov K, Dayton A, Hoffman M, Ryan RP, Skelton MM, Salehpour F, Ranji M, Geurts A. Hypertension. 2016. 67(2):440-50
- Molecular Approaches in HFpEF: MicroRNAs and iPSC-Derived Cardiomyocytes. Kriegel AJ, Gartz M, Afzal MZ, de Lange WJ, Ralphe JC, Strande JL. J Cardiovasc Transl Res. 2017 (in press).
- Exploring human disease using the Rat Genome Database. Shimoyama M, Laulederkind SJ, De Pons J, Nigam R, Smith JR, Tutaj M, Petri V, Hayman GT, Wang SJ, Ghiasvand O, Thota J, Dwinell MR. Dis Model Mech. 2016. 9(10):1089-1095
- Renal Tumor Necrosis Factor α Contributes to Hypertension in Dahl Salt-Sensitive Rats. Huang B, Cheng Y, Usa K, Liu Y, Baker MA, Mattson DL, He Y, Wang N, Liang M. Sci Rep. 2016. 6:21960
- Effects on breathing of agonists to μ-opioid or GABAA receptors dialyzed into the ventral respiratory column of awake and sleeping goats. Langer TM 3rd, Neumueller SE, Crumley E, Burgraff NJ, Talwar S, Hodges MR, Pan L, Forster HV. Respir Physiol Neurobiol. 2017. 239:10-25
- State-dependent and -independent effects of dialyzing excitatory neuromodulator receptor antagonists into the ventral respiratory column. Langer TM 3rd, Neumueller SE, Crumley E, Burgraff NJ, Talwar S, Hodges MR, Pan L, Forster HV. J Appl Physiol 2017. 122(2):327-338
- The NRF2 knockout rat: a new animal model to study endothelial dysfunction, oxidant stress, and microvascular rarefaction. Priestley JR, Kautenburg KE, Casati MC, Endres BT, Geurts AM, Lombard JH. Am J Physiol Heart Circ Physiol. 2016. 310(4):H478-87
- Detection of TRPV4 channel current-like activity in Fawn Hooded hypertensive (FHH) rat cerebral arterial muscle cells. Gebremedhin D, Zhang DX, Weihrauch D, Uche NN, Harder DR. PLoS One. 2017. 12(5):e0176796.

- Interleukin-6 inhibition attenuates hypertension and associated renal damage in Dahl salt-sensitive rats. Hashmat S, Rudemiller N, Lund H, Abais-Battad JM, Van Why S, Mattson DL. Am J Physiol Renal Physiol. 2016. 311(3):F555-61
- Novel adaptive and innate immunity targets in hypertension. Abais-Battad JM, Dasinger JH, Fehrenbach DJ, Mattson DL. Pharmacol Res. 2017. 120:109-115
- Intravital Imaging of the Kidney in a Rat Model of Salt-Sensitive Hypertension. Endres BT, Sandoval RM, Rhodes GJ, Campos-Bilderback SB, Kamocka MM, McDermott-Roe C, Staruschenko A, Molitoris BA, Geurts AM, Palygin O. Am J Physiol Renal Physiol. 2017 (in press).
- Lack of Effects of Metformin and AICAR Chronic Infusion on the Development of Hypertension in Dahl Salt-Sensitive Rats. Pavlov TS, Levchenko V, Ilatovskaya DV, Li H, Palygin O, Pastor-Soler NM, Hallows KR, Staruschenko A. Front Physiol. 2017. 8:227.
- The Role of Angiotensin II in Glomerular Volume Dynamics and Podocyte Calcium Handling. Ilatovskaya DV, Palygin O, Levchenko V, Endres BT, Staruschenko A. Sci Rep. 2017. 7(1):299.
- Upregulation of 20-HETE Synthetic Cytochrome P450 Isoforms by Oxygen-Glucose Deprivation in Cortical Neurons. Zhang H, Falck JR, Roman RJ, Harder DR, Koehler RC, Yang ZJ. Cell Mol Neurobiol. 2017. doi: 10.1007/s10571-017-0462-8.
- Renal sodium transport in renin-deficient Dahl salt-sensitive rats. Pavlov TS, Levchenko V, Ilatovskaya DV, Moreno C, Staruschenko A. J Renin Angiotensin Aldosterone Syst. 2016 17(3).
- Identifying Candidate Genes that Underlie Cellular pH Sensitivity in Serotonin Neurons Using Transcriptomics: A Potential Role for Kir5.1 Channels. Puissant MM, Mouradian GC Jr, Liu P, Hodges MR. Front Cell Neurosci. 2017 11:34.
- Redox Stress Defines the Small Artery Vasculopathy of Hypertension: How Do We Bridge the Bench-to-Bedside Gap? Touyz RM, Montezano AC, Rios F, Widlansky ME, Liang M. Circ Res. 2017. 120(11):1721-1723.
- SerpinC1/Antithrombin III in kidney-related diseases. Lu Z, Wang F, Liang M. Clin Sci (Lond). 2017. 131(9):823-831.
- Hypertension: From GWAS to functional genomics-based precision medicine. Mattson DL, Liang M. Nat Rev Nephrol. 2017. 13(4):195-196.
- Antithrombin III Protects Against Contrast-Induced Nephropathy. Lu Z, Cheng D, Yin J, Wu R, Zhang G, Zhao Q, Wang N, Wang F, Liang M. EBioMedicine. 2017. 17:101-107.
- Ushering Hypertension Into a New Era of Precision Medicine. Kotchen TA, Cowley AW Jr, Liang M. JAMA. 2016. 315(4):343-4.
- Pappa2 is linked to salt-sensitive hypertension in Dahl S rats. Cowley AW Jr, Yang C, Kumar V, Lazar J, Jacob H, Geurts AM, Liu P, Dayton A, Kurth T, Liang M. Physiol Genomics. 2016. 48(1):62-72.

Anethesiology

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 internally.

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

Studies involving Departmental Faculty in academic year 2017-2018 include the following:

1. Genomic Analysis of a Cohort with Infantile Hemangiomas Associated with Multi-Organ structural birth defects (Dawn Siegel, MD)
2. Development and Validation of a Gene Expression Assay to Predict Risk of Metastatic Disease in High Risk Cutaneous Squamous Cell Carcinoma (Julia Kasprzak, MD)
3. A Pilot Study of a Single, Easily Measurable Outcome for Psoriasis in Pediatric and Adult Patients (Kenneth Gordon, MD)
4. A Phase 3, Multi-Center, Randomized, Placebo-Controlled Double-Blind Study of the Efficacy and Safety of Apremilast (CC-10004) in Subjects with Moderate to Severe Plaque Psoriasis of the Scalp (Kenneth Gordon, MD)
5. Regeneron Pharmaceuticals, Clinical Trial R668-AD-1526 (Kristen Holland, MD)
6. Regeneron Pharmaceuticals, Clinical Trial PROSE R668-AD-1762 (Keri Chaney, MD)
7. Novartis Pharmaceuticals Corporation Clinical Trial - Adult Moderate to Severe Plaque Psoriasis (Kenneth Gordon, MD)

Other key accomplishments in academic year 2017-2018 include the following:

1. Dawn Siegel, MD was named the President of the Pediatric Dermatology Research Alliance (PeDRA)
2. Yvonne Chiu, MD was appointed to the Dermatology Foundation Executive Committee
3. Stephen Humphrey, MD was appointed to the Children's Hospital of Wisconsin Ambulatory Workgroup, Telemedicine Committee, and the Medical College of Wisconsin Clerkship Committee

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, 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 Milwaukee Clinical Translational Research Institute (CTSI), the MCW Cancer Center, Cardiovascular Research Center, 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 in order 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, American Heart Association, 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, 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 Basic Research faculty members are:

- **Andreas Beyer, PhD** studies the metabolic effects of aging, hyperglycemia, and oxidative stress on the peripheral microcirculation.
- **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. 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. Physiology of endothelial dysfunction in gestational diseases.
- **Jennifer Strande, MD, PhD** has research interests focused on the mechanisms underlying the cardiomyopathy of muscular dystrophy.
- **Michael Widlansky, MD** has efforts focused on the relationship between altered mitochondrial bioenergetics and endothelial dysfunction

- **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.

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 2017-2018 academic year, the Division of Gastroenterology and Hepatology has been involved in research spanning esophageal 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 Saltzman 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 five-year RO1 grant award for his proposal entitled "Mechanisms for Improving Pharyngeal and Esophageal Motor Functions"; this study will begin in September of 2018.
- **Dr. Banani Banerjee and Dr. Jyoti Sengupta** successfully submitted a competitive renewal of their R01 grant submission titled "Neuoromolecular Mechanisms of Chronic Pelvic Pain in Neonatally-induced Cystitis".
- **Dr. Banani Banerjee** received a seed grant from the DDC for his proposal entitled "The Role of Reactive Oxygen Species (ROS) in Esophageal Acid-Induced Cortical Sensitization".
- **Dr. Jyoti Sengupta** received a seed grant from the DDC for his proposal entitled "Effect of mu/delta Opioid Receptor Agonists for the Treatment of Pelvic Pain".
- **Dr. Achuthan Sourianarayanane** received a seed grant from the DDC for his proposal entitled "Serum Lipid Markers Based on Liver Tissue in NASH Diagnosis".
- **Dr. Andres Yarur** received a seed grant from the DDC for his proposal entitled "The Association Between Body Composition and Response to Biologic Therapy in Inflammatory Bowel Disease Patients".
- In June 2018, our Division presented a total of 27 posters and 8 presentations at Digestive Disease Week in Washington, D.C.

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 nineteen active clinical trials in our Division. This includes fourteen active IBD clinical trials (one run by Dr. Amir Patel, four run by Dr. Daniel Stein, nine run by Dr. Andres Yarur), two active esophageal stent trials run by Dr. Kulwinder Dua, and three active hepatology clinical trials (two run by Dr. Syed Rizvi, one run by Dr. Achuthan Sourianarayanane). We are in the process of starting *six* new clinical trials with several different Investigators including one motility clinical trial run by Dr. Reza Shaker, one hepatology clinical trial run by Dr. Kia Saeian, one IBD clinical trial run by Dr. Poonam Beniwal-Patel, and three IBD clinical trials run by Dr. Andres Yarur. Overall, we are working with ten 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 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, and Drs. **Timothy Fenske, James Thomas, Joshua Field and Wendy Peltier**, Section Heads for Blood and Marrow Transplant (BMT) and Hematologic Malignancies, Solid Tumor Oncology, Benign Hematology and Palliative Care, 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). He is developing clinical trials in the pre- and peri- transplant setting for high risk disease patients, with a goal of investigating methods to improve disease related outcomes.
- **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 acute lymphocytic leukemia (ALL) and chronic myelogenous leukemia (CML). He is co-Principal Investigator (PI) with Dr. Kathryn Flynn, MD in the Division of General Internal Medicine of an R01 from the National Cancer Institute (NCI) to evaluate stopping tyrosine kinase inhibitors in patients with CML who are in complete molecular remission.
- **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 and has an investigator-initiated clinical trial to study the outcomes of cancer patients with blood clots associated with intravenous catheters. Additionally, she is the institutional PI for an international randomized trial of direct oral anticoagulants vs. low molecular weight heparin for treatment of acute venous thrombosis in cancer patients. 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.
- **Alexandria Bear, MD's** research interests include experiential learning and development of end of life communication workshops.
- **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.
- **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 and evaluation of several potential biomarkers of treatment response in conjunction with Dr. Craig MacKinnon's Core Translational Research Lab.

- **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).
- **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.
- **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 high-risk plasma cell neoplasms. His current research interests include clinical trials (with focus on investigator-initiated trials) for drug development in the areas of plasma cell neoplasms and improving outcomes of allogeneic hematopoietic cell transplantation. He is a member of the New Investigators Committee of the ALLIANCE for Clinical Trials in Oncology. He is also involved in the BMT CTN studies, as site PI of CTN 1501 and as a protocol team member of the CTN 1801 study.
- **Christopher Chitambar, MD's** research focuses on the role of iron and iron proteins in tumor growth and the development of novel metallodrugs to target tumor iron homeostasis and mitochondrial function in non-Hodgkin's lymphoma and brain tumors. He also studies the role of mitochondrial dysfunction in the development of fatigue in patients with early stage breast cancer receiving adjuvant chemotherapy.
- **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. One is already published, and the other one is in the process of manuscript submission. He was recently awarded a pilot grant from American Cancer Society to explore the role of micro-RNA in multiple myeloma bone disease. Additionally, in collaboration with investigator from University of Wisconsin Madison, he was also 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. He has also successfully collaborated with Dr. Anand Padmanbhan from Blood Center of Wisconsin in understanding the novel diagnosis and treatment for patients with heparin-induced thrombocytopenia.
- **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. Dr. Drobyski has been continuously funded by NIH for this work since 1991. He currently has two 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 in patients.
- **Anita D'Souza, MD, MS** has 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. She has conducted multiple clinical trials in these diseases. She currently leads efforts to study quality of life and patient-reported outcomes in amyloidosis for which she received the 2016 Mentored Career Development Award. She mentors multiple trainees on research projects in these diseases.
- **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.
- **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). Dr. Foy 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. Dr. George 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 interests are enrolling patients on genitourinary clinical trials. Additionally, building 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.
- **Jonathan Gully, MD** is interested 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 residents interface with technology at bedside.
- **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 lymphoid malignancies, GVHD, and alternative donor allogeneic transplantation. He is the Scientific Director of the CIBMTR's Lymphoma Working Committee. He is currently the PI of two investigator-initiated clinical trials; one which looks at the role of immunomodulation with HMG-CoA reductase inhibitors for preventing acute GVHD (supported by a grant from Conquer Cancer Foundation of the American Society of Clinical Oncology) and another which understands the role of the novel proteasome inhibitor MLN9708 in preventing chronic GVHD. His expertise and focus on developmental therapeutics has led to at least five first-in-human phase I trials opening for patient accrual at MCW within the last one year.
- **Parameswaran Hari, MD** 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 a national trial evaluating allogeneic HCT 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 (pre-IND phase).
- **Mary Horowitz, MD, MS** leads two international programs to evaluate and improve outcomes of hematopoietic stem cell transplantation (HCT): the CIBMTR (described separately), funded by the NCI, NHLBI and NIAID and the Blood and Marrow Transplant Clinical Trials Network (BMT CTN), funded by NHLBI and NCI. The CIBMTR maintains a large outcomes registry compiling data on HCT recipients in more than 350 centers in more than 40 countries. The BMT CTN conducts large multicenter trials and enrolls patients from more than 100 centers in the US, Canada, France and Germany.

- **Siegfried Janz, MD**'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's work, which is supported by NCI grants and other external revenue streams, 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 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.
- **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 exosomal 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 Natural Killer cells (NK), and developing translational models to improve the anti-tumor efficacy of human NK cells. Research in his laboratory is supported by NCI, NIH, MACC Fund, Nicholas Family Foundation, and Lulu's Lemonade Stand.
- **Sean Marks, MD's** research interest is in Palliative Care Education among physicians in training, prognostication, and psychological issues at the end of life.
- **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 clinical trials, specifically cooperative group clinical trials and drug development.
- **Marcelo Pasquini, MD, MS's** research interest is clinical trials in HCT in multiple myeloma, acute leukemia, myelodysplasia, autoimmune diseases and in GVHD prophylaxis. Additionally, his research includes studying approaches to reduce post-transplant complications and applications of cellular therapies for treatment of different diseases.
- **Wendy Peltier, MD's** research interests include quality improvement models for 'upstream' palliative care in cancer and advanced heart failure, and creating models for inpatient hospice in the ICU setting.
- **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.

- **Mary Rhodes, MD's** research interests include 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.
- **Kimberly Ridolfi, MD's** research interests include treatment of solid tumors and quality care of our veterans.
- Research in **Matthew Riese, MD, PhD's** lab focuses on understanding how T cells are affected by the tumor microenvironment, and how they can be manipulated to overcome the inhibitory mediators present within that environment. Dr. Riese's laboratory focuses on diacylglycerol kinases, proteins that serve as intracellular brakes to dampen T cell activity, and PECAM-1, a cell adhesion proteins that is required for efficient TGF-beta signaling in T cells.
- **Paul Ritch, MD's** clinical research focus includes patients with gastrointestinal malignancies with particular interest in pancreatic cancer. He is part of a multidisciplinary research team conducting multimodality clinical trials in patients with early stage disease and is involved in protocols evaluating new strategies and novel agents targeting pancreatic cancer cells and tumor stroma and extracellular matrix in advanced disease.
- **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 interest is in understanding and optimizing communication between patients with advanced hematologic malignancies and their providers. She is particularly interested in how physicians help patients make decisions regarding their care. 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 endothelial, platelet and macrophage biology as they relate to common vascular diseases, including atherosclerosis, thrombosis and tumor angiogenesis. Dr. Silverstein's work centers on a cell signaling system mediated by the type 2 scavenger receptor CD36. As a receptor for thrombospondin in microvascular endothelial cells, CD36 mediates critical anti-angiogenic responses. 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.
- **Liza Thiel, MD, MS's** research interest is in Palliative Care Education in the community setting.
- **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.

- The laboratory of **Li-Shu Wang**, **MD** is investigating the ability and mechanisms of active metabolites from black raspberries (BRBs) to influence colon and pancreatic cancer immunology through epigenetic modifications. The results from animal models of both cancer types indicate that the berries dampen tumor-induced immune suppressive microenvironment by decreasing CD11b+ myeloid cells, and boosting CD8+ T-cell and natural killer cells. In an effort to translate these findings from laboratory to clinical use, Dr. Wang is collaborating with Dr. Ehab Atallah on the effects of black raspberries on DNA methylation in patients with myelodysplastic syndrome (MDS). This trial was awarded the Kurtis Froedtert CTO Seed Grant in January 2017. The aim of this clinical trial is to evaluate the hypomethylating properties of BRBs in patients with MDS monthly for 12 weeks of BRB supplementation.
- **Jo Weis, PhD's** research interests include psychological phenomena at the end-of-life including anticipatory grief and post-traumatic symptomatology.
- **Gilbert White, MD's** research focuses on the role that blood platelets play in heart disease and strokes. Specifically, he is using genetic and proteomic approaches to study the intracellular signaling pathways that mediate integrin activation, a key event in platelet aggregation. The overall goal of his work is to understand the signaling processes in order to identify drugable targets that will more safely and effectively modulate platelets. Rap1b is a small GTPase in platelets that has features of a bidirectional regulator of integrin activation. His current work is aimed at understanding the mechanism of rap1b action.
- **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. Dr. Wong received funding to develop a smartphone app for managing oral mucositis pain associated with head and neck radiation therapy. He also received an RO1 NIH grant with Ming You, MD. PhD, to study a new agent in patients with oral cancer.
- **Fenlu Zhu, PhD's** research interest has been focusing on immunotherapy especially preclinical process development and validations; large-scale cGMP manufacturing of cellular products including patient cell purification, expansion, transduction and formulation; product characterization and release testing; technology transfer from research bench to clinical production; quality control, FDA regulations and FACT accreditations; SOP preparation and investigational new drug (IND) applications; immune monitoring and correlative studies pre and after cellular therapy infusion. Related to this area, cellular therapy products have been manufactured under cGMP for clinical trials including multi-specific (EBV, CMV and Adenovirus) cytotoxic T lymphocytes (CTL) in G-Rex system and CD20_CD19 dual chimeric antigen receptor (CAR) T cells using CliniMACS Prodigy Device for the treatment of B cell malignancies.

Division of Infectious Diseases

The Division of Infectious Diseases is involved in multidisciplinary and collaborative research efforts with internal and external partners. Primary research components include:

Clinical Research:

Faculty are engaged in a variety of clinical research trials conducted in collaboration with research networks and industry sponsored-trials. Dr. 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. Several additional HIV treatment, HIV prevention, and Influenza Phase III drug trials and network trials are also in active enrollment, and will determine the safety and effectiveness of various new treatments.

The Division also studies infection control and hospital epidemiology. Dr. 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*. 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, the Clinical Microbiology Laboratory, and the Hematology-Oncology Department. 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.

Translational Research:

Dr. Cockerham is completing a study entitled "Diurnal variation in HIV Measurements and T Cell Populations". The aim of this study is to determine whether HIV DNA and RNA levels in the blood fluctuate during the day as preliminary data has shown that levels of unspliced HIV RNA may differ within the same individual depending on time of collection. This would greatly impact the design of HIV "cure" studies. Secondary aims include studying the trafficking of T cells subsets and levels of plasma cortisol and catecholamines over the course of the day and to determine how they might be related to fluctuations in HIV DNA/RNA levels.

Dr. Aldrete is conducting a study to better understand why some people living with HIV have poor CD4 cell recovery even while they are taking antiretroviral therapy. These individuals are known as immune non-responders (INR). She is interested in looking at how different CD4+ metrics predict the development of AIDS and non-AIDS related outcomes. She is performing a retrospective study that aims to compare the various definitions of INRs currently found in the literature in order to determine which definitions are most effective in identifying true risk for poorer long-term outcomes. This study is also identifying the CD4+ T-cell count recovery pattern most predictive of adverse events using a complex modeling approach. By providing a better definition for which patients are immune non-responders, this work has the potential to more precisely identify individuals at risk for increased morbidity and mortality and allow clinicians to focus their efforts on reducing these poor health outcomes.

In addition, a study is being conducted to determine the sensitivity and specificity of a new test for methicillin-resistant *Staphylococcus aureus* (MRSA). This test has the potential increase the likelihood of identifying MRSA carriers and identifying them more rapidly in a hospital or outpatient setting.

Banking Studies:

The Division conducts banking studies, in which data or biospecimens are collected and stored for future, unspecified research purposes. An observational, prospective study is currently enrolling persons who are hospitalized with suspected or confirmed Influenza or other targeted non-influenza viral respiratory infections, such as MERS-CoV and SARS-CoV. This study will provide information on risk factors for mortality and other adverse outcomes, as well as provide specimens for use in virus characterization, including subtyping, antigenic and genetic analyses, identification of signature mutations associated with antiviral drug resistance, mutational evolution, and additional re-assortment of the flu virus. The non-influenza respiratory virus study will characterize initial cases and their outcomes in order to develop more specific protocols that could help in the prevention and treatment of these new infections.

Behavioral and Community Research:

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. Dr. 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.

Bench Research:

There are several ongoing laboratory-based research projects headed by key members of the Infectious Diseases division.

Dr. 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.

Bench research is also aimed at addressing international health issues. Currently, an NIH-funded collaborative study led by Dr. Michael Kron is 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). 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, which, with 7,100 islands, is considered one of five biodiversity hotspots worldwide.

Division of General Internal Medicine

Overview

The Division of General Internal Medicine (GIM) has an active and nationally known research and scholarship program. Areas of focus within the research programs of GIM include patient outcomes, patient-physician communication and decision-making, and medication education. Research efforts are based at both the Medical College of Wisconsin campus and the Clement J. Zablocki VA Medical Center. The infrastructure to support research efforts in GIM includes standing research conferences twice a month, collaborative efforts with faculty in the Center for Advancing Population Science (CAPS), and a critical mass of clinician-investigators based in GIM. Faculty in GIM are actively involved in the dissemination of their work through peer-reviewed publications and participation at regional and national scientific meetings of the Society of General Internal Medicine (SGIM) as well as other professional organizations. Faculty in GIM have held national leadership positions in SGIM and the Society for Medical Decision Making (SMDM). Research efforts often involve collaborative work with other Divisions and Departments both within MCW and with other institutions.

Outcomes Research

One area of research focus in GIM is outcomes research. Faculty are engaged in research that utilizes large administrative and clinical databases to address questions regarding the relationship of patterns of care to clinical outcomes. The GIM research group has a large amount of experience and expertise in the use of Medicare and SEER (Surveillance, Epidemiology, and End Results) databases to address research questions regarding patterns of care and patient outcomes. Clinical areas of interest that are currently being evaluated with this methodology include screening and treatment patterns for breast cancer, prostate cancer and osteoporosis. The GIM faculty work closely with core faculty in the Center for Advancing Population Science (CAPS) who bring expertise in the areas of economics and psychometrics.

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.

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 six full-time clinical research coordinators, full-time research assistant, three basic science support staff and a part-time system specialist 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.

Ongoing clinical and translational research studies in the Division focus on:

- **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)** looking at long and short-term treatments and outcomes in conjunction with quality of life.
- **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 45 active projects, 27 industry, 18 IIT, 12 grants with 8 funding through the CTSI/AHW and 4 awards with the CF Foundation. These projects are primarily led by: J Biller, MD, V Bonne MD, R Franco MD, D Ishizawar MD, D Kogan MD, 9-R Lipchik MD, MD, R Nanchal MD, J Patel MD, K Presberg MD, V Ramalingam MD, A Taneja MD, T Ferrer Marrero MD, K Maso MD, & J Truwit MD. Supported by; Jeanette Graf RM, Rachel Harris and Stephanie Zellner CRC IIIs, Erin Hubertz and Ashley Wuerl CRC IIs, Amy Blair CRC I, Shama Sharwani System Specialist II and Shannon Broaddrick RA III.

2018 has brought several new opportunities of research and collaboration to our department, we look forward to the many new endeavors on the horizon.

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 SLE and scleroderma, and participating in clinical trials of SLE, scleroderma, myositis and rheumatoid arthritis. We are always interested in collaborations and have expertise that spans bench research, industry-sponsored clinical trials and investigator-initiated human studies. We have a full time clinical research coordinator at FMLH 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 laboratory 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 recently described as a novel mediator of ATP efflux in chondrocytes. She has also recently begun a project to explore the role of osteoprotegerin mutations in CPPD which involves studies of osteoclastogenesis. Current local collaborators at MCW include James Ninomiya, M.D. and Brian Volkmann, Ph.D.. Dr. Rosenthal is a standing member of the Skeletal Biology Structure and Regeneration study section at NIH, and a mentor for the US/Canada Bone and Joint Initiative Young Investigators Workshop. She also has active research interests in SLE, funded by the Lupus Foundation of Wisconsin. 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 Medical Director of the CTSI-funded VA Translational Research Unit.

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 in retroperitoneal fibrosis, IgG4-related diseases and currently participates in a clinical trial of polymyositis.

Division of Endocrinology, Metabolism, and Clinical Nutrition

The Division of Endocrinology, Metabolism, and Clinical Nutrition has continued to maintain a high level of research and scholarly activity. All of our current full-time faculty have been or are currently involved in our clinical or basic-science research programs. Our physicians and investigators collaborate with many basic and clinical departments in order to advance the research mission.

We would like to welcome Marcelo Bonini, PhD, and Zeljko Bosnjak, PhD. Dr. Bonini joined the Endocrinology Research team in February. His research is focused on how changes in the electrochemical potential of the cell (or organelles) impact how the cell works, behaves, interacts with neighbors and affects tissue or the body homeostasis. Dr. Bosnjak joined Endocrinology in March, transferring from the Department of Anesthesiology. His work is focused on cardioprotection by volatile anesthetics.

Endocrinology, Metabolism, and Clinical Nutrition has 19 active projects managed by eight faculty members: Robert Blank, MD, PhD; Marcelo Bonini, PhD; Zeljko Bosnjak, PhD; Carol Everson, PhD; Srividya Kidambi, MD; Theodore Kotchen, MD; Daisy Sahoo, PhD; Mary Sorci-Thomas, PhD. We are the recipients of funding through: Advancing a Healthier Wisconsin, National Institutes for Health, American Heart Association, Department of Defense, and the Veterans Health Administration. Our research has been published in: *American Journal of Hypertension, American Journal of Physiology, Lung, Cellular and Molecular Physiology, Biochimica et Biophysica Acta, Breast Cancer Research and Treatment, Case Reports in Oncology, Circulation Research, Current Opinion in Lipidology, Endocrine, European Journal of Endocrinology, Free Radical Research, Hypertension, Journal of the American Heart Association, Journal of American Society of Hypertension, Journal of Bioenergetics and Biomembranes, Journal of Biological Chemistry, Journal of Lipid Research, Journal of Trace Elements in Medicine and Biology: Organ of the Society for Minerals and Trace Elements (GMS), Metabolism: Clinical and Experimental, Nature Structural & Molecular Biology, Oncogene, Oncotarget, Physiological Reports, Research in Social & Administrative Pharmacy, Structure, The Hypothalamic – Pituitary – Adrenal Axis in Health and Disease, Cushing's Syndrome and Beyond, Toxicology, Transgenic Research*. Our areas of interest include: cholesterol metabolism and cardiovascular disease; bone metabolism; vascular biology; behavioral and neurological studies in rat models, and concussion; and metabolic syndrome, obesity, diabetes, hypertension, cholesterol, anesthetic cardioprotection, breast cancer and macrophage inflammation.

The TOPS Obesity Center, in partnership with the Division of Endocrinology, is exploring the causes and treatment of obesity through medical research. Thousands of TOPS members and their families have participated in research projects to unravel the genetic basis of obesity and the metabolic syndrome, the "TOPS Obesity Genes Project" being one of the largest projects.

Ongoing clinical and translational research studies in the Division focus on understanding the biology of different fat tissue depots, the differences between these types of fat tissue at the molecular level; how changes in dietary salt affect genes and ultimately the blood pressure; if the genetic material (DNA) obtained from the patient approximately 10 years ago is predictive of complications often associated with high blood pressure, including stroke, heart disease, and kidney disease; and ACTH and cortisol dynamics in human disease.

2018 has brought exciting opportunities of research to our Division, and we look ahead with enthusiasm to future research endeavors. We are dedicated to the mission and vision of this organization to further educate and improve the health of those we serve.

Division of Geriatrics & Gerontology

The Division of Geriatrics & Gerontology is engaged in a variety of clinical and educational research areas, which are intended to advance patient care and innovate/optimize geriatrics 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. These awards have sparked program and faculty development in the areas of undergraduate, graduate and continuing medical education.

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: The Geriatrics Workforce Enhancement Program (GWEP). One focus of this award is continuing professional development using geriatrics though the Part IV Maintenance of Certification (MOC) process targeting primary care providers at MCW as well as other GWEP affiliates (UW and Aurora). Another focus has been the maintenance and expansion of MCW's Geriatrics Fast Facts, a repository of brief, to-the-point summaries of a discrete clinical problem. Funding for this HRSA award has been extended through June 30, 2019.

The Division maintains a variety of clinical research interest areas. These include: geriatrics syndromes (falls, delirium, urinary incontinence); quality improvement studies; community home nursing care; hospice/end-of-life care; patient perceptions and self-management of chronic illnesses such as diabetes and congestive heart failure; application of technology for improving patient self-management and health behaviors; musculoskeletal conditions in aging; aging and immune function; multi-morbidity and frailty. Active, cross-disciplinary collaborations are addressing minority health disparities and obesity, Latino elders with dementia and their caregivers, physical activity and aging, and risks and potential interventions to address unplanned, post-surgical hospital readmissions. These research initiatives have been funded through the National Institutes of Health, the Agency for Healthcare Research and Quality (AHRQ), Veteran's Health Administration, and the Healthier Wisconsin Partnership Program, among others.

The Division participates in the MCW NIA T-35 award that supports 10 undergraduate medical students in summer research each year. Dr. Edith Burns is a Division faculty member and the Co-PI of this award that was successfully funded in 2017. In addition, Dr. Burns has been appointed a faculty member in the Graduate Studies program at MCW, and has mentored half a dozen faculty, doctoral and master's degree students in their thesis work. One of her students was awarded a MS at the MCW 2018 commencement. She has also been mentoring a junior faculty member at MCW and three junior faculty at Marquette University for the past several years.

Other Division research-related activities have included serving on AHRQ Study Sections as grant reviewers, committee work for the Society of Behavior Medicine (Medication Adherence Topic Chair for the annual meeting; Program Planning Committee for 2019), participation on the ZVAMC R&D committee, and on one of the MCW IRB committees.

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 fMRI, event-related potentials (ERP), magnetoencephalography (MEG), transcranial magnetic stimulation (TMS), and structural MRI. Clinical research focuses on new methods for quantitatively characterizing the structural and functional connections between brain regions that make up epileptic networks, language mapping prior to brain surgery, and on understanding recovery from 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 drug trials test the effectiveness of promising new therapeutics for the treatment of MCI and early AD as well as the prevention of AD in people with normal cognition 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).

Under the leadership of Dr. Janet Rader, Chair of OB/GYN and Dr. Ramani Ramchandran, Vice-Chair of Research in OB/GYN, 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 including from basic science to translational clinical science promoting collaboration. OBGYN Research faculty including lab staff meet once a month to discuss their work, topics of interest are discussed. Within FY18, the department has submitted over 25 grants application.

Notable accomplishments include:

- **Dr. Pradeep Chaluvally- Raghavan** received an extramural $563,272 grant award for 3 years from the Department of Defense to research his project titled, "*R- Targeting miR551b to Prevent Tumor Formation and Metastasis of Triple Negative Breast Cancer.* Dr. Chaluvally- Raghavan also received intramural totaling $70,000 from cancer center to research ovarian cancer.
- **Dr. Ling Wang** received an extramural $569,934 grant award for 3 years from the Department of Defense to research his project titled, "*R- Regulation of tumor cell ANGPTL4 by astrocyte-secreted TGF-beta2 in triple negative breast cancer brain metastases*"
- The Women's Health Research Program (WHRP) has awarded grant for research project to **Anna Palatnik, MD** assistant professor of OBGYN, along with Alison Kriegel, PhD associate professor of physiology, received funding for a project titled "*The role of micro-RNA 223 in the pathogenesis of preeclampsia"*
- **Dr. Janet Rader**, Professor and Chair of OBGYN along with Dr. Kristina Kaljo, assistant professor of OBGYN applied for R25 and received favorable outcome with pending decision from NIH.
- **Dr. Tamjid Chowdhury**, an OBGYN post-doctoral fellow in the Ramchandran laboratory received an American Heart Association post-doctoral fellowship award of $106,532 for 2 years
- First MFM research fellow graduation – **Dr. Anna McCormick** is first fellow to graduate 2018

Other key programmatic initiatives include:

- **WHRP SEMINAR SERIES:** This seminar series is held once every month on Thursdays 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. The seminar series has seen increased attendance over the years, and has increasing influence over OBGYN research trajectory.
- **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 met the midpoint in recruitment. We opened several phase I trials enabling cancer patients to receive novel drugs and early access to biologic agents. Maternal Fetal Medicine physicians have opened several fetal therapy and studies for the management of hypertension in pregnant women and recruitment is robust.
- **RESEARCH IN PROGRESS MEETINGS:**-Every Wednesday of the month, basic scientists and clinicians meet in the OBGYN department in a lab meeting format. This group is steadily growing to over 20 plus members each meeting. At each meeting, one member presents their work, and receives feedback on directions and resources available on campus or within department that might facilitate collaboration. This interactive format has resulted in progress of research projects, and general awareness of lab methodology and expertise of members in OBGYN 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. This meeting is chaired by Dr. Janet Rader.

- **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 group is a monthly meeting that 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:** Dr. Tamjid Chowdhury, an OBGYN post-doctoral fellow published a first author paper in the respected Arteriosclerosis, Thrombosis and Vascular Biology (ATVB) journal. Publications in other frontline journals from OBGYN faculty is available in the OBGYN web page. Abstracts were also presented at national and regional meetings.

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 faculties 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, from individual donations to National Institutes of Health grants, enables our researchers to take a multidisciplinary approach to improving the fundamental understanding, diagnosis and management of eye diseases. As a leader in clinical and translational research, Vision Science Research at MCW supports a solid platform for innovation, collaboration and discovery. Learn more about our Corporate Ventures.

CORE Grant for Vision Research

The Department of Ophthalmology is proud to be the center of a Core Grant for Vision Research from the National Eye Institute (NEI) that has been continuously funded for more than 40 years. The current grant supports four shared-use resource Modules under the direction of principal investigator, Dr. Joseph Carroll, Richard O. Schultz, MD / Ruth Works Professor in Ophthalmology, Co-Director, AOIP.

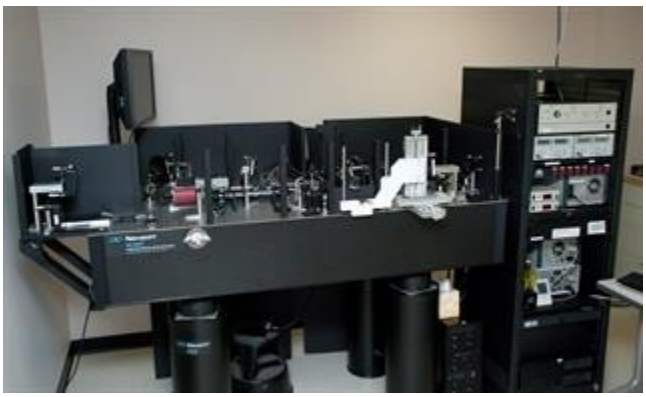
The research supported by the grant contributes to new knowledge about the development and function of tissues of the eye and for the prevention and treatment of many eye disorders. This grant supports four shared-use resource modules to assist scientists located at the Eye Institute as well as the vision scientists in the departments of anesthesiology, biochemistry, biophysics, pediatrics, radiology, and cell biology, neurobiology & anatomy for their studies of the eye and visual system.

Core Grant Modules

- Noninvasive Assessment of Animal Models, Joseph Besharse, PhD
- Biochemistry/Molecular Biology, Witold Karol Subczynski, PhD, DSc
- Morphology & Microscopic Imaging, Brian Link, PhD
- Engineering & Translational Imaging Module, Joseph Carroll, PhD

Advanced Ocular Imaging Program

The Advanced Ocular Imaging Program (AOIP) was created 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.



In 2011, Dr. Alfredo Dubra was recruited to the AOIP. Dr. Dubra had collaborated with Dr. Carroll since 2007 on the development and application of ophthalmic adaptive optics technology. The strength in adaptive optics imaging, specifically our commitment to apply the technology with the patient in mind, laid the foundation for the AOIP today.

In conjunction with Dr. Dubra's recruitment, the Department of Ophthalmology made a major investment to renovate the existing laboratory space on the 8th floor of the Eye Institute to house the AOIP. A dedicated waiting area for patients and their families, 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. In addition, there continues to be investment in the most valuable resource of the AOIP – people. The AOIP currently consists of over 40 faculty, staff, and students. In January of 2013, Dr. Dubra replaced Dr. Han and co-directed the program with Dr. Carroll until October of 2016 when he left for Stanford University.

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. In pursuit of this aim, OGTL actively focuses on several key areas of research.

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
dfriedland@mcw.edu

Pathology

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; serving our community; and developing leaders. Our vision is to be a nationally respected pathology department, leading the pursuit of cutting edge diagnostics, education, research, and community outreach.

Vision: A nationally respected 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 in campus and with outside institutions in funded research.

Active collaboration in funded projects is promoted through our Clinical and Translational Research Core Lab, which houses the capability to support researchers throughout campus with a variety of specialized molecular techniques on solid tissue samples. 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.

Cancer Genetics Program

The Cancer Genetics Program is an important component of the Department of Pathology's efforts at advancing cancer research in collaboration with the Cancer Center. The lab is located at the fourth floor of the Translational and Biomedical Research Building. The lab is equipped with state-of- the-art technology for modern molecular biology and genetics research. It provides research training opportunities for research fellows as well as clinical fellows. Currently, the lab is composed of one research technician who supports laboratory investigation and three postdoc fellows who are involved in intensive research training in the areas of Cancer Genetics, Translational Medicine and Bioinformatics.

The research focus of the lab is in genome variation and human cancer. Specifically, the lab is interested in investigating the genetic basis of human cancers including prostate, esophagus and lung cancer using gene expression profiling, genomewide SNP genotyping, systems biology-based network analysis and large scale case- control association studies. The lab is also interested in the development of cancer biomarkers including prostate, pancreas, colon and lung by testing blood/tissue DNA/RNAs in well-characterized patient populations using genome- wide methylation, next generation sequencing and bioinformatic approaches. Examples of the research efforts currently being carried out include a large scale RNA sequencing project that aims to analyze RNA sequences in over 500 prostate cancer patients. The goal is to identify genes and genetic variants that contribute to aggressive forms of prostate cancer. Another project is to identify blood-based biomarkers that can predict drug response and clinical outcomes in prostate and colon cancer patients. This project also uses large scale next generation sequencing technology and examines circulating RNAs as potential biomarkers for early detection and outcome prediction. In the next few years, the lab is expected to lay a solid foundation as a leader in this emerging cancer research field. The research activities of the lab are being supported by grants from the National Institute of Health and Advancing a Healthy Wisconsin Foundation.

Clinical and Translational Research Core Lab (CTRL)

The Clinical and Translational Research Core Lab (CTRL) combines two major components in one lab: histopathology and molecular pathology. The CTRL provides basic histopathology, research immunohistochemistry, tissue microarray, laser capture microdissection, and molecular biology services to researchers at the Medical College of Wisconsin and within the surrounding academic community.

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

Pediatrics

We value a diverse research agenda in the Department of Pediatrics. Our agenda is integrated through the priorities of our academic and hospital partners and includes a strong mentorship component for new investigators. The goal of this agenda is to improve the health of the children of our region. To reach this goal, we actively engage and coordinate investigative teams across divisions to take advantage of Departmental strengths.

Improving survival is a primary goal of our **oncology** program. Dr. Cindy Schwartz is the new leader of the Hematology-Oncology-Transplant Section. Dr. Schwartz comes to MCW from the MD Anderson Cancer Center, where she served as the Department Chair and the Director of Clinical and Translational Research for the Division of Pediatrics. In particular, her research has focused on the treatment of Hodgkin lymphoma. The group includes Dr. Jeff Medin a leading expert in lysosomal storage disorders and gene therapy, who directs the GMP facility as part of our MACC Fund Center Developmental Therapeutics program. Other key investigators involved in the cellular therapy program include Drs. Monica Thakar and Julie Talano. They are investigating the use of natural killer cell infusions to prevent relapse in patients with leukemia and the use of donor-derived cytotoxic T cells to prevent viral infections after transplants.

The Department of Pediatrics **hematology** program offers comprehensive services for the treatment of children with acute and chronic blood diseases, including sickle cell disease. The program is a nationally recognized, federally funded center of excellence for bleeding and thrombotic disorders, and includes one of the country's leading basic research programs in hemophilia and von Willebrand disease. Dr. Julie Panepinto uses patient reported outcomes to determine the comparative burden of disease in children with sickle cell disease. This multicenter study is funded by a U19 grant from the NIH. In another NIH-funded project, Dr. Veronica flood is investigating the molecular interactions between VWF and collagen 4 in hemostasis. For our entire hematology faculty, there is a close intertwining of research interests with clinical work to bring the lab to the bedside and the bedside to the lab.

A focus on **immunology** is another Departmental strength, where the theme of close cooperation between clinical and research faculty is also a priority. We approach the immune system through multiple perspectives, including those of immunodeficiency, neonatal lung disease, mucosal immunity, diabetes, inflammatory homeostasis and immunogenetics / epigenetics and immunotherapy. Drs. Jack Routes and James Verbsky utilize recent advances in immunogenetics to define the molecular basis of profound lymphopenia in infants. Dr. Ganesh Konduri studies how necessary respiratory interventions in the newborn often incite inflammation and lead to chronic lung disease. His work is complemented through the efforts of Dr. Joanne Lagatta. Dr. Lagatta studies how we treat infants with chronic lung disease. Other key investigators are Dr. Nita Salzman and Dr. Marty Hessner. Dr. Salzman's NIH-funded research focuses on the role of antimicrobial peptides produced by Paneth cells in host defense and gut homeostasis. The primary interest of Dr. Marty Hessner's laboratory involves using cytokine signatures to identify autoimmune profiles that predict the development of type 1 diabetes. Dr. Hessner' s work has led to the development of relevant bioassays. We are grateful for the support Dr. Hessner receives from the Max Magee Foundation, as well as the NIDDK.

Importantly, the Department of Pediatrics offers multiple structured opportunities for junior faculty to develop competitive grant proposals. These include a weekly "K Club" for the review of the Specific Aims page, and an annual 3-day grant writing retreat. These mentored activities are central to the success of our junior 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, under the direction of Ji-Geng Yan, MD, PhD, Associate Professor, 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. The laboratory is also active in fMRI research. Our commitment to community service is noted in our annual medical mission trip and in our community education presentations.

Psychiatry and Behavioral Medicine

The Department of Psychiatry and Behavioral Medicine is a dedicated community of compassionate, expert, inspired, professional clinicians, academicians, staff, and trainees committed to improving the lives of persons affected by psychiatric diseases, concurrent disorders, behavior-related illnesses, and social-environmental conditions impeding mental health. This mission is accomplished through the pursuit of six core values: (1) scholarship and research, (2) education, (3) clinical service, (4) community engagement, (5) bioethical principles, and (6) leadership and administration.

Current contributions by faculty within the Department of Psychiatry and Behavioral Medicine include:

Joseph S. Goveas, MD, Associate Professor

Depressive symptoms, Family History of AD, and Brain Structure and Function: This project will determine the independent and additive contributions of elevated depressive symptoms and family history of late-onset Alzheimer's disease on gray matter volumes, brain function and white matter microstructure in asymptomatic middle-aged adults.

Multimodal Imaging in Depressed Adults at risk for Alzheimer's Disease: This study will identify the functional and structural connectivity correlates in depressed adults at risk for Alzheimer's disease.

Retinal biomarkers of Alzheimer's disease: This is a collaborative project between MCW faculty from Departments of Psychiatry, Neurology and Ophthalmology that utilizes novel retinal imaging techniques to detect retinal phenotypes that discriminates patients with mild cognitive impairment and Alzheimer's disease from cognitive healthy volunteers.

Ultra-high-field Structural MRI in Late-Life Depression and Normal Aging: This collaborative project between MCW faculty from the Departments of Psychiatry, Biophysics and Radiology will utilize ultra-high-field structural brain image datasets obtained on 7T MRI to characterize the medial temporal lobe subregional volumes, and white matter hyperintensities and cerebral microbleeds that will differentiate late-life depression from healthy volunteers.

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 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.

Jeffrey A. Kelly, PhD, Professor

The **Center for AIDS Intervention Research (CAIR)** in the Department of Psychiatry & Behavioral Medicine was first established in 1994 and has successfully competed for renewed funding since then. The Center began its 25th year in 2018. CAIR adopted a mission statement that emphasized interventions as the Center's thematic focus. Much has changed in the field since that time, and CAIR's research has evolved in response to new needs. However, our thematic focus remains the **scientific study of HIV prevention interventions**:

"**CAIR's mission is to conceptualize, conduct, and scientifically evaluate the effectiveness of new intervention strategies to prevent HIV infection in populations vulnerable to the disease**. CAIR's research also develops improved strategies to promote health and alleviate adverse mental health consequences among persons living with HIV. 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 mission 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 HIV prevention methods.

CAIR is the only NIMH-supported HIV behavioral research Center located between the nation's east and west coasts. We are a resource to investigators, institutions, and service providers from across the broad midsection of the country. The Center is also a scientific field leader at both national and international levels.

Within the framework of its thematic mission on intervention research and emerging from intensive Center-wide priority-setting, the following specific aims guide CAIR's research:

(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 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-related disparities through research that identifies and responds to the needs of racial and ethnic minority populations with greatest HIV incidence and disease burden;

(5) As the only NIMH AIDS Research Center (ARC) located in the center of the United States, to develop, evaluate, and lead in the implementation of high-impact HIV prevention and to serve as a resource to health departments, providers, researchers, and community constituencies in mid-sized and underserved cities across the broad midsection of the country.

CAIR's Core Structure

Administration Core: Strategic planning, administrative oversight, integrated decision–making

Developmental Core: Innovative new and pilot project development, early-stage investigator support, Center seminars, conferences, and internal peer review

Qualitative Core: Qualitative and ethnographic research expertise and resource support to Center studies

Quantitative Core: Methodological, design, data management, and statistical analysis expertise

International Core: Resource, logistics, and cross-cultural research support for international studies

Dissemination and Implementation Science Core (DISC): Resources for partnership development, design, and evaluation of implementation science initiatives

Center leadership includes:

- Jeffrey A. Kelly, PhD. – Center Director
- Yuri A. Amirkhanian, PhD. – Director – International Core
- Julia Dickson-Gomez, PhD. –Director – Qualitative Core and Co-Director – Dissemination and Implementation Science Core
- Carol L. Galletly, J.D., PhD. – Director – Developmental Core
- Timothy McAuliffe, PhD. – Director – Quantitative Core
- Jennifer Walsh, PhD. – Co-Director – Dissemination and Implementation Science Core
- Karen M. Opgenorth, M.S. – Director - Administration Core

Jennifer M. Knight, M.D., M.S., Assistant Professor

Dr. Jennifer Knight has a research interest in **psychoneuroimmunology and cancer**, specifically regarding the **neuroimmune mechanisms** involved in mediating the relationship between **psychosocial factors and hematopoietic stem cell transplantation outcomes**. She has secondary appointments in the Departments of Medicine (Hematology/Oncology) and Microbiology & Immunology and works in conjunction with the MCW Clinical Cancer Center and the Center for International Blood and Marrow Transplant Research (CIBMTR) to investigate these mechanisms in both local clinical trials as well as nationally representative populations of stem cell transplant recipients. Dr. Knight is the recipient of a **Clinical and Translational Science Institute KL2 Career Development Award** granted to junior faculty with significant promise of establishing an independent research career in clinical and translational science.

With **American Cancer Society** funding, Dr. Knight and her collaborators Dr. J. Douglas Rizzo (MCW) and Dr. Steve W. Cole (UCLA) identified that stem cell transplant recipients of low socioeconomic status have altered gene transcription profiles previously characterized as the conserved transcriptional response to adversity (CTRA). Dr. Knight and her team identified that this shift in gene expression was also associated with adverse outcomes among transplant recipients. This work has been further corroborated and defined as part of Dr. Knight's KL2-funded project. Dr. Knight received **NCI/Leidos Biomed** funding to conduct a prospective randomized controlled trial of propranolol among autologous transplant recipients at MCW and demonstrated that this drug is capable of altering this adverse CTRA gene expression profile associated with social health disparities. Dr. Knight also collaborates with Dr. Carol Williams (cancer biology, MCW), to investigate how propranolol may be affecting Rap1b prenylation patterns, a mechanism of tumor spread and progression.

Dr. Knight also collaborates with Drs. Cecilia Hillard (Neuroscience) and William Drobyski (stem cell transplant) at MCW investigating the neuropsychiatric effects of inflammation as a function of tocilizumab administration among allogeneic transplant recipients (**Advancing a Healthier Wisconsin** funding). Their group has discovered that, counter to what supporting scientific literature had speculated, the anti-IL6 drug tocilizumab actually worsened depression, anxiety, sleep, and pain. This group is conducting ongoing work to better understand the mechanisms by which this is happening.

Jeffrey M. Engelmann, Ph.D., Assistant Professor

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.

New to MCW, 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 earliest research findings demonstrated that potentiated startle can be used as a measure of negative affect in both nicotine-dependent rodents and humans, demonstrating its translational potential and promise as a biomarker for negative affect in preclinical studies of new medications for nicotine dependence. In the human study, he expanded upon the traditional approach to studying cue reactivity that only compares responses to smoking cues and neutral stimuli to an

approach that compares the relative reactivity to smoking cues and neutral, pleasant, and unpleasant stimuli. With **National Cancer Institute funding**, Dr. Engelmann used fMRI to study the neurobiological basis of relative differences in cue reactivity. He found that brain responses to smoking-related and pleasant cues in the striatum, a brain area involved in reward processing, are predictive of long-term smoking cessation: smokers with larger responses to pleasant stimuli than smoking-related cues are more likely to successfully quit than those with larger responses to smoking-related cues than to pleasant stimuli. Interestingly, smokers in the "lower risk" (pleasant stimuli > smoking cues) group showed equal benefit from varenicline or bupropion for smoking cessation, but those in the "higher risk" (smoking cues > pleasant stimuli) were more likely to benefit from varenicline than bupropion, which suggests that pre-quit assessment of relative cue reactivity might contribute to the personalization of smoking cessation treatment. With startup funding from MCW, Dr. Engelmann is extending this finding to a more diverse and representative group of smokers, and he is applying for R21 funding to study whether individual differences in relative cue reactivity contribute to race-related disparities tobacco use.

Dr. Engelmann is also the recipient of a **mentored career development award from the National Institute on Drug Abuse**. The goal of this grant is to investigate the effect of the imminent possibility of smoking on brain responses to smoking-related cues, a condition that more closely resembles relapse. He is currently analyzing the data from this project and is also submitting an R03 application to conduct secondary analysis on the data collected from this study and another one of his fMRI studies, the goal of which is to examine the impact of mentholated cigarettes on brain responses to smoking cues. This secondary analysis will provide the preliminary data necessary for an R01 application aimed at studying the contributions of menthol to the addictiveness of tobacco products and to race-related disparities in smoking.

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: 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 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.

Under the leadership Dr. Vince Mathews, Chair of Radiology, and Dr. Kathleen Schmainda, Vice-Chair of Radiology Research, the research arm of radiology continues its efforts to further strengthen and better serve the research needs of the faculty, residents and fellows. This includes a quarterly "research forum" where research updates are given, topics of interest are discussed and collaborations promoted.

The radiology research seminar series continues with both internal and external speakers covering a wide range of topics from basic to translational clinical science. Most recently a database administrator has been hired with a goal of building the informatics networks that enable both research and clinical questions to be addressed in a more efficient fashion. This positions Radiology well in the new era of "big data".

Finally, a quantitative imaging lab (QIL), which expands the capabilities of Radiology to support clinical trials will be ready for business this year.

The benefits of an increased and strengthened research support staff are already apparent with two new NIH grants in the areas of brain cancer MRI, awarded to Dr. Peter LaViolette, and use of MRI in patients with musculoskeletal implants, awarded to Dr. Kevin Koch.

In addition, the Database Administrator is working to consolidate and build a robust system to aid in research. The planned solution uses data virtualization to reduce the amount of data stored redundantly and reduce the amount of computer programming required. Also included in the proposed solution is the ability to search note fields through the implementation of Natural Language Processing (NLP.) NLP is a method that analyzes free-form text or speech based on rules and patterns in the data and converts the data into a structured format that can be easily queried and manipulated. The resulting solution will not only allow for searches using data across the disparate systems, but also the ability to search through notes. Neither of these functions are presently available to the department. A small Proof of Concept implementation is under construction.

Overall research activity within the Department of Radiology continues to grow. Within the past year, the Department has submitted approximately 60 grant applications, and has collaborated on over 40 other grant applications. Current fiscal year research revenue includes a $ 950K NIH funding, which should exceed $1Mil. by Fiscal 17 year end, currently 25% over Budget. We also have several Multi-PI Federal Grants submitted with other Institutions.

Other Extramural revenue has increased 40% YTD compared to Fiscal Year 16. This increase is largely due to the Division of Interventional Radiology and the fellowship and clinical trial funds they seek annually. Sponsors with recognizable names such as Society of Interventional Radiology, Radiological Society of North America, Siemens, GE, Guerbet, CR BARD, Cook Medical, Penumbra, DFINE, W.L. Gore and Associates, Medtronic, InSightec, The Froedtert Hospital Foundation, The Musella Foundation have new and ongoing collaborations with the Department of Radiology.

We continue to receive awards on campus from the Cancer Center, CTSI, AHW, the Center for Imaging Research (CIR) Pilot grants. The Department is also just beginning several new Investigator Initiated Studies, to further the partnership with Industry. In Pediatric research, the department received Awards from the CRI and $50K directly from the Kelleigh's Cause Foundation. Those funds have allowed the recruitment of the first Kelleigh Gustafson AVM Research Fellow, Dr. Shahram, Eisa-Beygi to aid in the study of arteriovenous malformation.

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 2016-2017 academic year, the MCW Division of VIR continued to expand its clinical and translational research activities. The Division opened 1 new clinical trial and continued research activities in 9 ongoing clinical trials. Their research endeavors have resulted in 7 publications, 3 grants, 7abstracts and 13 poster presentations at national and international meetings. This research could not have been done without the dedication of the VIR research coordinator, Elizabeth Weil. Elizabeth has been working with the PIs and the IRB to utilize the IRB's new Flex Review process. Herein we will highlight some of the pivotal trials our faculty have been involved with over the past year:

- Vice-chair of Clinical Operations, **William S. Rilling, MD, FSIR** continues to build his research interests, which are focused on image guided therapy for cancer. SIRFLOX was completed this past year and we continue to enroll in the ongoing trial TS-102 EPOCH. A potential upcoming phase 2 HCC study will evaluate a new drug combating the hypoxic response in combination with transarterial embolization.
- VIR Division Chief**, Sean M. Tutton, MD, FSIR** completed enrollment of patients in the STARRT trial, that evaluated treatment of vertebral metastatic lesions with concurrent pathologic fractures. Dr. Tutton also launched multiple MR guided Focused UltraSound clinical trial protocols at MCW for the treatment of metastatic bone and soft tissue lesions.
- Chief of the Clement J. Zablocki VA Medical Center, **Robert A. Hieb, MD, FSIR** completed his study, where he serves as PI, evaluating 3D imaging to guide needle trajectory during TIPS. The data will be presented this fall in Copenhagen. He was also instrumental in getting BEST-CLI open at the VAMC.
- **Eric J. Hohenwalter, MD, FSIR** continues his work on IVC filters, and currently serves as PI for the PRESERVE study which evaluates 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.
- **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. He served as PI for the ATTRACT trial, whose data was presented in Washington, D.C.
- **Sarah B. White, MD, MS. FSIR** continues work in her translational research laboratory at MCW with an emphasis on interventional oncology. Her laboratory is highly collaborative, and she is working with Drs. Joshi, Flister and LaViolette. Her work received the top abstract of the year at the 2017 WCIO annual meeting. She is on her 2nd year of a 3 year 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. She is PI for the upcoming RETNET trial, evaluating the efficacy of liver directed therapy in metastatic neuroendocrine cancer.
- **William B. Lea, MD** continues to focus on utilizing navigational software to enhance current treatment algorithms, and has teamed up with Siemen's medical on ongoing trials.
- **Alexandra H. Fairchild, MD** recently joined the group and is currently working on evaluating the palliative care education among interventional radiology 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, General Surgery, Pediatric Surgery, Surgical Oncology, Transplant Surgery, Trauma and Critical Care, and Vascular Surgery. The Department's dedication to research is further demonstrated in the recent addition of 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 2017-18 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 Cardiothoracic Surgery, Adult

In clinical research, **David Johnstone, MD** is MCW Principal Investigator for the Spiration EMPROVE Clinical Trial for Severe Emphysema. The Spiration Valve is a small, umbrella-shaped, one-way valve placed inside the airways of one lung to redirect air from less healthy to more healthy parts of the lung. The goal is to reduce over-inflation and improve overall lung function and quality of life for people living with emphysema. The sponsor submitted a PMA to the FDA in January of this year.

George Haasler, MD is the Site Principal Investigator for the pilot study "Quantification of Cell Free DNA to Determine Rejection Following Lung Transplantation" sponsored by TAI Diagnostics, Inc. The objective of this study is to quantify levels of circulating donor-specific cell free DNA in lung transplant recipients. The study will allow investigators to describe relationships between cell free DN and important clinical events, such as rejection, which may allow use of this technology as a noninvasive alternative to biopsy for monitoring the health of transplanted lungs. William Ragalie, MD, Surgery Resident is managing this study.

David Joyce, MD is the MCW Principal Investigator for the "SynCardia 70cc Total Artificial Heart (TAH-t) for Destination Therapy (DT)". 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 this study 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 and are not eligible for heart transplantation. This use is called destination therapy (DT).

David Joyce, MD is the MCW Principal Investigator for the "SynCardia 50cc Temporary Total Artificial Heart (TAH-t) as a Bridge to Transplant (BTT)". The purpose of this study is to evaluate whether the 50cc TAH-t can support patients who are imminent risk of death from biventricular heart failure, are eligible for heart transplantation, and for whom the 70cc TAH-t is not appropriate due to size of the chest cavity.

David Joyce, MD is the MCW Principal Investigator for the "TandemHeart Experiences and Methods THEME Registry". The TandemHeart percutaneous extracorporeal ventricular assist system is used to support circulation. It is anticipated that THEME Registry analysis will provide insight into disease defining characteristics resulting in the clinical decision to use TandemHeart for mechanical support and enhance knowledge of best practice regarding clinical management, weaning and removal.

Chart Review Studies:

- Short and Long-Term Outcomes in Mechanical Circulatory Support (MCS) Devices (D. Joyce)
- A Retrospective Chart Review Study of the Safety and Efficacy of a Modified Del Nido Cardioplegia Protocol in Complex Aortic Surgery Involving the Use of Deep Hypothermia and Circulatory Arrest (C. Rokkas)
- Comparison of Traditional Transhiatal Esophagectomy to Transhiatal Esophagectomy with Transcervical Endoscopic Esophageal Mobilization (D. Johnstone)
- Outcomes in Solid Organ Transplantation; A review of the UNOS Database (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 also 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.

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.

Michael E. Mitchell, MD and **Aoy Tomita-Mitchell, PhD** manage 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. Dr. Michael Mitchell is PI of the CHD Tissue Bank, a biorepository of DNA and surgical discards from CHD patients. He is the PI of an AHW grant investigating the role of the *MYH6* gene in Hypoplastic Left Heart Syndrome (HLHS) using patient specific induced pluripotent stem cells. Dr. Aoy Mitchell and her collaborators received a CTSI grant to study the effect of *MYH6* variants on cardiomyocyte biomechanics and patient outcomes in HLHS. She and her collaborators have also received a grant from the Greater Milwaukee Foundation to bioprint patient-specific cardiac cells on a 3D tissue construct. Other significant studies in the Mitchell lab include investigating the etiology of Ebstein's Anomaly with Left Ventricular Noncompaction, and testing 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. Dr. Michael Mitchell is also the PI of a multi-site, five year, NHLBI/NIH R01 grant to study cell-free DNA in cardiac transplant rejection.

Professor **John Baker's** research program serves as a nexus to translate basic science discoveries into clinical applications. Dr. Baker is collaborating with cardiac surgeons and cardiologists to improve outcomes in children with congenitally corrected Transposition of the Great Arteries. He is also studying why survivors of childhood cancer, who have been treated with radiation therapy, have an increased risk for heart disease and how to mitigate this deleterious outcome. 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 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 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. Dr. Ludwig has national reputation as an expert in the surgical treatment of rectal cancer with special emphasis on sphincter sparing techniques.

Dr. Mary Otterson's primary research effort is currently focused on a rodent model of radiation enteritis. This work is done in collaboration with Dr. Gourlay (Pediatric Surgery) and Dr. Baker (Cardiothoracic Surgery). Dr. Otterson has been exploring the role of intestinal alkaline phosphatase in the prevention of the acute intestinal response to radiation. The team is currently using a knock out and heterozygous rat model. Interestingly, diminished levels of intestinal alkaline phosphatase are found in patients with Crohn's disease. Dr. Otterson is working with Dr. Carrie Peterson on the efficacy of neurostimulation in reducing postoperative pain. She is completing a long-term project on colonic and bladder function in spinal cord injured veterans.

Dr. Timothy Ridolfi was awarded the American Society of Colon and Rectal Surgeons Career Development Award. This three-year award is funding a project that is aimed at evaluating the changes that occur within the enteric nervous system following resection for rectal cancer. This work builds on our previous work in the basic science lab utilizing an animal model. Dr Ridolfi's second grant funds a project utilizing 7 Tesla MRI to evaluate the quality of excised rectal cancer specimens and response to neoadjuvant therapy. This MRI equipment is one of only 20 such devices worldwide and is located within the MACC fund building at MCW. This work is done in collaboration with the departments of Pathology, Radiology, and Biophysics. Dr. Ridolfi was also awarded access to the NCDB database for rectal, colon and anal cancers.

Dr. Carrie Peterson continues to pursue her research interests in minimally invasive colorectal surgery and surgical outcomes. She is involved in several research projects evaluating improvements in postoperative pain control and perioperative process improvements. She is currently the principal investigator of a study evaluating the efficacy of neurostimulation in reducing postoperative pain. Dr. Peterson recently completed a Masters' Degree in Clinical and Translational Science, with her thesis being a meta-analysis of the utility of intravenous acetaminophen in reducing opioid use in patients undergoing colorectal resection.

The division is excited to welcome **Dr. Hu** as the 2018-2020 Colorectal Research Resident. Dr. Hu is completing her General Surgery residency at the Medical College of Wisconsin (MCW) and will be working with the Division for 2 years. She will have a very active role in the multitude of current ongoing projects within the division.

Utilizing funds from the Lachman Family Summer Research Student Foundation and the Quasi endowment, this year, our Division supported the summer research efforts of three medical students. Projects this summer included, evaluating functional outcomes following chemo-radiation for anal cancer and evaluation utilization and response rates to induction chemotherapy for 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.

Division of General Surgery

The Division of General Surgery supports the Department's commitment to excellence in education and research. Over the 2017-2018 academic year, faculty and research staff collaborated to develop 18 new research protocols, added to ongoing investigations through 45 more, showcased the institution's innovative efforts through presentations at 34 local, regional, and national meetings, and brought in over $350,000 in research funding. Throughout the academic year the division faculty mentored 18 medical students and 3 general surgery residents. Our research is focused in the domains of foregut surgery (upper GI, esophagus, stomach), bariatric surgery (metabolic and weight loss surgery for obesity), hernia surgery, and surgical quality.

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. In the Fall of 2017, we were fully reaccredited for the maximum 3-year cycle. Reaccreditation is a rigorous process that requires collaboration between research staff (who maintain the quality outcomes database and help organize quality improvement efforts), bariatric surgeons, hospital personnel, and the entire multidisciplinary bariatric surgical team. To remain accredited requires an annual Quality Improvement Project. We turned our QI projects ultimately into research and were fortunate enough to improve quality and outcomes while presenting our work on a national stage and publishing our findings in major peer reviewed journals. These QI projects and their associated manuscripts were entitled "Perioperative Factors Influencing Urinary Retention after Laparoscopic Inguinal Hernia Repair", "Perioperative Bleeding and Blood Transfusion is a Major Risk Factor for Venous Thromboembolism Following Bariatric Surgery", and "Perioperative complications increase the risk of venous thromboembolism following bariatric surgery".

We continue to explore outcomes following bariatric surgery using both our own institutional data and national datasets such as NSQIP, the national MBSAQIP registry, and the Truven Marketscan database. **Tammy Kindel, MD, PhD** collaborated with faculty from the Comprehensive Weight Loss Center, the Center for Microbiome Research, and the Genome Sciences and Precision Medicine Center on a protocol exploring the influence of perioperative antibiotic use on gastrointestinal microbial composition to determine whether it impacts post-operative hypertension resolution in gastric bypass patients. **Rana Higgins, MD** and Tammy Kindel, MD, PhD also collaborated with faculty from the Department of Anesthesia to develop a randomized, prospective study on the impact of preoperative carbohydrate loading on postoperative nausea and vomiting.

We have an ongoing and successful collaboration with Srividya Kidambi, MD, MS, an Endocrinologist and researcher in obesity. Current collaborative projects include studies exploring the relationship of adipose tissue specific microRNA with obesity and type 2 diabetes mellitus, as well as adiposity distribution and MicroRNA in obesity pathogenesis.

Throughout the academic year the division's faculty, staff, residents, and students published 17 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, Surgery, and the Journal of Laparoendoscopic* and *Advanced Surgical Techniques*.

Foregut Surgery

In the 2017-18 academic year, the division participated in numerous multi-institutional sponsored trials on gastroesophageal reflux disease (GERD) surgical outcomes using implantable medical devices. We enrolled patients a randomized controlled trial designed to compare outcomes following surgery to implant a magnetic sphincter augmentation device (LINX) with acid suppression medications on GERD. We also participated in post-market studies on the magnetic sphincter device and studied outcomes following implantation of a novel biologic mesh at the diaphragm in hiatal hernia repair. Faculty teamed with colleagues from across Wisconsin to examine long-term patient experiences following implantation of a gastric electrical stimulation device (Enterra) in patients with medically refractory gastroparesis. **Dr. Gould** presented these findings at Central Surgical Association and the results were accepted for publication in *Surgery.* The Division's fellow, quality resident, and students participated in several research projects in foregut surgery outcomes and presented their findings at Wisconsin Surgical Society, Academic Surgical Congress, and Society of American Gastrointestinal and Endoscopic Surgeons (SAGES). Peer-reviewed manuscripts were accepted to Annals of Surgery, *Journal of Laparoendoscopic* and *Advanced Surgical Techniques, Surgical Endoscopy, the Journal of Gastrointestinal Surgery,* and *Surgery.*

Hernia Surgery

Hernia surgery outcomes is an area of clinical excellence and academic interest for faculty in the Division. Sponsored projects and investigator-initiated studies in the hernia domain included studies designed to evaluate outcomes following implantation of numerous different types of mesh, studies evaluating recovery from hernia surgery and mechanisms to enhance this recovery, and quality focused initiatives.

Joseph Helm, MD, general surgery resident, was mentored by Rana Higgins, MD, on a quality initiative exploring the influence of blood transfusions on the important metric of surgical site infections. Dr. Helm's project entitled, "Perioperative Blood Transfusions Increase Risk of Surgical Site Infection Development in Ventral Hernia Repairs" was the recipient of the 2018 MCWAH Research and Quality Award. Dr. Helm presented his research at the 2018 International Hernia Congress.

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 through identifying and implementing best practices, benchmarking MCW's outcomes to peer institutions, and providing real-time feedback to surgeons. The Division's hernia research efforts were presented locally at MCW, regionally at the *Wisconsin Surgical Society*, and nationally at meetings of the *Academic Surgical Congress, Southwest Surgical Association,* and the *International Hernia Congress*.

Surgical Quality

Dr. Gould was appointed Vice Chair for Quality in the Department of Surgery and worked to continue joint research efforts between General Surgery and other departments including *Otolaryngology and Communication Sciences* and *Medicine*, *Gastroenterology,* and *Endocrinology,* as well as expand the Division's role in surgical quality.

Lindsey Clark, MD, served as the 2017-2018 Surgical Quality Improvement and Research Resident under the mentorship of Dr. Gould. Throughout the academic year, Dr. Clark served as a member on several institutional quality committees including the Rothman Index Workout Group, Discharge When Medically Ready Team, 7 and 8 NT Accountable Care Teams, and Froedtert Hospital's Safety and Adverse Events Committee. Dr. Clark also worked with Chief Quality Officer Siddhartha Singh, MD and Dr. Gould to investigate the causes of very early readmissions (within 72 hours) following surgical procedures on a national level. This work was presented at the 2018 Academic Surgical Congress and is to be published in a peer reviewed surgical journal. During her research year, Dr. Clark presented her work on the podium at 3 national surgical society meetings and will finish with at least 3 peer reviewed publications. In addition, Dr. Clark worked hard to improve the visibility and knowledge of quality improvement projects and patient safety to faculty, APPs, and residents through initiatives such as the Quality Minute" and the Quality in Training Initiative (QITI) through the American College of Surgeons National Surgical Quality Improvement Program (NSQIP). Throughout the academic year, **Matthew Goldblatt, MD**, surveyed operating room staff, nurse anesthetists, surgical specialties residents, and faculty to characterize the culture of reporting adverse events and breaks in the sterile field. Dr. Goldblatt is designing educational initiatives for the 2018-2019 academic year as a result of his findings.

The Division of General Surgery is proud of the quality people and projects it produces year after year and looks forward to continuing this work in 2018-19 and beyond.

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** was awarded an NIH R01 grant for his research on mechanisms of oxidative stress and inflammation in sickle cell disease. He has also begun research 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. Robert Miao's** lab is also NIH funded and investigates the roles of Nogo-B receptor (NgBR) in the pathogenesis of various diseases, including fatty liver diseases, tumor resistance to chemotherapy, and cerebral cavernous malformation.

Our clinical research program is one of the founding members of the Midwestern Pediatric Surgical Consortium (MPSC), through which our division is a collaborator on several multi-institutional studies. As part of the MPSC, a number of our surgeons participate in clinical studies examining congenital pulmonary airway malformations, anorectal malformations, spontaneous pneumothorax, esophageal atresia and tracheoesophageal fistula (EA/TEF), and appendicitis.

One of the first major initiatives of the MPSC was led by **Dr. Dave Lal** to examine the treatment of EA/TEF. This work led to several published manuscripts on the diagnosis. Dr. Lal is also the site PI for the MPSC 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, MPSC** is also developing a protocol to prospectively study venous thromboembolism prophylaxis in trauma patients. Dr. Gourlay is also co-Investigator on an NIH study to investigate mechanisms of injury and need for a trauma center in pediatric patients.

We have the good fortune to work collaboratively in large, multi-institutional studies in the United States and abroad. **Dr. Casey Calkins** is our site's PI in a NIH funded study led by Vanderbilt University examining early versus late repair for neonates with inguinal hernias, in what is known as the HIP study. In addition to this, Dr. Calkins is a steering committee member of a national registry of anorectal malformations (Pediatric Colorectal and Pelvic Learning Consortium). This multi-center consortium will investigate variations in care of these patients that lead to optimal outcomes.

As Surgical Program Director of Fetal Concerns Center of Wisconsin and an investigator associated with the North American Fetal Therapy Network, **Dr. Amy Wagner** oversees the GOOD study, a large, multi-institutional study examining the outcomes of early versus late delivery in prenatally diagnosed gastroschisis. She has a number of research projects related to maternal-fetal care.

Dr. Marjorie Arca leads many quality improvement initiatives as leader of the division's Pediatric National Surgical Quality Improvement Program and is currently working with providers across Wisconsin to create a collaborative to implement QI initiative for umbilical hernias. Dr. Arca also maintains a vast surgical case log that serves as a valuable tool in many quality improvement projects.

Dr. Keith Oldham is the PI of Children's Hospital of Wisconsin's Clinical Outcomes Registry (COR), which continues to collect annual quality of life data from over 400 neonatal surgery patients. Dr. Oldham is also a founding board member of the GICS which aims to improve pediatric surgery care across of the globe.

Dr. Sabina Siddiqui is the division's global health liaison, studying surgical illness across the globe and a member of Global Initiative of Children Surgery (GICS). Dr. Siddiqui is establishing partnerships to examine improvement is 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.

Dr. John Densmore has a strong clinical interest in Congenital Chest Wall Malformations and currently investigating the use of non-operative means to correct chest wall anomalies.

Dr. Thomas Sato spearheaded a study examining the clinical course and healthcare costs of patients with acute appendicitis, specifically looking at differences of duration of symptoms at time of presentation, perforation rates, length of hospital stay, and complications of patients with private insurance and patients who are uninsured or are covered by government assisted programs.

Lastly, our program has several retrospective chart review projects, including projects investigating the pain management and opioid use in appendicitis patients, the role of hypothermia in surgical site infections, outcomes in ovarian torsion, and surgical site infection prophylaxis in neonates.

Division of Transplant Surgery

The Research Program in the Division of Transplant Surgery focuses on liver and kidney transplantation and surgical diseases of the liver and bile duct. As a multi-faceted program, basic science research is undertaken in the laboratory of Chief and Professor **Johnny Hong, MD**; clinical science and translational research is pursued by transplant faculty and researchers at Froedtert Hospital, Children's Hospital of Wisconsin, The Blood Center of Wisconsin, UW Milwaukee, Concordia University, Cleveland Clinic, and Washington University in St. Louis. MCW Transplant Surgeons have served over 5000 patients since 1967.

Our comprehensive clinical data from years of patient care is a critical element of the Transplant Division's growing research infrastructure. As part of the Transplant Surgery's academic infrastructure over the years, an extensive clinical database has been maintained; in 2014, the MCW Institutional Review Board (IRB) approved a transition of that clinical database, with IRB approval, to a REDCap database now entitled the Solid Organ Transplantation Data Bank, with data available for program management, quality assurance, and research.

Another element of the research infrastructure is Dr. Johnny Hong's basic science laboratory housed in the Cardiovascular Research Center at MCW. Current research is focused on regulated hepatic reperfusion, to mitigate the adverse effects of ischemia and reperfusion injury (IR) in porcine circulatory death liver transplant model. In addition, Dr. Hong's lab is studying the effects of hepatic steatosis on IRI in a rat model, and the influence of extracellular adenosine in a mouse IRI model.

Current ongoing studies involving Divisional Faculty in academic year 2017-2018 include the following:

- TRANSFORM: A 24 month multicenter, randomized, open label safety and efficacy study of concentration – controlled everolimus in kidney transplant recipients.
- Determine the effect of regulated hepatic reperfusion in a DCD swine liver transplant model and mitigate IRI through novel treatment.
- Assessment of hepatic IRI measured by bile transporter expression in a rat IRI model with hepatic steatosis.
- Investigate the influence of extracellular adenosine signaling on leukocyte-mediated hepatic injury in a mouse IRI model.
- Pre-Habilitation in Patients Awaiting Liver Transplantation.
- Incompatible Organ Transplantation in High Risk Donors.
- Cycle Ergometer Therapy in Transplant ICU patients.
- Liver Biopsies to study Ischemic Reperfusion Injury
- A Randomized, Controlled, Open Label Clinical Trial of Thymoglobulin Induction and Extended Delay of Calcineurin Inhibitor Therapy for Renal Protection after Liver Transplantation.
- Staged Bile Duct Reconstruction in the Share 35 Era
- Outcomes in Transplant Mental Health Group Therapy
- Platelet Refractoriness and Alloimmunization in Liver Transplantation
- A Phase 3 Study to Compare the Efficacy and Safety of Humacyte's Human Acellular Vessel with that of an Autologous Arteriovenous Fistula in Subjects with End-Stage Renal Disease

Collaborative efforts with other MCW researchers include:

- Testing new interventions for discharge teaching of post-transplant patients at Froedtert Hospital under the direction of Stacee Lerret, Ph.D., Assistant Professor of Pediatrics at MCW.
- Application of novel cardiac blood enyzyme tests for the solid organ transplant population under the direction of Michael Mitchell, MD, Professor of Surgery in the Pediatric Congenital Cardiac Surgery Division at MCW, sponsored by TAI Diagnostics.
- Studying the role of myeloperoxidase inhibition in hepatocellular injury in collaboration with Kirkwood Pritchard, Ph.D., Professor of Pediatric Surgery at MCW.
- Addiction in End Stage Renal Disease: Identification of Neurocognitive Profiles and Risk Factors for Transplant with David Sabsevitz PhD, Professor of Clinical Neuropsychology at MCW.

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 2018 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 includes global health and randomized controlled trials for improved surgical outcomes in trauma patients.

Dr. Marshall Beckman's research is focused on the management of hypothermia.

Dr. Tom Carver completed a randomized controlled trial of early ketamine administration in adult and elderly multiple rib fracture patients in hopes to reduce pain and to decrease overall opiate requirements and side effects.

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. Chris Davis is investigating the role of the Stop the Bleed training on students and computed tomography prediction of need for rib stabilization.

Dr. Chris Dodgion is researching the burden of surgical disease on global populations including in Haiti and utilizing national databases to understand the incidence of acute medical issues in need of surgical intervention.

Dr. Joshua Hunt utilizes advanced statistical methods to understand factors that constitute PTSD and the confluence in risk for poor outcomes in those with and without a traumatic brain injury.

Dr. Jeremy Juern is conducting research on the utility of endoscopic retrograde cholangiopancreatography in bile leaks.

Dr. David Milia's research focus includes a multicenter trial relate to venous thromboembolism in trauma patients, complications related to tracheostomies, and incidence of UTIs in trauma patients.

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. Jacob Peschman is evaluating airway device management in trauma patients, delirium in the geriatric trauma patient, and education level of discharge materials for trauma patients.

Dr. Colleen Trevino leads research focused on understanding the conversion from acute to chronic pain in adult injured patients and developing novel models of 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.

Continuing Research Education: Drs. Joshua Hunt and 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 Surgery continued to expand its clinical research activities throughout the Academic Year 2017/2018 by continuing a NIH trial in collaboration with the Division of Interventional Radiology, an Aortic Device Trail and a Phase I drug trial. Additionally, the division participated in several clinical outcome reviews, vascular device registries, and device trials.

Peter Rossi, MD, as site PI (Principal Investigator) at FH (Froedtert Hospital), is one of the top enrollers 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 Bolton Medical. Dr. Rossi continues to run 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 data collection to assess the outcomes associated with the use of the GORE® EXCLUDER®, an approved iliac graft. Dr. Rossi continues to acquire clinical outcome data for two projects: "Vascular Surgery Groin Infections" and "Outcomes of Ruptured Abdominal Aneurysms".

Cheong Jun Lee, MD, and Parag Patel, MD, Interventional Radiologist, serve as site co-PIs in their respective fields for 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. As of summer 2018, national enrollment has reached nearly 1400 patients with MCW as one of the top enrolling sites. Vascular Surgery and Interventional Radiology continue to collaborate on four active trials evaluating new technical devices for endovascular therapy.

Dr. Lee is also the Medical Director of the Vascular Quality Initiative at FH which is a collaborative of regional quality groups collecting and analyzing vascular data with efforts to improve patient care. Recently, in conjunction with Standford University faculty, he co-authored a paper which has received top awards in a SVS poster competition with the manuscript submitted to the Journal of Vascular surgery for publication. Dr. Lee continues as site PI for two Endologix clinical trials, the Nellix® EndoVascular Aneurysm Sealing System and the LEOPARD trial in which patients are randomized to the Endologix AFX® system or the leading competitor devices for EVAR (Endovascular Aneurysm Repair). Both continue to follow patients for outcomes. Additionally, he continues to conduct several projects, "Outcomes after EVAR", "Infection Outcomes When IrriSept is Used in Lower Extremity Bypass and/or Endarterectomy Procedures" and "Outcome Differences after Carotid Intervention". Most recently Dr. Lee has opened a Phase I Trial with Proteon Therapeutics in patients with PAD.

Max Wohlauer, MD recently authored "Walking Capacity of patients with Claudication in Lower Extremities Following Ischemic Preconditioning". Studying the effects of patient-initiated therapy and is currently planning an investigator-initiated trial studying the platelet responsiveness to assess the most effective antiplatelet therapy for patients after vascular intervention. Earlier this year Dr. Wohlauer spearheaded the expansion of the MCW tissue lab trial into the FMLH clinics starting with our own Vascular Surgery clinic.

Vascular Surgery faculty **Brian Lewis, MD, Kellie Brown, MD and Michael Malinowski, MD** participate as co-investigators on all Vascular Surgery clinical trials and protocols. Charles Edmiston, PhD, Emeritus Professor, continues to publish on a variety of topics related to the prevention of surgical site infections. The faculty are also involved in clinical trials and outcomes research at the Clement J Zablocki VA Medical Center.

Contribution to the division's research efforts by MCW 2017/2018 Vascular Surgery fellows, **Abby Rothstein MD**, who recently joined our faculty, and **Nicholas Saguan MD**, along with the department's research residents, medical students and Research Nurse Coordinator, **Beth Weseman, RN** are invaluable and remain a critical element of 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), **Caitlin R. Patten, MD, Miraj G. Shah-Khan, MD, Alonzo P. Walker, MD, 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 (formerly MCW's Patient Care and Outcomes Research Center). Our faculty also collaborate with the basic science faculty at the medical school on translational research projects.

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 and National Surgical Adjuvant Breast and Bowel Project (NSABP). Tina Yen, MD, MS, serves as the institutional principal investigator for the Alliance for Clinical Trials in Oncology cooperative group and Alonzo Walker, MD, is the institutional surgical oncology leader for the NRG 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 – 2018 academic years, the Endocrine Surgery research program had >20 oral/poster presentations at the national/regional/local level and published >30 peer-reviewed publications and book chapters. During the 2018-2019 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.

Our faculty are also actively engaged in both the Surgical Oncology Tissue Bank and the MCW Central Tissue Bank to store healthy and tumor tissue that would otherwise be discarded at surgery. This tissue is then made available to cancers researchers who have obtained the proper institutional permissions to conduct research using it. The Section also has

received funding, secondary to submission of tissue to The Cancer Genome Atlas (TCGA) Pheochromocytoma/Paraganglioma (PCPG) and is a member of the TCGA PCPG Analysis Working Group.

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. As active members of the MCW Cancer Center, Surgical Oncology GI Faculty participate in numerous NIH-sponsored cooperative group clinical trials coordinated by the Cancer Center Clinical Trials Office (CTO).

Two areas of translational research include: the use of natural products for chemoprevention in hepatobiliary cancers (**Dr. Muthusamy Kunnimalaiyaan and Dr. T. Clark Gamblin**) in addition to the study of cell free DNA as a therapeutic biomarker (**Dr. Susan Tsai**). Dr. Tsai also spearheads the pancreas cancer Tumor Donation Program which allows patients to provide metastatic tissue for use by qualified research teams. The Division also coordinates a high risk pancreatic cancer screening clinic, which is co-directed by a genetic counselor (**Jenny Geurts, CGC**).

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. Based on the belief that tissue and blood specimens are an invaluable resource, the Surgical Oncology Tissue Bank (SOTB) was established in 2010. This bank stores blood throughout a patient's oncologic treatment from the time of diagnosis onward. The SOTB also stores oncology patients' resected tumors. Benign and malignant pancreas, liver and adrenal tissues that would otherwise be discarded at surgery are also stored. Clinical data is linked to stored tissue, blood and data which are then available to qualified researchers. Located in and managed by the Tsai laboratory, the SOTB has created a rich resource for investigation and collaboration. The Tissue Bank was identified as an essential core facility in a recent P01 application to study the basic and translational biology of pancreatic cancer and continues to support multiple research collaborations including external collaborations with MIT, Van Adel Institute, Baylor University, and the Wisconsin Donor Network as well as internal collaborations within MCW.

Division of Research

Together, our mission in the Division of Research is to advance the careers of research-intensive faculty, enhance the departmental culture of academic achievement, foster inter-division, interdepartmental and inter-institution collaborations, and facilitate the resident research program. We are committed to continuing our own research as well serving as advocates for research in the department. We will work tirelessly to fulfill our vision to be *leaders in surgical research*, *advancing medicine through scientific discoveries*.

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.

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.

Michael James, PhD, has a laboratory focused on understanding key tumor cell survival and therapy resistance mechanisms and exploiting them for better cancer therapy. Broadly, his expertise lies in molecular and cellular pathobiology of cancer. He applies this expertise to the functional evaluation of novel tumor-associated proteins. The application of murine modeling, cell biology and molecular biology techniques has allowed him to elucidate CLPTM1L/CRR9 as a novel anti-apoptotic oncology target that is necessary for oncogene-induced transformation and tumorigenesis. Dr. James has developed disease-representative, patient-derived, 3D organoid models of pancreatic cancer in collaboration with Drs. Evans and Tsai, building upon their surgical biorepository for pancreatic cancer. These personalized models have been utilized in the study of stromal and immune interaction with pancreatic tumor tissues. Dr. James has been awarded WeCare and ACS grants for his work on CRR9-mediated chemotherapy resistance and several recognition awards, investments, and in-kind awards for his efforts to drive novel anti-CRR9 therapeutics to first-in-human trials through a biotechnology startup spun out of MCW.

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

- Multicenter industry sponsored randomized trial of abobotulinum toxin (Dysport) for the management of neurogenic bladder
- 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

Education

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