Research Week

April 17 – 21, 2023

Presented by the Office of Research

Digital Event Catalog

Welcome!

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

This week is designed to inspire new knowledge, boost collaboration, and spark discovery with a variety of programming from researchers at all levels. Events include five poster sessions, nine unique mini-symposiums designed by our research centers, multiple talks by national speakers, and a day of programming devoted to our exceptional research cores. We are pleased to host Research Week in person this year with hybrid options for many events.

Thank you to everyone who has contributed to Research Week. We look forward to engaging and collaborating during this celebration of research at MCW.

Table of Contents

Specialty Programs, Cores, and Shared Resources

Schedule of Events

Monday, April 17

10:00 a.m. – 11:00 a.m.

MFRC #3075 and via Zoom

Zoom

Add to Calendar

Mellowes Center for Genomic Sciences & Precision Medicine Mini Symposium

"Facilitating and Implementing Science in 'Omics and Systems Biology"
Speakers: Dr. Angela Mathison, Dr. Victor Jin and Dr. Michael Zimmerman

The Mellowes Center provides cutting-edge NGS and large-scale assays to investigate the role of the genome, transcriptome, epigenome, proteome, and other 'omics in the molecular mechanisms of cellular processes and human diseases. From extraction to library preparation and sequencing, our team uses a variety of platforms, including Illumina's NovaSeq 6000 and NanoString's nCounter, to generate novel data. Our Bioinformatics Analysis Shared Resource provides comprehensive solutions to a wide variety of research areas and 'omics data types, delivering robust analysis and interactive web-based reports. These two Mellowes Center labs support research in the Center's four pillar programs and additionally develop custom preparations and analyses to meet research needs and publication requirements for investigators throughout MCW.

10:00 a.m. – 10:30 a.m.

H1270

Add to Calendar

Core Breakout Session: Histology

"Histology – An Open Forum"
Speaker: Christine Duris

Join histology core staff to discover more about Histology Core services, explore frequent histology mistakes, and inquire about any ongoing histology projects – whether they're successful or challenging.

10:00 a.m. – 11:00 a.m.

H1320

Add to Calendar

Core Breakout Session: Translational Metabolomics (TRaM) + Imaging + MS + Redox

"Introduction of Translational Metabolmics Shared Resources (TraM SR), MCW Cancer Center"
Part 1: QIL and pre-clinical imaging (Drs. Peter LaViolette and Amit Joshi)
Part 2: Redox and Bioenergetic, and mass spectrometry (Drs. Jacek Zielonka and Kazuhiro Aoki)

The Translational Metabolomics Shared Resource (TraM SR) is a newly developing core comprised of historically separate imaging and bioenergetics cores, now complimented by new initiatives in mass spectrometry and comprehensive Multi-Omics analyses. The TraM SR provides expertise and state-of-the-art instrumentation for MCW members to investigate disease metabolism by providing services in mass spectrometry analysis, bioenergetic and redox function analyses, pre-clinical imaging, and clinical trial response assessments. The TraM SR ensures high-quality sample preparation, vetted protocols, standard operating procedures, and knowledgeable, well-trained staff. The TraM SR works with investigators on all aspects of experimental design, execution, data analysis, and manuscript preparation.

10:00 a.m. – 11:30 a.m.

H1310

Add to Calendar

iLab Support Sessions

Presenter: Erin Bentley

10:00 = General drop-in, questions, system help
10:30 = Introduction to iLab for first time or new users
11:00 = Using iLab for Poster Printing Requests

11:00 a.m. – 11:30 a.m.

H1270

Add to Calendar

Core Breakout Session: Flow Cytometry – Sorting

"How to Sore Cells Effectively, Easily and of High Quality?"
Presenter: Galina Petrova, PhD, Flow Cytometry Core

Traditional high-speed cell sorters expose cells to high pressure, charge and decompression that often damage cells and, as a result, reduces viability and may change functionality. This presentation will cover technologies and resources available at MCW that allow safe, sterile, and gentle cell sorting and yield healthy, viable cells.

11:30 a.m. – 1:30 p.m. Alumni Center Add to Calendar	**Cores Fair** Stop by to learn more about the exciting technologies and scientific support services available at MCW. 36 research cores and shared resources will be represented. Meet with core personnel to discuss your projects, ask questions, and make new connections. This is an open-house style event; refreshments will be provided. JUMP TO CORES FAIR MAP & PARTICIPANTS
12:30 p.m. – 1:00 p.m. H1320 Add to Calendar	**Core Breakout Session: Advanced Cell Imaging Core** **"Breaking the resolution limit: Super-resolution imaging as a new tool for biomedical research"** *Presenter: Xuelin Lou, PhD* This session will give you an overview of super-resolution imaging nanoscopy methods and their applications in cell biology, neuroscience, immunology, and pathology.
1:30 p.m. – 2:00 p.m. H1270 Add to Calendar	**Core Breakout Session: Flow Cytometry – Spectral** **"Spectral Flow Cytometry Delivers High-Resolution Data at the Single Cell Level"** *Presenter: Galina Petrova, PhD, Flow Cytometry Core* The Cytek Aurora system uses full spectrum flow cytometry to detect the entire fluorochrome emission and allows users to run multicolor panels without sacrificing data resolution. Use of multicolor panels provides more information from one tube and reduces the number of tubes needed in an assay, which saves precious sample, reagents, acquisition time and reduces lab operating costs. Attend this session to learn more about how the Aurora spectral flow cytometry system delivers high resolution data at the single-cell level to resolve the most challenging cell populations, such as cells with high autofluorescence or low levels of expression of key biomarkers.
2:00 p.m. – 3:00 p.m. H1310 Add to Calendar	**iLab Support Sessions** *Presenter: Erin Bentley* 2:00 = Overview of iLab billing, invoicing, and payment information 2:30 = General drop-in, questions, system help 3:00 = General drop-in, questions, system help
2:00 p.m. – 3:00 p.m. MFRC #3075 and via Zoom Zoom Add to Calendar	**Neuroscience Research Center Mini-Symposium** **"New Models for Neuroscience Delivery"** *Presenters: Allison Ebert, PhD, Pui Ying Lam, PhD, Lezi E, PhD, Ross Collery, PhD and Matthew Hodges, PhD* Attendees will learn about non-rodent preclinical models that are being used at MCW to study the nervous system.
3:00 p.m. – 4:00 p.m. MFRC #3075 and via Zoom Zoom Add to Calendar	**Cancer Center Mini-Symposium** **"Cancer Center Programs and Leadership Overview"** *Presenters: Gustavo Leone, PhD, Carol Williams, PhD, Joan Neuner, MD, MPH and William Drobyski, MD* Hear presentations on the goals, approaches, and personnel of the MCW Cancer Center, including "Cancer Center Director's Overview," "Cancer Biology Research Program Overview," "Cancer Control Research Program Overview", and "Discovery & Developmental Therapeutics Program Overview."

Tuesday, April 18

10:00 a.m. – 11:00 a.m.

Dunn Conference Room

Add to Calendar

Poster Session: Community, Education, Population Science & More

JUMP TO POSTER SESSION MAP & PARTICIPANTS

12:00 p.m. – 1:00 p.m.

Kerrigan Auditorium and via Zoom

Zoom

Add to Calendar

Distinguished Faculty Seminar in Infectious Diseases*

"The Human Genetic and Immunological Determinates of Life-Threatening COVID-19"

Jean-Laurent Casanova, MD, PhD
Levy Family Professor
Head of Laboratory, St. Giles Laboratory of Human Genetics of Infectious Diseases
Senior Attending Physician Investigator, Howard Hughes Medical Institute
Member, National Academy of Science
Member, National Academy of Medicine
The Rockefeller University

**In lieu of a Center Mini-Symposium, the Center for Infectious Disease Research invites individuals to attend Dr. Casanova's talk. The Seminar is jointly sponsored by CIDR, the department of Microbiology & Immunology, the Medical Scientist Training Program, Adult Infectious Diseases, Pediatric Infectious Diseases, and the Office of Global Health.*

1:00 p.m. – 2:00 p.m.

MFRC #3075 and via Zoom

Zoom

Add to Calendar

Center for Advancing Women in Science & Medicine Mini-Symposium

"Gender Equity at MCW: Measuring and Promoting Change"
Speakers: Leon J. Gilman, MS, Data Analyst, AWSM and ODI; Amy H. Farkas, MD, MS, Assistant Professor GIM, AWSM Women's Leadership Learning Collaborative Lead; Elizabeth (Libby) Ellinas, MD, MS, Professor of Anesthesiology, Founding Director, AWSM

The Center for the Advancement of Women in Science and Medicine (AWSM) will share data and research efforts around its three major initiatives: trend analysis, culture, and women's leadership. Participants will:

- Understand trends by gender in academic medicine at MCW and nationally.
- Follow complexities regarding AWSM's IWill, WeWill, and MCWill equitable-culture initiatives.
- Consider the effects of a women's leadership program on culture, equity and women's success.

2:00 p.m. – 3:00 p.m.

MFRC #3075 and via Zoom

Zoom

Add to Calendar

Institute for Health & Equity Mini-Symposium

"Institute for Health & Equity Research"
Speakers: Dr. Laura Cassidy; Dr. Julia Dickson-Gomez; Dr. Connie Kostelac; Dr. Aniko Szabo; Dr. Art Derse; Dr. Ryan Spellecy; Dr. Fabrice Jotterand and Dr. John Meurer

Attendees will understand and might later collaborate with IHE researchers

- Dr. Cassidy: Epidemiology and global health collaborations
- Dr. Dickson-Gomez: Tackling public health emergencies: opioid misuse and the shortage of affordable housing
- Dr. Kostelac: The role and value of data in community-engaged research and partnerships
- Dr. Szabo: Turning data into insight through collaboration with a biostatistician
- Drs. Derse, Spellecy, and Jotterand: The doctor-patient relationship, professional identity formation, and perils and pitfalls of informed consent in research
- Dr. Meurer: Evaluating coaching and a video game to improve trust, resiliency, kindness, responsibility and schoolwork in 5th to 9th graders in Milwaukee

Wednesday, April 19

9:00 a.m. – 10:00 a.m.

Dunn Conference Room

Add to Calendar

Poster Session: Clinical Research (1 of 2)

JUMP TO POSTER SESSION MAP & PARTICIPANTS

11:00 a.m. – 11:50 a.m.

Lois Martin Conference Room and via Zoom

Zoom

Add to Calendar

Center for AIDS Intervention Research Mini-Symposium

"Updates on Critical HIV and LGBTQ Research Happening at CAIR"
Speakers: Yuri Amirkhanian, PhD; Steven A. John, PhD, MPH; Jeffrey A. Kelly, PhD and Katherine Quinn, PhD

This session will include four brief presentations by CAIR investigators, highlighting some of the ongoing HIV and LGBTQ health research happening at CAIR. Topics will include the importance of social networks in HIV prevention and care, the impact of racism on efforts to end the HIV epidemic, and the effects of community and police violence on engagement in HIV care.

12:00 p.m. – 1:00 p.m.

Kerrigan Auditorium and via Zoom

Zoom

Add to Calendar

Research Week Keynote Talk

"Use of Nano-enabled Immunotherapy for Cancer and Treatment of Allergic and Autoimmune Disease at CNSI/UCLA"

Andre Nel, MD, PhD
Distinguished Professor of Medicine
Chief of the Division of NanoMedicine
Research Director, California NanoSystems Institute
Director, UC Center for the Environmental Impact of Nanotechnology
University of California, Los Angeles
Nanosafety Center Director, University of California Center for Enviornmental Implications of Nanotechnology
Associate Editor, ACS Nano

1:00 p.m. – 2:00 p.m.

Dunn Conference Room

Add to Calendar

Poster Sessions: Basic Science

JUMP TO POSTER SESSION MAP & PARTICIPANTS

2:00 p.m. – 3:00 p.m.

Lois Martin Conference Room and via Zoom

Zoom

Add to Calendar

Center for Imaging Research

"Providing Support for Imaging Research, Imaging Technology Transition, and Advanced Clinical Care"
Speakers: Kevin Koch, PhD, and Andrew Nencka, PhD

The MCW Center for Imaging Research has recently undergone significant expansion. The Daniel M. Soref Imaging Research Facility, strategically situated between the HUB and the MACC Fund Research Building, now hosts two cutting-edge 3T MRI systems. These systems facilitate a range of activities, including research projects, technology development, clinical trials, and advanced clinical care. Additionally, the facility houses a 9.4T pre-clinical small bore MRI scanner. To further support imaging research projects, the center also features a technical service core, providing access to skilled personnel.

3:00 p.m. – 4:00 p.m.

Lois Martin Conference Room and via Zoom

Zoom

Add to Calendar

Center for Advancing Population Science Mini-Symposium

"Highlights from Programs in the Center for Advancing Population Science (CAPS)"
Speakers: Leonard Egede, MD, MS; Joni Williams, MD, MPH; Joan Neuner, MD, MPH; Muska Nataliansyah, PhD and Rebekah Walker, PhD

Research in CAPS is organized within programs, allowing our multidisciplinary investigators to develop, test, and implement innovative strategies for transforming healthcare. This center mini-symposium will start with an overview of CAPS, including our vision, mission, and structure designed to support population health research. This will be followed by presentations by four of our Center programs: Collaborative for Healthcare Delivery Science (CHDS), Health Equity Research Group (HERG), Older Women's Health, and Global Health Research.

Thursday, April 20

9:00 a.m. – 10:00 a.m.

Virtual

Zoom

Add to Calendar

Comprehensive Injury Center Mini-Symposium

"An Overview of the Science and Programs in the Comprehensive Injury Center (CIC"
Speakers: Terri deRoon-Cassini, PhD; Sara Kohlbeck, PhD; Maureen Busalacchi; Reggie Moore and Constance Kostelac, PhD

The comprehensive injury center is focused on preventing injury across the lifespan. Injury in Wisconsin is driven by disparities and the CIC is focused on addressing such inequities to improve health. This session will focus on the research and programs of the CIC so the audience can gain a better understanding of potential collaborations.

11:00 a.m. – 12:00 p.m.

Dunn Conference Room

Add to Calendar

Poster Session: Translational Research

JUMP TO POSTER SESSION MAP & PARTICIPANTS

12:00 p.m. – 1:00 p.m.

Innovation Center, 1st Floor; Hub for Collaborative Medicine

Add to Calendar

Research Support & Resource Expo

Find information on administrative research resources from central offices and programs, including services, training or learning opportunities, and ask questions. This is an open-house style event; refreshments will be provided.

JUMP TO RESOURCE EXPO MAP & PARTICIPANTS

2:00 p.m. – 3:00 p.m.

Virtual

Zoom

Add to Calendar

Cardiovascular Center Mini-Symposium

"Human Induced Pluripotent Stem Cell (iPEC) Program in the Cardiovascular Center"
Speaker: Gracious Ross

In this session, attendees will learn:

- Reprogramming of somatic cells into stem cells (iPSCs)
- Differentiation of iPSCs into desired cell types
- Characterization of iPSCs / differentiated cells
- Applications of Human iPSC Technology
- Available iPSC Services at MCW-CVC hIPSC Core facility

3:00 p.m. – 4:00 p.m.

Alumni Center and via Zoom

Zoom

Add to Calendar

Research Week Translational Talk

"Reducing Global Incidence of Myopia in Kids with an MCW Technology: A Journey from Idea to a Breakthrough Product"

Jay Neitz, PhD
Professor, Ophthalmology
University of Washington

Dr. Neitz was a Professor at MCW from 1991-2008. The Neitz lab designed novel, contrast-reducing spectacle lenses to help patients manage myopia (near-sightedness).

4:00 p.m. – 5:00 p.m.

Dunn Conference Room

Add to Calendar

Poster Session: Clinical Research #2

JUMP TO POSTER SESSION MAP & PARTICIPANTS

Friday, April 21

In lieu of Research Week programming, please consider attending another research event on campus:

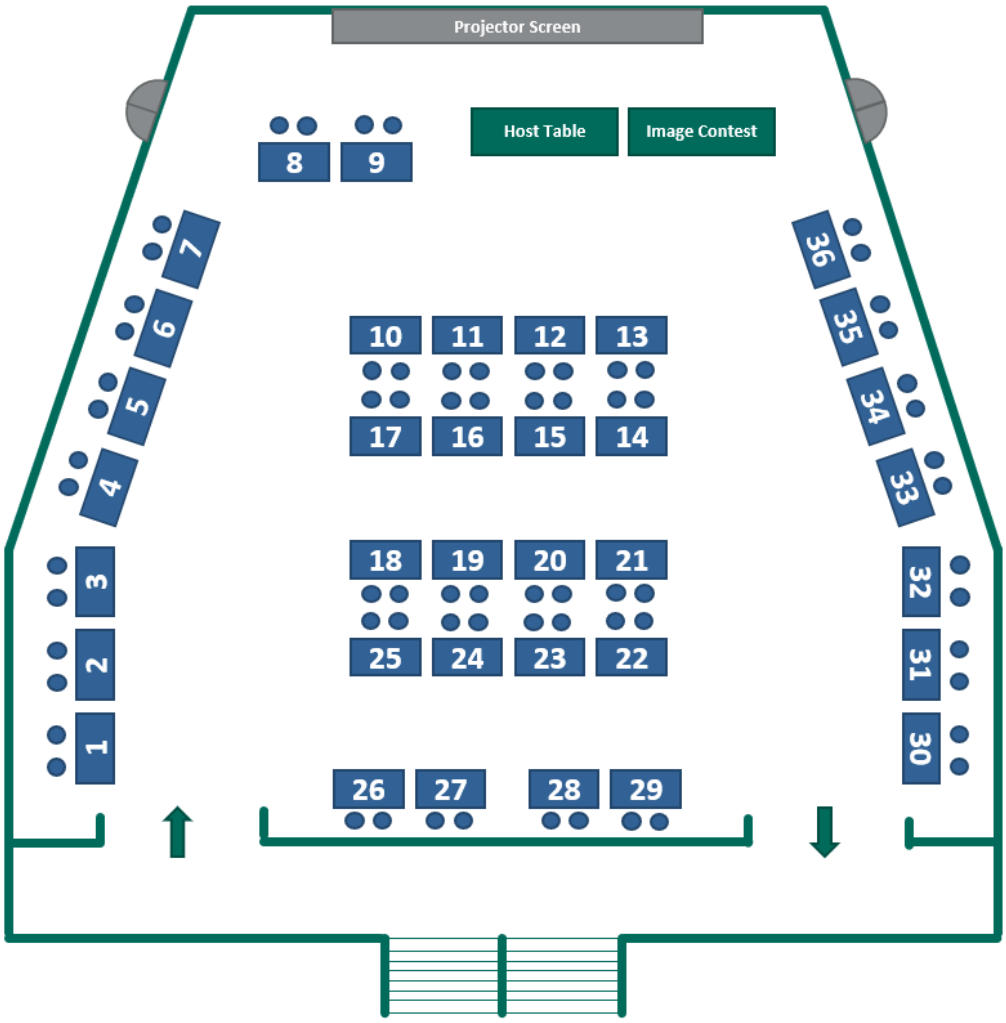
Cancer Center Trainee Symposium
8:00 a.m. - 5:00 p.m. @ Alumni Center

- Keynote Addresses from Julien Sage, PhD, and Rosalie Sears, PhD
- Trainee Presentations/Poster Session (high school to postdoc to clinical fellows)
- View flyer or register online

6th Annual Graduate Student Association (GSA) Symposium
11:00 a.m. - 5:00 p.m. @ Milwaukee County Zoo – Zoofari Conference Center

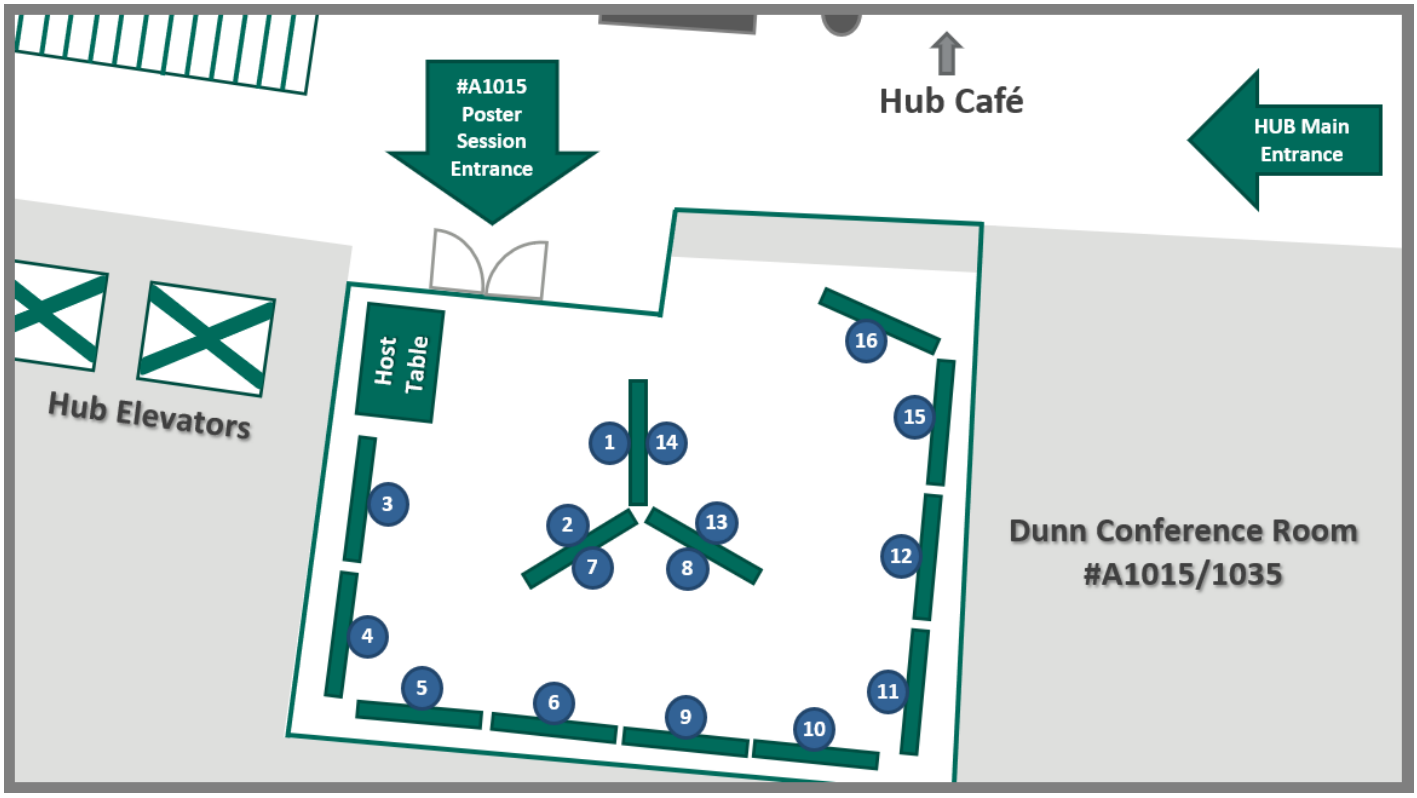
- Keynote Address from Francesca Marassi, PhD
- Student Talks/Poster Session
- Organized by MCW graduate students for MCW graduate students
- View flyer or contact Skylar Eisman

Cores Fair | Alumni Center | Monday, April 17, 11:30 a.m. – 1:30 p.m.



1. Translational Metabolomics Shared Resource, Cancer Center
2. IncuCyte
3. Biochemical Assay Core
4. Mouse Transgenic Core
5. Rat Models and Genotyping Service Center
6. Neuroscience Research Center Microscope Core
7. Neuroscience Research Center Rodent Behavior Core
8. Comprehensive Rodent Metabolic Phenotyping Core
9. MCW Engineering Core
10. Advanced Cell Imaging Core (ACIC)
11. Electron Microscopy Core
12. Physiology & Cardiovascular Center Microscopy Cores
13. Human Induced Pluripotent Stem Cell (iPSC) Core
14. Children's Research Institute Imaging Core
15. Children's Research Institute Histology Core Lab
16. Children's Research Institute Flow Cytometry Core
17. Versiti Blood Research Institute Flow Cytometry Core
18. Marquette University Visualization Laboratory
19. Biacore S200 - Surface Plasmon Resonance
20. Echocardiography Core
21. Shared High-Frequency Ultrasound Imaging Facility
22. Center for Microbiome Research
23. Cell Therapy Laboratory
24. MCW Tissue Bank
25. Pediatric Biobank & Analytical Tissue Core
26. Mellowes Center for Genomic Sciences and Precision Medicine
27. Precision Irradiation Core
28. Shared Mass Spectrometry (MSMS) Facility - Small Molecules
29. Structure Biology Shared Resource
30. Therapeutic Accelerator Program
31. Qualitative Research Consulting Service
32. Geospatial, Epidemiology and Outcomes Shared Resource
33. Biostatistics Consulting Service
34. CTSI Adult Translational Research Unit (ATRU)
35. CTSI Clinical Trials Office (CTO)
36. Clinical Research Data Warehouse

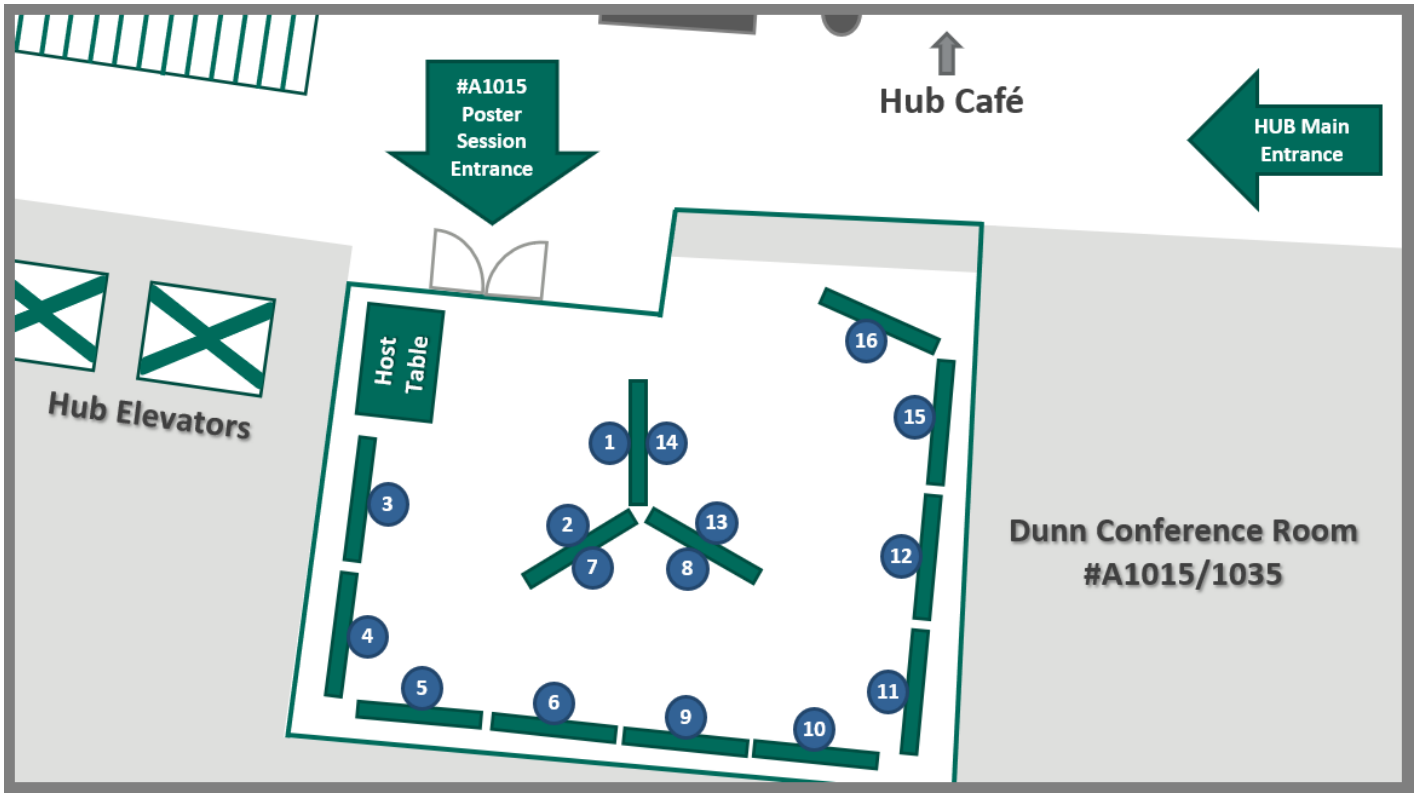
Poster Session | Dunn Conference Room | Tuesday, April 18, 10:00 – 11:00 a.m.



Community, Education, Population Science & More

1. **Michael Tschannen**, Advancing Precision Medicine with Basic and Translational Research Tools, Services, and Assays at the Mellowes Center
2. **Athena Dong**, The World Traveler: A Case of Multiple Infectious Diseases in an Immunocompromised Patient
3. **Melissa Drezdzon**, Association between BMI and Early-Onset Colorectal Cancer
4. **Maie Zagloul**, Evaluation of social and clinical determinants of health on dysphagia care pathways at a tertiary care facility
5. **Mohammad Titi**, Flight COVID Milwaukee: Protective Behaviors and Risk Communications Associated with the COVID Pandemic
6. **Cailey O'Neill**, Implementing Vaccine Initiatives at Student-Run Free Clinic
7. **Buruj Mohammed**, Implementation of a DSMES Educator Program in Port Harcourt, Nigeria
8. **Anum Khan**, The Impact of Mass Shootings in Schools: How we can aid those affected individuals and communities
9. **Jenna Hansen**, Associations Between Chronic Stress Exposures, Stress Hormones, and Biological Aging in Midlife Adults
10. **Jaime Wendt Andrae**, Advancing our Understanding of Diseases and Cellular Biology through Transcriptomic Sequencing
11. **Juliana Alvarez-Argote**, Long term expression of anti-sickling transgenic beta-globin after non-myeloablative conditioning lentiviral gene in a sickle-cell disease murine model
12. **Neshatul Haque**, Development of prediction model for variant effect assessment of RAG1/2 complex
13. **Salomao Jorge**, Integrative Modeling, Molecular Mechanics, and Molecular Dynamics Evaluation of Genomics Variants in KMT2C (MLL3), a Gene Involved in Kleefstra Syndrome II
14. **Guile Urrutia**, Pharmacological Targeting of PRMT5 in Pancreatic Cancer disrupts cell cycle progression and RNA splicing
15. **Morgan Maring**, ECMO for COVID-19 related Acute Hypoxic Respiratory Failure: The Association between Age and Mortality Outcome

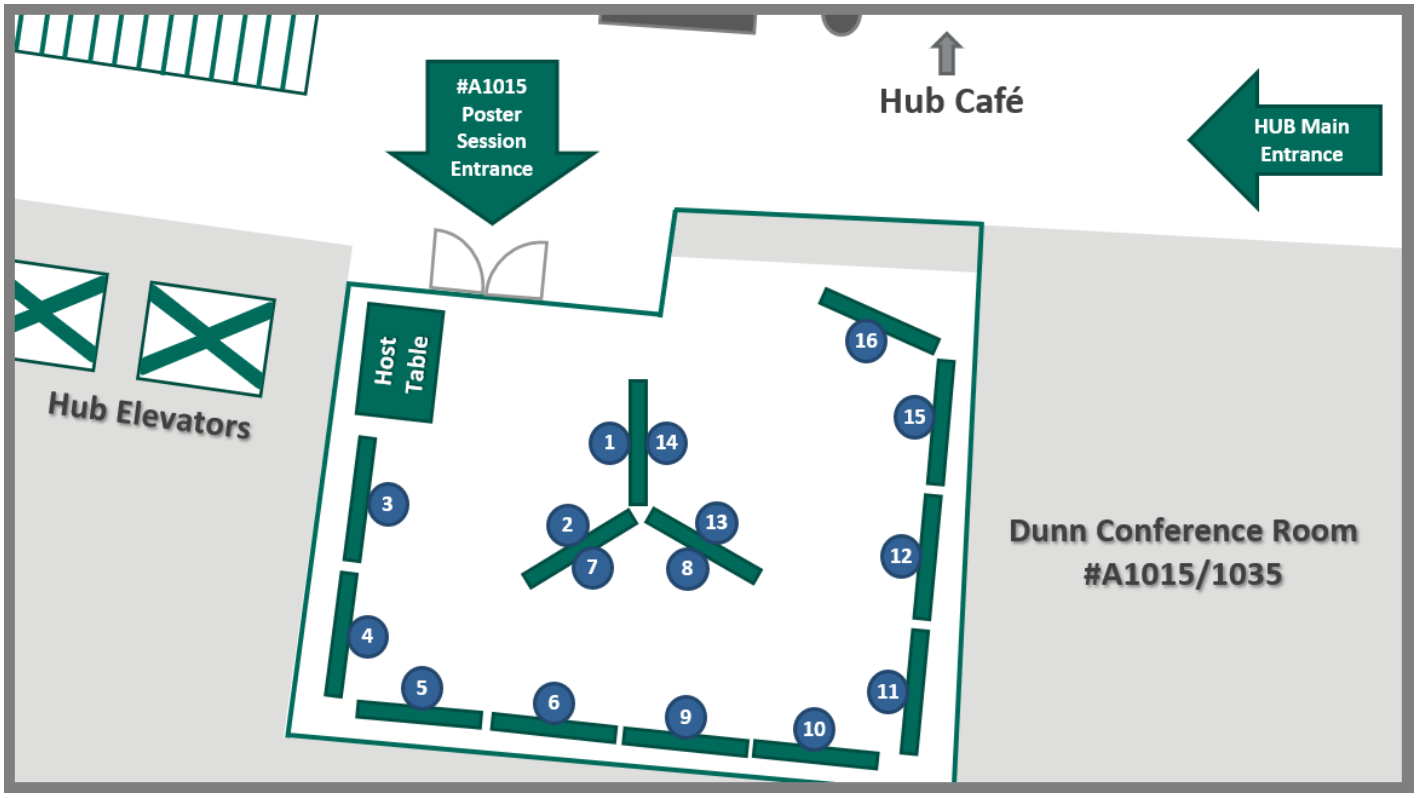
Poster Session | Dunn Conference Room | Wednesday, April 19, 9:00 – 10:00 a.m.



Clinical Research (1 of 2)

1. **Kaila Herold**, Robotic-assisted surgical repair of rectus diastasis and abdominal bulge following abdominal based breast reconstruction
2. **Kayleigh Cook**, Strengthening Surgical Systems in Ethiopia: An Assessment of Sustainability in Data Practices
3. **Bryce Patin**, VTE chemoprophlaxis within 24 hours of stable TBI: safe and effective
4. **Monet Woolfolk**, Early Post-Discharge Self-Reported Mental and Physical Health Outcomes in Gunshot Wound Survivors
5. **Maya Subramanian**, Assessing variability in reporting severity of the same symptom (fatigue) in context of different psychiatric syndromes
6. **Benjamin Seadler**, The Impact of Increasing Tolerance for Donor Heart Travel Distance on Transplant Outcomes
7. **Marie Luebke**, Developing a Urinary Incontinence Care Pathway: A mixed methods study
8. **Morgan Tentis**, Implementation of the 300cc-Rule Safely Decreases Chest Tub Placement in Traumatic Hemothorax
9. **Elise Biesboer**, An Estimated Blood Volume-Based Enoxaparin Dosing Protocol Improves Venous Thromboembolism Prophylaxis in Emergency General Surgery Patients
10. **Abdul Hafiz Al Tannir**, Evaluation of a Safe Volume Cut-off to Observe Traumatic Hemothoraces
11. **Craig Miller**, Leveraging Patient and Family Perspectives to Improve Systems of Care for Traumatic Brain Injury: A Qualitative Study
12. **Brian Conway**, The Cost-Effectiveness of Gender Affirming Mastectomy
13. **Nicole Sequeira**, Syndromes of Concurrent Hypertension, Diastolic Dysfunction, and Pulmonary or Peripheral Edema in Cardio-Oncology: A New Classification System and Case Series
14. **Kearnin Van Bortel**, Age of First Concussion Is Associated with Total Concussions and Symptom Endorsement
15. **Brandon Patterson**, Using microscale thermophoresis for primary hit identification in fragment based lead discovery with ULK3 kinase
16. **Sumaya Ahmed**, O-GlcNAcylation is required for the abscission checkpoint

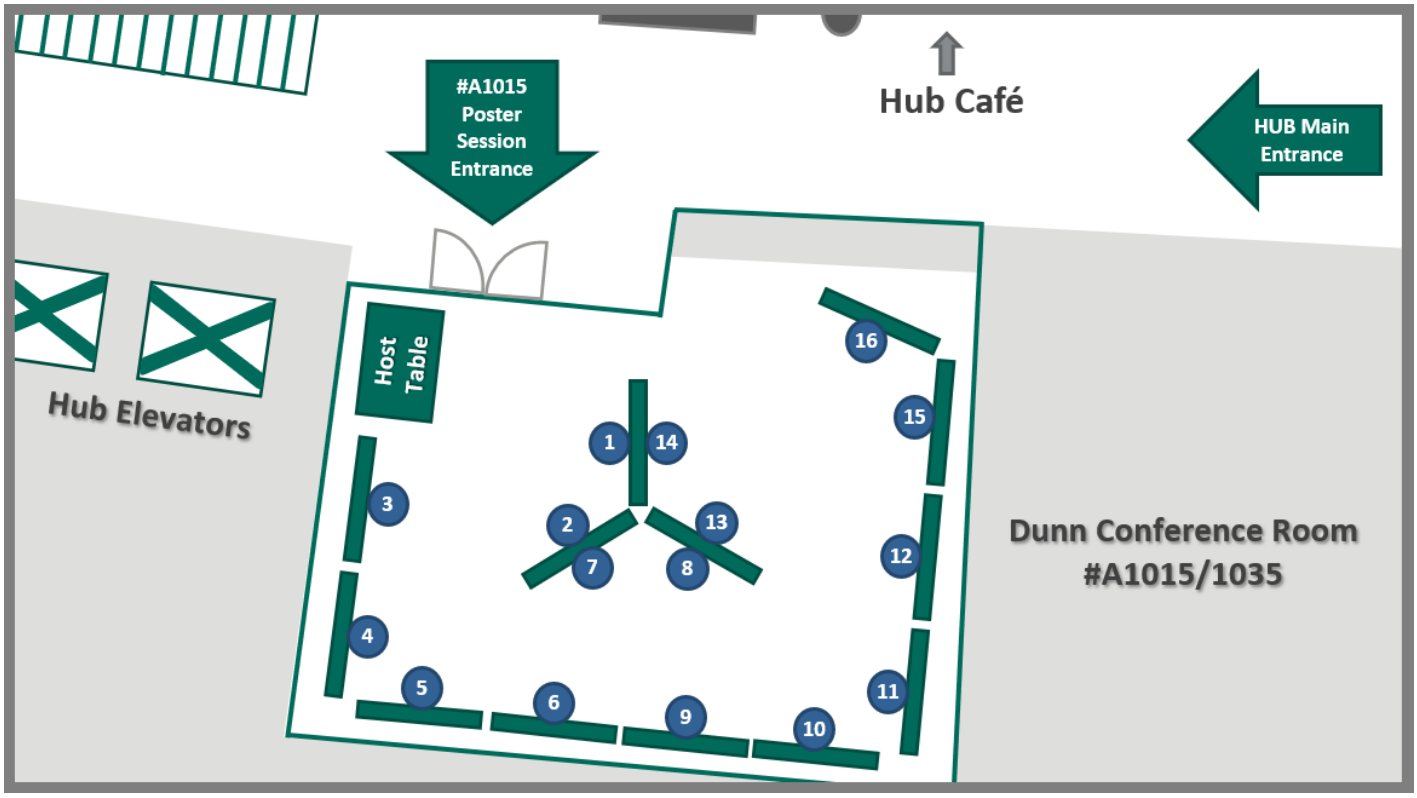
Poster Session | Dunn Conference Room | Wednesday, April 19, 1:00 – 2:00 p.m.



Basic Science

1. **Amanda Miller**, Mellowes Center Bioinformatics Shared Resources: Single-cell RNA-seq Analysis
2. **Meera Krishna**, The Neuroprotective Role of Skin Collagens in Aging
3. **Jue Zhang**, CD36 Mediates Mitochondrial Reactive Oxygen Species Production thorough PKM2 in Macrophages
4. **Julia Jezykowski**, Interleukin 8-CXCR2 Mediated Neutrophil Extracellular Trap Formation in Biliary Atresia
5. **Asad Akhter**, Mass Spectrometry Identification of Novel Immunotherapy Targets for Osteosarcoma
6. **Brian Ratnasinghe**, Molecular Dynamics Simulations for Cancer Genomics: Distinction Between KRAS Variants
7. **Jitka Rybova**, Hematopoietic Stem Cell Transplantation in Farber Disease and Spinal Muscular Atrophy-Like Mouse models of Acid Ceramidase Deficiency
8. **Angela Mathison**, The Spatial Biology Revolution: Revealing new Layers of Transcriptional Changes in Tissues
9. **Jessica Wagenknecht**, ABCC6 3-State Structural Model Enhances Functional Interpretation of Genetic Variants
10. **Jessica Zhou**, Hydrocele Risk with Tunica Vaginalis Closure in Scrotal Surgery
11. **Morgan Briggs**, Assessment of Uterine Fibroid Knowledge and Education Interests Amongst Healthcare Professionals
12. **Nathan Schloemer**, Mutant Thymidylate Kinase Mediated Modulation of IL-12 Transduced Sarcoma NK cell Activation
13. **Muhammad Khokhar**, The Effects of Spinal Orientation on Lumbar Spine Fractures
14. **Thiago Milech De Assuncao**, Heterogeneity In Transcriptional Initiation Signals For Pancreatic Cancer Is Achieved By The Expression Of Different Pancreatic Cancer-Associated Mutants
15. **Kun Fang**, NucHMM: a method for quantitative modeling of nucleosome organization identifying functional nucleosome states distinctly associated with splicing potentiality
16. **Justin Page,** The functional role and therapeutic potential of heme binding proteins after cervical SCI

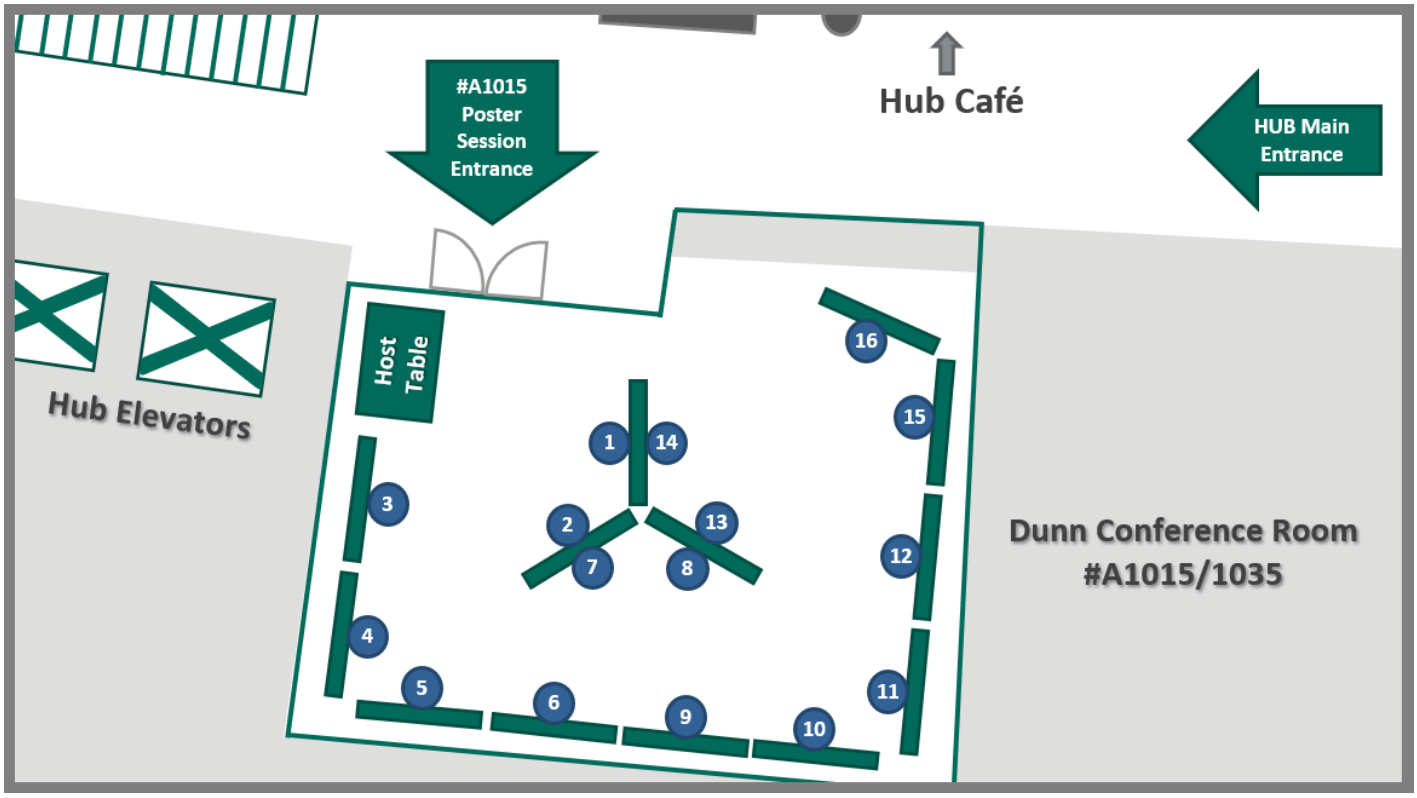
Poster Session | Dunn Conference Room | Thursday, April 20, 11:00 a.m. – 12:00 p.m.



Translational Research

1. **Bethany Corbin**, From Pediatric to Adult Medicine: What is the Patient and Family Experience in Translational Care?
2. **Grace Wittenberg**, Design of a Nursing Home Infection Control Peer Coaching Program
3. **Margaret Stebbins**, SOX2 Positive Glioblastoma Invasion Beyond Contrast Enhancement Detected with Radio-Pathomic Maps of Cell Density
4. **Ally Lesnick**, Toxicology of Inhaled Fosamprenavir as a Dry Powder for Laryngopharyngeal Reflux
5. **Chuck Hay**, The Design and Development of Novel Bispecific Anti-CD30/Anti-CD3 Antibodies
6. **Asha Raghavan**, Optimization of Behavioral Assessments for Prediction of Functional Outcomes of Spinal Cord Injury
7. **Mary L. Faber**, Characterization of a Novel Anti-CD30/Anti-CD3 Bispecific Antibody Conjugate for Immunotherapy for CD30+ Malignancies: Preparation for a Phase I Clinical Trial
8. **Mary Jo Rademacher**, Establishment of a Pediatric Sarcoma Patient-Derived Orthotopic Xenograft Program
9. **Andrew Liermann**, Clinical-Scale Production of Lentiviral Vectors at a New Academic cGMP Facility
10. **Xuejun Wang**, Development of a Mass Spectrometry-Based Assay for the Detection of Endogenous and Lentiviral Engineered Enhanced Hemoglobin in Sickle Cells and Mice
11. **Young-In Chi**, Structural Genomics Studies Shed Light on the Mechanisms of Dysfunction of the KDM5C A388P Mutation in a Developmental Disability Child
12. **Lavanya Choppavarapu**, Genome-wide analysis and characterization of 3D chromatin architecture in breast cancer endocrine resistance
13. **Gareth Pollin**, Functional inferences derived from defining the interactome of the H3K9me2 Writers and Readers
14. **Anju Thomas**, G9a Responds to KRAS-Mediated Replication Stress by Increased Origin Licensing
15. **Monica Seadler,** FEASIBILITY OF siRNA BASED APPROACHES FOR KNOCKING DOWN BLOOD PROTEINS IN SWINE
16. **Maria Replogle,** Evaluating the functional impact of a deep intronic variant in RARB associated with complex microphthalmia

Poster Session | Dunn Conference Room | Thursday, April 20, 4:00 – 5:00 p.m.



Clinical Research (2 of 2)

1. **Hope Reecher**, Awake Craniotomy for Supratentorial Tumors and Epileptogenic Lesions in the Pediatric Population: A Case Series
2. **Lauren L. Titus, MD**, Disproportionate Enforcement of a Hospital's Safe Sleep Policy in Racial and Ethnic Minority Families
3. **Anna Kerschner**, Tubulovillous Adenoma Identified on Transvaginal Ultrasound: A Case Report
4. **Morgan Leissring**, Comparison of a Person-Administered vs Automated Screening Tool for PTSD in Traumatically Injured Patients
5. **Rana Aliani**, Impact of Race, Insurance, and Procedural Timing on Sterilization Method
6. **Haley VanBeek**, A Single Institution Experience on Efficacy and Safety of Endovascular Mechanical Aspiration
7. **Nitin Somasundaram**, Left Ventricular Lead Placement in Patients with Prior Sternotomy Utilizing the Robotic Platform
8. **Athena Dong**, The Impact of Surgery on Functional and Cognitive Outcomes after Traumatic Brain Injury. A TRACK-TBI Study
9. **Jacob Lindemann**, Robotic-Assisted Left Atrial Appendage Exclusion After Prior Sternotomy in Patients with Long-Standing Atrial Fibrillation
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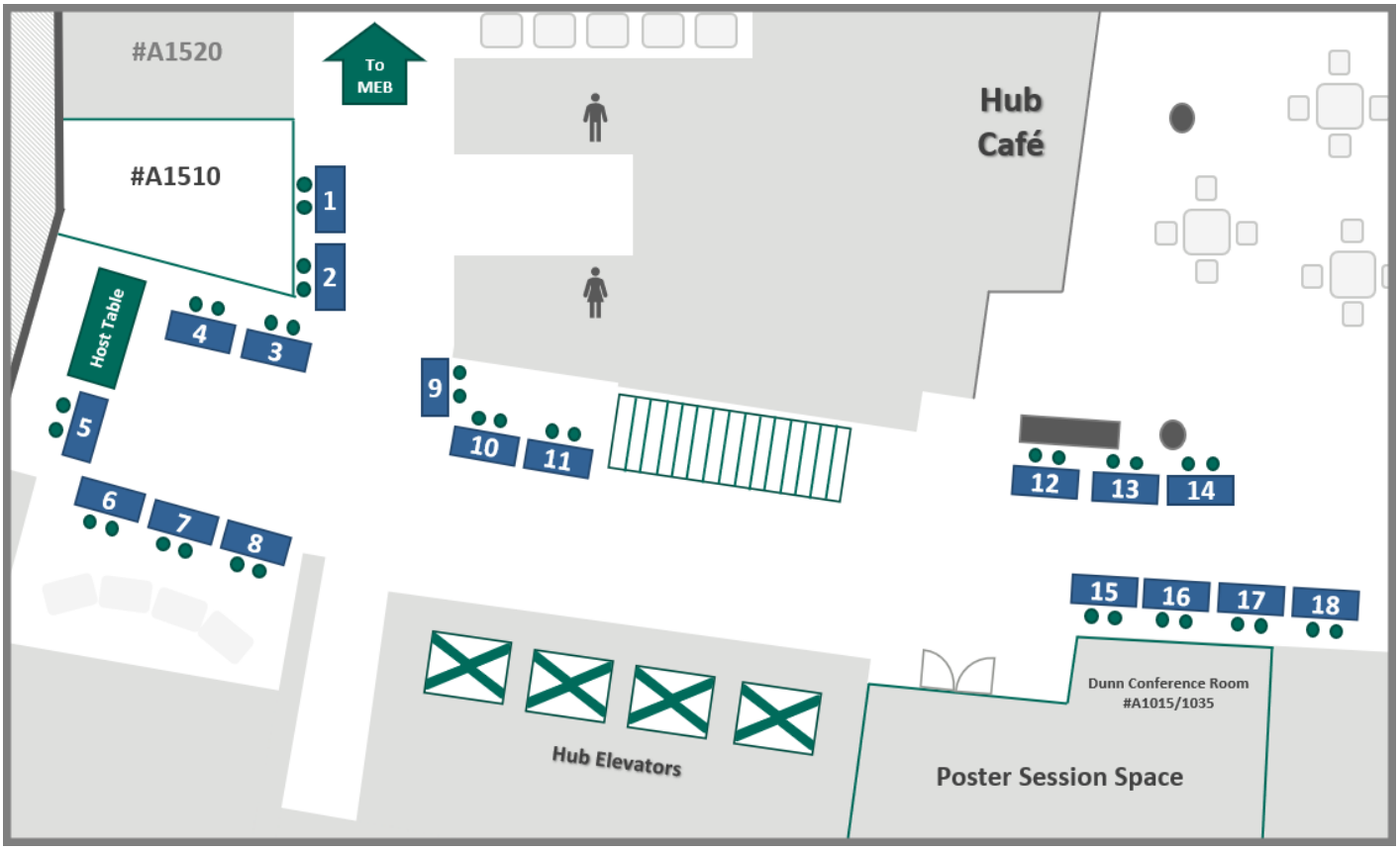
Research Support & Resource Expo | 1st Floor Hub | Thursday, April 20, 12:00 – 1:00 p.m.



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2. Therapeutic Accelerator Program
3. Early-Stage Research Regulatory Oversight Program
4. Human Research Protection Program
5. Research Systems
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7. MCW Clinical Trials Office
8. Clinical & Translational Science Institute (CTSI)
9. Association of Clinical Research Professionals: Wisconsin Chapter
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11. MCW Libraries
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Research Week Abstracts

A few notes regarding the abstracts:

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

- Some researchers will present their abstracts as posters during Research Week. These poster sessions will take place at MCW-Milwaukee's campus in the Dunn Conference Room on the 1st Floor of the Hub for Collaborative Medicine.

Session	Map	Date & Time
Community, Education, Population Sciences & More		Tuesday, April 17 10:00 a.m. – 11:00 a.m.
Clinical Research #1		Wednesday, April 18 9:00 a.m. – 10:00 a.m.
Basic Sciences		Wednesday, April 18 1:00 p.m. – 2:00 p.m.
Translational Research		Thursday, April 20 11:00 a.m. – 12:00 p.m.
Clinical Research #2		Thursday, April 20 4:00 p.m. – 5:00 p.m.

Category	Allergy, Immunity & Infectious Disease, #1
Primary Author	Athena Dong, BS
Secondary Authors	Meghan Conroy, BS and Julie Hansen, MD
Title	The World Traveler: A Case of Multiple Infectious Diseases in an Immunocompromised Patient
Introduction	In this case, we present a 31-year-old South Asian male with no significant past medical history who presented with several weeks of diarrhea after recent travel in Africa and Europe. The patient started typhoid and malaria prophylaxis in the US 3 days before leaving. He previously lived in Las Vegas, where he had many sexual partners with inconsistent condom use. He spent 2 weeks in Sierra Leone, where he slept with no bed nets and experienced mosquito bites. After arrival, he experienced 24 hours of fever, chills, and diarrhea. He consumed local food, drank tap water, and swam in the ocean. He also traveled briefly to Senegal and Morocco. The patient then spent 2 weeks in Portugal, during which he drank tap water and hiked barefoot. He also stopped taking his malaria prophylaxis. After several days, he developed fever, chills, fatigue, and non-bloody diarrhea. Symptoms persisted through his return to the US.
Methods	Although public health measures have reduced risks of contracting infectious disease during travel, it is still crucial to be aware of how to coordinate management of a patient who becomes infected while abroad. Immunodeficiency increases susceptibility to opportunistic infections. Infection with multiple organisms, in addition to preexisting immunodeficiency, can lead to a complicated and extensive hospital course.
Results	Giardia is a parasite that causes gastrointestinal illness, manifesting as non-bloody steatorrhea, abdominal pain, and nausea. Since it is often transmitted via contaminated water, it is possible that the patient may have contracted giardiasis from drinking tap water while abroad. Similarly, Cryptosporidium causes gastrointestinal illness that can present as watery diarrhea, abdominal pain, nausea, vomiting, and fever. However, in immunocompetent patients, cryptosporidiosis is usually self-limited. Our patient experienced diarrhea for several weeks without improvement, which raised concern for possible immunodeficiency. This led us to discover that the patient was HIV positive. Clinicians should be aware of similar warning signs of immunodeficiency, and that co-infection with HIV and opportunistic organisms can be common. Malaria commonly presents with fever, chills, headache, nausea, vomiting, and anemia. Africa is home to 95% of all malaria cases across the globe. Previous research has suggested that HIV infection is associated with more frequent episodes of symptomatic malaria and higher parasitemia. However, more research is needed on the impact of HIV and malaria coinfection.
Conclusions	It is important for travelers to be made aware of infectious diseases endemic to their destinations and appropriate precautions. In turn, it is important for clinicians to share this awareness and understand the presentation of infectious diseases in order to manage them in the hospital setting. This case highlights the importance of considering and testing for multiple infectious agents in patients with non-specific symptoms and a history of travel.
Acknowledgements	We would like to express our thanks to Dr. Julie Hansen, Dr. Veronica Quintern Pujol, Dr. Ananda Ray, and Dr. Janak Wagle for their guidance in managing the care of this patient.
Reference 1	Patnaik, P., Jere, C. S., Miller, W. C., Hoffman, I. F., Wirima, J., Pendame, R., Meshnick, S. R., Taylor, T. E., Molyneux, M. E., & Kublin, J. G. (2005). Effects of HIV-1 serostatus, HIV-1 RNA concentration, and CD4 cell count on the incidence of malaria infection in a cohort of adults in rural Malawi. The Journal of infectious diseases, 192(6), 984â€“991. https://doi.org/10.1086/432730
Reference 2	Hochman, S., & Kim, K. (2009). The Impact of HIV and Malaria Coinfection: What Is Known and Suggested Venues for Further Study. Interdisciplinary perspectives on infectious diseases, 2009, 617954. https://doi.org/10.1155/2009/617954
Reference 3	Roupa, Z., Zikos, D., Vasilopoulos, A., & Diomidous, M. (2012). Common Health Risks, Required Precautions of Travelers and their Customs Towards the Use of Travel Medicine Services. Materia socio-medica, 24(2), 131â€“134. https://doi.org/10.5455/msm.2012.24.131-134
Ancillary Materials	VIEW MY POSTER

Category	Allergy, Immunity & Infectious Disease, #2
Primary Author	Mohamed Khalil
Secondary Authors	Scott Terhune and Subramaniam Malarkannan
Title	Single cell transcriptomes reveal a unique NKG2CHigh subset from the spleen of HCMV+ donors represent memory NK cells
Introduction	Infection with human cytomegalovirus (HCMV) can result in severe morbidity and mortality to the developing fetus and immunocompromised individuals. Natural killer (NK) cells are cytotoxic lymphocytes that are required to manage and control HCMV infections. The NKG2C receptor expressed by NK cells recognizes and responds to infected cells expressing HLA-E loaded with HCMV UL40-derived peptide. NKG2C+ NK cells possess features of adaptive immunity and are at greater percentages in HCMV seropositive individuals. The molecular mechanisms by which adaptive NK cells are generated and their transcriptomic signatures remain unknown
Methods	Eight healthy spleens from four HCMV+ and four HCMV- donors were obtained and their NK cells were sorted and captured for scRNA-seq. Donor median age was 59 [IQR 48.5-56.5], 50% (n=4) were female, 50% (n=2) of females were HCMV seropositive and 50% (n=2) of females were HCMV seronegative.
Results	Using scRNA-seq, we observed elevated levels and numbers of NKG2C+ adaptive NK cells in HCMV+ individuals when compared to HCMV- individuals. In addition, we identified a set of transcription factors and markers that are potentially responsible for the development and function of adaptive NKG2C+ NK cells, including CD52, B3GAT1, FCGR3A, CD3E, and KIR3DL1. Our developmental trajectory analysis of adaptive NKG2C+ NK cells revealed a unique branch point of true memory NK.
Conclusions	Here, we demonstrate that HCMV infection can induce the formation of adaptive NKG2C+ NK cells that display a unique transcriptional and developmental profile. These findings have the potential to influence the future application of adaptive NK cells in cellular immunotherapies.
Acknowledgements	This work is supported by the National Center for Advancing Translational Sciences, National Institutes of Health, through grant number TL1TR001437

Category	Cancer, #3
Primary Author	Amy Yoonjin Lee, BA
Secondary Authors	Anna Lyons, BS; Vaia Markis, BS; Sailaja Kamaraju, MD, MS; Melinda Stolley, PhD; Joan Neuner, MD, MPH; Kathryn E. Flynn, PhD
Title	Attribution of symptoms to adjuvant endocrine therapy and association with adherence among older women with breast cancer: a qualitative study
Introduction	Oral adjuvant endocrine therapy (AET) is an effective treatment for hormone receptor positive breast cancer shown to decrease recurrence and mortality. However, adherence to AET is poor, with 1/3 of patients not completing the recommended 5-year treatment. Studies suggest that symptoms of the medication, including joint pain, hot flashes, and fatigue, are associated with AET discontinuation. While previous studies focused on symptoms post-AET initiation, preliminary evidence suggests that pre-AET symptoms may predict early medication discontinuation. We used qualitative interviews to explore adherence to AET and patientsâ€™ attribution of symptoms to AET amongst adherent and discontinued patients to better understand attitudes regarding AET.
Methods	Participants were recruited from the Froedtert/MCW Cancer Center registry, stratified by adherence to/discontinuation of AET. Semi-structured phone interviews followed an interview guide based on constructs identified in the literature as having strong associations with AET adherence. Interviews were recorded and transcribed. A multidisciplinary team developed a codebook based on themes that emerged from the data.
Results	Interviews were conducted with 33 participants; ages ranged from 57-86 years. Participants included 10 patients who discontinued AET & 23 patients who completed AET or were adherent at the time of interviewing. Major themes amongst discontinued patients included: worries, inability to deal with symptoms/precedence of quality of life, inadequate support and communication and symptom management strategies. Major themes amongst adherent patients included: trust, self-efficacy, receiving adequate support, and necessity of AET. While both adherent and discontinued patients reported experiencing symptoms throughout the course of treatment, adherent patients were more likely to attribute these symptoms to factors other than AET including older age, comorbidities, and recent completion of other cancer treatments. In contrast, patients who discontinued therapy were more likely to attribute symptoms to AET itself and frequently cited this as a primary reason for stopping treatment.
Conclusions	The experience of symptoms during AET may influence a patient’s attitudes and actions regarding therapy completion. Symptom attribution may be a key factor leading to discontinuation of AET, and a better understanding of this observation may assist in the identification of patients who are at higher risk of discontinuation.

Category	Cancer, #4
Primary Author	Anju Elizabeth Thomas
Secondary Authors	Thiago M. De Assuncao, Gareth Pollin and Gwen Lomberk
Title	G9a Responds to KRAS-Mediated Replication Stress by Increased Origin Licensing
Introduction	The COVID-19 pandemic has disproportionately affected nursing home (NH) residents, and emerging evidence suggests quality, location, resident demographics, and staffing levels may be related to COVID-19 incidence within facilities. We describe the distribution of COVID-19 cases in Wisconsin from January 2020 to October 2020, the effect of rural vs urban location of NHs on COVID-19 incidence, and temporal changes in COVID-19 incidence.
Methods	We generated an inducible KRAS model in an hTERT-immortalized human non-cancerous pancreatic ductal cell line to study the cellular response to RS.
Results	Induction of KRAS for 48 hours in this model activated the ATR RS-response pathway, as indicated by increased levels of P-T1989-ATR, P-S345-CHK1, and P-S33-RPA32 by western blot and microscopy. The G9a epigenomic complex, along with ORC1 and ORC2 and several other pre-RC proteins, also showed increased levels. Co-immunoprecipitation of G9a revealed interaction with ORC2 protein under conditions of oncogene-induced RS. Our in vitro and in vivo studies suggest that the G9a complex targets Orc2 for methylation. Inhibition of G9a with UNC0642 during KRAS-induced RS resulted in a decrease of chromatin-bound ORC1 and ORC2, as well as pre-RC proteins in subcellular fractionation experiments, indicating a role for G9a function in origin licensing.
Conclusions	Our findings suggest that G9a directly interacts with the pre-RC during origin licensing under conditions of RS. G9a-mediated methylation of ORC2 reveals a potential regulatory mechanism of the pre-RC through histone mimicry. Our study provides insight for a mechanism by which KRAS mutated cancer cells respond to rapid cellular proliferation during RS, reinforcing the role of G9a as a promising therapeutic target for PDAC.

Category	Cancer, #5
Primary Author	Asad Ahkter
Secondary Authors	Mary Jo Rademacher BS; Lauren E. Ball PhD; Jeffrey A. Medin PhD; Nathan J. Schloemer MD
Title	Mass Spectrometry Identification of Novel Immunotherapy Targets for Osteosarcoma
Introduction	Osteosarcoma is the most common bone cancer of children and young adults. Metastatic and recurrent disease have dismal survival and there has been no substantial improvement in outcomes since the 1980s despite intensification of conventional chemotherapy and surgery. Additionally, current standard of care therapy has devastating short- and long-term toxicities that accumulate and leave survivors with long-term functional disabilities. Novel treatments must be able to address metastatic disease and limit toxicities to impact survival and patient quality of life. Immunotherapy has thus far demonstrated inadequate efficacy in sarcoma with a paucity of specific targets recognized as a key limitation. We sought to use mass spectrometry of osteosarcomas to identify novel surface protein targets for future immunotherapy development.
Methods	Three distinct osteosarcoma cell lines (143B, MG-65, and KHOS-240) were subjected in three technical replicates to Liquid Chromatography with Tandem Mass Spectrometry (LC-MS/MS). Whole cell lysate proteins were identified based on the Uniprot database, normalized and quantitatively reported by Label Free Quantitation (LFQ) intensity assessment scoring. Proteins with inconsistent expression were eliminated. Resultant proteins were scored on the bioinformatic tool, Surface Genie (www.cellsurfer.net/surfacegenie) to rank predicted surface expression consistency.1 Proteins were prioritized based on quartiles of quantitative expression. Finally, proteins with consistent surface expression were sorted via Human Protein Atlas, version 22, (www.proteinatlas.org), for patterns of expression in 256 healthy/normal tissues based on RNA-seq by normalized Transcripts Per Million (nTPM). An nTPM of >100 was categorized as high expression.
Results	We identified 3,254 target proteins in triplicate assessment of three distinct osteosarcoma cell line samples. Elimination of low-frequency expression resulted in 2,541 target proteins which were subjected to Surface Genie assessment. 72 proteins demonstrated high Surface Prediction Consensus (SPC) scoring. Bottom quartile of LFQ expressions was excluded and the remaining 33 target proteins were categorized by Human Protein Atlas as above into categories of High uniform expression (n=3), High expression on critical tissue (n=6), High expression on non-essential tissue only (n=8) and Low uniform expression (n=16). 13 of the 24 proteins with High expression on non-essential tissue or Low uniform expression were found on all three osteosarcomas. Validation of protocol is noted by two of the 13 identified on all samples are currently or have previously been the targets of therapeutic clinical trials for osteosarcoma.
Conclusions	We have identified potential novel targets for the development of antibody directed immunotherapy for osteosarcoma. Immunohistochemical (IHC) confirmation of our prioritized target proteins on primary patient samples collected as part of ongoing patient derived orthotopic xenograft program is ongoing. IHC confirmation of our resultant protein targets will also validate our mass spectrometry identification and stepwise sorting protocol for subsequent application to additional sarcomas and solid malignancies.
Acknowledgements	Supported in part by MACC Fund Start-up Grant, Snowdrop Foundation Grant and Sharon K. Wadina Foundation's Sarcoma Foundation of America Grant through the MCW Cancer Center.
Reference 1	Waas M, Snarrenberg ST, Littrell J, et al. SurfaceGenie: a web-based application for prioritizing cell-type-specific marker candidates. Bioinformatics. 2020;36(11):3447-3456.
Ancillary Materials	VIEW MY POSTER

Category	Cancer, #6
Primary Author	Brandon Patterson
Secondary Authors	Akanksha Gurtu, Rafael Toro, Dawn Wenzel
Title	Using microscale thermophoresis for primary hit identification in fragment-based lead discovery with ULK3 kinase
Introduction	Cell division is regulated by cell cycle checkpoints that naturally possess mechanistic on-and-off switches that make attractive drug targets. Cancerous cells constantly divide and are therefore more susceptible to cell cycle checkpoint disruption than normal cells. However, there is currently a lack of therapeutics that target cell cycle checkpoints, including the under-characterized abscission checkpoint that regulates cytokinesis. ULK3 is a serine/threonine kinase required for the abscission checkpoint and is upregulated in colon and many other cancers. Overexpression in acute myeloid leukemia and bladder cancer promotes cell proliferation and is even considered a poor prognostic marker in certain cancer contexts. Despite the potential for ULK3 as a drug target, specific small-molecule inhibitors are lacking.
Methods	To identify small molecule binders of ULK3, we are screening using microscale thermophoresis (MST). Rather than screening typical drug-sized molecules, fragment-based lead discovery allows piecing together the final molecule optimized for specific protein targets. MST uses a fluorescent target and a laser-induced temperature gradient to monitor binding events and is scalable to be a primary hit detection method in a fragment-based lead discovery campaign. MST has several advantages over other biophysical binding techniques, including detecting interactions in solution and measuring binding events that involve a small mass change of the labeled target. Additionally, MST is highly sensitive and can detect interactions between chemical fragments and picomolar concentrations of fluorophore-labeled protein.
Results	Here we report an MST fragment-based screening pipeline to identify chemical modulators of ULK3 kinase activity. Using known ligands, we demonstrate that fluorophore-labeled ULK3 reliably reports on binding throughout the entire ULK3 molecule and will therefore be able to detect allosteric binding sites. As a proof of concept, we screened ULK3 with a small (<150) pool of fragments and show that we can successfully identify weak affinity (KD>100 ÂµM) binders. Confirmatory assays with orthogonal methods, such as nano-differential scanning fluorimetry and kinase assays, are underway to cross-validate hits.
Conclusions	With this approach, we aim to identify new inhibitors of ULK3, which will allow testing the utility of disrupting the abscission checkpoint for cancer therapeutics. Our data also suggest a general protocol for using an MST fragment-based screening approach to identify chemical modulators of kinases and other protein targets.
Acknowledgements	Brian Smith, Blake Hill, Brian Volkman, Davin Jensen

Category	Cancer, #7
Primary Author	Brian D. Ratnasinghe
Secondary Authors	Neshatul Haque, Jessica B. Wagenknecht, Angela J. Mathison, Davin R. Jensen, Elise N. Leverence, Thiago Milech De Assuncao, Gwen Lomberk, Brian C. Smith, Brian F. Volkman, Raul Urrutia, Michael T. Zimmermann
Title	Molecular Dynamics Simulations for Cancer Genomics: Distinction Between KRAS Variants
Introduction	There has been great progress in the field of genomics regarding the number of people who have been sequenced, leading to a large number of genetic variants collected. However, our ability to functionally interpret this wide array of genetic variants lags their identification. Recent studies have demonstrated the utility of 3D protein structure and structure-based calculations for better understanding the effects of inter-individual human genetic variation. Here we aim to take this idea to its logical next step by analyzing a complete ensemble of 3D protein structures generated via Molecular Dynamics simulations for the purpose of interpreting genetic information.
Methods	Our first application is to the RAS family of genes and their encoded proteins. When RAS is mutated in the germline, the associated collection of rare diseases is referred to as RASopathies. Additionally, somatic RAS mutations are well-established to contribute to malignant transformation in cancer. As such, we aim to apply our new structural genomic methods to KRAS, which is has the highest potential for cancer causing genetic variation among the GTPase class of proteins. We aim to use the conformational ensemble of KRAS disease variants to elucidate a new potential avenue for cancer treatment via small molecule targeting of mutationally-restricted conformations, or intermediates produced by the mutations.
Results	To contextualize the conformational ensemble obtained via MD we calculated a series of distance monitors that have previously established biophysical characteristics describing and distinguishing between disease and non-disease KRAS conformations. We also compared various MD analysis methods such RMSD, RMSF, and Eint to our measurements of thermostability (Tm), for each variant. The distance monitors and Tm data associate strongly with MD-based scores, establishing the biophysical value of the latter and increasing our confidence in the capacity of Molecular Dynamics to properly describe effects of genetic variation. Using these analysis methods, we generate a series of scores allowing us to develop a meta classification system to subdivide groups of KRAS variants that have different effects.
Conclusions	Indeed, we suspect that we have established a workflow that has great potential in precisely describing the effects of genetic variation. We additionally anticipate that our approach can be used to identify mutation specific conformations, amenable to small molecule screening and the development of more precise therapy targeting approaches across rare diseases and cancer.
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Category	Cancer, #8
Primary Author	Charles E. Hay
Secondary Authors	Mary Faber, Jeffrey A. Medin
Title	The Design and Development of Novel Bispecific Anti-CD30/Anti-CD3 Antibodies
Introduction	CD30 is a transmembrane domain protein of the TNFR family. CD30 signaling is involved in memory cell survival and controlling bacterial infections amongst other roles. In healthy tissues, CD30 is expressed on B cells and T cells. However, CD30 has been found to be a biomarker for Hodgkinâ€™s lymphoma, anaplastic large cells lymphoma (ALCL), and peripheral T cell lymphomas (PTCLs). Further, it is estimated that CD30 is expressed on the surface of over 30% of all known cancer types. This prevalence in various tumors shows the potential widespread therapy that immunotherapies targeting CD30 could provide.
Methods	A common immunotherapy is bispecific antibodies, which can be used to bring effector cells near the cancer cells by binding antigens on both cell types. Bispecific antibodies are synthetically designed antibodies that can bind two different antigens. Bound effector cells can release their cytotoxic granules to kill the target cell and release cytokines to recruit other immune cells to the cancerous tissue. Our lab has developed two generations of an anti-CD30/anti-CD3 antibody, where CD3 is a protein subunit of the T cell receptor expressed on T cells. The first-generation bispecific antibodies (BiAbs) consist of two different IgG antibodies chemically conjugated together. Our second-generation bispecific antibodies (Grapplers) are expressed as single proteins with scFvs on either end with Fc regions in the center.
Results	Thirteen different cell lines of various origins were used to model non-solid cancers for this project. Three of these cell lines were known to be CD30 negative. The rest of the lines were known to express CD30 naturally or were made to express CD30 via genetic modification. Using Quantibrite kits, the relative level of CD30 expressed by the various cell lines was determined. Primary T cells armed with either BiAbs or Grapplers were incubated with the various tumor cell lines. Both the BiAbs and Grapplers were shown to be able to simultaneously bind both CD3 on primary T cells and CD30 on the cell lines that were confirmed to be CD30+ via flow cytometry. Chromium release assays showed the levels of specific lysis effected by the primary T cells corresponded to CD30 levels on the tumor cells.
Conclusions	Furthermore, T cells armed with either BiAbs or Grapplers showed specific engagement when incubated with CD30+ cells; releasing significantly greater levels of IFN-g, IL-2, and TNFa compared to incubation with CD30- cells. Future steps will be to show in vivo efficacy and determining the pharmacokinetic properties of the BiAbs before moving towards an IND application.

Category	Cancer, #9
Primary Author	Guillermo A. Urrutia-Perez, MD
Secondary Authors	Anju Thomas, Madeline Dzikowski, Xuan Li, Michael T. Zimmermann, Raul Urrutia, Gwen Lomberk
Title	Pharmacological Targeting of PRMT5 in Pancreatic Cancer disrupts cell cycle progression and RNA splicing
Introduction	Pancreatic ductal adenocarcinoma (PDAC) is one of the most lethal cancers. There is an urgent need for the development of novel therapeutic strategies for PDAC, and the identification of druggable targets. Protein arginine methyltransferase 5 (PRMT5), a type II histone arginine methyltransferase involved in various cellular processes, has emerged as a promising target for cancer due to its oncogenic activity in multiple tumor types, including pancreatic cancer, among others, and its high expression correlates with worse prognosis. In fact, several PRMT5 inhibitors (PRMT5i) are currently undergoing evaluation in clinical trials for various solid and blood cancers. However, there remain critical gaps in the current knowledge regarding the molecular mechanisms underlying the contribution of PRMT5 to both normal cellular physiology and tumorigenesis.
Results	In this study, we evaluate the response of basal and classical PDAC cell lines to PRMT5 inhibition, using the Incucyte live cell imaging system. While both PDAC subtypes respond to PRMT5 inhibition, we find that basal PDAC cells are sensitive at nanomolar doses. Using flow cytometry and pBOB EF1 Fucci-expressing cells, we demonstrate that this inhibition disrupts cell cycle progression via G2/M arrest. At the molecular level, PRMT5 inhibition dramatically reduces levels of ATM transcript and protein, as well as promotes the accumulation of DNA damage along with markers of G2/M arrest. Interestingly, RNA-seq and non-coding transcript analysis of PRMT5i-treated pancreatic cancer cells reveals RNA splicing alterations enriched for genes involved in mitosis and DNA repair. Congruently, we detect morphological changes in the nuclei of cells treated with PRMT5i that are consistent with disruption of the spliceosome complex, as evidenced by SC35 immunofluorescence.
Conclusions	Inhibiting the PRMT5 methyltransferase triggers G2/M phase cell cycle arrest and accumulation of DNA damage, which coincides with reduced levels of ATM. Moreover, PRMT5 inhibition alters the transcriptome of PDAC cells, which is characterized by disruption of the spliceosome machinery and increased alterations in RNA splicing. In summary, our data provides mechanistic insight into the effects of PRMT5 inhibition, which holds promise as a valuable therapeutic strategy for PDAC.

Category	Cancer, #10
Primary Author	Jessica Liu, BS
Secondary Authors	Kelly Cohesey MOT, OTR/L; Whitney A. Morelli, PhD
Title	Development of a Remotely Delivered Functional Fitness Assessment for Older Clinical Populations
Introduction	Functional fitness assessments measure an individual's ability to safely perform tasks of daily living appropriate to their age group. Adapted from the fitness arena, these assessments are now implemented into clinical practice and research by providing supporting evidence in designing, testing, and improving treatments and therapies. Through the advancement of technology and increasing utilization of Telehealth there is ample opportunity for new modes of assessment delivery. The purpose of this study was to outline the development of a remotely delivered functional fitness assessment detailing program considerations, design, and method of delivery
Methods	We conducted a literature review on barriers to technology use, needs and preferences for remote assessment of function, and safety of remote administration of functional assessments. The initial draft underwent review by fitness assessment experts to provide feedback on design and content. The user manual and assessment script were revised and will be evaluated by participants in a needs assessment study.
Results	The final remote assessment consisted of six functional assessments relevant to predicting functional trajectories in clinical populations: (1) 6-minute walk test (2) Balance test (3) One leg stand test (4) Gait speed test (5) Chair stand test (6) 8 foot up and go test. Design considerations that were employed include visual and verbal instructions through recorded videos, diagrams, illustrative examples, video conferencing for real-time assessment with a staff member, a written script to standardize assessment delivery, and safety precautions.
Conclusions	The final product was a remotely administered functional fitness assessment to promote a safe, reliable, and equitable way to increase the reach of functional assessments for clinical populations. Future research will evaluate the understandability, actionability, and patient satisfaction of the remotely delivered functional fitness assessment.
Acknowledgements	This work was funded by ACS-IRG/ MCW Cancer Center Award #19-138-34 (PI: Morelli)
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Category	Cancer, #11
Primary Author	Justin L. Greene, MD
Secondary Authors	Matthew J. Scheidt, MD; Eric J. Hohenwalter ,MD; William S. Rilling, MD; Sarah B. White, MD, MS; Amanda R. Smolock MD, PhD
Title	Liver directed therapy for hepatocellular carcinoma with portal vein tumor thrombus
Introduction	The purpose of this study was to review outcomes for patients with hepatocellular carcinoma (HCC) and portal vein tumor thrombus (PVTT) who underwent liver directed therapy targeting the PVTT.
Methods	This was an IRB-approved retrospective study evaluating patients with HCC and tumor thrombus undergoing chemoembolization (TACE) and radioembolization (TARE) from 2013 to 2022. The query yielded a total of 118 procedures in 60 patients. Cases were excluded due to lack of follow up or if treatment did not target PVTT. Medical records were reviewed for demographics, Child-Pugh score, MELD, total bilirubin levels, and imaging response to treatment. Studentâ€™s t test was used for continuous variables, and Chi Square test was used for categorical variables. P<0.05 was considered statistically significant.
Results	A total of 9 patients (7 males) with a mean age 68 +/- 6.4 years underwent TACE and 18 patients (14 males) with mean age 67 +/- 6.7 years underwent TARE for HCC with PVTT. The majority of patients in each group had preserved liver function with Child-Pugh A cirrhosis in 6/9 (67.7%) receiving TACE and 16/18 (88.9%) receiving TARE. Average MELD was 9 +/- 1.9 for patients undergoing TACE and 7.7 +/- 1.5 for patients undergoing TARE. Total bilirubin before and after treatment was not statistically significant different. Seven of 9 (77.8%) patients that received TACE and 15/18 (83.3%) patients that received TARE demonstrated disease control with stable disease, partial response, or complete response on imaging.
Conclusions	Liver directed therapy should be considered as a treatment option in patients with PVTT, as it provides effective local control without significant associated toxicities.

Category	Cancer, #12
Primary Author	Lavanya Choppavarapu
Secondary Authors	Kun Fang, Yini Yang, Jingwei Li, Ke yang, Yufan Zhou, Junbai Wang, Ismail Jatoi, Victor X. Jin
Title	Genome-wide analysis and characterization of 3D chromatin architecture in breast cancer endocrine resistance
Introduction	Breast cancer is heterogeneous and classified into three main subtypes based on the presence or absence of hormone receptors ERÎ±, PR and HER2. Among them, 70% are classified as ERÎ± positive breast cancers with a standard anti-hormone therapeutic treatment including tamoxifen. Even though success in the endocrine therapies, around 30-50% patients eventually develop the resistance to these agents. Hence, understanding the mechanisms of driving breast cancer progression and endocrine resistance is extremely important.
Methods	In our recent studies, we demonstrated that gene regulation controlled by three-dimensional (3D) chromatin looping interactions was lined to breast cancer endocrine resistance. We further showed that many differential topologically associated domains (TADs) and looping genes are reversible after treatment with sapitinib, a dual tyrosine kinase inhibitor of EGFR/HER2, suggesting that EGFR/HER2 signaling might play an important role in reshaping and rewiring the high order genome organization. We also explored the chromatin interactions in 3D model system by establishing and performing Hi-C on 3D spheroids of three breast normal and cancer cells MCF10A, MCF7 and MCF7TR and compared TADs and looping genes with those in 2D monolayers.
Results	Our results demonstrated thousands of 3D-growth-specifc TADs and looping genes in 3D spheroids of breast cancer cells and observed that the strengths of looping genes were statistically different between 2D monolayers and 3D spheroids. Furthermore, we identified novel 3D growth-specific looping genes within Hippo relevant pathways, of which two genes showed potential prognostic values in measuring the outcome of the endocrine treatment. Finally, we confirmed a few selected genes in Hippo relevant pathways with enhanced looping in organoids of breast cancer tumor tissues.
Conclusions	We are currently conducting the genome-wide functional characterization of 3D chromatin architecture and looping in breast cancer tumor tissues. The results from our tissue data will further improve our understanding of the 3D-regulated inter-tumor heterogeneity in tamoxifen-treated recurrent breast cancer.

Category	Cancer, #13
Primary Author	Madeline Dzikowski
Secondary Authors	Gwen Lomberk
Title	Investigating Interactions between G9a and the ATM/ATR Pathways to Assess Synthetic Lethality Strategies in ATM-deficient Pancreatic Ductal Adenocarcinoma
Introduction	Pancreatic ductal adenocarcinoma (PDAC) remains a highly lethal cancer with an urgent need for more effective therapeutic strategies. Genomic analyses suggest that upwards of 25% of PDAC patients have mutations in DNA damage response (DDR) pathway genes, including ATM, BRCA1/2, and PALB24. Mutation in ataxia telangiectasia mutated (ATM) kinase, a major kinase involved in recognizing double- strand breaks, occurs in upwards of 6% of PDAC patients. If ATM is mutated, then the cells must rely on the related ATR pathway for sensing DNA damage. G9a, a histone methyltransferase, is recruited to the site of DNA breaks via its phosphorylation by ATM or binding to RPA, a target of ATR kinase5,6. G9a is upregulated in pancreatic cancer and its inhibition abrogates cell growth, suggesting G9a as a potential therapeutic target6,7. If G9a plays a critical role in the ATR and/or ATM pathways, it may be possible to leverage G9a inhibition in ATM-deficient PDAC patients to develop more effective therapeutic strategies.
Methods	Previously, our lab has performed experiments demonstrating that combined targeting of G9a and a downstream effector of ATR, CHK1, synergistically inhibit PDAC growth8. However, the functional interaction between G9a and the ATM or ATR proteins remains unclear. Using linear motif analysis, we identified two potential phosphorylation sites, in addition to the previously described S569, that may be involved in ATM/ATR signaling, namely S525 and S579..
Results	Indeed, in vitro kinase assays demonstrated ATM- and ATR-mediated phosphorylation of G9a at these 3 sites. We also found increased G9a automethylation in the presence of ATM or ATR, suggesting that phosphorylation stimulates the catalytic activity of this methyltransferase. Furthermore, affinity purification of G9a followed by mass spectrometry showed interaction with ATM, ATR and ATRIP in cells.
Conclusions	To better understand the role of G9a in both ATM and ATR signaling, we are studying the impact of G9a knockout on DDR effector signals upon induction of DNA damage through single-stranded (ATR) or double-stranded (ATM) breaks. This research will provide key insight into the functional interactions between the signaling pathways associated with ATM and ATR kinase activation and the methyltransferase G9a and the rationale to further investigate leveraging G9a inhibition in ATM-deficient PDAC for synthetic lethality approaches.

Category	Cancer, #14
Primary Author	Margaret A Stebbins, BSc.
Secondary Authors	Dr. Samuel Bobholz, Allison K. Lowman, Savannah R. Duenweg, Aleksandra Winiarz, Fitzgerald Kyereme, Dr. Jennifer Connelly, Dr. Dylan Coss, Dr. Dr. Wade M. Mueller, Dr. Mohit Agarwal, Dr. Anjishnu Banerjee and Dr. Peter S. LaViolette
Title	SOX2 Positive Glioblastoma Invasion Beyond Contrast Enhancement Detected with Radio-Pathomic Maps of Cell Density
Introduction	In the treatment of glioblastoma (GBM), MRI is used to determine the location and extent of cancer. Often regions of tumor invasion occur outside of gadolinium contrast enhancement, and more research is needed to better detect these regions of infiltrative glioblastoma. This study compares radio-pathomic maps of cell density to autopsy tissue samples stained with SOX2 to determine the extent of tumor invasion beyond contrast enhancement.
Methods	A 48-year-old male diagnosed with a primary GBM with an overall survival of 155 days was included for this study. Three autopsy tissue samples were analyzed for HE and SOX2 positive cell staining outside of contrast enhancement. Pre- and post-contrast T1-weighted images (T1, T1C), T2-weighted FLAIR images, and apparent diffusion coefficient (ADC) images obtained 12 days prior to death were used for this study. A radio-pathomic model was applied to predict pathological features including cellularity (Cell) and tumor probability maps (TPM)
Results	In each of the three samples, SOX2 staining identified tumor cell invasion beyond regions of contrast enhancement that were highlighted by both the cell density map and TPM. Slices 1 and 2 (Figure 2) display SOX2 positive invasion beyond regions of contrast enhancement, but within the TPM-identified tumor region. Slice 3 (Figure 2) displays SOX2 positive invasion farther outside regions of contrast enhancement, where both TPMs and histological signatures do not suggest invasive tumor.
Conclusions	Radio-pathomic maps of cellularity and tumor probability highlight regions of infiltrative glioblastoma cells beyond contrast enhancement that were identified with SOX2 staining. Additionally, SOX2 staining demonstrated the potential for identification tumor invasion not previously identified by H&E and traditional histological signatures. These results highlight the need for improvement in tumor invasion identification techniques at both a microscopic and macroscopic level.
Reference 1	Bobholz et al. MedRXiv 2022, doi:10.1101/2022.08.17.22278910.

Category	Cancer, #15
Primary Author	Mary L. Faber, PhD
Secondary Authors	Robyn AA Oldham, Archana Thakur, Steven A Gifford, Theresa A Dlugi, Mary Jo Rademacher, Lawrence G Lum, Nathan J Schloemer, Jeffrey A Medin
Title	Characterization of a Novel Anti-CD30/Anti-CD3 Bispecific Antibody Conjugate for Immunotherapy of CD30+ Malignancies: Preparation for a Phase I Clinical Trial
Introduction	Chimeric antigen receptor (CAR) modified T cells have delivered clinical successes for patients with leukemia and lymphoma, though responses are frequently marred by life-threatening toxicities such as cytokine release syndrome. Gene modified autologous T cell products can also be expensive and complex to produce. Bispecific antibody (biAb) armed T cells can similarly redirect autologous T cells to kill tumor-associated antigen expressing cells and are more straightforward to manufacture. CD30 is a promising immunotherapeutic target due to its expression on a number of malignancies including Hodgkinâ€™s lymphoma, some non-Hodgkin lymphomas in both adult and pediatric disease, pediatric AML, and about 30% of all non-lymphoid malignancies. Expression of CD30 on normal tissues is limited, with low expression on activated T and B cells. Several approaches targeting CD30 are currently being evaluated in preclinical and clinical settings, including an antibody-drug conjugate and CAR-T therapies.
Methods	The aim of the present study is to develop and assess efficacy of our novel CD30/CD3 biAb armed T cells. Five novel anti-CD30 monoclonal antibodies were characterized by epitope mapping, and DNA and protein sequencing. Two that bind different epitopes of CD30, 8D10 and 10C2, were selected for further development. Each was heteroconjugated with anti-huCD3 antibody (OKT3) to produce anti-CD3x8D10 (bi8D10) and anti-CD3x10C2 (bi10C2). BiAb-T cells were assessed by flow cytometry for cell conjugation ability, by standard.^{51} Cr-release assay for *in vitro* cytotoxicity, and by ELISA for cytokine production, each after co-culture with target cells.
Results	Bi8D10-T cells efficiently bound CD30+ tumor cells and were cytotoxic to all CD30+ cell lines tested. Bi10C2-T cells were less effective. When co-cultured with CD30+ tumor cells, bi8D10-T cells and bi10C2-T cells robustly produce IL-2 and IFN- Î³. Neither bi8D10-T cells nor bi10C2-T cells are cytotoxic to or produce cytokines in response to CD30- or CD30low cells. The ability of bi8D10-T cells to combat a CD30+ malignancy was assessed in an *in vivo* mouse model. The bi8D10-T cells were more effective than unarmed T cells. In preparation for the Phase I clinical trial, 8D10 was screened for binding to over 6000 human membrane proteins to determine off-target binding. This membrane proteome analysis confirmed that 8D10 binds primarily to CD30. 8D10 was also subcloned and a MCB prepared under GMP conditions at UVa.
Conclusions	The results and conclusions above support our novel bi8D10 as a promising candidate for the clinic. We have filed an IND application with the FDA and have a clinical trial listed with clinical trials.gov (NCT05544968).
Acknowledgements	
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Category	Cancer, #16
Primary Author	Mary Jo Rademacher, BS
Secondary Authors	Nathan J. Schloemer, MD and Kathleen M. Bone, PhD, MS
Title	Establishment of a Pediatric Sarcoma Patient-Derived Orthotopic Xenograft Program
Introduction	There has been minimal survival outcome improvement of pediatric sarcomas over the past 40 years despite intensification of conventional chemotherapy, surgery and radiation. Immunotherapy and precision medicine promise to be the novel therapies to impact cure rates. These treatments require nuanced disease models to appropriately assess efficacy and safety. Patient derived orthotopic xenografts (PDOX) offer the potential to predict patient responses most accurately but have limited availability in the rare and heterogenous pediatric sarcomas. To establish models to capture the diverse pediatric sarcoma populations we established a protocol to collect fresh tissue following patient/family consent from all Children's Wisconsin patients with sarcoma diagnosis to develop patient derived orthotopic xenografts.
Methods	We collected tumor specimens at clinically indicated surgical procedures for patients with an established sarcoma diagnosis or a diagnostic biopsy due to concern for sarcoma. Submitted tumor specimens underwent orthotopic surgical implantation into NOD.Cg-Prkdcscid Il2rgtm1Wjl/SzJ (NSG) mice. Mice were monitored weekly for tumor growth, weight maintenance, and disability. Upon tumor growth to 2 cm in largest diameter, disability, or 20% weight loss the tumors were considered engrafted. Engrafted sarcomas were passaged to subsequent generations of PDOX, cultured in vitro and underwent molecular assessment or cytogenetics to assess for alignment with existing clinical patient sample testing.
Results	Twenty-six patients enrolled on study. Eighteen (69.2%) patients had adequate residual tumor tissue for submission and 15 (83.3%) of those had eligible sarcoma diagnoses. 66.6% (10/15) samples were submitted following interventional radiology biopsy. Two patients had submission of samples eligible to implant following cryopreservation and demonstrated a tumor engraftment rate of 16.7% (1/6). Eleven patients submitted sample adequate for fresh implantation and demonstrated an engraftment rate of 45.5% (5/11) in first generation PDOX models. Subsequent passage to a second generation PDOX demonstrated a 58.3% (7/12) engraftment rate. Second generation PDOX models have demonstrated localized (42.9%), metastatic (42.9%) and combined (14.3%) disease. Successful passage to third and fourth generation PDOX as well as engraftment from cryopreserved PDOX sample have been performed. Cytogenetics and fluorescent in-situ hybridization (FISH) have confirmed persistent molecular characteristics of the primary human sarcomas including Ewing sarcoma and osteosarcoma.
Conclusions	We have established a protocol for the generation of pediatric sarcoma PDOX models from the residual tissue of clinically indicated oncologic surgical procedures. We developed PDOX models for a broad group of pediatric sarcomas including osteosarcoma, Ewing's sarcoma, and non-rhabdomyosarcoma soft tissue sarcomas. Cytogenetics and FISH have verified stable propagation of human malignancy. Investigation into pediatric sarcoma biology and immunotherapy target screening are ongoing. We anticipate utilization of these PDOX models for future in vivo preclinical testing of novel therapies.
Acknowledgements	We thank the patients and families who so generously donated tissue for this project, the clinical trials office teams for transport of samples and maintenance of data, and TBRC technicians for care of mice. Supported in part by MACC Fund Start-up Grant and Sharon K. Wadina Foundation - Sarcoma Foundation of America Grant through the MCW Cancer Center.
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Category	Cancer, #17
Primary Author	Nathan J. Schloemer, MD
Secondary Authors	Mary Jo Rademacher BS, Jeffrey A. Medin PhD.
Title	Mutant Thymidylate Kinase Mediated Modulation of IL-12 Transduced Sarcoma NK cell Activation
Introduction	There has been minimal survival outcome improvement for pediatric patients with sarcomas over the past 40 years despite intensification of treatments. New therapies are desperately needed. Immunotherapy, harnessing the immune system to destroy cancer, despite successes in several malignancies has thus far disappointed in sarcoma. Existing immunotherapies are largely dependent on T cell effector functions. NK cells offer an additional therapeutic cell to engage. We have shown that human sarcoma with a LV/hu-IL-12 transduction in a humanized NSG.Tg(hu.IL-15) mouse with mature human NK cells elicited a robust and specific NK cell-mediated anti-sarcoma immune response.1 However, systemic inflammation led to off-target toxicities. Introduction of a regulatory mechanism to control systemic inflammation while maintaining local NK cell augmentation to elicit a specific immune response is required prior to human implementation.
Methods	Sarcoma cell lines and primary human sarcoma short-passage samples were transduced with LV/hu-IL-12 vector containing a mutant thymidylate kinase (mTMPK) fate control, a.k.a. “suicide system”, to allow for AZT induced termination of IL-12 production. We assessed in vitro and in vivo properties of these transduced cells and their ability to modulate NK cell effector functions of inflammatory cytokine production and cytotoxicity.
Results	Lentiviral transduction (LV/hu-IL-12_mTMPK) of human Ewing sarcoma, osteosarcoma, and rhabdomyosarcoma cell lines as well as low passage primary human sarcomas, engendered robust expression of human IL-12 abrogated by AZT administration. Activation of the fate control system also elicited a dose dependent cytotoxic effect specific to the LV/hu-IL-12_mTMPK transduction. This was measured by metabolic activity (WST-1) and direct cytotoxicity (Incucyte). NK92mi IFN-gamma production was significantly augmented when co-cultured with AZT exposed transduced sarcomas. Cytotoxic granule release (CD107a) effector function was also augmented in Ewing sarcoma and rhabdomyosarcoma. Fate control activation significantly and preferentially augmented sarcoma surface expression of NK cell activation ligands for the NKG2D receptor in LV/hu-IL-12_mTMPK transduced sarcomas. However, immunocompromised NSG murine in vivo trials following orthotopic implantation of LV/hu-IL-12_mTMPK transduced sarcomas demonstrated neither IL-12 regulation nor restriction of primary tumor growth with AZT administration. No systemic toxicities of in vivo AZT administration were noted.
Conclusions	We conclude that LV/hu-IL-12_mTMPK transduction of sarcoma elicits a specific NK cell mediated immune reaction that can be modulated with induction of the mTMPK fate control system via AZT delivery. The engagement of the fate control system efficiently and specifically induces transduced sarcoma cell death and can further localize the NK cell mediated immune response through surface ligand induction. Murine AZT metabolism limits in vivo systemic assessment of this fate control system. Prior to immunocompetent efficacy evaluation, an alternative host or localized AZT delivery is required to assess the in vivo regulation of LV/hu-IL-12_mTMPK transduced sarcomas.
Acknowledgements	We thank the patients and families who so generously donated tissue for this project. Supported in part by MACC Fund Start-up Grant, Snowdrop Foundation Grant and Sharon K. Wadina Foundation’s Sarcoma Foundation of America Grant through the MCW Cancer Center.
Reference 1	Rademacher MJ, Cruz A, Faber M, et al. Sarcoma IL-12 overexpression facilitates NK cell immunomodulation. Sci Rep. 2021;11.
Ancillary Materials	VIEW MY POSTER

Category	Cancer, #18
Primary Author	Nicole Sequeira, MBBS
Secondary Authors	Rana Aliani; Rebekah Summey; Lindsey McAlarnen; Tahseen Shaik; Denise Uyar; Sherry-Ann Brown
Title	Syndromes of Concurrent Hypertension, Diastolic Dysfunction, and Pulmonary or Peripheral Edema in Cardio-Oncology: A New Classification System and Case Series
Introduction	As cancer treatment improves, patients are living long enough to develop chronic diseases of aging including cardiovascular disease. Oncology patients are at additional risk of developing cardiovascular disease from antineoplastic therapies and systemic effects of malignancy. Symptoms of cardiovascular toxicity including edema, heart failure, and hypertension can pose a diagnostic challenge, as the etiology could be cardiovascular, malignancy-related, or both.
Methods	This case series and classification system proposes a systematic methodology to categorize patients with cancer into syndromes of edema, diastolic dysfunction (DD) and/or hypertension (HTN) to aid in early detection and treatment of cardiovascular dysfunction.
Results	A three-tier cardio-oncology classification system for syndromes of edema, HTN and DD was defined, and an algorithm was developed for categorization into one of the types. A separate algorithm was developed to identify diastolic dysfunction based on echocardiography. The three proposed categories are pulmonary or peripheral edema without HTN or DD, edema caused by HTN or DD, and cancer-related edema associated with HTN or DD. Six patients with diagnoses of malignancy and cardiovascular disease who fit one of these three proposed categories were identified. Charts were reviewed to extract information regarding oncologic, medical and cardiovascular histories. Review of their cardiovascular evaluation and treatment course supports utilization of the proposed algorithms.
Conclusions	When evaluating cardiovascular symptoms in cancer patients, it can be difficult to determine if symptoms are related to underlying cardiovascular disease, cancer, therapies received, or a combination. By creating a classification system to organize patient symptoms, we hope to aid in the early diagnosis and treatment of cardiovascular toxicity in oncology patients.
Ancillary Materials	

Category	Cancer, #19
Primary Author	Philip T. Skummer, MD
Secondary Authors	William S. Rilling, MD, Eric J. Hohenwalter, MD, Sarah B. White, MD, MS, Amanda R. Smolock, MD, PhD
Title	Transarterial Yittrium-90 Radioembolization as Salvage Treatment for Patients with Breast Cancer with Hepatic Metastases
Introduction	The purpose of this study is to review a single center experience with transarterial radioembolization (TARE) for metastatic breast cancer involving the liver in the salvage setting.
Methods	This was an IRB-approved retrospective, single center study evaluating patients undergoing TARE for metastatic breast cancer between 2013 and 2022. Demographic data, prior therapies, extent of disease (intra- and extra-hepatic), treatment intent, dose of Y-90, site of Y-90 delivery, response rates, hepatic progression free survival, complications according to CTCAE v5.0, and overall survival from initial TARE were recorded. Descriptive statistical analysis was performed.
Results	A total of 9 females with a mean age of 58 +/- 15 years underwent a total of 14 procedures. All patients were ER+/HER2-, and 7/9 patients were PR+. Glass microspheres were used in most procedures (13/14, 92.8%). Most patients had bilobar (7/9, 77.8%) and extrahepatic (7/9, 77.8%) disease at time of treatment. All patients with extrahepatic disease had osseous metastases. All procedures were performed as salvage therapy. The average dose of Y-90 delivered to the treatment area was 1.87 +/- 1.08 GBq with most treatments delivered to a lobe (11/14, 78.6%). Only one grade 3 complication occurred which was a right hepatic artery dissection requiring treatment. There were otherwise no significant toxicities following treatment. Eight of 14 treatments (57%) demonstrated stable disease or partial response at the last imaging examination. The median hepatic progression free survival after TARE was 2.5 months (range: 1-27 months). The median overall survival after initial TARE was 6 months (range: 2-56 months).
Conclusions	TARE for chemorefractory liver dominant metastatic breast cancer with oligoprogression is an emerging indication. This small retrospective series demonstrates safety of TARE for chemorefractory hepatic metastatic breast cancer in the salvage setting. Further studies are warranted to better define patient selection and optimal timing of intervention yielding a survival benefit.

Category	Cancer, #20
Primary Author	Radha Vaddavalli, PhD
Secondary Authors	Venkateswara Gogineni, PhD, Sarah White, MD, MS, Amanda Smolock, MD, PhD
Title	Impact of probe tip orientation and distance on collecting system injury during renal microwave ablation in a porcine model
Introduction	The purpose of this study was to evaluate the effect of microwave ablation (MWA) probe tip and orientation relative to the central renal collecting system on the incidence of collecting system injury.
Methods	A single MWA probe (NeuWave PR 15, Madison, WI) was placed under ultrasound guidance into the lower pole of each kidney in 6 pigs (female, ~50kg). Perpendicular and parallel orientation relative to the collecting system was alternated and distance of tip to collecting system was varied. All ablations were performed at 65W for 5 minutes. Non-contrast CT was obtained to document probe position followed by contrast-enhanced CT to evaluate ablation zone and any complications. Kidneys with proximal ureter were fixed in formalin. Histologic assessment was made for damage to the collecting system and ureter and graded using a standard system.
Results	The median distance of probe tip to collecting system was 1.75 (0.1-3.2) cm in the parallel group and 0.85 (0.1-1.3) cm in the perpendicular group. Mean maximum probe temperature in the parallel group was 118.7 (+/- 8.5) Â°C and in the perpendicular group was 109.5 (+/- 6.8) Â°C. Ablation zones abutted the collecting system in 67% of the parallel group and 83% of the perpendicular group. Four of 12 (33%) ablations resulted in injury to the collecting system/ureter. One was in the parallel group with injury to the renal pelvis identified as mucosal epithelium attenuation and ulceration. Three were in the perpendicular group demonstrating acute injury to the ureter with ureter muscularis hemorrhage and necrosis. All injuries were seen when ablation zones abutted the collecting system/ureter. There were no findings on CT that appeared to be predictive of histological evidence of ureteral injury. A hematoma with contrast extravasation confirmed on pathology was seen in 1/12 ablations. There were no urine leaks on CT or histopathology.
Conclusions	Ablation zones that contact the collecting system/ureter, regardless of orientation of probe placement, appear to cause acute damage. However, transmural injury causing urine leak was not seen in any case. Survival studies are needed to fully elucidate the long-term significance of the findings of acute injury.

Category	Cancer, #21
Primary Author	Rebekah Summey
Secondary Authors	Deepak Parashar, Marissa Iden, Rachel Schmidt, Janet S. Rader, Elizabeth Hopp
Title	Exploration and exploitation of hormonal pathways in adult granulosa cell tumors for development of targeted therapeutics
Introduction	A combination anti-hormonal drug regimen for complete hormonal blockade may be an effective treatment for recurrent adult granulosa cell tumors of the ovary (AGCT). This study aimed to investigate the efficacy of a combination anti-hormonal drug regimen and to elucidate hormone pathways affected by the hallmark FOXL2C134W mutation in AGCT.
Methods	To perform this study, we developed patient-derived cell lines from two AGCT tissue samples and performed Sanger sequencing to confirm the FOXL2C134W mutation. We confirmed androgen receptor (AR) and gonadotropin-releasing hormone receptor presence with Western blot. Next, we established IC50s of each drug (bicalutamide, anastrozole or leuprolide acetate) alone and in combination via MTS-based cell proliferation assays. Organoids were then created from a primary tumor sample and a combination dose response experiment was repeated. We then used a publicly available RNA sequencing dataset to investigate upstream and downstream effects of androgen, estrogen and GnRH signaling. Gene ontology, Singscore analysis, weighted correlation network analysis, ingenuity pathway analysis and gene set variation analysis were performed to illustrate up and down regulation within these pathways.
Results	AR and GnRHR presence was confirmed in our patient-derived and commercial cell lines. Cancer cell proliferation was significantly decreased after treatment with bicalutamide and with anastrozole. A minimal effect on proliferation was seen with leuprolide acetate alone. IC50s for bicalutamide, anastrozole and leuprolide acetate were determined to be similar when used in combination, but with improved suppression of viability than seen in single medication treatment. In our organoid experiments, organoid size was decreased up to 72.9% with combination therapy, as compared to 54.5% with any medication alone. In our RNA sequencing analyses, 38 tumors were included following outlier exclusion. The hallmark of cancer pathways regarding early and late estrogen signaling, as well as androgen signaling, were found in the top 15 pathways identified with the Singscore multiScore.
Conclusions	Complete hormonal blockade with a triplet regimen of an androgen receptor blocker, aromatase inhibitor and GnRH receptor agonist may be a promising treatment for recurrent or persistent AGCT.
Reference 1	Suntsova, M., Gaifullin, N., Allina, D.A et al. “Atlas of RNA sequencing profiles for normal human tissues.” Sci Data 6, 36 (2019).
Reference 2	Andersson N, Haltia UM, Färkkilä A, Wong SC, Eloranta K, Wilson DB, Unkila-Kallio L, Pihlajoki M, Kyrönlahti A, Heikinheimo M. Analysis of Non-Relapsed and Relapsed Adult Type Granulosa Cell Tumors Suggests Stable Transcriptomes during Tumor Progression. Curr Issues Mol Biol. 2022 Jan 28;44(2):686-698.
Ancillary Materials	VIEW MY POSTER

Category	Cancer,#22
Primary Author	Savannah R. Duenweg
Secondary Authors	Samuel A. Bobholz, Allison K. Lowman, Aleksandra Winiarz, Fitzgerald Kyereme, Kenneth A. Iczkowski, and Peter S. LaViolette
Title	Comparison of voxel-wise intensity identification of prostate cancer on T2-weighted MRI with and without an endorectal coil
Introduction	The use of an endorectal coil (ERC) for prostate cancer (PCa) MRI has previously been assessed to determine if it aids in image contrast and detection of cancer foci. While studies have found ERC to increase contrast and cancer detection, particularly in small or low-grade lesions[1, 2], there has been a recent phasing out of ERC use due to patient discomfort and increased patient cost. This study tested the hypothesis that voxel-wise T2WI intensity from images without an ERC would better detect tumor presence than those with an ERC.
Methods	This study used data from 69 prospectively recruited patients (mean age 60.7 years) with pathologically confirmed prostate cancer (PCa). Patients underwent multiparametric MRI prior to surgery on a 3T MRI scanner (General Electric, Waukesha, WI, USA or Siemens Healthineers, Erlangen, Germany) with an ERC and after removal of ERC. Masks of the prostate were created using AFNI (Analysis of Functional NeuroImages, https://afni.nimh.nih.gov/) for both images. After surgery, tissue was sliced using custom 3D-printed slicing jigs modeled using the ERC-based masks, processed, hematoxylin and eosin (H&E) stained, digitized at 40x resolution using a sliding stage microscope, and finally annotated for tumor presence by a board-certified genitourinary pathologist (KAI) (n = 207 slides, 3 per patient). T2WI were Z-score intensity normalized, and slides and annotations were nonlinearly aligned to the T2WI using custom in-house control-point based MATLAB software[3]. Lesion annotations were matched to voxel-wise intensity on both T2WI, and receiver operating characteristic curves (ROC) were plotted. The area under the curve (AUC) was calculated and compared between the ERC and non-ERC images.
Results	Voxel-wise intensity from T2WI without an ERC were better able to predict tumor presence than images with an ERC in place (AUC = 0.58, 0.53, respectively).
Conclusions	Our results suggest that T2-weighted MR images without an endorectal coil may better predict voxel-wise lesion presence than acquisitions with an ERC. This may aid in MR-guided biopsy targets and subsequent treatment guidance.
Reference 1	Turkbey B, Merino MJ, Gallardo EC, et al. Comparison of endorectal coil and nonendorectal coil T2W and diffusion-weighted MRI at 3 Tesla for localizing prostate cancer: correlation with whole-mount histopathology. J Magn Reson Imaging 2014;39:1443-1448
Reference 2	Dhatt R, Choy S, Co SJ, et al. MRI of the Prostate With and Without Endorectal Coil at 3 T: Correlation With Whole-Mount Histopathologic Gleason Score. AJR Am J Roentgenol 2020;215:133-141
Reference 3	McGarry SD, Bukowy JD, Iczkowski KA, et al. Gleason probability maps: A radiomics tool for mapping prostate cancer likelihood in mri space. Tomography 2019;5

Category	Cancer, #23
Primary Author	Sumaya Ahmed
Secondary Authors	Dawn Wenzel
Title	O-GlcNAcylation is required for the abscission checkpoint
Introduction	Mitosis concludes with the physical separation of daughter cells in a process called abscission. Like other stages of the cell cycle, progression through abscission is regulated by a checkpoint known as the abscission checkpoint. The abscission checkpoint prevents premature abscission and arrests abscission in response to cell cycle errors, including lagging chromatin in the intercellular bridge. The molecular mechanisms underlying how cells detect cell division problems and respond by inhibiting the abscission machinery is currently not well understood. Here we show that the post-translational modification, known as O-GlcNAcylation is required for a robust abscission checkpoint. O-GlcNAcylation is an intercellular glycosylation of proteins where the monosaccharide N-acetylglucosamine is covalently O-linked to serine and threonine residues, much like phosphorylation.
Methods	All O-GlcNAcylation in the cell is driven by only two enzymes: glycosylation by O-GlcNAc Transferase (OGT) and de-glycosylation by O-GlcNAcase (OGA). We find that disruption of O-GlcNAc flux through siRNA depletion of either OGT or OGA prevents a robust abscission arrest. To develop a mechanistic explanation for the dependence of the abscission checkpoint on O-GlcNAcylation, we are taking multiple approaches to discover specific substrates of OGT.
Results	Using publicly available resources including The O-GlcNAc Database (www.oglcnac.mcw.edu), and confirming with experiments in cells, we have found that key proteins in the Endosomal Sorting Complexes Required for Transport (ESCRT) pathway can be O-GlcNAcylated. ESCRT proteins perform the membrane constriction and fission step of abscission, and we hypothesize that O-GlcNAcylation regulates their activity.
Conclusions	Our discovery that O-GlcNAcylation is required for the abscission checkpoint emphasizes the dynamic nature of the O-GlcNAc modification, and adds to the known regulatory mechanisms whereby cells ensure faithful cell division

Category	Cancer, #24
Primary Author	Suraj Prakash, MD
Title	A case series of patients undergoing transarterial chemoembolization of musculoskeletal tumors with drug-eluting beads
Introduction	Drug-eluting bead transarterial chemoembolization (DEB-TACE) is an established endovascular treatment for the treatment of unresectable hepatocellular carcinoma. This treatment is based on the use of microspheres to release chemotherapeutic agents within a target lesion with controlled pharmacokinetics. The safety and efficacy of DEB-TACE in the treatment of tumors outside of the liver is unknown. We aimed to assess the feasibility and safety of DEB-TACE with doxorubicin-loaded microspheres in the treatment of patients with primary and metastatic musculoskeletal tumors that are deemed unresectable or not amenable to percutaneous ablation.
Methods	A single institution retrospective analysis was performed on all patients undergoing DEB-TACE of primary and metastatic tumors of the musculoskeletal system between August 2021 and November 2022. All procedures were performed under fluoroscopic guidance using either a transfemoral or transradial arterial approach. A 4 or 5 French size base catheter was used to identify the tumor feeding artery or arteries supplying the target tumor. A microcatheter was advanced selectively into the feeding artery or arteries through which 100-300 Âµm Doxorubicin loaded beads mixed with iodinated contrast were delivered until an angiographic endpoint of near stasis was achieved. In situations in which this endpoint could not be achieved with DEB-TACE alone, additional bland embolization with 150-500 Âµm polyvinyl alcohol beads was performed. Patients were followed up by a combination of inpatient rounds, telephone follow up, and/ or outpatient clinic visits.
Results	Over the time period studied, four patients underwent a total of five DEB-TACE procedures of musculoskeletal tumors. Two of these patients underwent treatment for desmoid tumors. One patient with a desmoid tumor underwent a second DEB-TACE treatment 6 months after their first procedure with embolization performed from a different vascular territory. The other two patients studied underwent treatment of metastatic RCC lesions. Technical success was achieved in all treated patients and procedures. One patient reported the development of a lace-like rash within a few days after DEB-TACE, however this was completely resolved by 2 weeks post-procedure. One patient with metastatic RCC died 2-3 months after DEB-TACE due to systemic progression of malignancy. There were no treatment-related deaths or severe adverse events.
Conclusions	DEB-TACE with doxorubicin-loaded microspheres is a safe and feasible palliative treatment option for patients with primary and metastatic musculoskeletal tumors that are deemed to be surgically unresectable or not amenable to percutaneous ablation.

Category	Cancer, #25
Primary Author	Thiago Milech De Assuncao
Secondary Authors	Elise Leverence, Angela Mathison, Salomao Doria-Jorge, Juan Iovanna, Michael Zimmerman, Gwen Lomberk and Raul Urrutia
Title	HETEROGENEITY IN TRANSCRIPTIONAL INITIATION SIGNALS FOR PANCREATIC CANCER IS ACHIEVED BY THE EXPRESSION OF DIFFERENT PANCREATIC CANCER-ASSOCIATED MUTANTS
Introduction	Pancreatic ductal adenocarcinoma (PDAC) is a highly aggressive malignancy with a poor prognosis, accounting for approximately 3% of all cancers and 7% of all cancer-related deaths. KRAS, which encodes a small GTPase and plays a critical role in regulating cellular signaling pathways, is mutated, at distinct residues with different substitutions, in approximately 95% of PDAC. The current study represents the first comparative characterization of the most common mutants that mediate PDAC initiation.
Methods	To perform this analysis, we engineered pancreatic ductal, non-cancerous, HPNE cells to allow inducible expression of the G12C, G12D, G12R, G12V, G13D, Q61H, Q61K, and Q61R mutants and the controls EV, WT, and S17N (dominant-negative mutant). We evaluated the similarities and differences of the mutants in terms of: 1. downstream signaling, 2. nuclear transcriptional response, and 3. production of secreted mediators that reprogram the tumor microenvironment.
Results	Signaling studies demonstrated that, after induction of the various G12 and Q61 mutants, the pAKT and pERK signaling pathways are activated, except for the control S17N. The G12R mutant, however, did not activate the pathways as robustly as the other mutants. Analyses of the transcriptional landscape induced by each mutant using RNA-seq showed significant heterogeneity in gene expression pathways, as demonstrated by PCA plots and heatmaps. Pathway enrichment analysis of epigenetic genes revealed the ability of these mutants to upregulate universal stripe factors, known to pioneer the opening of chromatin, as measured by ATAC-seq. Moreover, we observed common as well as divergent regulation of gene networks that support various processes involved in cancer initiation. Deeper data analyses demonstrated that distinct subsets of KRAS mutants produce diverse mediators to reprogram the tumor microenvironment.
Conclusions	In conclusion, while we find similarities among the most frequent PDAC-associated KRAS mutants, they also display notable differences. Considering the critical role of these oncogenes in cancer initiation, the therapies being developed for their targeting, and the distinct mediators of tumor microenvironment reprogramming, this study bears not only mechanistic importance but also significant biomedical relevance.

Category	Cancer, #26
Primary Author	Venkateswara Gogineni, PhD
Secondary Authors	Kevin Koch, PhD Charles Bradley, VMD, Sean M. Tutton, MD, Sarah B. White, MD, MS
Title	Bone Ablation with a Saline-Infused System
Introduction	Mitigation of deleterious carbonization (charring) and off-target thermal damage is critical for heat-based thermal ablation in bone and specifically the spine. The purpose of this study was to evaluate the effect of bone radiofrequency ablation (RFA) in the spine with and without controlled saline infusion.
Methods	RFA with and without controlled saline infusion was performed in the vertebral bodies of 2 swine with real-time temperature and impedance recordings. All animals had probes placed at 3 levels. Group 1 underwent RFA alone. Group 2 underwent RFA with controlled saline infusion. Group 3 underwent RFA and controlled methylene blue infusion and group 4 underwent controlled methylene blue infusion only. Both pigs were euthanized, 1 immediately after ablation and 1 after MRI was obtained at 4 hours post ablation. Tissue was harvested. Histology and MRI were reviewed to evaluate ablation zone size, breach of spinal canal, damage to spinal cord and nerves, and any adverse events related to needle insertion, ablation, and/or infusion. The ablations were performed using a RFA device currently under FDA 510(k) review.
Results	Technical success for bone ablation was 100%. There was no difference in maximum and mean temperatures between controlled saline and non-infusion groups. All groups achieved temperatures above 90Â°C. Only one ablation performed without infusion had a high impedance value and low power output. Otherwise, impedance and power output were not significantly different between groups. MRI demonstrated ablation zones confined within vertebral bodies. No breach of or ablation effect at the posterior cortex or spinal cord injury was seen at any level on MRI or histology. Decreased hematopoietic cellularity around needle paths at all sites was compatible with ablation effects in the early phase on hematoxylin and eosin stains. No nerve or ganglion injury was identified on histology.
Conclusions	Bone RFA with and without controlled saline infusion can be performed safely in the spine. Concurrent saline infusion may mitigate against carbonization and does not adversely affect production of ablation zone or cause unintended collateral damage. Controlled saline infusion with thermal ablation may increase the operatorâ€™s confidence in applying thermal ablation to bone tumors in the spine.

Category	Cardiovascular & Heart, #27
Primary Author	Annie Kleynerman
Secondary Authors	Jitka Rybova, Murtaza S. Nagree, Theresa A. Dlugi, Mary L. Faber, William M. McKillop, Caitlin C. O'Meara, Jeffrey A. Medin
Title	Impaired Cardiac Function and Pathology in Acid Ceramidase Deficient Mice
Introduction	Farber Disease (FD) is an ultra-rare, autosomal-recessive, lysosomal storage disorder caused by acid ceramidase (ACDase) deficiency due to ASAH-1 gene mutation. Patients with classic FD often present with lipogranulomatosis, respiratory involvement, and neurological deficits, dying before 2 years of age. Our group developed an ACDase deficient murine model in a mixed background and published evidence of significant pathology in the hematopoietic system, central nervous system, liver, eyes, and lungs. Clinical cases suggest the heart is also affected in FD. Our group found preliminary evidence of ceramide accumulation, decreased ACDase activity, and histiocytic infiltrations in the hearts of their mixed background ACDase deficient mice, indicating notable cardiac involvement. However, specific and long-lasting consequences of ACDase deficiency on cardiac development and function have not yet been determined. Analyzing cardiac pathology in FD is beneficial for the development of new treatments that will reduce or prevent the harmful symptoms associated with ACDase deficiency. We hypothesize that ACDase deficiency and ceramide accumulation significantly affects cardiac function in novel BL/6 ASAH-1 mutant FD mice.
Methods	Specific Aims: 1.Breed the Medin lab ASAH-1 mutant mouse model into a pure BL/6 background, allowing for direct comparison to the wild type and helping facilitate downstream experiments. 2. Broadly assess the novel BL/6 ASAH-1 mutant mouse model. 3.Evaluate cardiac stress using clinically relevant assays. 4. Present physical evidence of cardiac pathology. BL/6 FD mice were generated by multiple backcrosses with a pure BL/6 line. Strain purity was assessed by Jackson Labs. To supplement the findings relating to the heart, parameters such as lifespan and weight were monitored. Complete Blood Counts were collected from peripheral blood at 3, 5, and 7 weeks. Following standard cardiomyopathy diagnostics, echocardiograms were obtained at 5 weeks of age to assess various functional cardiac parameters. Troponin I level, a common biomarker of cardiac stress and damage, was measured in serum at 7 weeks. To detect physical evidence of cardiac pathology, histological assessments were conducted. Using standard histological methods, heart tissues from 7-week-old mice were stained with H&E, Masson's Trichrome, and antibodies for Mac-2 and Cathepsin-D. Transmission electron microscopy was used to image cardiomyocytes, and Farber bodies, a cellular feature commonly observed in FD. Data are presented as mean results Â± standard error of the mean. Statistical comparisons were performed using two-tailed, unpaired Student's t-tests with unequal variances and One-way ANOVA followed by Dunnett's multiple comparisons. Statistical analyses of survival data were done using the Mantel-Cox log-rank test (GraphPad Prism, GraphPad Software, San Diego, CA). p-Values <0.05 were considered significant.
Results	We demonstrate significant impaired cardiac function and histopathology in a mouse model of ACDase deficiency. Visually smaller in size, BL/6 FD mice had decreased lifespan, lowered body weight, and decreased heart weight compared to strain controls. Troponin I was elevated in FD mice at 7 weeks. Complete blood counts demonstrated microcytic anemia and leukocytosis in the peripheral blood. Ventricular atrophy, valve dysfunction, bradycardia, decreased cardiac output, and lowered stroke volume were present in echocardiogram results. Histopathological analyses revealed cellular disarray, tissue fibrosis, increased staining for lysosomes, and elevated presence of macrophages. Upon ultrastructural analysis, heart tissue was found to have infiltrating macrophages containing excessive storage vacuoles with Farber body inclusions. FD cardiomyocytes displayed elevated amounts of cytosol with increased storage vacuoles.
Conclusions	These data demonstrate that consequences of ACDase deficiency cause cardiac pathology, leading to impaired cardiac function. Future experiments will be to measure ACDase activity and ceramide accumulation in heart tissue. FD heart tissue will be histologically accessed for lipids, vascularization, and cardiomyocyte size. Additionally, our next goal is to elucidate the mechanism behind the involvement of ACDase in cardiac development.
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Category	Cardiovascular & Heart, #28
Primary Author	Benjamin D Seadler, MD
Secondary Authors	Hamsitha Karra BS, James Zelten MS, Lisa Rein MS, Mohammed Kamalia BS, Takushi Kohmoto MD, Lucian A Durham MD PhD, Lyle D Joyce MD PhD, David L Joyce MD MBA
Title	The Impact of Increasing Tolerance for Donor Heart Travel Distance on Transplant Outcomes
Introduction	The revised 2018 UNOS Adult Heart Allocation System ranks candidates within a 500-mile radius and prioritizes highest medical urgency and best projected outcomes over geographic proximity to the recipient hospital. Since this change, a decrease in waitlist mortality and increase in transplant rate for waitlisted candidates have been described, but there is a lack of evidence comparing outcomes between transplant centers and travel distance. We investigated whether transplant center travel distance impacted the likelihood of patient transplant and 1-year posttransplant outcomes.
Methods	We queried the UNOS registry for adult patients waitlisted for an isolated heart transplant from 2016-2021 and excluded patients with a previous transplant or wait-listed at a center with < 10 annual adult transplants. Centers with â‰¥ 50% of annual transplanted donor hearts from 250 or more miles from the transplant center were defined as high tolerance centers while centers with <50% were defined as low tolerance centers for waitlisted patients and transplant recipients. Waitlist mortality, the incidence of transplantation, overall survival, and graft survival were modeled using Cox proportional hazard regression.
Results	Despite changes to the allocation system, significant variability exists amongst transplant centers regarding how far they are willing to travel on average for a donor heart. This diversity in strategy has a notable effect on transplant. For example, the average wait times were significantly lower at high tolerance centers (86.6 days vs 149.2 days, Wilcoxon rank-sum test P<0.001), the annual number of transplants at high tolerance centers were significantly higher (45.7 vs. 37.9, Wilcoxon rank-sum test p<0.001), and the ischemic time at high tolerance centers on average was 18 minutes more than low tolerance centers (3.2 hrs vs. 3.5 hrs, Wilcoxon rank-sum test p< 0.001). Additionally, a Cox proportional hazard regression showed that waitlist mortality and overall survival did not differ significantly before and after the allocation change. The only significant difference in the adjusted regression results was a higher incidence of transplant in the high tolerance centers compared to the low tolerance centers in the post-2018 allocation change period. There was no significant difference observed in the pre-2018 period. Lastly, there was a significant difference in travel distance comparing those waitlisted pre vs post 2018 allocation change Wilcoxon rank-sum test for travel distance compared by time period (pre and post Oct 18), p < 0.001).
Conclusions	Our findings suggest that before and after the 2018 revision, high tolerance transplant centers with a median donor heart acceptance distance of over 250 miles had a significantly shorter waitlist time with no difference in waitlist mortality and overall survival compared to low tolerance centers, even though ischemic time was slightly higher on average. Whether this increase in ischemic time outweighs the benefits of reducing waitlist time should be further investigated.

Category	Cardiovascular & Heart, #29
Primary Author	El-Sayed Ibrahim
Secondary Authors	Jason Rubenstein, Antonio Sosa, Ivor Benjamin
Title	Cardiac magnetic resonance imaging provides early markers of myocardial involvement post COVID-19
Introduction	Myocardial involvement showed to be associated with unfavorable prognosis in patients with COVID-19, which could lead to fatal outcomes as in myocardial injury-induced arrhythmias and sudden cardiac death. We hypothesize that cardiac magnetic resonance imaging (MRI) myocardial strain parameters are sensitive markers for identifying subclinical cardiac dysfunction associated with myocardial involvement in post-acute sequelae of COVID-19 (PASC).
Methods	Based on clinical presentations, this study evaluated a total of 115 subjects including 65 consecutive COVID-19 patients using cardiac MRI for assessment of either post-COVID-19 myocarditis or other cardiomyopathies. Subjects were categorized, based on results of the MRI exams, having either â€˜suspectedâ€™ or â€˜excludedâ€™ myocarditis. A control group of 50 matched individuals was studied. Along with parameters of global cardiac function (ejection fraction, volumes, mass), the MRI images were analyzed for measurements of myocardial T1 and T2 relaxation parameters, extracellular volume (ECV), strain, and strain rate.
Results	MRI excluded myocarditis in 15 out of 22 patients referred due to concern of myocarditis. In this group, strain significantly differentiated between suspected and excluded myocarditis patients. Similarly, strain rate significantly differentiated between suspected and excluded myocarditis patients in the group of patients referred due to concerns of other cardiomyopathies. For all studied subjects, global longitudinal strain (11Â±4% vs 14Â±4% vs 16Â±3%), global circumferential strain (13Â±5% vs 17Â±5% vs 19Â±2%), and global radial strain (20Â±9% vs 28Â±10% vs 34Â±7%) in the suspected myocarditis group were significantly smaller than those in the excluded myocarditis group, which in turn were significantly smaller than those in the control group. Similarly, global longitudinal strain rate (0.6Â±0.24s-1 vs 0.7Â±0.22s-1 vs 0.9Â±0.27s-1), global circumferential strain rate (0.6Â±0.23s-1 vs 1.0Â±0.32s-1 vs 1.0Â±0.24s-1), and global radial strain rate (1.0Â±0.49s-1 vs 1.8Â±0.73s-1 vs 1.9Â±0.65s-1) in the suspected myocarditis group were smaller than those in the excluded myocarditis group, which in turn were smaller than or equal to those in the control group. The results showed significant correlations between strain, strain rate, and global cardiac function parameters.
Conclusions	This study emphasizes the value of multiparametric cardiac MRI for differentiating patients with myocardial involvement in PASC based on changes in myocardial contractility pattern and tissue structure. Especially, myocardial strain and strain rate showed to be sensitive parameters that can detect subclinical cardiac dysfunction in patients at-risk of cardiac complications post COVID-19.
Reference 1	Xie et al. Nat Med. 2022;28(3):583-590.
Reference 2	Wang et al. J Cardiovasc Magn Reson. 2021;23(1):14
Reference 3	E Ibrahim. Heart Mechanics. Magnetic Resonance Imaging. CRC Press. 2017
Ancillary Materials	VIEW MY POSTER

Category	Cardiovascular & Heart, #30
Primary Author	Haley VanBeek, BS
Secondary Authors	Benjamin Seadler, MD, Dalip Singh, MD, G Hossein Almassi, MD, David Joyce, MD, MBA, Sarah B. White, MD
Title	A Single Institution Experience on Efficacy and Safety of Endovascular Mechanical Aspiration
Introduction	Endovascular mechanical aspiration is a catheter-based system approved for the percutaneous removal of unfavorable intravascular material found throughout the cardiovascular system. As utilization of mechanical aspiration devices rapidly increases, the indications and uses of these devices continue to be refined. We aim to use our single-center experience to provide additional insight into the application, efficacy, and safety of mechanical aspiration devices in a variety of clinical scenarios utilizing a commercially available device.
Methods	In this retrospective case series, we describe our experience with catheter-based mechanical aspiration through an analysis of all cases completed between July 2017 and July 2022 of patients aged 18 years and older. Data points collected include demographics, pertinent medical history, indication, intra-operative and post-operative complications, and hospital length of stay.
Results	A total of 13 patients met inclusion criteria. Indications included endocarditis with valvular vegetations (54%), right heart thrombus (38%), and arterial thromboembolism (8%). Aspiration was successful in 11 of the 13 patients. Intra-operative complications were rare, consisting of one aborted aspiration due to hypotension immediately pre-procedure requiring conversion to open pulmonary artery thrombectomy. Post-operative complications included the need for post-operative ECMO (15%) and death (8%). There were no cases of post-procedure pseudoaneurysm or operative site infection.
Conclusions	Review of these cases revealed high success rates utilizing a catheter-based aspiration system in a wide variety of indications. Rates of complications and mortality were low in this patient population that typically carries a high mortality rate. Catheter-based endovascular aspiration is a safe and viable treatment option for valvular vegetations, right heart thrombi, and arterial thromboembolism. This device may be a useful alternative therapy for critically ill patients who are poor surgical candidates. The use of this device in healthier patient cohorts as an alternative to more invasive procedures continues to be explored.

Category	Cardiovascular & Heart, #31
Primary Author	Hamsitha Karra
Secondary Authors	Benjamin Seadler, MD; Lisa Rein; David Joyce, MD
Title	Going the Distance: An Assessment of Donor Heart Acceptance Radius
Introduction	To address geographic inequity in organ sharing, the revised 2018 UNOS Adult Heart Allocation System mandated that Status 1 and Status 2 candidates receive priority for organs within the donor service area (DSA) and within 500 miles of the transplant center before lower priority candidates within the DSA. We hypothesized that transplant centers in low population-density UNOS regions were more likely to accept organs from a greater radius as compared to high population-density regions in the post-revision era.
Methods	Data was obtained from the United Network for Organ Sharing (UNOS) registry to include adults wait-listed for a heart transplant from 2016-2021 and exclude patients with previous transplants or wait-listed at a center with < 10 annual adult transplants. Transplant centers were grouped by travel distance tolerance. High tolerance centers received ~ 50% of annual transplanted donor hearts from 250 miles or more from the transplant center, while low tolerance centers received <50%. Regional population density was estimated using 2019 US Census data.
Results	Centers with lower population density do not necessarily have increased tolerance for donor organ travel. For example, UNOS Region 6 has the lowest population density but did not have a single transplant center with an average travel distance of greater than 250 miles. Region 11 has a population density that is nearly 4 times greater than Region 6, but an equivalent percentage of high tolerance transplant centers.
Conclusions	Analysis of this data set did not support our hypothesis that transplant centers in low-population density UNOS regions would have a higher tolerance for donor organ travel distance. This finding merits further investigation, including whether the number of transplant centers within a given region had an impact on each center's willingness to travel further. It is also worth assessing whether the utilization of the organ care system (OCS) machine would affect tolerance.

Category	Cardiovascular & Heart, #32
Primary Author	Jue Zhang, MD, PhD
Secondary Authors	Jackie Chang, Mirza Ahmar Beg, Vaya Chen, Yiliang Chen
Title	CD36 Mediates Mitochondrial Reactive Oxygen Species Production through PKM2 in Macrophages
Introduction	Excessive mitochondria-derived reactive oxygen species (mtROS) are associated with foam cell formation and atherosclerosis progression in both animal models and human patients. We previously showed that oxLDL/CD36 signaling stimulated mtROS production and facilitated diet-induced atherosclerosis in mice. However, underlying mechanisms by which oxLDL/CD36 pathway mediates mtROS production during atherosclerosis remain elusive. Pyruvate kinase M2 (PKM2) is a glycolytic enzyme recently discovered to facilitate foam cell and atherosclerosis development. We hypothesize that oxLDL/CD36 signaling mediates mtROS production by stimulating PKM2 mitochondrial translocation.
Methods	We separated mitochondria and cytosol fractions in murine peritoneal macrophages. OxLDL treatment upregulated PKM2 protein level in mitochondria fractions in a time-dependent manner (peak at 3h, ~2.5 fold), but not in cytosol. Confocal imaging further confirmed a translocation of PKM2 to mitochondria induced by oxLDL. This phenomenon was not observed in CD36-deficient macrophages.
Results	To investigate the mechanism, we immunoprecipitated PKM2 followed by mass spectrometry analysis of proteins associated with PKM2. GRP75, a known chaperone protein that imports cytosol proteins to the mitochondria was identified. Co-IP assay confirmed the interaction between GRP75 and PKM2, which was augmented by oxLDL (~3 fold). Moreover, UQCRC1, a subunit of mitochondrial electron transport chain (ETC) complex III, a major site of mtROS production, was also identified from mass spectrometry. Increased interaction between PKM2 and UQCRC1 induced by oxLDL (~3 fold) was further validated by coIP and in situ proximity ligation assay, which was dependent on CD36. In addition, PKM2 inhibitor Shikonin and PKM2 siRNA both inhibited the oxLDL-induced mtROS generation (by 50% and 100% respectively) in murine macrophages and human monocytes-derived macrophages.
Conclusions	OxLDL/CD36 axis promotes PKM2 translocation to mitochondrial which facilitates mtROS production in macrophages. It highlights the novel role of PKM2 in mtROS production during atherosclerosis and implicates GRP75-PKM2-UQCRC1 axis as a potential therapeutic target.

Category	Cardiovascular & Heart, #33
Primary Author	Nitin Somasundarum, BS
Secondary Authors	Benjamin Seadler MD, Mami Sow BS, Ali Syed MS, Hossein Almassi MD, Mario Gasparri MD, Stefano Schena MD PhD
Title	Left Ventricular Lead Placement in Patients with Prior Sternotomy Utilizing the Robotic Platform
Introduction	Cardiac resynchronization therapy (CRT) has been shown to improve cardiac function and slow the physiologic decline associated with chronic heart failure or left ventricular (LV) dysfunction. Patients with anomalous anatomy or prior pacemaker insertion may be unable to undergo endovascular insertion of an LV lead. In patients with prior median sternotomy, minimally invasive options for LV lead placement have often been foregone out of concern for post-operative adhesions increasing the risk of iatrogenic injury. Successful placement without thoracotomy or repeat sternotomy would decrease the morbidity associated with the procedure. In this case series we present a cohort of patients with prior median sternotomy who have undergone robotic-assisted LV lead placement.
Methods	A single-center retrospective review of all patients from 2018 to 2023 who were referred for LV lead placement and previously underwent sternotomy were included in this study. The cohort only included cases that utilized the robotic platform. Primary outcome was successful lead placement. Additional outcomes include conversion to open procedure and lead failure within 1 year.
Results	There were 6 patients that met inclusion criteria. The median age was 75 and 83% were male. Indications for CRT included ventricular dyssynchrony in 1 patient, declining LV function in 2 patients, and chronic heart failure in 3 patients. Prior operations included CABG, MAZE, mitral valve repair, congenital AV canal defect, and VSD repair. All leads were placed successfully, however; one patient required conversion to thoracotomy due to dense adhesions. There were otherwise no intraoperative or postoperative bleeding complications. The median length of stay was 2 days and 30-day mortality was 0%. No patients required re-intervention on their CRT system at 1-year post-placement.
Conclusions	The findings of this case series underscore that LV lead placement can reliably be achieved utilizing the robotic platform in patients with prior sternotomy. It may be that the population of patients who were traditionally considered contraindicated for minimally invasive LV lead placement may be able to benefit from robotic-assisted placement. A larger cohort size is needed to confirm the efficacy and safety demonstrated in these findings.

Category	Genomics, Precision Medicine & Data Science, #34
Primary Author	Amanda Miller
Secondary Authors	Hongfei (Sophie) Liu, PhD; Angela Mathison, PhD; Michael Zimmermann, PhD; Victor X. Jin, PhD; Raul A. Urrutia, MD
Title	Mellowes Center Bioinformatics Shared Resources: Single-cell RNA-seq Analysis
Introduction	Single-cell RNA sequencing (scRNA-seq) is a powerful genomic technology for characterizing cellular heterogeneity by profiling the transcriptome of thousands of individual cells. Its ability to make new biological discoveries has led such technology an explosion of use in biomedical research areas, such as oncology and immunology. The Mellowes Center Bioinformatics Shared Resources provides the bioinformatics service to analyze scRNA-seq data with a standardized workflow to investigators across the Medical College of Wisconsin (MCW), including a web-based report and an interactive easy exploration of results. In brief, the bcl2fastq tool is first performed to de-multiplex raw reads, Cell Ranger software from 10x Genomics is then used to align reads, generate feature-barcode matrices and perform initial clustering and gene expression analysis.
Methods	Additional outputs from Cell Ranger provided to investigators include web summaries and cloupe files which can be uploaded to the Loupe Browser for data visualization. The R package Seurat is further used to perform quality control (QC), data filtration/normalization, calculation of high-variance genes, dimensional reduction, graph-based clustering, and the identification of cluster markers.
Results	The interactive HTML web-based report summarizing the sequencing and analysis results is finally generated. In addition to the standard report, more custom analyses based on the investigator's needs, such as supervised assignment of cluster identity, pathway enrichment and pseudo-time analysis, can also be performed.
Conclusions	In addition to scRNA-seq data analysis, our services within the shared resources provide other bioinformatics analyses, including bulk RNA-seq, DNA-seq, ATAC-seq, CUT&RUN, ChIP-seq, Spatial Transcriptome and many others.

Category	Genomics, Precision Medicine & Data Science, #35
Primary Author	Gareth Pollin
Secondary Authors	Thiago M. De Assuncao, Salomao Doria Jorge, Young-In Chi, Michael T. Zimmermann, Raul Urrutia, Gwen Lomberk
Title	Functional inferences derived from defining the interactome of the H3K9me2 Writers and Readers
Introduction	The H3K9Me2-driven histone code pathway has emerged as key for cancer initiation and progression. The H3K9Me2 mark is written by the lysine methyltransferases Euchromatic Histone Lysine Methyltransferases, EHMT1 and EHMT2, and read by the heterochromatin protein 1 (HP1) chromobox (CBX) protein family. Currently researchers are evaluating the inhibition of regulators involved in this pathway for therapeutic purposes. Thus, knowledge on the complexes which are operational to support the function of these writers and readers during the process of cell proliferation is critical for our understanding of their role in carcinogenesis. Here, we define and comprehensively analyze the interactome for these proteins during the cell cycle.
Methods	We immunopurified each of these proteins individually and performed mass spectrometry of the associated proteins at two different phases of the cell cycle, namely G1/S and G2/M.
Results	Our findings identify novel binding proteins for these writers and readers, as well as confirm known interactors, to show the formation of distinct protein networks in a cell cycle phase-specific manner. Through a multi-tiered bioinformatics-based approach, we reveal that many interacting proteins exhibit histone mimicry, based on a H3K9-like linear motif. Gene ontology analyses, pathway enrichment, and network reconstruction inferred that these comprehensive H3K9me2 writer and reader-associated interacting protein networks participate in various functions, including transcription, DNA repair, splicing, and membrane disassembly.
Conclusions	â€¯â€¯Combined, our data reveals relevant complexes to elucidate key functions of this epigenomic pathway, which provides insight for a better understanding the biochemistry of cell cycle-associated epigenomic processes that are also highly significant in carcinogenesis.

Category	Genomics, Precision Medicine & Data Science, #36
Primary Author	Jaime Wendt Andrae, MB(ASCP)cm
Secondary Authors	Michael Tschannen, Angela Mathison, Michael Zimmermann, Victor Jin, Raul Urrutia
Title	Advancing our Understanding of Diseases and Cellular Biology through Transcriptomic Sequencing
Introduction	Transcriptomic sequencing, or RNA-Seq, is a next generation sequencing (NGS) technique that is used to interrogate the transcriptome of an individual tissue type or a population of cells. We highlight here the progression of transcriptional assays that can be utilized on translational and basic science research samples to uncover mechanistic and cellular changes that result from a variety of diseases and treatments. The Research and Development (R&D) team at the Mellowes Center (MC) have established end-to-end RNA-Seq pipelines as part of the greater menu of genomic services offered to MCW investigators. Researchers can interrogate the transcriptome of cells, tissues (fresh frozen or FFPE), single cell dissociated tissues, and much more. By understanding and checking the quality of the RNA, the R&D team adjusts protocols to produce the most accurate and relevant data.
Methods	Bulk RNA-Seq can be initiated from 100pg to 1000ng of high quality RNA (RNA Quality Number (RQN) of 6-10 as measured by Agilentâ€™s Fragment Analyzer or equivalent) and undergo a polyA tail enrichment. If working with lower quality RNA (RQN 4-7 and DV200 score â‰¤60%), the MC utilizes a ribosomal depletion method to focus on the transcriptome. The workflow used in this kit takes advantage of an innovative technology allowing removal of ribosomal cDNA (cDNA fragments originating from rRNA molecules) after cDNA synthesis using probes specific to mammalian rRNA. rRNA depletion methods are especially well-suited for working with very small quantities of total RNA or cells, including intact single cells.
Results	Once quality standards are met for all prepared libraries, paired-end sequencing is completed on the Illumina NovaSeq 6000. In instances where tissue is limited or RNA is highly degraded (FFPE samples), investigators can work with the MC to utilize or develop a capture panel allowing identification and transcript counting via NanoString technology. Finally, MC workflows are established to provide insight about the transcriptomics of individual cells within a mixed population of cells. Understanding the diversity of cell types and changing transcriptomics from a heterogenous tissue can reveal the critical and unique characteristics of a tissue or organ.
Conclusions	For all MC services, bioinformatic support is available to collaborate, analyze, interpret, and integrate these diverse data sources. The MC's vision is to innovate and drive cutting-edge technologies that will advance basic mechanistic understanding of disease etiology, pathophysiology, and potential therapeutics with the goal of increasing the knowledge base in translational, personalized medicine research. Using experience from a variety of projects, we will tailor assays, provide services, and collaborate to address the current and future needs of researchers throughout MCW.

Category	Genomics, Precision Medicine & Data Science, #37
Primary Author	Jessica Wagenknecht
Title	ABCC6 3-State Structural Model Enhances Functional Interpretation of Genetic Variants
Introduction	Mutations of ATP Binding Cassette Subfamily C Member 6 (ABCC6) protein cause either Pseudoxanthoma Elasticum (PXE) or the more severe condition, Generalized Arterial Calcification of Infancy (GACI). However, the underlying molecular underpinnings are unknown for how mutations alter ABCC6 protein function, and if those differences contribute to some patients developing PXE versus GACI. These two diseases are both characterized by calcification of body tissues via hydroxyapatite deposition, yet have drastic differences in age of onset, phenotype, progression, and prognosis.
Methods	Without an experimentally solved protein structure, functional interpretation of genetic variants within the protein is quite difficult. To better interpret the genetic variation within ABCC6, we used an integrative hybrid approach to generate three structural models, which capture the main conformations ABCC6 takes including unbound, substrate-bound, and ATP-bound. These models were used in structural calculations of both clinically observed genetic variants and variants from nationwide databases
Results	Structure-based calculations categorize the effects of variants in more specific ways and enable us to interpret the functional mechanism of more variants than with any single 3D model. Use of multiple functional conformations and structure-based calculations enabled us to analyze a broad portfolio of genetic variants efficiently, with analysis of how mutations alter the dynamic interconversion between these states left for future study.
Conclusions	Our results not only aid in mechanistic understanding of PXE and GACI, but also reveal a novel method of high throughput bioinformatic protein variation analysis through multi-conformational models that are informed by functional data.

Category	Genomics, Precision Medicine & Data Science, #38
Primary Author	Michael Tschannen MB(ASCP)cm
Secondary Authors	Jaime Wendt Andrae MB(ASCP)cm, Dr. Angela Mathison Ph.D, Dr. Raul Urrutia Ph.D
Title	Advancing Precision Medicine with Basic and Translational Research Tools, Services, and Assays at the Mellowes Center
Introduction	Every day, Omics techniques are used to understand, prevent, detect, and treat diseases with precision. The Mellowes Center (MC) is at the forefront of these innovative discoveries with our ability to pair cell and molecular biology techniques with Next Generation Sequencing (NGS). Integration and customization of NGS assays allows for mechanistic dissection of the initiation, establishment, and progression of diseases. At MCW, our goal is to allow the efficient translation of new technologies and applications to basic, translational, and clinical research to address the unmet needs of the research community. Consultations are available with the MC to facilitate and ensure the focus is aligned and service products are appropriate to the hypotheses being asked. Working with investigators, we can initiate the experimental plan, customize and trouble shoot assay design, plan state-of-the-art library preparations and sequencing technologies, and prepare bioinformatic support for translating data to knowledge. All of these services are available to basic and translational researchers to ensure that Precision Medicine becomes a reality for all patients.
Methods	The MC has experience deploying methods using DNA and RNA from blood, formalin-fixed paraffin-embedded (FFPE), and fresh frozen cells or tissues. By understanding the input source material, the Research and Development (R&D) team can adjust protocols to produce the accurate and relevant data. Once extracted, our team applies optimized methods to interrogate intact or degraded DNA through genome, exome, or custom targeted sequencing. The MC also provides dynamic snapshots of cellular activity at the molecular level through transcriptomic sequencing (RNAseq), targeted transcriptome identification and screening (Nanostring), and several epigenomic sequencing offerings including reduced representation bisulfite (RRBS), chromatin immunoprecipitation (ChIP) sequencing, Assay for Transposase-Accessible Chromatin sequencing (ATAC-seq), Cleavage Under Target and Tagmentation (CUT&Tag), and Cleavage Under Target and Release Using Nuclease (CUT&RUN).
Results	We continuously look to extend and expand our services and have recently completed several single cell and spatial transcriptomics projects (10X Genomics Chromium and Visium). Each of these â€˜Omics technologies is supported through bioinformatic services available at the MC making the data accessible and adding cellular and molecular knowledge to disease phenotypes.
Conclusions	The vision of the MC is to innovate and drive cutting-edge technologies that will advance basic mechanistic understanding of disease etiology, pathophysiology, and potential therapeutics with the goal of increasing the knowledge base in translational, personalized medicine research. Using experience from a variety of projects, MC will tailor assays, provide services, and collaborate to address the current and future needs of researchers throughout MCW.

Category	Genomics, Precision Medicine & Data Science, #39
Primary Author	Neshatul Haque, PhD
Secondary Authors	Tomoki Kawai, Brian D. Ratnasinghe, Raul Urrutia, Luigi D. Notarangelo, Michael T. Zimmermann
Title	Development of prediction model for variant effect assessment of RAG1/2 complex
Introduction	Every individual's genome is unique, yet we assume they perform identical functions at the population level. Diseases like cancer, autoimmune disorders, and inborn errors of immunity, have strong genomic drivers, highlighting the uniqueness of our medically relevant genomic variations. Therefore, such diseases require individualized approaches for diagnosis, mechanistic inference, and treatment. Diagnosis of human conditions from genomic variation has potential to significantly improve because of cheap, accessible, and robust sequencing techniques. Despite these gains, the clinical understanding of the relation among the genetic variations, human phenotypes, and diseases is lacking because of the complex nature of the functioning genomic products encoded by genes. Unlike the sequence-based methods for assessing the effect of genetic variations that are currently in widespread use, we have developed an integrative prediction model by incorporating sequence and 3D structural characteristics of the protein â€“ and from the functional multi-protein complex environment.
Methods	For the development of such methods, we have selected one of the clinically significant RAG recombinase enzymes system. Genomic variations in RAG1 and RAG2 (RAG1/2) have been reported to cause may immunity related fatal diseases like CHIDG, SCID and Omen Syndrome. To develop our prediction model, we generated experimental data on 182 RAG1/2 missense variantsâ€™ enzyme function. Then, we developed full length 3D models of RAG1/2 complex in four states, and calculated 68 different distinct scores. Multiple linear regression (MLR) and partial least square regression (PLSR) were implemented to develop the prediction model by leveraging experimental enzymatic assay data and the scores, characteristic to each distinct variant. The regression model was separately developed for RAG1 (R2 = 0.914 and enzyme activity RMSE = 10.34%) and RAG2 (R2 = 0.973; RMSE = 9.57%) to predict RAG activity changes from structure-based scores.
Results	The method, with ~10% error, proved to be very successful and can be used to develop and implement specific models for other clinically significant enzymes.
Conclusions	Thus, our approach to studying human genetic variation via the encoded gene products in 3D, is a key advance for interpreting causes of inborn errors of immunity, and generalizable to other rare diseases and cancer.
Reference 1	Liu, Xiaoming, et al. "dbNSFP v4: a comprehensive database of transcript-specific functional predictions and annotations for human nonsynonymous and splice-site SNVs." Genome medicine 12.1 (2020): 1-8.
Reference 2	Delmonte, Ottavia M., Catharina Schuetz, and Luigi D. Notarangelo. "RAG deficiency: two genes, many diseases." Journal of clinical immunology 38 (2018): 646-655.
Reference 3	Delmonte, Ottavia M., Anna Villa, and Luigi D. Notarangelo. "Immune dysregulation in patients with RAG deficiency and other forms of combined immune deficiency." Blood 135.9 (2020): 610-619.

Category	Genomics, Precision Medicine & Data Science, #40
Primary Author	Young-In Chi
Secondary Authors	Salomão D. Jorge, Thiago M. De Assuncao, Angela J. Mathison, Gwen Lomberk, Michael T. Zimmermann, Donald G. Basel, James W. Verbsky, and Raul Urrutia
Title	Structural Genomics Studies Shed Light on the Mechanisms of Dysfunction of the KDM5C A388P Mutation in a Developmental Disability Child
Introduction	Histone modifications are at the center of epigenetic regulations and many human diseases are caused by mutations in the components of epigenetic apparatus. From the inpatient child with developmental defects and protein losing enteropathy, we identified the A388P missense mutation in KDM5C, a H3K4 lysine-specific histone demethylase. To elucidate the underlying mechanism of molecular dysfunction, we carried out the multi-layered mechanistic-based analyses along with known pathogenic and neutral variants as control. We used both the universal and protein-specific metrics from each protein layer including 3D structure and 4D all atom molecular dynamics (MD) to assess the damaging effects of the variants and gain better mechanistic insights.
Methods	We used a set of metrics that has been previously identified as functionally relevant and effective measures of functional disruption for non-heme Fe(II) histone methyltransferases. Individual scores were combined with equal weights to generate the overall damaging scores to make overall damaging assessment. As expected, all pathogenic control variants are predicted to be damaging by our analysis. They are expected to disrupt the structural aspects of the protein such as protein stability, folding, local geometry, and global pKa values which can affect the catalytic activity of pH-dependent oxidative enzymes such as KDM5C, and/or the dynamics aspects of the protein such as coordinated molecular fluctuations (RMSF), substrate/Zn interactions and optimal Fe(II)-methyl distances. Likewise, the case variant A388P is also predicted to be damaging by severely disrupting the protein stability, but not the key parameters associated with the optimal catalytic activity such as substrate/Zn interactions or Fe(II)-methyl group distances. More importantly, this A388P mutation is expected to disrupt the inter-domain communication that is essential for concerted motions of individual domains for both reader and writer functions. On the other hand, the neutral control variant D723N is expected to be damaging by our analysis although it is currently annotated as likely benign in the genomic variation database. The D723 residue is located right next to one of the zinc ligation sites and its mutation is expected to cause structural perturbation, reduced substrate/Zn interactions, and notable pKa shift within the protein. Due to these conflicting predictions, we reclassified it as a variant of uncertain significance (VUS)
Results	The results of this comprehensive study reveal the key biophysical mechanisms underlying the disfunction of this common disease-causing variant. This type of comprehensive structure- and MD-based analyses should help develop improved impact scoring systems to interpret the damaging effects of variants as well as provide detailed mechanistic insight that is not currently predictable from sequence alone.
Conclusions	This new knowledge will be of benefit to the increasing number of patients carrying this mutation, by shedding light on the molecular mechanisms of their disease and potentially leading to new avenues for therapy.

Category	Geriatrics & Aging, #41
Primary Author	Grace F. Wittenberg
Secondary Authors	Ann Reddy, MPH; David R. Gifford, MD, MPH; Marguerite M. McLaughlin, MA; Vivian Leung, MD; Rosa R. Baier, MPH
Title	Design of a Nursing Home Infection Control Peer Coaching Program
Introduction	To pilot test and refine an infection control peer coaching program, Infection Control Amplification in Nursing Centers (ICAN) in partnership with long-term providers.
Methods	This was a quality improvement intervention design and pilot test. Participants were infection preventionists (IPs) from seven Connecticut nursing homes (NHs). We co-designed and pilot tested the ICAN program with NH IPs. The initial program involved designating peer coaches to provide real-time feedback on infection control practices to coworkers and targeting coachesâ€™ observations using data from both observations shared by coaches in daily huddles and weekly audit data about hand hygiene, masking, and transmission-based precautions. IPs tested the initial program while providing feedback to the research team during weekly calls. We used information from the calls, participant surveys, and the pilot process to update the program.
Results	Despite IPs reporting that the initial program highly aligned with facility priorities and needs, their weekly call attendance dropped as they dealt with short staffing and COVID-19-related outbreaks, and none implemented all of the program's components as intended. Most IPs described making changes to increase feasibility and reduce burden on staff amidst short staffing and other ongoing issues exacerbated by the SARS-CoV-2 pandemic. We used information from the IPs and the pilot to update the program, including shifting from having IPs lead implementation by themselves to using a team-based approach. The updated program retains peer coaches and audit data, while broadening the mode of feedback from huddles to communication using other means like email in addition to huddles. It also provides NH staff with flexibility to tailor implementation to each of their needs and constraints.
Conclusions	Working with staff, we developed an infection control peer coaching program that may be of use to NH leaders seeking strategies to strengthen infection control practices. Future work should involve implementing and evaluating the updated program.
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Category	Geriatrics & Aging, #42
Primary Author	Jenna L. Hansen, BS
Secondary Authors	Judith E. Carroll, PhD, Teresa E. Seeman, PhD, Steve W. Cole, PhD, & Kelly E. Rentscher, PhD
Title	Associations Between Chronic Stress Exposures, Stress Hormones, and Biological Aging in Midlife Adults
Introduction	Psychosocial stress and adversity have been linked to accelerated aging and increased risk for age-related diseases. Animal and in vitro studies have demonstrated that exposure to stress hormones (catecholamines, glucocorticoids) can impact biological aging processes such as DNA damage and cellular senescence, suggesting they play a key role in links between stress and aging; however, these associations have not been well investigated in humans. This study examined associations between chronic stress exposures, stress hormones, and biological aging markers in midlife adults, and whether stress hormones mediated associations between stress and aging.
Methods	Participants were 543 adults aged 26-78 years (Mage=54.0, 50.5% female) in the nationally representative Midlife in the United States Refresher cohort. They reported their chronic stress exposures in childhood and adulthood (Stressful Life Event Inventory) and provided 12-hour urine samples that were used to assess norepinephrine (NE), epinephrine (E), and cortisol. RNA sequencing of whole blood derived aging biomarkers: cellular senescence marker p16INK4a (CDKN2A), the DNA damage response (DDR), and the pro-inflammatory senescence-associated secretory phenotype (SASP).
Results	Multiple regression models adjusting for age, sex, race/ethnicity, BMI, smoking status, alcohol use, and medications revealed that more childhood exposures were associated with higher NE (ï•¢=0.08, p=.047) and marginally higher E (ï•¢=0.08, p=.08). Higher NE related to elevated DDR expression (ï•¢=0.16, p<.001), and higher NE (ï•¢=0.14, p=.002) and E (ï•¢=0.11, p=.01) related to elevated SASP expression. Higher cortisol was associated with lower p16INK4a mRNA (ï•¢=-0.10, p=.02). In tests of mediation, NE mediated associations between childhood exposures and both DDR (ï•¢ab=0.01, 95% CI [0.001, 0.03]) and SASP (ï•¢ab=0.01, 95% CI [0.0004, 0.03]), such that more exposures were associated with higher NE, which related to elevated DDR and SASP. Further adjustment for mRNA markers of cell subsets in the leukocyte pool suggested that leukocyte composition may mediate associations between NE and DDR and SASP.
Conclusions	Findings provide preliminary evidence in humans that stress hormones may impact key biological aging processes in the stress-senescence-inflammation pathway and may be a mechanism linking chronic stress exposures in childhood to accelerated aging.

Category	Geriatrics & Aging, #43
Primary Author	Tarini Mitra
Secondary Authors	Kelly Clohesey, MOT, OTRL; Whitney Morelli, PhD
Title	iWear: The Future of Monitoring Older Patients' Health Outside the Clinic to Prevent Functional Decline
Introduction	Older adults' healthcare costs on average about 3 times greater than those of the average working adult. In addition to an increased prevalence of chronic disease, functional decline and functional limitations account for 64% of emergency department visits in adults above 65. With decreasing time providers have to spend with patients, integrating wearable activity monitors (such as an Apple Watch or Fitbit) into the healthcare setting for older adults to be used to remotely monitor and assess (1) changes to patients' functional status, (2) adherence to rehabilitation programs, and (3) early referral and intervention when clinically significant changes are detected. The purpose of this study is to 1) to assess the ability of an activity monitor to remotely detect differences among functional status and 2) to assess the feasibility and acceptability of older adultsâ€™ compliance to wear an activity monitor over a period of time.
Methods	Older adults participating in remotely-delivered physical activity study with complete data (N=89) were included. Participants were mailed an ActiGraph GT3X+ activity monitor and were instructed to wear the activity monitor on their right hip, during all waking hours. Participants recorded any times the activity monitor was removed. Additionally, participants completed an online questionnaire to assess their self-reported present health and completed a walk test wearing the activity monitor to assess their current functional status (gait speed, time spent sedentary, in light, moderate, and vigorous physical activity, and sit-to-stand transitions). Feasibility and acceptability of activity monitor wear compliance was assessed using percent of valid wear data. Assessment of activity monitor differences among functional status was assessed using ANOVA.
Results	All findings are significant. Results indicated participants without history of falls had faster gait speed (2.3(0.7 sec) vs 1.8 (0.6) sec), less sedentary time (669(118) min/d vs 784.3(92) min/d) and had more daily sit-to-stand transitions (73(13) transitions/day vs 42(21) transitions/day) compared to those with a reported fall ($p<0.05$). Participants without a history of falls engaged in more active behaviors overall, and more time in higher intensity activities than those with a reported fall ($p<0.05$). We showed high adherence rates to activity monitor wear, with 94% of the sample returning the activity monitor with seven-days of valid data on a seven-day wear protocol.
Conclusions	Results indicate wearable devices provide a feasible and acceptable way to remotely monitor older adults' activity. Further, evidence indicates gait speed, time spent in physical activities, and sit-to-stand transitions, as assessed by an activity monitor, may be used a digital biomarker to remotely detect change in functional status and early intervention to reduce functional decline and/or functional-related injuries and hospitalizations. This preliminary data provides foundational evidence to explore implementation strategies for using wearable devices to remotely monitor patients between provider visits.
Acknowledgements	This work was funded by NCI K01CA255414 (PI: Morelli)
Ancillary Materials	VIEW MY POSTER

Category	Hematology & Blood, #44
Primary Author	David Scott, MS
Secondary Authors	Lisa Baumann Kreuziger MD, Damon Houghton MD MS
Title	Validation of Natural Language Processing for the Identification of Venous Thromboembolism in Radiologic Reports.
Introduction	Natural Language Processing (NLP) is a software driven method of evaluating information of interest. NLP allows for the rapid identification and distinction between disease states, such as acute and chronic venous thromboembolism (VTE), desirable in large datasets.
Methods	The aim of this study was to externally validate the use of NLP algorithms developed and internally validated at Mayo Clinic to identify the presence of acute pulmonary embolism (PE) or acute deep vein thrombosis (DVT) from radiologic reports. A dataset of adults who underwent relevant imaging within 90-days after COVID-19 vaccination between 11/1/2020 and 11/1/2021 was used. Verification was achieved by use of two configuration files for radiologic reports (one with CT reports and one with venous duplex ultrasound reports of the extremities) in conjunction with the open-source software SimpleNLP. The data from the NLP analyses were then compared to a blinded determination if the report showed an acute VTE event performed separately by two individuals (DS, LBK). A random sample of 50 reports determined by the NLP algorithm to be positive and 50 negative reports were reviewed.
Results	A total of 3,499 images were identified in patients within 90 days of a COVID-19 vaccination (CT scan, n=2431, ultrasound (n=912, lower extremity =790, upper extremity=122). Of the patients who had a chest CT, 96 were identified by the NLP as positive for acute PE and 2335 as negative. Within the random sample of the radiology reports, 49/50 positive and 50/50 negative scans were confirmed, resulting in 100% sensitivity and 98% specificity. The scan falsely identified with acute PE by the NLP noted “A tiny focus of hypoattenuation” which could represent a small nodule adjacent to the vessel, although a very tiny pulmonary embolus is possible.” Of the patients who underwent US for suspected DVT, 100 were identified as positive. Within the random sample, 49/50 ultrasounds were confirmed positive and 50/50 were confirmed negative for acute DVT resulting in a 100% sensitivity and 98% specificity. The ultrasound that was falsely identified with acute DVT said “No definitive central deep venous thrombus in the right upper extremity. Adjacent to the brachial artery courses a hyperechoic structure with no internal flow. It is possibly though less likely an occlusive thrombus in a paired brachial vein.”
Conclusions	The PE and DVT NLP algorithms have been externally validated to accurately identify acute VTE and exclude chronic VTE event. Ambiguous imaging results led to limited false positive results. The validated NLP algorithms provide a more accurate identification of acute VTE than ICD-10 codes and can be used in large datasets.

Category	Hematology & Blood, #45
Primary Author	Juliana Alvarez-Argote, MD
Secondary Authors	Theresa A. Dlugi, PhD., Xuejun Wang, PhD., Teresa Sundararajan, Mary L. Faber, PhD., William M. McKillop, PhD., Jeffrey A. Medin, PhD.
Title	Long term expression of anti-sickling transgenic beta-globin after non-myeloablative conditioning lentiviral gene therapy in a sickle cell disease murine model
Introduction	Sickle cell disease (SCD) results from a sequence defect in the adult hemoglobin (HbA) Î²-globin chain. This disease causes acute and chronic multiorgan failure, and reduced lifespan despite current advances in medical management. To improve these outcomes, gene therapy is being studied in the preclinical and early clinical setting. We have engineered a novel lentiviral vector based on the Lenti/Î²AS3-FB construct. The Î²AS3-globin transgene expressed from this vector contains the mutations G16D, E22A and T87Q that increase affinity for healthy Î²-globin and inhibit axial and lateral contacts with sickle Î²-globin, thereby conferring anti-sickling properties.
Methods	We have successfully used our vector in a gene therapy model in the Townes mouse model for SCD. Recipients underwent a non-myeloablative conditioning regimen of 6Gy whole body irradiation and each received 1 million donor cells via retro-orbital injection. We optimized the survival of the mice by implementing a transfusion program following cell injection. Furthermore, we successfully detected lentiviral vector-encoded Î²AS3-globin in peripheral blood after gene therapy.
Results	We followed these mice over 30 weeks post-BMT and report stable peripheral blood vector copy number as well as persistent Î²AS3-globin measured by mass-spectrometry (see our corresponding poster). We analyzed several parameters in these mice including some for the first time in a Townes mouse gene therapy setting. We assessed complete blood counts (CBC), in vitro sickling of peripheral blood red blood cells, urine osmolality and urine albumin/creatinine ratio. We also completed non-invasive echocardiography, whole body non-invasive plethysmography, von Frey behavioral assay, and a pathologic evaluation by hematoxylin and eosin and Prussian blue staining in transplanted mice.
Conclusions	Our findings suggest several readouts that will be useful in evaluating gene therapy approaches in the Townes mouse model of SCD.
Acknowledgements	This project was supported by funding from the Midwest Athletes Against Childhood Cancer Fund, Inc. (MACC Fund), and the Greater Milwaukee Foundation (GMF) Russell J. and Betty Jane Shaw Fund. We give special thanks to Dr. Steve Faber for building the von Frey and cold assay supporting structures; Dr. Kirkwood A. Pritchard and his laboratory for sharing their experience with the Townes mice; Dr. Cheryl Stucky and her laboratory for sharing their expertise in behavioral studies; the Neuroscience Research Center's Rodent Behavior Core at MCW for providing training and the facilities for the behavioral studies; Teresa Michalkiewicz, Dr. Girija Ganesh Konduri and Dr. Gary Mouradian and their laboratories at MCW for sharing their expertise and equipment for the plethysmography procedures; the Research and Education Initiative Fund, a component of the Advancing a Healthier Wisconsin Endowment at MCW for their support of our project.
Ancillary Materials	VIEW MY POSTER

Category	Hematology & Blood, #46
Primary Author	Lana Mucalo
Secondary Authors	Shuang Jia, Mark F. Roethle, Ashima Singh, David C. Brousseau, Julie A. Panepinto, Martin J. Hessner, Amanda M. Brandow
Title	Identification of hub genes associated with acute pain episodes in individuals with sickle cell disease
Introduction	Sudden, unpredictable, severe acute pain episodes are the most common sickle cell disease (SCD) complication. Some SCD patients experience frequent pain episodes while others experience rare episodes. Knowledge of the biology driving this variability is limited. Using gene transcription analyses, we previously showed an elevated inflammatory response is associated with increased SCD pain episode frequency. We sought to replicate these findings in a larger SCD cohort and identify hub genes closely associated with increased pain frequency.
Methods	We conducted plasma-induced transcription analyses in 132 SCD patients (baseline health) and 60 Black controls (4-21 years, both groups). 3028 differentially expressed genes between SCD patients and controls were retained for subsequent analyses with Weighted Gene Co-Expression Network Analysis (WGCNA). WGCNA was used to define modules (functionally grouped genes) and we correlated these modules with number of pain episodes requiring health care utilization in prior three years.
Results	Of 11 identified modules, four showed significant correlation with number of pain episodes. Database for Annotation, Visualization, and Integrated Discovery (DAVID) was used for ontological analysis of the four significant modules and key biological processes identified were inflammatory response and cellular response to lipopolysaccharide. Cytoscape was used to construct a protein-protein interaction network and the 10 top hub genes identified in hierarchical order were: TNF, CCR5, CCR1, CCL2, CXCL2, ITGAM, CCL7, CXCL3, TLR2 and MMP9. These genes, as part of the inflammatory response, support the immune system contributes to increased pain episode frequency.
Conclusions	Identified hub genes may be leveraged as therapeutic targets for reducing SCD pain episodes.

Category	Hematology & Blood, #47
Primary Author	Rivka Franklin, BA, MPH
Title	Case: A 67-Year-Old Woman with CLL and Acute Liver Failure
Introduction	A 67-year-old African American female with a past medical history of indolent chronic lymphocytic leukemia (CLL) diagnosed in 2002, Type II Diabetes Mellitus, and Hypertension presented to the Emergency Department on 10/28/2022 with acute hepatic failure. Biopsy workup indicated hepatic involvement of the patients known CLL/SLL, staged as Ann Arbor Stage: IV and Binet Stage: B.

Category	Kidney, Diabetes & Digestive, #48
Primary Author	Buruj Mohammed
Secondary Authors	Ashanti Johnson, Katie Seibold, Elyssa Marmolejo, Lolia Abibo MD, MS
Title	Implementation of a DSMES Educator Program in Port Harcourt, Nigeria
Introduction	Diabetes prevalence in Nigeria has skyrocketed and in 2017, the national prevalence of diabetes was 5.77%. This along with the complications associated with diabetes have placed a large burden on public health in Nigeria. With this growing trend, culturally sensitive diabetes self-management education and support (DSMES) is needed to equip healthcare professionals with the necessary knowledge on diabetes management. DSMES programs have been increasingly implemented worldwide. Studies have shown these programs can improve HbA1c by up to 1% and have been associated with improved long-term health outcomes and self-management behaviors in patients with Type 2 Diabetes.
Methods	After completion of the educator curriculum, we hypothesize that 80% of the healthcare professionals will meet the passing benchmark on the post-test for the course. Additionally, we hypothesize a least 10-point increase in scores from pre-test to post-test. The goal of this study is to provide a nationally recognized diabetes management education program at the University of Port Harcourt Teaching Hospital (UPTH) in Nigeria. This will serve to educate health professionals on working with diabetic patients and standardize the type of care this patient population receives. This project aims to develop a standard DSMES program that reflects the cultural and healthcare practices of Nigeria. Healthcare professionals enrolled in the course will be given pre- and post-course examinations that will be used to analyze the effectiveness of the course.
Results	Out of the ten healthcare professionals enrolled in the program, two did not meet the passing benchmark. We reject the null hypothesis and found that 80% of healthcare professionals met the passing benchmark for the course. Test scores increased from pre-test to post-test by an average of 12.5 points. The 95% confidence interval for Î¼d is (8.20, 16.80). The test statistic is t = 6.58, with 9 degrees of freedom, and p = 0.0001. Because the p-value is less than Î±=0.05, we reject the null hypothesis and state that there is a difference, on average, in test scores between the pre-test and post-test.
Conclusions	Completion of this program saw the certification of a DSMES curriculum at the UPTH and to the graduation of eight healthcare professionals who are now able to instruct DSMES programs at their own institutions. The diabetes educator program provided them with the necessary knowledge and skills to educate and support patients with Type 2 Diabetes. This study enhanced the need to educate healthcare professionals on delivering evidence-based education and counseling, allowing for successful patient-centered care and long-term chronic condition management. The findings of this study will provide a rationale for DSMES programs to be implemented at a national level in Nigeria.

Category	Mental Health, Abuse & Addiction, #49
Primary Author	Anum S. Khan, MD
Secondary Authors	Karolina Kalata MS-1 and Sarah Farhan MS-2
Title	The Impact of Mass Shootings in Schools: How we can aid those affected individuals and communities
Introduction	The incidents of mass shootings across the United States have continued to spike over the last two decades. Research has shown that a number of risk factors collectively contribute to mass violence in schools. Risk factors are multifactorial and stem from a variety of areas including past trauma, degree to exposure to an event, school environment/climate, interpersonal issues, parenting, media violence, and access to guns. We present all of the data and risk factors that contributes to gun violence and mass trauma in schools. We also discuss various violence prevention programs and their efficacy. As we know, programs that support student social and emotional learning, positive behavioral interventions, improving school climate, and promoting collaboration amongst school personal and mental health professionals has been shown to decrease the risk the violence risk. We also explore ways in which mental health professionals can approach those individuals and communities exposed to mass violence and what interventions may be helpful.
Ancillary Materials	VIEW MY POSTER

Category	Mental Health, Abuse & Addiction, #50
Primary Author	Maya Subramanian, BA, BS
Secondary Authors	Timothy McAuliffe, PhD, MS, BA. Himanshu Agrawal, MD, DFAPA.
Title	Assessing variability in reporting severity of the same symptom (fatigue) in context of different psychiatric syndromes
Introduction	Fatigue is a common symptom experienced by individuals with Major Depressive Disorder (MDD) and Generalized Anxiety Disorder (GAD). The symptom is included in the diagnostic criteria for both disorders in the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5). However, there may be variations in the way patients perceive and report the symptom of fatigue depending on the specific disorder being assessed. The aim of this study is to examine the variability in the self-reported fatigue symptom severity in MDD compared to GAD.
Methods	This study was conducted as a retrospective chart review of 100 patients who were evaluated for fatigue using depression and anxiety questionnaires at MCW Outpatient Psychiatry Clinic at Tosa Center between July 1st, 2017, and June 30th, 2022. All patients included in the study had been diagnosed with concomitant MDD and GAD based on DSM-5 criteria at the time of their visit. The study divided the patients into two groups, with the first group being asked depression-related questions first and the second group being asked anxiety-related questions first. The median differences in fatigue scores were calculated for each group and compared using the Independent-Samples Mann-Whitney U Test. The significance level used was 0.05.
Results	The study found that there was a statistically significant difference in the median difference of the paired depression fatigue and anxiety fatigue scores (Depression score - Anxiety score) with a p-value of .008. This suggests that patients may perceive and report fatigue differently when it is assessed in the context of MDD versus GAD.
Conclusions	This study's findings indicate that the symptom of fatigue may be perceived differently by patients based on the context of the syndrome being assessed. This highlights the importance of considering the context of symptom reporting in diagnostic and treatment strategies for individuals with MDD and GAD. As fatigue is a common symptom in both disorders, it is important to be aware of the possible variations in the way it is perceived and reported. This can help improve diagnostic methods and inform treatment strategies for individuals suffering from MDD and GAD.

Category	Mental Health, Abuse & Addiction, #51
Primary Author	Morgan Leissring, BS
Secondary Authors	Elise A Biesboer, MD, Amber Brandolino, MS, Rachel Weber, BS, Terri deRoon-Cassini, PhD, MS & Mary E Schroeder, MD
Title	Comparison of a Person-Administered vs Automated Screening Tool for PTSD in Traumatically Injured Patients
Introduction	The development of post-traumatic stress disorder (PTSD) is a prevalent problem for patients suffering from injuries and has major implications for post-injury quality of life. Early identification of high-risk patients to prevent adverse mental health consequences can contribute to improved outcomes. As of January 2023, the American College of Surgeons Committee on Trauma (ACS CoT) has mandated that trauma centers have mental health screening and referral protocols in place for traumatically injured patients. Various screening tools are available to assess for PTSD, each with their advantages and disadvantages. Two of these include the Injured Trauma Survivor Screen (ITSS), a person-administered 9-item screener, and an electronic medical record-based automated screener. This study aims to prove the ITSS as a better predictor for PTSD against the automated screener. The goal of this study is to inform trauma centers creating screening protocols regarding the performance of these two tools in the same population.
Methods	A cohort of traumatically injured patients (n=207) at a Midwest Level 1 trauma center who had ITSS and clinician-administered PTSD Scale for DSM-5 (CAPS-5) results available were retrospectively reviewed via the EMR for the automated screening tool variables. A receiver operating characteristic (ROC) curve analysis was then conducted to compare the screening tools. PTSD diagnosis was determined using the CAPS-5, which was administered 6-months post-injury.
Results	The ITSS and automated screener performed similarly in predicting PTSD risk at 6-months post-injury in the same population. Trauma centers should focus on the impact their screener choice will have on resource allocation. Their differential resource considerations are that the ITSS simultaneously screens for depression risk, while the automated screener does not require person administration. These differential impacts on resource allocation may instead guide the decision-making process for trauma centers as they determine a screening tool most beneficial to their trauma center to meet the ACS CoT's new screening mandate.
Conclusions	This safety net provided families with real time problem solving for an urgent need post-discharge such as triaging patients symptoms at home, counseling on medication questions, information about timeline of illness recovery, and provision of additional resources.

Category	Neuroscience & Neurology, #52
Primary Author	Alexandra Bachmann
Secondary Authors	Anthony Raimondi, Antje Kroner
Title	Maraviroc treatment reduces secondary damage following SCI in mice
Introduction	Spinal cord injury (SCI) is a severe condition that significantly impacts the affected individualâ€™s life. Depending on the level and severity of the injury, SCI can result in impaired sensorimotor control of upper and lower limbs, respiratory, and autonomic function. Tissue damage from SCI is caused by mechanical trauma (primary damage), followed by a cascade of events that exacerbate damage (secondary damage). One of the primary drivers of secondary damage is inflammation. While inflammation does have beneficial effects after SCI, exacerbated inflammation leads to tissue damage, neuronal death and worsened functional outcomes. Specific chemokines have been shown to play a major role in the immune response that creates secondary damage following SCI. Chemokine (C-C motif) ligand 3 (CCL3) is one of the signaling molecules involved in these negative outcomes. Our previous work showed that CCL3 knockout mice had reduced lesion sizes, axonal injury, and immune cell recruitment to the spinal cord following thoracic SCI compared to wild-type mice, leading to improved functional recovery. Antibody-mediated inhibition of CCR5, the preferred receptor for CCL3, also showed improved functional outcome. These results make inhibition of CCR5 a potential therapeutic treatment to improve functional outcome following SCI. Maraviroc is an FDA approved CCR5 inhibitor that is currently used for human immunodeficiency virus (HIV) treatment, preventing virus entry into cells. It has also been successfully used in models of neurological conditions, such as neuropathic pain, stroke, multiple sclerosis, and traumatic brain injury. We hypothesize that treatment with maraviroc will improve functional outcome, neuronal survival, and tissue preservation in a mouse model of contusion SCI.
Methods	A mouse model of thoracic contusion SCI (T10-11, 50 kdyne) was used. Starting the day of injury, mice received 0.1 mL intraperitoneal injection of either 50 mg/kg maraviroc treatment or the control (DMSO and saline) daily for 14 days. Locomotor recovery was assessed through the Basso Mouse Scale (BMS) on days 1, 3, 5, 7, 10, 14, 21, 28, and 35 post injury. Horizontal ladder walk was used once weekly from day 14 post injury on. Mice were transcardially perfused using 4% paraformaldehyde at day 35. Immunohistochemistry staining of the spinal cord was done to assess neuronal survival, synapse density, and lesion sizes.
Results	Histological analysis uncovered improvements in neuronal cell preservation, synapse density, and a reduction in lesion volume in maraviroc-treated animals compared to controls. No significant differences were detected between groups pertaining to functional outcomes.
Conclusions	Preliminary data suggests that maraviroc treatment leads to tissue preservation around the lesion following SCI. Further testing will need to be done to see if this preservation leads to beneficial sensorimotor outcomes, and to assess the mechanisms behind CCR5 inhibition.
Acknowledgements	We would like to acknowledge AHW and the Craig H. Neilsen Foundation for their support in this project.

Category	Neuroscience & Neurology, #53
Primary Author	Ana Mia Corujo Ramirez
Secondary Authors	Mi-Hyeon Jang, Alfredo Oliveros, Ki-Hyun Yoo, Jun Tang, Yuanhang Liu, Danielle Brogren
Title	The Adenosine A2A Receptor as a Preventative Therapy For Cisplatin Induced Cognitive Dysfunction
Introduction	Cisplatin is a platinum-based chemotherapy clinically reported to potentiate cognitive impairments known as chemobrain. Finding novel therapeutic options for cancer survivors suffering from chemobrain is imperative.
Methods	Utilizing an in vivo model of cisplatin-chemobrain we performed RNA-sequencing in the hippocampus, a critical brain structure for learning and memory. This revealed robust elevations in the adenosine A2A receptor (A2AR), an important regulator of cognition.
Results	Remarkably, we found that istradefylline (KW-6002), an FDA approved specific A2AR antagonist, prevented cisplatin-induced hippocampal impairments in neurogenesis and dendrite spine formation while improving memory and anxiety-like behavior. Notably, KW-6002 did not promote tumor growth or interfere with cisplatin's anti-tumor efficacy. Mechanistically, we found that cisplatin targets mouse hippocampal neurons in vivo and human cortical neurons downstream of A2AR, in a CREB and ERK dependent manner
Conclusions	Collectively, A2AR, CREB and ERK are key chemobrain contributors that can be therapeutically targeted to improve quality of life for cancer survivors.

Category	Neuroscience & Neurology, #54
Primary Author	Andrew L. DeGroot, BS
Secondary Authors	Daniel L. Huber, MPH; John Leddy, PhD; Hershel Raff, PhD; Michael A. McCrea, PhD; Blair D. Johnson, PhD; Lindsay Nelson, PhD
Title	Utility of Structured Oculomotor, Balance, and Exercise Testing in Civilian Adults with Mild Traumatic Brain Injury (mTBI)
Introduction	Office-based assessments of oculomotor, balance, and exercise function are purported to be useful to detect individual differences in response to mild traumatic brain injury (mTBI) and direct personalized treatments. While these assessments are well-accepted to evaluate athletes with sport-related mTBI, they are relatively unstudied in broader adult community ("civilian") mTBI population. Objective. Evaluate the performance of adult level 1 trauma center patients with mTBI on tests of oculomotor functioning (near point of convergence [NPC] and accommodation [NPA]), balance (Balance Error Scoring System [BESS]), and exercise tolerance (Buffalo Concussion Treadmill Test [BCTT]).
Methods	Prospective, observational, longitudinal Setting. Academic medical center Participants. N=37 adults treated in a level 1 trauma center emergency department with mTBI. Main Measures. Participants were assessed twice three weeks apart (1 week and 1 month post-mTBI) for NPC and NPA, BESS, a 15-minute version of the BCTT, and the Rivermead Post Concussion Symptoms Questionnaire [RPQ]. Analyses characterized the prevalence of impairment on the tests and examined the association between test performance and mTBI-related symptom burden (RPQ scores).
Results	Participants frequently met impairment criteria on the tests, with the prevalence of impairment highest for oculomotor tests (e.g., 73.5% on NPC-recovery at 1 week), followed by balance (e.g., 44.1% at 1 week) and exercise (36.1% discontinued at 1 week due to mTBI-related symptom exacerbation). Participants displayed diverse profiles of impairment across assessments. Medium to large correlations were observed between poorer NPC and BCTT performance and greater mTBI symptom burden.
Conclusions	Clinical examinations of oculomotor function, balance function, and response to exercise adopted from commonly used sport-related concussion assessments frequently detect impairment in adult community members with mTBI. While larger-scale replication is needed, the findings imply that incorporating these relatively simple, structured exams into the office-based assessment of mTBI may facilitate more personalized, active management strategies.
Ancillary Materials	WATCH MY PRESENTATION

Category	Neuroscience & Neurology, #55
Primary Author	Asha Raghavan
Secondary Authors	William Eastham, Briana Meyer, Matthew Budde, PhD
Title	Optimization of Behavioral Assessments for Prediction of Functional Outcomes of Spinal Cord Injury
Introduction	Traumatic spinal cord injury to the cervical cord causes deficits in gait, posture, and motor coordination, particularly affecting the forelimbs. Historically, the Forelimb Locomotor Assessment Scale (FLAS) has been used to measure forelimb movement coordination and compensatory behaviors post injury in an animal model. Our previous study demonstrated that FLAS scores were significantly correlated with injury severity. DeepLabCut is a deep learning software that measures kinematic variables such as joint angles, paw placement, and step lengths which can then be coupled with analysis tools such as Automated Limb Motion Analysis (ALMA). In this study, the purpose of this study was to compare the accuracy and efficiency of two forms of behavioral assessments, FLAS and DeepLabCut, in relation to predicting functional outcomes of spinal cord injuries at varying severities using a rodent model.
Methods	Male and female adult Sprague Dawley rats (n= 38) received cervical contusion injuries of varying severity at the C5 level of the spinal cord. Injuries were administered using the Multicenter Animal Spinal Cord Injury Study Impactor in which the impactor was dropped from heights varying from 5mm to 25mm, and the impactor software was used to record the maximum cord compression measured as the displacement of the impact from the surface of the pre-injury spinal cord to the point of maximum compression of the spinal cord. Functional capabilities were assessed 57 days post injury using FLAS) for subjective assessments. DeepLabCut was first trained by placing limb position markers on videos from 8 animals across 960 frames. Linear regressions will be used to measure the correlation between impact height/injury severity, FLAS scores, and DeepLabCut metrics.
Results	FLAS scoring was consistent with our previous study showing a strong relationship between it and the measured impact height/injury severity. DeepLabCut was trained to capture the limb position of 16 separate markers of the limbs in videos captured at 60 frames per second. It successfully identified the limb positions from both a lateral and ventral view of the animal captured simultaneously. After training, both right and left sides were identified on separate video of right-to-left or left-to-right walking.
Conclusions	A custom behavioral alley to capture both lateral and ventral views of rats performing locomotor behaviors was developed and in combination with DeepLabCut was able to automate the collection of limb placement positional information. Work is ongoing to convert limb positions into kinematic measures such as joint angles, step distances, and left-right coordination after which we will assess whether the accuracy of automated gait analysis using DeepLatCut can match or surpass non-automated and subjective FLAS scores in predicting injury severity measures biomechanically. These processes are expected to accelerate discovery and testing of therapies to treat the injured cord.

Category	Neuroscience & Neurology, #56
Primary Author	Athena Dong, BS
Secondary Authors	Lindsay D. Nelson, PhD; Nancy R. Temkin, PhD; Jason Barber, MS; Geoffrey T. Manley, MD, PhD; Claudia S. Robertson, MD, Alex B. Valadka, MD; John Yue, MD; the TRACK-TBI Investigators; and Christopher J. Roberts, MD, PhD
Title	The Impact of Surgery on Functional and Cognitive Outcomes after Traumatic Brain Injury: A TRACK-TBI Study
Introduction	Traumatic brain injury (TBI) is a leading public health issue that affects a diverse range of patients, increases healthcare costs, and is associated with persistent functional and cognitive deficits. Clinical management of TBI patients necessitates the prevention of secondary insults that would further complicate or exacerbate the initial brain injury. The implications of exposure to surgery/anesthesia following TBI warrant investigation, given that both surgery and anesthesia have physiologically disruptive and neurotoxic effects. The objective of this study is to determine whether exposure to extracranial (EC) surgery/anesthesia is associated with worse functional and neurocognitive outcomes after TBI.
Methods	This study is a retrospective, secondary analysis of the TRACK-TBI dataset, a collection of longitudinal outcomes of patients enrolled at 18 level-1 trauma centers in the US from February 2014 to August 2018. Subjects (n=1835) were â‰¥ 17 years old, presented within 24 hours of trauma, were admitted to an inpatient unit from the emergency department (ED), had known Glasgow Coma Scale (GCS) and head computed tomography (CT) scan status, and did not undergo cranial surgery. Patients that underwent EC-surgery during the index admission (n=486) were compared to patients with no surgery (n=1349) in groups that had a peripheral orthopedic injury or a TBI, classified as uncomplicated mild (GCS 13-15, negative CT; CT-mTBI), complicated mild (GCS 13-15, +CT scan; CT+mTBI), or moderate/severe (GCS 3-12; m/sTBI). The primary outcomes were functional limitations quantified by the Glasgow Outcome Scaleâ€“Extended for all injuries (GOSE-ALL) and brain injury (GOSE-TBI), and neurocognitive outcomes quantified by the Wechsler Adult Intelligence Scaleâ€“Fourth Edition Processing Speed Index (WAIS-PSI), Trail Making Test (Trails), and Rey Auditory Verbal Learning Test (RAVLT). Outcomes were assessed at 2 weeks and 6 months post-injury.
Results	EC-surgery patients across all TBI severities scored significantly worse on the GOSE-ALL at 2 weeks and 6 months compared to nonsurgical counterparts. At 6 months post-injury, m/sTBI and CT+mTBI patients who underwent EC-surgery exhibited significantly worse GOSE-TBI scores (-1.11 [95% CI -0.68 to -1.53] and -0.39 [95% CI -0.01 to -0.77]) and performed worse on Trails B (30.1 [95% CI 11.9 to 48.2] and 26.3 [95% CI 11.3 to 41.2]). Exposure to EC-surgery/anesthesia is associated with both acute and lasting adverse effects on functional outcomes and executive functioning post-TBI.
Conclusions	This association warrants further examination of the mechanisms and clinical implications, which, if replicated, could impact decisions regarding surgical interventions in TBI patients.
Acknowledgements	This study was supported and funded by the Medical College of Wisconsin Department of Anesthesiology and the Summer Academic programs for Medical Students Medical Student Summer Research Program (SAMS-MSSRP). Special thanks to the University of Washington Biostatistics Team for their assistance in statistical analysis for this study, the Transforming Research and Clinical Knowledge in Traumatic Brain Injury (TRACK-TBI) project for providing the source patient database, and Dr. Christopher Roberts for providing invaluable leadership and mentorship.
Ancillary Materials	VIEW MY POSTER

Category	Neuroscience & Neurology, #57
Primary Author	Craig R. Miller, MA MS
Secondary Authors	Jeanine Merrill, Grace Amadon, Staci Young, PhD, Lindsay D. Nelson, PhD
Title	Leveraging Patient and Family Perspectives to Improve Systems of Care for Traumatic Brain Injury: A Qualitative Study
Introduction	Traumatic brain injury (TBI) is a common cause of disability for Wisconsin residents. Individuals with TBI often have to cope with the direct consequences of brain injuryâ€”such as headache, mood changes, and thinking problemsâ€”as well as other bodily injuries and the difficult circumstances resulting from the injury-inducing event. Yet for many individuals, TBI care is often fragmented, poorly coordinated, and of insufficient duration given the prolonged recovery course that often follows a TBI. Further, prior research has shown that patients/families often feel unsupported during early inpatient treatment experiences, find it challenging to navigate transitions from acute to post-acute rehabilitation services, have difficulty accepting the loss of autonomy and disability experienced due to TBI, and experience anxiety due to perceived dissonance between their goals and the goals of their providers. Study Aim: The present qualitative study aims to better understand the perspectives of Froedtert Hospital patients and caregivers, with a focus on understanding their experiences of TBI care and perceived gaps in care. This study is part of a larger mixed-methods study seeking to understand TBI recovery, with the goal of developing concrete initiatives to improve TBI outcomes in Southeastern Wisconsin.
Methods	Two groups of adult TBI patients treated through Froedtert Hospital were selected for inclusion: those experiencing mild TBI (i.e., discharged from the Emergency Department without acute intracranial findings on neuroimaging) and those with moderate-to-severe TBI (i.e., those admitted with positive neuroimaging evidence of TBI) to compare/contrast patients' experiences of care and recovery. Data collection is ongoing, with a total of 14 interviews completed to date. Qualitative data are being gathered using an open-ended, semi-structured interview protocol. Data are analyzed in an iterative, collaborative coding process to identify consistent themes across cases. (IRB PRO#: 35743)
Results	Several themes emerged specific to gaps in care. Participants discussed a need for clearer communication from providers during the acute care phase about patient's TBI diagnosis and potential ongoing symptoms patients might encounter. For example, some participants noted that they were never told that they had a TBI/concussion. Several participants with more severe injuries also described acute care of both TBI- and non-TBI-related injuries as disjointed. Others noted that providers attended more to patient's visible physical injuries and did not attend as closely to the potential effects of the TBI. Participants also noted non-clinically related challenges in care, including financial concerns, lack of transportation, insurance difficulties, and legal involvement as significant contextual factors affecting their treatment course and recovery.
Ancillary Materials	VIEW MY POSTER

Category	Neuroscience & Neurology, #58
Primary Author	Deepali Bhalla, B.S.
Secondary Authors	Elias Granadillo, MD
Title	Brainstem Atrophy across the AD Spectrum and its Correlation with Markers of Cognitive Decline, Sleep, and Mood Disturbance: An Automated Volumetric MRI Study.
Introduction	Alzheimer's disease (AD) is the most common dementia that causes progressive problems with memory, critical thinking, and behavior. Studies have shown brainstem displaying earliest signs of AD progression (2,3). Midbrain structural changes are linked to AD symptoms i.e., memory impairment, sleep disorders, and emotional disturbances. The purpose of this study is to investigate changes in brainstem volumes (BS-V) and elucidate the differences in BS atrophy patterns across the AD spectrum utilizing MRI automated volumetric assessment (NR). Potential correlations between BS-V and biomarkers of cognition, sleep, and mood disturbances are evaluated.
Methods	A retrospective review of 60 AD spectrum patients who had NR, and sleep and cognitive tests was performed. BS-V and Hippocampal volumes (Hip-V) for 3 groups of 20 patients each: Subjective cognitive impairment (SCI), Mild cognitive impairment (MCI), and AD were collected. Multiple regression models corrected for age and gender were obtained, to determine group-wise differences in BS-V and Hip-V with SCI set as the comparison group. Pearson correlations between BS-V, sleep biomarkers, and cognitive test scores were assessed.
Results	No difference in BS-V or BS-V corrected for total intracranial volume (BS-VM) across AD spectrum compared to SCI. Hip-V difference between AD and SCI remained significant after adjustment for age ($p=0.014$). Female gender was a significant predictor of lower brainstem volumes ($\hat{I}^2$ =-0.382, $p=0.004$) but when corrected for total intracranial volume (BS-VM), male gender was associated with lower brainstem volumes ($\hat{I}^2$ =-0.356, $p=0.009$). Female gender was also a significant predictor of lower raw hippocampal volumes ($\hat{I}^2$ =-0.403, $p=0.002$), consistent with AD literature suggesting a differential gender-based susceptibility to AD pathology (1). Inverse correlation between SE and BS-V noted, contrary to prevailing literature that needs further exploration.
Conclusions	Significant results obtained from this study can be explored further towards establishing a few non-invasive clinical biomarkers that could be utilized for early AD detection as well as assessing AD progression. Characterizing the brainstem atrophy rate in AD spectrum patients and correlating with accompanying clinical manifestations such as sleep and mood disorders could refine the diagnostic algorithm leading to earlier diagnosis, appropriate change in care, and possible treatments of patients.
Acknowledgments	Research reported in this publication was supported by the National Heart, Lung, And Blood Institute of the National Institutes of Health under Award Number T35HL072483. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.
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Ancillary Materials	VIEW MY POSTER WATCH MY PRESENTATION

Category	Neuroscience & Neurology, #59
Primary Author	Justin Page
Secondary Authors	Shannon Kafura, Alexandra Bachmann, Antje Kroner
Title	The functional role and therapeutic potential of heme binding proteins after cervical SCI
Introduction	Spinal cord injury (SCI) is a severe condition with a significant impact on the life of affected individuals. Cervical SCI (cSCI) accounts for approximately 60% of SCIs and can impair motor and sensory function of upper and lower limbs, respiration, and the function of the autonomic nervous system. SCI associated tissue damage occurs in two major phases: Primary damage is caused by mechanical trauma, followed by secondary damage, which is mediated by a range of factors including inflammation and hemorrhage.
Methods	Hemorrhage worsens the outcome of SCI patients and contributes to secondary tissue damage via different mechanisms. First, hemoglobin released from lysed red blood cells and its breakdown products, such as heme and iron, are highly reactive and introduce an abundance of reactive oxygen species (ROS), resulting in oxidation of DNA, protein, and lipids. In addition, hemorrhage is a direct inducer of potentially harmful inflammation. Professional binding proteins, like haptoglobin and hemopexin are produced in the liver and, to a lower extent, in the Central Nervous System (CNS) where they capture and sequester hemoglobin and heme until they can be taken up by macrophages. However, other proteins present in the blood and tissue can also bind heme: Alpha-1 anti-trypsin (A1AT) and alpha-1 microglobulin (A1M) protect against heme and iron toxicity under various pathological conditions. Importantly, their protective function might be attributed to more than their heme-binding ability as they also have striking tissue protective, anti-inflammatory, and radical scavenging properties. A1M treatment has been shown to remarkably reduce tissue damage and inflammation in a model of intraventricular hemorrhage. We hypothesized that the presence of A1M and A1AT in the spinal cord has a beneficial effect after SCI. In this study, we quantified the expression of A1M and A1AT in the injured spinal cord, followed by an assessment of which cell types express these proteins after SCI.
Results	Our work shows that both A1AT and A1M are significantly upregulated after SCI and expressed by various resident CNS cells following SCI. Next, we investigated the ability of A1AT to reduce ROS production in vitro following treatment with hemin. Using cultures for bone marrow derived macrophages and astrocytes, we found a significant reduction of ROS levels and cell death in hemin treated macrophages and astrocytes. To assess the therapeutic potential of these heme binding proteins after SCI, we are using a proof-of-concept approach: A1M is overexpressed in the cervical spinal cord, utilizing a viral AAV vector, followed by C5 contusion injury. Three weeks after injection, a C5 cervical SCI was induced, and mice were assessed behaviorally.
Conclusions	Preliminary data indicate improved functional recovery. Confirmation studies and parallel investigations of A1AT overexpression are ongoing.
Acknowledgments	We would like to thank Wings for Life for their support.

Category	Neuroscience & Neurology, #60
Primary Author	Kearnin M. Van Bortel, B.S.
Secondary Authors	Keeley E. Hamill, B.S., Timothy B. Meier, PhD.
Title	Age of First Concussion Is Associated with Total Concussions and Symptom Endorsement
Introduction	There is rising concern over the potential cumulative and long-lasting effects of prior concussions, particularly in the >40 million young athletes who are concomitantly undergoing critical periods of neurological development. According to national injury databases, an estimated 1.1-1.9 million sport- and recreation-related concussions occur annually in children under 18, with many going undiagnosed or unreported to healthcare providers (Bryan et al., 2016). There is some evidence that having a younger age of first concussion (AFC) is a risk factor for sustaining an increased number of future concussions given the increased window of vulnerability (Moody et al., 2022; Schmidt et al., 2018). The goal of the current project was to replicate and extend these prior findings. We hypothesized that younger AFC would be associated with more total concussions and more subjective symptom reporting in active, collegiate-aged athletes. Moreover, we also investigated whether AFC is associated with current symptom reporting when accounting for total number of prior concussions.
Methods	A total of 91 collegiate-aged athletes met strict enrollment criteria and reported at least 1 prior concussion (Mage=21.23, SD=1.63; 70.3% men) retrospectively assessed based on structured interviews using American Congress of Rehabilitation Medicine criteria. Total severity of endorsed symptoms at time of scan was self-reported using the Sport Concussion Assessment Tool (SCAT5). A Poisson generalized linear model tested the association between AFC and total number of concussions. A linear regression model tested the association between AFC and log-transformed symptom severity. An additional linear regression model tested the association between AFC and symptom severity, controlling for the total number of concussions. Sex and years of contact sport exposure were controlled for in all models.
Results	AFC was significantly associated with having more total concussions at age of scan (X2 (1, N=91)=18.77, B(SE)=-.068(.016), p<.001). Additionally, AFC was significantly associated with endorsing more severe symptoms (X2 (1, N=91)=12.80, B(SE)=-.097(.027), p<.001), as was years of exposure (X2 (1, N=91)=4.51, B(SE)=0.035(.017), p=.034). After controlling for total number of concussions, only AFC remained a significant predictor of symptom severity (X2 (1, N=91)=5.84, B(SE)=-.074(.03), p=.016).
Conclusions	The finding that a younger AFC may be a risk factor for subsequent injury was replicated. It was further found that athletes with a younger AFC tended to report more severe symptoms at time of study involvement even when accounting for total number of prior concussions. These results suggest that having a younger AFC may be a salient predictor of long-term concussion-related outcomes which supports efforts to minimize the risk of concussions occurring at younger ages. Future studies should aim to increase diversity representation and to investigate differences in concussion diagnosis and symptom endorsement across races and ethnicities.
Reference 1	Bryan, M.A., Rowhani-Rahbar, A., Comstock, R.D., & Rivara, F. (2016). Sports- and recreation-related concussions in US youth. American Academy of Pediatrics, 138(1), e20154635. https://doi.org/10.1542/peds.2015-4635
Reference 2	Moody, J.N., Hayes, J.P., Buckley, T.A., Schmidt, J.D., Broglio, S.P., McAllister, T.W., McCrea, M., Pasquina, P.F., Caccese, J.B., & CARE Consortium Investigators. (2022). Age of first concussion and cognitive, psychological, and physical outcomes in NCAA collegiate student athletes. Sports Medicine, 52(11), 2759-2773. https://doi.org/10.1007/s40279-022-01719-7
Reference 3	Schmidt, J.D., Rizzone, K., Hoffman, N.L., Weber, M.L., Jones, C., Bazarian, J., Broglio, S.P., McCrea, M., McAllister, T.W., & CARE Consortium Investigators. (2018). Age at first concussion influences the number of subsequent concussions. Pediatric Neurology, 81, 19-24, https://doi.org/10.1016/j.pediatrneurol.2017.12.017
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Category	Neuroscience & Neurology, #61
Primary Author	Meera Krishna
Secondary Authors	Ariel Franitza, Bradey Stuart, Lezi E
Title	The Neuroprotective Role of Skin Collagens in Aging
Introduction	The interactions between non-neural and neural tissue are a potential key factor in the underlying mechanisms that drive the initiation of aging in the nervous system. Skin is densely innervated by various sensory neurons and has been established as a critical component in neurodevelopment and nerve injury repair to support a healthy nervous system. The goal of this study is to investigate the interactions between the skin and nervous system over the course of normal aging and determine if the interactions influence the aging process of neurons.
Methods	To examine this connection, we leveraged several genetics approaches using a cutaneous mechanosensory neuron in C. elegans as a model. Our data revealed that with increasing age in wild-type animals, this sensory neuron displays an excessive dendritic branching phenotype that is associated with a functional change in the proprioception of the animals.
Results	The skin also undergoes changes with age, with several skin collagens showing decreased expression, a phenomenon observed in mammalian systems as well. Surprisingly, the loss of the same skin collagens leads to an early-onset of excessive branching in the sensory neuron as well as associated-functional decline, while the overexpression of those collagens in wild type animals delays the onset of the aging-associated excessive branching. Additionally, the loss of an integrin was also found to lead to a similar premature aging-associated excessive branching, though further genetic experiments will be needed to investigate whether the integrin functions as a key intermediate molecule linking the skin collagens to neuronal health during aging.
Conclusions	These findings point to a novel role for the skin in the aging of the nervous system, implying that the initiation of neural aging processes could originate from proximal non-neural tissues. Additionally, it also indicates that some of the aging-associated structural changes that are observed in the neuron can be delayed by targeting the external initiator of the changes.

Category	Ophthalmology, #62
Primary Author	Maria R. Replogle
Secondary Authors	Samuel Thompson; Linda M. Reis; Elena V. Semina
Title	Evaluating the functional impact of a deep intronic variant in RARB associated with complex microphthalmia
Introduction	Retinoic acid receptor beta (RARB) is a transcriptional regulator crucial for coordinating retinoic acid-mediated morphogenic movements, cell growth and differentiation during eye development. RARB coding variants have been associated with microphthalmia, coloboma and anterior segment defects. Recently, we identified a novel, de novo RARB deep intronic variant (c.157+1895G>A) in a patient with syndromic microphthalmia consistent with RARB disruption. Here we evaluate the impact of the non-coding variant on the transcriptional or post-transcriptional activities of RARB in order to discover the underlying mechanism.
Methods	Minigene splicing assays and luciferase reporter assays were designed to functionally test the effect of the variant on mRNA splicing and transcriptional regulation of RARB in human lens epithelial cells and human embryonic kidney cells. The effects of pharmacologically or genetically induced RARB overexpression on retinoic acid-related gene expression, cell growth and viability were assessed in human cultured cells using RT-qPCR and trypan blue assay.
Results	Minigene splicing assays performed in both cell lines showed no effect on RARB mRNA splicing in the presence of the deep intronic variant. Interestingly, the variant is located in a highly conserved intronic region containing a candidate cis-regulatory element identified through ENCODE. Evaluation of this region specifically in human lens epithelial cells showed a significant increase in luciferase reporter activity in the presence of the candidate enhancer harboring the variant when compared to the wild-type enhancer or the promoter alone, suggesting that the variant may promote RARB overexpression during eye development. RARB overexpression in cultured cells resulted in increased cell proliferation and increased expression of FOXC1, a known downstream target of retinoic acid signaling during ocular development.
Conclusions	These results support a novel role for the candidate cis-regulatory element in modulating RARB gene expression and indicate that the deep intronic variant may disrupt proper regulation of RARB and downstream target gene expression, resulting in aberrant cell proliferation during eye development. Further investigation into mechanisms affected by RARB overexpression will clarify how the deep intronic variant contributes to human ocular dysgenesis

Category	Pediatrics & Child Health, #63
Primary Author	Amina Bedrat
Title	Plasma induced signatures measured at Type 1 diabetes (T1D) onset correlate with post-onset beta cell function and support the existence of inflammatory biased endotypes.
Introduction	Recent studies have highlighted the heterogeneous nature of autoimmune and immune-mediated diseases (Lupus, Celiac disease, multiple sclerosis, asthma, Type 1 diabetes), and emphasize on the enlarging portfolio of host-targeted therapies that are used to control the excessive pro-inflammatory signaling. In the field of T1D, the varying disease progression and different response observed during numerous trials therapies have drawn attention to the significant phenotypic diversity that exists among recent onset patients. The definition of patient subtypes is an important step towards more effective and personalized treatments.
Methods	We studied 566 new onset patients that had participated in six different TrialNet clinical trials (placebo and treated) using a novel plasma-based bioassay. We used the unbiased weighted gene co-expression network analysis (WGCNA) to associate Affymetrix microarray transcripts with phenotypes (traits) related to the disease progression and therapeutic responsiveness, and to distinguish potential endotypes. At the baseline sampling, a total of 6 networks (modules), spanning the 2854 transcripts, were characterized. For the placebo arms, we observed several modules exhibiting significant association with phenotypes related to future beta-cell function. In the treated arms, fewer module:trait associations were identified , consistent with varying degrees of immunomodulation being achieved even in the trials that did not show efficacy.
Results	Next, Graph-based clustering using Hierarchical clustering and principal component analysis (PCA) of the 2854 transcripts suggest that the studied samples fall into two distinct groups that we identified as Endotypeï•¡ and Endotypeï•¢. To better characterize the two endotypes, we implemented the random forest (RF) classifier to characterize the two endotypes based on TrialNet cohort, then the accuracy of the classifier was evaluated using a local cohort of 80 patients. The RF classifier trained on TrialNet showed an AUC = 0.98, the local cohort model explained 82% of the variance and reached an AUC = 0.75. Finally, with the help of pathway enrichment analysis, we observed that Endotypeï•¡ showed a high inflammatory bias with significant enrichment of patients with rapid disease progression (23% vs 7% $p<0.05$). Moreover, patients in Endotypeï•¡ also exhibits significantly higher cytokine level such as INFï•§, IL6 and IL10 and a higher memory:naive T-cell ratio than Endotypeï•¢.
Conclusions	In these analytic studies, we have confirmed the existence of 2 major subgroup that differ in levels of systemic inflammation, a more rapid loss in post-onset beta cell function, and a more robust response to post-onset immunotherapy.

Category	Pediatrics & Child Health, #64
Primary Author	Bethany Corbin, MD
Secondary Authors	Jessi Schnell, MD, Megan Teed, MD, Lauren Younker, Molly Paul
Title	From Pediatric to Adult Medicine: What is the Patient and Family Experience in Transitional Care?
Introduction	With the growing population of children with medical complexity (CMC) reaching adulthood, there is an urgent need for institutions to have proper resources and processes in place to help these patients transfer to adult providers. Each institution has its own unique barriers and patient factors to identify and address prior to creating a standardized process for transitional care. The aim of this project was to understand the patient/family transition experience at Medical College of Wisconsin-Children's Wisconsin (MCW-CW), with an overarching aim to identify barriers to address prior to the creation of a successful transition process for CMC.
Methods	For this single institution qualitative study, we recruited CMC and their families to participate in a 10-question semi-structured interview about their experience transitioning from pediatric to adult care. Eligible participants had (A) transitioned within the last 5 years and (B) been in the Complex Care Program at MCW-CW. Interviews were recorded via Zoom, transcribed, and coded by 5 independent coders using the Delphi Method. Codes were discussed to reach consensus (>80% consensus). Codes were then used to develop themes related to the patient/familyâ€™s transition experience. We present data from the first 3 interview questions: (1) How old was your son/daughter when they transitioned? Do you think this was the right age, and why? (2) When did you start planning for transition? At what age do you think discussions and planning for transition should start, and why? And (3) How did you choose where to transition your care to?
Results	Ten participants completed interviews. Age at transition ranged from 18-24 years. Analysis identified 7 main themes related to patient/family experience during the transition period: (1) Gradual, (2) Health Status, (3) Emotional State, (4) Provider Knowledge Base, (5) Models of Care, (6) Preparedness, and (7) External Barriers (see Table 1 for operational definitions). Representative quotes from each theme are included in Table 2.
Conclusions	The patient and family experience during this period of healthcare for CMC should be a key driver in developing institutional transitional care processes, and should frame the resources and protocols needed to ensure a smooth and safe transition period. This study provides important insight into what CMC and families value most during this period of their care. Future work will include administering pediatric and adult provider surveys with the ultimate goal of improving transitional care processes for CMC.

Category	Pediatrics & Child Health, #65
Primary Author	Christina M. McKinney, MD
Secondary Authors	Amy Pan, PhD, Melodee Liegl, MA, Glenn Bushee, MS, MA, Patrick J. McCarthy, MD, MME, Kelsey Porada MA, Erin Preloger, MD, Michelle Mitchell, MD, Kelly Graff, MD, Sarah Corey Bauer, MD
Title	Impact of the Diagnostic Pursuit of Multisystem Inflammatory Syndrome in Children (MIS-C) on Laboratory Utilization in Hospitalized Pediatric Patients with Common Bacterial Infections
Introduction	Multisystem inflammatory syndrome in children (MIS-C) is a potentially life-threatening disease without specific pathognomonic features or tests that emerged during the COVID-19 pandemic. MIS-C has varied clinical features that may overlap with common bacterial illnesses, possibly resulting in increased use of diagnostics for children with these conditions. Certain labs used in the diagnostic evaluation of MIS-C are not often ordered for common bacterial infections, thus typical values for these conditions are not established.
Methods	To compare laboratory utilization patterns for pediatric patients hospitalized with common bacterial infections with features that may overlap with MIS-C prior to and during the COVID-19 pandemic and determine median and mean values of these studies for each condition. A retrospective cohort study was conducted at a tertiary care, free-standing children's hospital between 2018-2022. The study period was divided into pre-pandemic (Mar. 2018-Feb. 2020) and pandemic (Mar. 2020-Feb. 2022) intervals. Patients >60 days and < 22 years of age discharged from the hospitalist service with cellulitis, lymphadenitis, pneumonia, or urinary tract infection were included. Patients diagnosed with MIS-C or similar syndrome were excluded. Use of C-reactive protein (CRP), procalcitonin (PCT), ferritin, B-type natriuretic peptide (BNP), D-dimer, troponin, and their initial values during patient encounters were compared and described using descriptive statistics.
Results	602 encounters met inclusion criteria. Demographics were similar, except for a higher proportion of females in the pandemic group. Ferritin, BNP, D-dimer, and troponin were more frequently utilized during the pandemic, without difference in CRP or PCT utilization. Mean and median laboratory values were determined and stratified by specific infection.
Conclusions	Patients hospitalized with otherwise common bacterial infections may incur unnecessary work ups in the COVID-19 era due to pursuit of MIS-C, as demonstrated by a significant increase in ferritin, BNP, troponin, and D-dimer utilization in the pandemic interval. Utilization of CRP and PCT was unchanged, suggesting their routine use in bacterial infections at baseline. Attention to specific MIS-C epidemiologic factors may help limit laboratory overuse and mitigate the potential for increased costs. Laboratory values in common bacterial conditions are reported, with unclear utility in differentiation from MIS-C. Limitations include small sample size, underrepresentation of some bacterial infections, and retrospective design.

Category	Pediatrics & Child Health, #66
Primary Author	Jacqueline Tran, BS
Secondary Authors	Bernard Cohen, MD
Title	Tinea Capitis in a 14-Day Old Infant
Introduction	Tinea capitis is a superficial fungal infection of the skin of the scalp with a propensity for invasion of the hair shafts and follicles. Common pathogenic causes are dermatophyte fungal geni including Trichophyton and Microsporum. Although tinea capitis affects predominantly African American children, infants and adults of all racial and ethnic backgrounds could be affected. Existing reports of tinea capitis in infants are rare, which may be attributable to the lack of reporting at this stage of life. In infancy, the presentation of alopecia, scaling, and flaking associated with tinea capitis are often misdiagnosed as eczema or seborrheic dermatitis.[1]
Methods	We present a case of a 14-day-old Caucasian boy evaluated for an annular, scaly plaque on the scalp. Examination of the specimen obtained included KOH slide preparation and fungal cultures. KOH preparation indicated broken hairs, spores, and an endothrix infection on the residual hair. Fungal cultures were positive for M. Canis. The patient was prescribed 15mg/kg/day of griseofulvin ultra-micro size tablets which were crushed and mixed with water, taken orally for 10 weeks. No side effects were reported. The patient exhibited clearance with no recurrence at the time of 3 months follow-up.
Results	There are limited treatment guidelines for children less than two years of age presenting with tinea capitis. The American Association of Pediatrics Red Book reports that griseofulvin is FDA approved for children two years and older and terbinafine is approved for use in those four years and older.[2] Currently, for children less than two years of age, terbinafine has been used off label for treatment of tinea capitis. However, there is no consensus for standard of care for treatment of tinea capitis in this patient population. Our case depicts successful use of griseofulvin in the treatment of tinea capitis in a 14-day-old infant. In support, a literature review of the treatment of tinea capitis in infants reported that children less than two years of age treated with oral anti-fungal agents had nearly 100% cure rates without recurrence at time of follow-up.[3] It is essential to establish a consensus and best practice guidelines to offer the best care for this patient population.
Conclusions	Further efforts are underway to survey pediatricians and pediatric dermatologists in the United States to obtain a more accurate representation of tinea capitis cases in young infants and determine a consensus when treating tinea capitis in this population.
Reference 1	Ely JW, Rosenfeld S, Seabury Stone M. Diagnosis and management of tinea infections. Am Fam Physician. 2014;90(10):702-710.
Reference 2	Lynfield, R., & Sawyer, M. H. (2021). Red Book (2021): Report of the Committee on Infectious Diseases (32nd Edition). American Academy of Pediatrics, 755â€“759. https://doi.org/10.1542/9781610025225
Reference 3	Zampella JG, Kwatra SG, Blanck J, Cohen B. Tinea in Tots: Cases and Literature Review of Oral Antifungal Treatment of Tinea Capitis in Children under 2 Years of Age. J Pediatr. 2017;183:12-18.e3. doi:10.1016/j.jpeds.2016.12.042

Category	Pediatrics & Child Health, #67
Primary Author	Jarrett Judkins
Secondary Authors	Matthew C. Scanlon M.D., Kari Rajzer-Wakeham CPNP, Binod Balakrishnan M.D.
Title	Stat Head CTs in the PICU: much risk for little reward?
Introduction	In pediatric intensive care units (PICUs), head computer tomograms are frequently ordered â€œstatâ€• (without delay) to assess acute intracranial pathology. Obtaining a â€œstatâ€• head CT (SHCT) may result in delays in therapy, as well as decompensation during patient transport. There are no studies evaluating whether SHCTs lead to changes in patient care in the PICU setting. We studied the indications for and findings of SHCTs, as well as any resultant interventions.
Methods	After obtaining approval from the investigational review board, we retrospectively analyzed the records of PICU patients who underwent SHCTs at a free-standing childrens's hospital over a two-year period. Abstracted data included demographics, primary diagnoses, indication for SHCT, illness severity (SOI), and both neurologic pupil index (NPI) and any post-SHCT interventions within two hours of imaging. SHCT finding were recorded as no change, new findings, progression of known findings. SHCT indications include altered mental status (AMS), seizure (SZ), neurosurgical team request (NS), increasing intracranial pressure (ICP), pupillary changes (PC), focal neurologic deficits (FND), electroencephalogram (EEG) changes, and vital sign changes (VS). Descriptive statistics were used to describe the study population. A general estimating equation (GEE) model was used to identify factors associated with new findings and interventions.
Results	Ninety-eight patients (54% male) underwent 112 SHCTs during the study period. New SHCT finding was noted in 35% of studies, with only 12% of SHCTs resulting in a post-SHCT intervention. Most common indications were AMS (25.0%), SZ (14.3%) and ICP (12.5%) Indications associated with most new findings included PC (80.0%), ICP (64.3%) and FND (50.0%). AMS had the lowest proportion with a new SHCT finding (10.7%). NPI<3, trauma status and SOI were associated with new SHCT findings.
Conclusions	Most SHCTs performed in the PICU have clinically insignificant findings and are not associated with intervention(s). Similar prior studies, AMS was least associated with a new SHCT finding. Prospective studies are needed to inform appropriate use of stat SHCTs.

Category	Pediatrics & Child Health, #68
Primary Author	Jitka Rybova
Secondary Authors	Teresa Sundararajan, Theresa Dlugi, and Jeffrey A. Medin
Title	Hematopoietic Stem Cell Transplantation in Farber Disease and Spinal Muscular Atrophy-Like Mouse Models of Acid Ceramidase Deficiency
Introduction	Farber disease (FD) and Spinal Muscular Atrophy with Progressive Myoclonic Epilepsy (SMA-PME) are ultra-rare lysosomal storage disorders caused by deficient acid ceramidase (ACDase) activity. Although both conditions result from mutations in the ASAH1 gene, their clinical presentations differ dramatically. FD patients manifest a spectrum of symptoms including formation of nodules, swollen and painful joints, and a hoarse voice. FD patients usually die in childhood. SMA-PME patients manifest neurological symptoms including seizures and uncontrollable muscle jerks (myoclonic epilepsy), as well as muscle weakness and wasting (atrophy). SMA-PME patients can survive until early adulthood and longer. Currently, there is no cure for ACDase deficiency. Treatment approaches focus on symptom management.
Methods	To study ACDase deficiency, we have generated and thoroughly characterized mouse models of both FD (P361R-FD) and SMA-PME (P361R-SMA). These mouse models display very different manifestations, though both recapitulate the human disorders closely. Histiocyte infiltration is seen and ceramide accumulates across many tissues. Enzyme replacement therapy and pharmacological chaperone therapy are being investigated for these conditions but are not curative therapies. Gene therapy is a possible curative approach and is being investigated for the treatment of a number of lysosomal storage disorders. To inform our future gene therapy efforts targeting autologous hematopoietic cell and systemic correction, here we conduct hematopoietic stem cell transplants (HSCTs) of healthy mouse bone marrow into P361R-FD and P361R-SMA mice.
Results	HSCT improved lifespan and performance on behavioral tests in both P361R-FD and P361R-SMA recipient mice. Treatment also normalized spleen and liver size and plasma levels of monocyte chemoattractant protein 1 (MCP-1) and Interleukin 6 (IL-6), and significantly reduced histiocytic infiltration and lysosomal accumulation in the spleen, liver, spinal cord and brain in both P361R-FD and P361R-SMA mice. HSCT prevented lesion development and reduced demyelination of the spinal cord reported in P361R-SMA mice. These results suggest that successful engraftment of HSCs ameliorates pathology described in ACDase deficiencies.
Conclusions	Future studies will extend this HSCT protocol to treating P361R-FD and P361R-SMA mice with ex vivo lentiviral vector modified HSCs with the long-term goal being clinical translation of this work.
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Category	Pediatrics & Child Health, #69
Primary Author	Julia Jezykowski
Secondary Authors	Yuhuan Luo, Lisa Fraser, Cara Mack
Title	Interleukin 8-CXCR2 Mediated Neutrophil Extracellular Trap Formation in Biliary Atresia
Introduction	Biliary Atresia (BA) is a neonatal, sclerosing lesion of the hepatic biliary tract, progressing to obstruction of bile flow in infancy. The etiology of BA is unknown, but is likely multifactorial, with possible origination of the disease from viral or bacterial infections, genetic factors, and environmental or autoimmune responses. Previous work from our lab has shown that IL-8 (neutrophil chemokine) neutrophil extracellular traps (NETs) correlated with worse patient outcomes.
Methods	The goal of this study was to characterize both neutrophil activation in BA and the ability of neutrophils to stimulate hepatic stellate cells (HSC), the major collagen-producing cells of the liver. BA patient blood was obtained at the time of diagnosis and transplant. Flow cytometry was performed on healthy donor isolated neutrophils co-cultured with BA patient (or other liver disease control) plasma for analysis of neutrophil activation markers. Quantitative multiplex immunohistochemistry (IHC) of markers of neutrophil activation was performed on liver tissue. QPCR of fibrotic gene markers is planned for the HSC LX-2 cell line after co-culturing with neutrophils or isolated NETs.
Results	Healthy donor neutrophils co-cultured with BA plasma produced more NETs than control. NET production correlated with higher IL-8 levels and lower levels of the IL-8 receptor, CXCR2, indicating activation of the pathway. Multiplex IHC identified increased expression of NETs containing tissue factor and IL-17, two proteins known to activate HSCs, that colocalized with markers of biliary fibrosis. Preliminary work with the LX-2 cell line revealed that these cells can be activated and show an upregulation of gene markers of fibrosis after addition of TGF-b1 in vitro.
Conclusions	Biomarkers of liver fibrosis and NETosis are chronically present in BA patients, suggesting that the IL-8-CXCR2 mediated NETosis pathway is involved in the pathogenesis of BA. HSCs are major contributors to fibrogenesis, and studies are ongoing to determine the impact of neutrophils and NETs in HSC activation.

Category	Pediatrics & Child Health, #70
Primary Author	Linda M Reis, MS, CGC
Secondary Authors	Huban Atilla, Peter Kannu, Adele Schneider, Samuel Thompson, Tanya Bardakjian, Elena V Semina
Title	Variants in histone lysine methyltransferases resulting in Axenfeld-Rieger and Peters-plus like phenotypes.
Introduction	Axenfeld-Rieger (ARS) and Peters plus syndromes (PPS) are distinct genetic conditions causing anterior segment dysgenesis phenotypes in combination with non-ocular anomalies. While specific genetic causes have been identified, in PITX2 (ARS type 1), FOXC1 (ARS type 3), and B3GLCT (PPS), some patients receive a clinical diagnosis based on overlapping clinical features but remain unexplained genetically.
Methods	Exome sequencing was undertaken in individuals with ARS, PPS, and overlapping phenotypes but negative analysis of known genes.
Results	We identified pathogenic variants in KMT2D and SETD1A (KMT2F), lysine methyltransferases that mediate methylation of histone H3, in four individuals. Retrospective analysis showed phenotypic overlap with the genetically diagnosed congenital regulopathy, but these conditions were not initially considered, likely due to the lack of previous association with anterior segment ocular anomalies and phenotypic overlap with known anterior segment syndromes of ARS and PPS. KMT2D has been associated with other developmental ocular anomalies and is known to be important in neural crest development, so an expansion to include anterior segment dysgenesis is consistent with known functions. SETD1A is less well-characterized but does show strong enrichment in the developing mouse eye.
Conclusions	KMT factors are a novel cause of anterior segment dysgenesis. The presence of rare anterior segment anomalies can distract from identification of other known genetic syndromes, thus unbiased genetic analysis is important for accurate diagnosis.
Acknowledgements	We are thankful to families for participating in this study and to collaborating clinicians for sharing information with families.

Category	Pediatrics & Child Health, #71
Primary Author	Madeleine Nowak
Secondary Authors	Amanda Rogers, MD
Title	Mind the Gap: Understanding the Timeline of Medical Readiness and Discharge
Introduction	Efficient discharges lead to decreased length of stay and improved hospital flow. An efficient discharge requires both timely recognition of patient's medical readiness for discharge (MRD) and effective preparation of logistical discharge needs. Our objective was to better understand Pediatric Hospital Medicine (PHM) discharges to inform future targeted discharge improvement work by 1. analyzing time of MRD throughout the day, 2. assessing the time from MRD to discharge, and 3. categorizing commonly identified discharge delays.
Methods	We completed a retrospective chart review of PHM patients hospitalized with one of 4 common pediatric diagnoses (status asthmaticus, brief resolved unexplained event, hyperbilirubinemia, and rule out sepsis) between 09/2021-09/2022). The time of MRD was determined by reviewing the electronic health record (EHR) for time of completion of previously established diagnosis specific criteria. The time of MRD was compared to the time of discharge order and to the time of discharge as recorded in the EHR. If the time from MRD to discharge exceeded 2 hours, the discharge was considered delayed and further chart review was completed to identify potential reasons for the delay. MRD and discharge timing was analyzed using descriptive statistics and discharge delays were assessed by content analysis.
Results	100 discharge events were analyzed, 25 from each of the four selected diagnoses. MRD occurred throughout the day (33% morning, 43% afternoon, 143% evening and 101% night) with a median hour of 11 am. The median time from MRD discharge was 1.7 hours (0.5 hours from MRD to discharge order and 0.9 hours from discharge order to discharge) with the longest duration from MRD to discharge occurring in patients with status asthmaticus. 40% of patients had a delayed discharge, with patients with status asthmaticus having the most discharge delays. Identified reasons for delays were categorized into coordination of discharge medications, family education, vaccinations, social barriers, and transportation.
Conclusions	MRD occurred throughout the day suggesting that time from MRD to discharge may be a more informative metric of discharge efficiency than discharges by a set time of day. While the majority of patients were discharged within 2 hours of MDR, themes of common discharge delays were identified. Next steps include the development of forward facing EHR timestamps noting MRD for improved tracking and real-time communication about this informative metric and targeted interventions to address commonly identified reasons discharge delays.

Category	Pediatrics & Child Health, #72
Primary Author	Narmeen Khan
Secondary Authors	Michael Levas, Danny Thomas, Catherine Ferguson, Marlene Melzer-Lange, and Katherine O'Brien
Title	Increasing Project Ujima Referral Rates at Children's Wisconsin EDTC
Introduction	Milwaukee County is one of the top counties in the United States for firearm injuries. Project Ujima is a collaborative program that supports pediatric victims of violence ages 7 to 18 years of age in Milwaukee County and their families throughout the hospitalization process and after discharge. The program provides resources including housing, mental health, job security, and legal support as these individuals try to recover from their trauma and navigate societal stressors. The purpose of our project is to increase Ujima referral rates in Children's Wisconsin Emergency Department Trauma Center (EDTC) so that more eligible patients can reap the benefits and resources of Ujima.
Methods	We used a quality improvement approach to understand the specifics, including barriers, that play a role in the Ujima consult placement process as it already exists. We used data from 2019 to current and looked at several variables, including the patient’s chief complaint, to create p-charts to assess such barriers.
Results	Based on this data gathering, our primary interventions will be to modify the already-existing best practice advisory for Ujima consults and to increase resident education about Ujima.
Conclusions	Future goals include implementing plan-do-study-act (PDSA) cycles to test whether these two interventions increase Ujima referral rates within a 12-month time frame.

Category	Pediatrics & Child Health, #73
Primary Author	Nawara Abufares, MS
Secondary Authors	Staci Young, PhD, Siobhan McDonnell, MS, Bethany Klett, MD, Mir Basir, MD, MS
Title	Baby Talk: Exploring barriers and facilitators to parent-physician communication in the NICU
Introduction	The NICU is often a gateway to long-term complex healthcare needs. Parent's most frequent complaints are that physicians do not listen to their concerns, care about their problems, or provide adequate information about treatment. Effective parent-physician communication is vital to developing a healing relationship that. optimizes health outcomes. Objective: Identify parent and physician behaviors that act as barriers or facilitate communication.
Methods	Parents with ≥7 days NICU experience were selectively recruited to ensure diversity in race, socioeconomic status, and gender. After consent, participants completed the Perceived Efficacy in Patient-Physician Interactions questionnaire and Medical Term Recognition Test. One-hour Zoom or in-person semi-structured interviews explored participant experiences of communication with physicians and perceived barriers to efficacy. Interviews were audio recorded and transcribed. Thematic analysis with MAXQDA was performed to understand communication facilitators and barriers.
Acknowledgements	The John A. & Linda Mellowes Family Endowed Chair in Intensive Care Fund Drs. Elsa B. and Roger D. Cohen Endowed Chair in Medical Education

Category	Pediatrics & Child Health, #74
Primary Author	Xuejun Wang
Secondary Authors	Theresa A. Dlugi
Title	Development of a Mass Spectrometry-Based Assay for the Detection of Endogenous and Lentiviral Engineered Enhanced Hemoglobin in Sickle Cells and Mice
Introduction	Sickle cell disease (SCD) results from a sequence defect in the adult hemoglobin (HbA) Î²-globin chain. SCD is traditionally diagnosed by cellulose-acetate hemoglobin (Hb) protein electrophoresis or high-performance liquid chromatography (HPLC). While clinically useful, these methods have sensitivity limitations.
Methods	In efforts towards implementing a gene therapy approach for SCD, we first developed a novel mass spectrometry (MS)-based method for the rapid, sensitive, and highly quantitative detection of endogenous and lentiviral-encoded therapeutic Î²-globin. We have engineered a novel lentiviral vector based on the Lenti/Î²AS3-FB construct. The Î²AS3-globin transgene expressed from this vector contains the mutations G16D, E22A and T87Q that increase affinity for healthy Î²-globin and inhibit axial and lateral contacts with sickle Î²-globin, thereby conferring anti-sickling properties. Utilizing synthetic signature peptides for wild-type human Î²-globin, sickle Î²-globin, and Î²AS3-globin, we developed sample preparation methods and a MS-based assay to simultaneously detect each of these globins in cultured cells and small quantities of mouse peripheral blood.
Results	Using these MS methods, we have successfully phenotyped homozygous HbA (AA), heterozygous HbA-HbS (AS), and homozygous HbS (SS) Townes mice. We detected lentiviral vector-encoded Î²AS3-globin in transduced erythroid cell cultures and in transduced human CD34+ cells after erythroid differentiation. We also detected therapeutic Î²AS3-globin in peripheral blood six weeks post-transplant of transduced Townes SS bone marrow cells into Townes SS mice. This Î²AS3-globin persisted over 24 weeks post-transplant.
Conclusions	With several genome-editing and gene therapy approaches for severe hemoglobin disorders currently in clinical trials, this MS detection method will be useful for patient assessment before treatment and during follow-up.
Ancillary Materials	VIEW MY POSTER

Category	Population Health, Disparities & Outcomes, #75
Primary Author	Ana Johnson Escauriza
Secondary Authors	Berenice Ramirez-Leal, Babyle Medina Vega, Magnalena Marisol Garcia, Wilfredo Marcial Santiesteban Herrera, Geydis Costa Ortiz, Arianna Guelmes Lavandero, Nerli Montero Laffita, Alicia Sende, Jara McLarren, Katie Iverson, Marc A. de Moya
Title	Culture of Patient Safety and Team Communication in the Operating Room of a University Hospital in Cuba
Introduction	The General Calixto-Garcia University Hospital has been one of the largest trauma centers in La Habana, Cuba, with a yearly admission of approximately 3,000 trauma patients. As in other Latin American countries, Cuba has experienced a rise in surgical interventions. Therefore, efforts to improve surgical outcomes have been analyzed and subsequently implemented. Culture of patient safety and team communication have been marked as critical for the safety and prevention of poor surgical outcomes. Therefore, simulation-based interventions such as TeamSTEPPS, a teamwork system designed to improve institutional collaboration and communication relating to patient safety, can improve teamwork and communication throughout surgery. And thus, strengthen patient safety culture. Currently, there are no available programs validated in Latin America. Specific Aims: To analyze and identify the Cuban culture of patient safety and communication among the operating room (OR) teams of the General Calixto-Garcia University Hospital. Hypothesis: We hypothesized that the design, translation, and implementation of TeamSTEPPS, tailored for the faculty and professionals of the General Calixto-Garcia University Hospital, will enhance team communication and functioning in the OR, thus increasing patient safety.
Methods	A multi-disciplinary operating room staff of the Calixto-Garcia University Hospital identified challenges via semi-formal focus groups in June 2022. The utilization of TeamSTEPPS to target these issues was proposed and implemented. Four of its original eight modules were utilized. These were: Module 1 - Introduction, Module 6 - Communication, Module 7 - Mutual Support, and Module 8 - Summary/Putting it All Together. They were translated from English to Spanish and combined for pilot use with this OR staff.
Results	Two focus groups were completed, and their responses were recorded and three themes emerged. They identified significant gaps between the discussion about holistic surgical team communication satisfaction and quality of patient safety culture. The gaps in communication within the OR team provided an opportunity to focus the future training. Most notable gaps included poor or limited communication due to unclear communication, experience level and autonomy. Additionally, staff with less experience agreed that there is a difficulty in voicing a perceiving a problem with surgical methods and/or patient care. Hence, there is a need of initiating a culture of patient safety that includes all OR staff. Four multidisciplinary simulation-based teaching modules were selected for implementation, and the design and individualization of standardized pre-operative, intra-operative and post-operative checklists and hospital-specific protocols were completed with the aid of the local Cuban faculty and physicians. Validation of the checklists and protocols were printed in June 2023, thus, it is currently ongoing.
Conclusions	Multidisciplinary communication plays an important role in both the causation and prevention of poor surgical outcomes leading to more effective and efficient patient care. Hence, simulation-based interventions focusing on communication and leadership can enhance performance and culture of safety. TeamSTEPPS has been employed by the General Calixto-Garcia University Hospital to develop superior interdisciplinary communication and improve the culture of safety. The four simulation-based education modules will be validated for hospital-wide implementation. Additionally, implementation of checklists and protocols are to be completed by the surgeon, anesthesiologist, and operating nurse. Our goal was to promote a collective culture of safety and communication to foster teamwork, therefore, TeamSTEPPS was and will be a great tool to accomplish such.
Ancillary Materials	WATCH MY PRESENTATION

Category	Population Health, Disparities & Outcomes, #76
Primary Author	Iaong Vang
Secondary Authors	Athena Dong, Danica Vendiola, Melissa Chiu MD, Caitlin Kaeppler, MD
Title	Assessing a Refugee Health Curriculum on Medical and Pharmacy Students' Confidence and Comfort in Providing Cross-Cultural Care
Introduction	Despite growing numbers of resettled refugees, many medical trainees lack formal education and feel underprepared to provide care. A former study at the Medical College of Wisconsin (MCW) created a refugee health curriculum and assessed its efficacy in improving participantsâ€™ knowledge, awareness, and confidence in providing cross-cultural care. The curriculum improved knowledge and awareness, but had no significant improvement in confidence. This study sought to revise and further develop the curriculum to increase participant confidence.
Methods	A 5-module curriculum was developed and presented to medical trainees at MCW. Participants completed pre- and post-surveys adapted from "The Cross-Cultural Competency Survey"•. Survey results were evaluated using non-parametric statistical analyses.
Results	Out of 41 participants, 17 completed pre-surveys (41.5%) and 10 completed post-surveys (24.4%). On a 7-point Likert scale, pre-survey results indicated a lack of education on refugees (median=2, IQR=1) and little confidence in providing cross-cultural care (median=3, IQR=2) and comfort taking histories (median=4, IQR=2). Evaluation of the curriculum’s impact showed statistically significant improvements in knowledge and awareness, confidence in providing cross-cultural care, and comfort when working with interpreters and taking histories ($p<0.05$). However, the curriculum had no statistically significant improvements in comfort when interacting with non-English speaking individuals and individuals with different cultural backgrounds.
Conclusions	This study continues to demonstrate a need for education on refugee health. The revised curriculum was effective in improving participants' confidence in providing cross-cultural care; however, trainees may benefit from additional sessions working with interpreters and interacting with individuals with different cultural backgrounds. Future directions include expanding the curriculum to provide hands-on experience.

Category	Population Health, Disparities & Outcomes, #77
Primary Author	Kara J. Kallies, MS
Secondary Authors	Laura D. Cassidy, PhD, MS; Constance A. Kostelac, PhD; Terri A. deRoon-Cassini, PhD, MS; Carissa W. Tomas, PhD
Title	Traumatic Injuries by Area Deprivation Index and Social Vulnerability Index in Milwaukee County
Introduction	Predisposing factors for traumatic injuries are complex and variable; in addition to individual factors, the neighborhood environment may influence injury mechanisms or outcomes. The Social Vulnerability Index (SVI) identifies areas at risk for emergencies and is used in disaster preparedness; Area Deprivation Index (ADI) measures socioeconomic disadvantage and is used for policy development. The objective of this study was to assess the relationship between SVI or ADI and hospital length of stay (LOS), and mortality for injured patients to determine whether SVI or ADI indicate areas where targeted injury prevention may be most impactful.
Methods	Patients (≥18 years old) who resided in Milwaukee County and were treated for injuries from 2015-2021 at a level I trauma center were included. Injured patients' addresses were geocoded and merged with 2020 state-level SVI and ADI. SVI ranks census tracts from 0-100% from least to most vulnerable. ADI ranks census block groups from 1 (least disadvantaged to 10 (most disadvantaged). The highest SVI or ADI decile indicated high vulnerability/disadvantage. Regression models for hospital LOS and in-hospital mortality were adjusted for either SVI or ADI within separate models, and age, gender, race/ethnicity, mechanism of injury, injury severity score (ISS).
Results	12,413 patients were included; 63% were male. The median total hospital LOS was 4 (0-313) days, and in-hospital mortalities occurred in 5% of patients. Based on SVI and ADI, 4,541 (37%) patients resided in high vulnerability areas and 4,750 (39%) lived in highly disadvantaged areas, respectively. After adjusting for patient factors, SVI deciles 6-10 were associated with increased hospital LOS, as were pedestrian injuries (Î²=1.1, 95%CI:0.37-1.78; p=0.003). When adjusted for SVI, firearm (OR=4.7, 95%CI:3.32-6.63; p<0.001) and suicide (OR=16.4, 95%CI:1.48-182.45; p=0.023) injuries were associated with in-hospital mortality. In an adjusted model using ADI, the 2nd, 7th, and 10th deciles were associated with increased hospital LOS. Similar to SVI, pedestrian injuries were associated with increased hospital LOS (Î²=0.9, 95%CI:0.15-1.58; p=0.018), and firearm (OR=4.7, 95%CI:3.28-6.68; p<0.001) and suicide (OR=15.9, 95%CI:1.36-185.71; p=0.028) injuries were associated with in-hospital mortality. SVI and ADI were not independently associated with in-hospital mortality. Increasing age and ISS were associated with increased hospital LOS and in-hospital mortality.
Conclusions	SVI and ADI identified a similar proportion of patients in high vulnerability or disadvantaged areas. Increased SVI was associated with increased hospital LOS, Similarly, some increased ADI areas were associated with increased hospital LOS. Neither SVI nor ADI was independently associated with in-hospital mortality. Pedestrian injuries were associated with increased hospital LOS, while firearm and suicide injuries were associated with in-hospital mortality after adjusting for either SVI or ADI. These data indicate that there may be some influence of neighborhood environments on hospital LOS, a social vulnerability that can impact hospital factors and overall health.
Ancillary Materials	VIEW MY POSTER

Category	Population Health, Disparities & Outcomes, #78
Primary Author	Lauren L. Titus MD
Secondary Authors	Natalie Yass BS, Anika Nelson MD, Kelsey Porada MA, Fatima Anibaba MS, Sarah Bauer MD
Title	Disproportionate Enforcement of a Hospital's Safe Sleep Policy in Racial and Ethnic Minority Families
Introduction	The negative effects that race and ethnicity-based biases have on patient health outcomes have been well documented. However, the effects of bias on patients' families during hospitalization has not been robustly explored. We hypothesize that implicit bias may impact family-provider communication through the enactment of our hospital's safe sleep policy, specifically with families of color. Objective: Investigate the demographic makeup of families who are involved with staff-initiated warnings within Children's Wisconsin's safe sleep policy and determine if there are racial disparities in how this policy is enacted.
Methods	We performed a retrospective chart review of enactments of the staff-initiated safe sleep policy. Encounters were identified by searching the electronic health records (EHR) for variations of the terms "co-sleeping" or "safe sleep". Inclusion criteria included: encounters for patients â‰¤12 months, hospitalized on an acute care floor at a tertiary children's hospital between January to December 2021, and a documented incident of unsafe sleep during admission. Descriptive statistics and bivariate analysis were applied to this data to evaluate for associations between demographic data and encounter details.
Results	Out of 114 hospital unsafe sleep encounters included in our study, we found a disproportionate number to be Black infants (55.3%) when compared to the overall demographics of hospitalized infants (16.7% Black). Families of Black and Asian infants received significantly more warnings about safe sleep during hospitalization than families of Non-Hispanic White infants ($p = 0.027$ and $p = 0.029$). Families who spoke a language other than English were also significantly more likely to receive more warnings than English-speaking families ($p = 0.008$). Families of Black infants and non-English-speaking families had more Social Work consults for unsafe sleep concerns. Families of Black infants had more encounters that escalated to having hospital security involved. Finally, there was a difference noted between the mean time between warnings for families of Black infants (mean 21.4 hours, SD = 21.5) and families of Non-Hispanic White infants (mean 55.1 hours, SD 67.9). This difference approached statistical significance ($p = 0.054$), suggesting that encounters with Black infants escalated more quickly, though more data is needed to fully understand the significance of this difference.
Conclusions	Our results suggest that our safe sleep policy is enacted disproportionately with more warnings going to Black, Asian, and non-English speaking families, and more frequent escalation to involve hospital security for Black families. The consequence of frequent warnings and escalation to security is ultimately limiting parent visitation to the hospital, which could result in decreased understanding about their child's condition and eroding trust in the medical system over time. Our study suggests that we need to further examine the ways in which our hospital policies contribute to institutional racism and harm systemically marginalized groups.

Category	Population Health, Disparities & Outcomes, #79
Primary Author	Mohammad Titi
Secondary Authors	Aliyah Keval, Julia Dickson-Gomez, Staci Young, John Meurer
Title	Fight COVID Milwaukee: Protective Behaviors and Risk Communications Associated with the COVID Pandemic
Introduction	Fight COVID Milwaukee is a community-engaged research project that utilizes antibody test data, surveys, focus groups, and health records from adults living in Milwaukee County to analyze COVID-19 risks from a population perspective. This effort examines the ways in which individuals responded to the COVID pandemic by making lifestyle modifications to mitigate potential risks, as well as the significant emotional impact that resulted from these changes Additionally, using information from focus group discussions with community members, Fight COVID MKE provides a better understanding of how adults, and people of color in particular, view the risks of COVID, and how to effectively communicate information about personal risk with the public. This information provides public health officials with knowledge to help guide and improve risk communication and public health policy.
Methods	Information letters were sent to patients of 20 primary care health centers, members of 12 community and faith partners, and participants in a COVID antibody/survey study in Milwaukee to recruit diverse adults, especially underrepresented, low-income, and elderly populations. 79 adults volunteered to join 9 Zoom focus groups. Groups discussed feelings about medical research, understanding of COVID, protective behaviors, and vaccines. Facilitators showed an initial version of a web-based risk assessment tool. Comments were transcribed and analyzed using MAXQDA.
Results	Analyses revealed 3 broad themes: (1) Participants had high levels of self-adherence to safety guidelines and public health recommendations but many reported observing non-adherence in others and felt discouraged and uncertain about future social reintegration. (2) Adherence to public health recommendations, particularly during the lockdown period, led to profound feelings of isolation and loneliness, exacerbated by virtualization which provided unfulfilling social interactions. (3) Effective risk communication strategies include using open and consistent messaging, using personal experience and local trusted community members to disseminate information, using layman's terms, clearly outlining risks and having individualized risk communication, and utilizing social media platforms for wider outreach.
Conclusions	The COVID pandemic had a profound impact on society and presented a considerable public health challenge to governments, public health, and health care systems around the world. Risk communication plays an important role in mitigating the spread of disease by informing individuals and allowing them to prepare for and respond to public health emergencies in an effective and timely manner. Our findings reveal public experiences with COVID, including protective behaviors and public perspectives on effective risk communication methods. These findings can help guide risk communication efforts and public health policy interventions for other infection outbreaks in the future.
Ancillary Materials	VIEW MY POSTER

Category	Resources, Tools & Methods, #80
Primary Authors	Cailey O'Neill and Victoria Le
Title	Implementing Vaccine Initiatives at Student-Run Free Clinic
Introduction	People who are uninsured face additional barriers to accessing preventative health services, including immunizations1. Adequate immunity is essential for individual and public health. Thus, improving access to immunizations is a priority for the Public Health Committee of the Saturday Clinic for the Uninsured (SCU), a student-run clinic for uninsured members of the Milwaukee community.
Methods	Over the last year, SCU established a multi-dimensional approach to improving access to immunizations and providing vaccine-specific education to patients that includes monthly in-house vaccine clinics, a novel volunteer position, influenza vaccine vouchers, and in-house influenza vaccines. Beginning in September 2022, in partnership with the Milwaukee Health Department (MHD), SCU began hosting monthly vaccine clinics open to SCU patients and other uninsured members of the community. At these clinics, MHD staff collaborated with SCU's new volunteer position, Vaccine Volunteers, to educate and vaccinate SCU patients and uninsured members of the community without cost or an appointment. Sixty-four total vaccines were provided to 36 different people from September 2022 - January 2023. Before this partnership began, SCU's only immunization options were referring patients to MHD facilities or providing in-house influenza vaccines when supplies were available. At each monthly clinic, the MHD offered SCU patients and community members the following vaccines: MMR, influenza, COVID-19 main series and boosters, Tdap, Hep A, Hep B, and Varicella.
Results	The Vaccine Volunteer role was implemented at SCU in October 2022. Vaccine Volunteers screen patients to determine immunization status, meet with patients individually during their visit to provide education about the importance of immunizations, determine patient eligibility, and connect SCU patients with internal and external immunization resources. Thus far, Vaccine Volunteers have met with sixty-four patients and from there, fourteen patients went on to receive vaccines at SCU that day, and 19 appointments were made to receive vaccines at a future date. Additionally, SCU offered Walgreens flu vaccine vouchers so that patients, especially those needing high-dose flu vaccine not offered by MHD, could obtain the recommended vaccines at no cost.
Conclusions	The monthly MHD vaccine clinics, implementation of the Vaccine Volunteer position, in-clinic flu vaccines, and flu vaccine vouchers facilitated improved access to immunization for SCU patients.
Acknowledgements	We would like to thank Dr. Rebecca Lundh and Dr. Rachele Harrison for their support of this project.
Reference 1	Lu PJ, O'Halloran A, Williams WW. Impact of health insurance status on vaccination coverage among adult populations. Am J Prev Med. 2015 Jun;48(6):647-61. doi: 10.1016/j.amepre.2014.12.008. Epub 2015 Apr 15. PMID: 25890684; PMCID: PMC5826635.
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Category	Resources, Tools & Methods, #81
Primary Author	Cesar A. Moncada
Secondary Authors	Andrew Liermann, Charlie M. Lewis, Jeffrey A. Medin, William M. McKillop
Title	Clinical-Scale Production of Lentiviral Vectors at a New Academic cGMP Facility
Introduction	Lentiviral vector (LV)-mediated gene delivery has shown clinical promise in the gene and cell therapy field. LVs offer a high rate of transduction into many cell types, the ability to transduce non- dividing cells, stable gene integration, and a reduced risk of insertional mutagenesis when compared to gamma-retroviruses. However, the production and purification of high-quality LVs for clinical trials remains challenging. The MCW/BCW GMP Vector Production Facility's mandate is to produce high-titer, clinical-grade LV for use in early-stage trials at the Milwaukee Regional Medical Center (MRMC).
Methods	Herein we describe a method to scale-up production of high-titer LVs that are capable of transducing multiple cell types under GMP conditions. We package our LV using HYPER technology, a commercially available, fully closed, and disposable system composed of multiple layers of a gas-permeable, tissue culture-treated, growth surface. Following packaging, we purify LV by post-harvest clarification and Mustang Q anion-exchange membrane chromatography. Scale-out experiments have provided encouraging recovery yields from clarification (83%) and Mustang Q chromatography (67%) resulting in a 1000-fold volume reduction with excellent viral recovery (60-70% of starting input LV). The chromatography eluate is subsequently diluted and concentrated using tangential flow filtration (TFF) and treated with Benzonase endonuclease (50 U/ml) at 37C. TFF is then repeated to further concentrate the LV down to 200 ml of deliverable product
Results	To evaluate compliance with current FDA guidance for clinical application, we analyzed samples from our production and purification process to assess LV purity and titer. We report functional titers between 1.3 x 10^7 TU/mL and 2.2 x 10^8 TU/mL for clinically relevant vectors. Our purification method results in minimal endotoxin detected (<100 EU/ml). Furthermore, post purification residual plasmid DNA, host-cell DNA, and host-cell protein were reduced >98%, >99%, and >98%, respectively.
Conclusions	The HYPER LV packaging strategy, Mustang Q chromatography, and TFF purification regimen described here is a practical method for LV scale-up to early-stage clinical trial volumes using affordable disposable laboratory supplies.
Ancillary Materials	VIEW MY POSTER

Category	Resources, Tools & Methods, #82
Primary Author	David R. Friedland, MD, PhD
Secondary Authors	Ryan Spellecy PhD; Bradley W. Taylor MBA FAMIA; Kathryn Gaudreau
Title	Facilitating Clinical Outcomes Research: A CTSI and HRPP Collaborative Improvement Project
Introduction	The Center for Biomedical Informatics (CBMI) of the Clinical and Translational Science Institute (CTSI) of Southeast Wisconsin has developed a nationally recognized Clinical Research Data Warehouse (CRDW). Through collaboration with the Human Research Protection Program (HRPP) of the Office of Research, the CRDW has institutional banking and IRB approval to facilitate investigators in performing deidentified cohort discovery using tools such as i2b2 and TriNetX. While this is invaluable for assessing demographic patterns for specific diseases and disciplines, evaluating clinical outcomes often requires identified patient data and additional manual chart review activities. In addition, on a departmental level, there may be multiple subspecialty specific disorders of interest for outcomes assessment. Traditionally, this would require each analysis of a specific disorder to have its own individual IRB submission and review. We present a collaborative effort among the Department of Otolaryngology and Communication Sciences, the CBMI/CRDW, and the HRPP/IRB to develop a department wide IRB-approved platform for performing retrospective medical record reviews using the CRDW. In addition, this IRB process has been templated to facilitate other departments and academic units in submitting their own global Clinomics IRB applications to expedite review and approval. This collaborative effort will stimulate activities that can improve clinical outcomes research, provide preliminary data for grant submissions, provide academic projects for resident and medical student education, engage faculty in clinical self-assessment and quality improvement, and enhance the academic culture of departments and divisions, while still adhering to regulatory and ethical requirements for research.
Ancillary Materials	VIEW MY POSTER WATCH MY PRESENTATION

Category	Resources, Tools & Methods, #83
Primary Author	Kun Fang
Secondary Authors	Victor Jin
Title	NucHMM: a method for quantitative modeling of nucleosome organization identifying functional nucleosome states distinctly associated with splicing potentiality
Introduction	Our knowledge at the quantitative aspect is very limited about the degree of nucleosome positioning, the spacing between two dyads of the nucleosomes, the phasing of a nucleosome array, and the extent to which the combinatorial epigenetic pattern influences nucleosome organization. In this study, we develop a novel computational method, NucHMM, to identify functional nucleosome states associated with cell type-specific combinatorial histone marks and nucleosome organization features such as phasing, spacing and positioning. We test it on publicly available MNase-seq and ChIP-seq data in MCF7, H1 and IMR90 cells and identify 11 distinct functional nucleosome states in which each is characterized with distinct nucleosome phasing, spacing, positioning and genomic location. Furthermore, we developed quantitative measures and demonstrate these nucleosome states are distinctly associated with the pioneer capacity of transcription factors and the splicing potentiality of skipping exons. Finally, we apply NucHMM on the prostate cancer system that consist of a primary prostate cancer cell line and a castration-resistant prostate cancer cell line, LNCaP and Abl and study the role of functional nucleosome states related skipping exons in the system. This work advances our understanding of the chromatin function at the nucleosome level, offers insights into the interplay among nucleosome organization, pioneer factors and splicing processes and provides a new perspective to study the role of nucleosome organization related splicing process in driving castration-resistant prostate cancer.

Category	Resources, Tools & Methods, #84
Primary Author	Megan Amarbayan, MPP
Secondary Authors	Jamie Aranda, MD, Nancy Jacobson, MD, Matthew Chinn, MD, Jonathan Rubin, PhD
Title	Internet scout page clicks as a surrogate marker for clinical pathway utilization within the emergency department
Introduction	Clinical pathways (CPs) are structured plans used by care teams when treating specific patient cases. The primary goal of CPs is to align evidence-based practices with patient care and optimize clinical outcomes while improving the efficiency of the healthcare system. CPs operationalize best evidence recommendations and clinical practice guidelines into an easily accessible pathway to be used at bedside. In the emergency department (ED), there is an intranet page that displays and promotes the usage of CPs. One way to track the usage of CPs is using scout page clicks as a surrogate marker and determine which CPs ED physicians are viewing within their practice. Determining which CPs are most frequently viewed will provide opportunities for quality improvement initiatives within our system of academic and community EDs. Aim/purpose: The purpose of this study is to determine the most frequently referenced clinical pathways on the ED scout page.
Methods	We obtained 6 months of hospital intranet traffic for the Emergency Medicine Clinical Pathways page. Additionally, we evaluated which pathways were the result of collaborations between different specialties and disciplines. Descriptive statistics were used to analyze the data.
Results	During the 6-month period, there were 1917 individual clicks reported on individual pathways and guidelines on the Emergency Department Clinical Pathway page. The ten most clicked pages were for pathways addressing the following conditions/subjects: atrial fibrillation, vertebral compression fracture, anticoagulation reversal, congestive heart failure, buprenorphine induction, acute bacterial skin and skin structure infection, traumatic brain injury, chronic obstructive pulmonary disease, pre-eclampsia, and behavioral health transfers. All ten of the most viewed pathways represent collaborations between the emergency department and other specialties. We are in the process of evaluating pathway page traffic over time to identify trends.
Conclusions	This analysis describes the most frequently viewed CPs on the Emergency Medicine Clinical Pathway intranet page. It may represent a surrogate marker for which pathways are being utilized in the ED. Though the amount of collaboration between departments was evident in the data, this could suggest that individuals in other departments may be contributing to the intranet traffic. Our findings have identified opportunities for educational interventions or operational changes to the usage and promotion of CPs for those CPs with the least number of views. One limitation of our study is that the intranet page clicks for each CP may not fully represent physician utilization. Physicians could be clicking on the pathway and may not be implementing into their practice. Alternatively, physicians who are using the CP may not necessarily need to derive it from the webpage. Future studies may be developed to investigate the extent which physicians are incorporating CPs within their care for patients, perhaps through technology embedded in the electronic health record.
Ancillary Materials	VIEW MY POSTER

Category	Surgery, #85
Primary Author	Abdul Hafiz Al Tannir
Title	Evaluation of a Safe Volume Cut-off to Observe Traumatic Hemothoraces
Introduction	Traumatic hemothoraces (HTXs) may be selectively observed. We sought to determine the safety of observation for traumatic HTXs, derive predictors of failed observation, and assess a safe HTX volume cut-off.
Methods	This is a 4-year retrospective study of all adult patients admitted to a Level 1 trauma center with a HTX on computed tomography (CT) from 2018 to 2021. Patients with tube thoracostomy (TT) placement prior to CT scan, concurrent pneumothorax >20mm, or mortality within 5 days of admission were excluded. HTX volume was calculated using Mergo's formula: V=d2xL (d: Depth; L: length). When comparing outcomes between early TT (TT placement≤24 hours of admission) and observation failure (TT placement >24 hours of admission), patients with a HTX>500cc were excluded..
Results	A total of 420 patients met inclusion criteria, of which 70% were initially observed. Fifty-Nine (20%) patients failed initial observation and progression or retained HTX (64%) was the most common reason. When compared to early TT, patients who failed observation had similar pulmonary complication (36% vs 35%; p-value=0.75), 30-day readmission (6% vs 7%; p-value=0.72), and 30-day mortality (6% vs 5%; p-value=0.73) rates. On multivariable analysis, HTX volume, number of ipsilateral rib fractures, flail chest, bilateral HTXs, and mechanical ventilation were independent predictors of observation failure (Table 1). On curve estimation regression, the risk of observation failure increased when HTX volume reached 400cc (Figure 1).
Conclusions	Observation of traumatic HTX is safe in select patients. Larger multi-institutional trials are warranted to evaluate a volume of 400cc as a safe observation cut-off point
Ancillary Materials	VIEW MY POSTER

Category	Surgery, #86
Primary Author	Alexandra O Polovneff, BS
Secondary Authors	Vienne Seitz, B.S.; Janet Panoch, PhD; Gwendolyn Hoben, M.D., PhD
Title	Spare The Limb And Spoil The Outcome: Why Do Some Osteosarcoma Patients Pursue Revision Amputation And Does The Amputation Improve The Outcome?
Introduction	There is tremendous emphasis on limb sparing surgery (LSS) in osteosarcoma. However, a substantial number of LSS patients choose to transition to an amputation-type revision, including rotation-plasty and turn-up plasty. Prior research has examined the psychosocial and physical outcomes, and overall satisfaction associated with secondary surgical interventions. However, little is known about subjective preoperative and postoperative pain and outcomes following secondary intervention. The purpose of this study was to determine motivating factors for revision and whether those interventions better address the motivating factors.
Methods	We identified the most popular public Osteosarcoma Facebook group by searching the keywords “osteosarcoma support group.” We selected posts containing comments regarding osteosarcoma interventions from June 1, 2021 through June 30, 2022. We excluded posts regarding non-surgical osteosarcoma interventions. We used iterative inductive and deductive thematic analysis to collect qualitative data on common topics, frequent questions, and knowledge gaps. Two investigators independently coded all posts and resolved discrepancies by discussion.
Results	A total of 14 posts and 378 comments from the Osteosarcoma and Ewing's Sarcoma Support Group were analyzed. Three themes emerged: (1) There is a lack of options presented to patients seeking treatment of osteosarcoma. (2) Many patients were unsatisfied and regretted their decision to undergo LSS because of numerous revisions, physical limitations, and chronic pain. (3) Many patients treated primarily or secondarily (following LSS) with rotation-plasty were satisfied with their lifestyle outcomes and mentioned improved mobility, range of motion, and limited chronic pain.
Conclusions	LSS can result in significant morbidity and despite sparing the limb, some patients are choosing to pursue amputation. Further work will need to examine amputation interventions to ensure that they can successfully address the problems identified with LSS, including mobility and pain. Prior concerns with amputation, including phantom limb pain, can now be addressed with targeted muscle reinnervation and regenerative peripheral nerve interfaces. Moreover, these options may deserve more discussion in the setting of the primary surgery.
Ancillary Materials	VIEW MY POSTER

Category	Surgery, #87
Primary Author	Ali Syed, MS
Secondary Authors	Benjamin Seadler MD, Jacob Lindemann BS, James Oujiri MD, David Joyce MD MBA, Stefano Schena MD PhD, Mario Gasparri MD
Title	Robotic-Enhanced Convergent Plus Procedure for Epicardial Left Atrial Ablation and Appendage Exclusion in Patients with Long-Standing Atrial Fibrillation: A Single Center Experience
Introduction	The Convergent Plus Procedure (CPP) is a hybrid treatment for patients with long-standing atrial fibrillation (AF). It combines a subxiphoid/left thoracoscopic epicardial ablation of the posterior wall of the left atrium with exclusion of the left atrial appendage (LAA) and a catheter-based endocardial ablation. We report the first series of a robotic enhanced CPP.
Methods	We retrospectively reviewed prospectively collected data of patients with AF who underwent robotic-enhanced CPP in the past 2 years. The lesion set adopted consists of division of the ligament of Marshall, ablation lines on the roof and floor of the left atrium, circumferential ablation of left pulmonary veins, semi-circumferential ablation of the right pulmonary veins and isthmus of the LAA, as well as LAA epicardial occlusion with clip. A traditional subxiphoid approach with ablation of the posterior wall of the left atrium completes the procedure. Rhythm follow-up was performed at 3 and 12 months through a combination of EKG, Holter, or interrogation of implanted devices. At 3-months, LAA closure was assessed with CT and TEE.
Results	There were 37 patients (average age: 64 years, 70% males) with a mean AF duration of 5.2Â±4.1 years. Mean LVEF,CHA2DS2-VASc and HAS-BLED scores were 53.4%, 2.3 and 3.1 respectively and 24% had NYHA Class III symptoms. Approximately 95% underwent endocardial catheter ablation prior to surgery with an average of 2 catheter-directed procedures performed. No cases required thoracotomy and the median LOS was 1 day. There were 3 postoperative complications (pleural effusion, pericardial effusion, costochondral fracture). Mean follow-up duration was 7.8 months. LAA occlusion was confirmed in 96% of patients. Freedom from AF at 12 months was 89%, 60% of patients discontinued Class I/III antiarrhythmics, and 56% of patients discontinued anti-coagulants.
Conclusions	In our experience, a robotic-enhanced CPP has rates of LAA occlusion and freedom from AF that are comparable to other techniques with minimal morbidity and a shorter length of stay. The robotic platform provides advantages such as increased dexterity, improved exposure of targeted anatomy, ease in LAA occlusion, and most of all, opportunities for a more comprehensive ablation. Discussion: Atrial fibrillation is a complex disease with many modalities for management. Based on contemporary data, a hybrid approach to AF can result in outcomes comparable to the current surgical gold standards. Our robotic approach provides increased visualization and dexterity allowing for more comprehensive ablative lesions and accuracy of LAA occlusion. Similar to current partnerships by interventional cardiology and cardiac surgery for the management of structural heart diseases, a multidisciplinary approach to atrial fibrillation between electrophysiologists and surgeons may allow for continued advancements in the field through more effective and less invasive treatment options.

Category	Surgery, #88
Primary Author	Anna Kerschner, BA
Secondary Authors	Morgan Briggs, MD; Jed Calata, MD; Kathleen Bhatt, MD; Benjamin Beran, MD
Title	Tubulovillous Adenoma Identified on Transvaginal Ultrasound: A Case Report
Introduction	Colorectal cancer is the second leading cause of death by cancer among North Americans, and most colorectal cancers develop from adenomas. Tubulovillous adenomas are a subtype of colonic polyp with relatively high potential for malignancy. Polyps such as these are typically identified on colonoscopy, but literature has shown cases of colorectal polyps found via ultrasound. We present a case of colonic tubulovillous adenoma first discovered on gynecologic transvaginal ultrasound (TVUS).
Methods	The patient was a 42-year-old gravida 2 para 2 female with symptoms suggestive of endometriosis, including left lower quadrant pain, heavy menstrual bleeding, urinary urgency, and dyschezia. The patient underwent TVUS following the International Deep Endometriosis Analysis (IDEA) protocol that identified an intermediate echogenicity, vascular solid mass measuring 1.2 x 0.8 cm within the rectosigmoid lumen. Consequent colonoscopy and polypectomy revealed tubulovillous tissue negative for high grade dysplasia or malignancy.
Results	Colonoscopy is the mainstay in identifying and treating colonic polyps, and early polyp removal is essential because most colorectal cancers arise from advanced adenomatous polyps. Furthermore, colorectal cancer among individuals under the age of 50 is on the rise, and this population of patients often lacks clear risk factors that would qualify them for early cancer screening. Evaluation of the rectosigmoid colon by ultrasound provides an opportunity for the identification of colonic polyps that might have otherwise gone undetected.
Conclusions	This case report highlights the importance of gynecologists developing an acute awareness of colonic pathologies that might be encountered while performing endometriosis ultrasounds with direct assessment of the rectum.
Ancillary Materials	VIEW MY POSTER

Category	Surgery, #89
Primary Author	Berenice Ramirez Leal, B.S.
Secondary Authors	A.J. Johnson Escauriza1 , Y. Valdes Gonzalez2 , K. Dieguez2 , S. Celestrin Marcos2 , M. Durruthy Alvarez2 , E. Hernandez Morales2 , M.A. Gonzalez2 , M. Perez Escalante2 , D. Milian Valdes2 , J. Roger Cordero2 , K. Iverson1 , C. Pain1 , M.A. De Moya1
Title	Real-Time Electronic Record and Clinical Guidelines Implementation in a University Hospital in Cuba
Introduction	The Calixto-Garcia Hospital is one of the largest trauma centers in Havana, Cuba, admitting approximately 3,000 trauma patients annually. The hospital is known as one of the leading institutions in trauma care and as a training hub. Although barriers such as accessibility and availability can hinder care in low and middle-income countries (LMICs), interventions to improve healthcare can be cost-effective [1]. Studies have shown that implementing clinical quality registries can improve health outcomes and reduce healthcare costs [2]. This is significantly important as most deaths following a trauma occur in LMICs where survival rates are lower than in high-income countries [3]. To improve patients' healthcare in emergency/trauma, this study aims to adapt a real-time electronic record and clinical practice guideline platform based on the resources and needs of its trauma center. The T6 platform is an iPad application that intends to facilitate decision-making in emergency and trauma patients by collecting patients' vital signs, and critical states/injuries and providing real-time analytics, risk prediction, and clinical decision support.
Methods	A total of six focus groups, ranging from five to eight hours, were conducted and recorded in May-August 2022 with the trauma and emergency team. Transcriptions were reviewed and coded to identify what sections of the T6 platform could be adapted. Two site visits were conducted to assess where the platform would be implemented within patient care processes.
Results	Three major themes emerged regarding the adaptability of the T6 platform for the institution. First, the lack of technological resources for effective communication between the pre-hospital and hospital teams hinders the ability to use the pre-hospital portion of the T6 platform. Second, some imaging tools, medications, and laboratory tests are unavailable in the institution and will not be part of the adaptation. An important realization was the need for Abbreviated Injury Scale (AIS) training, a large section of the T6 platform and integral in trauma care. Third, the Clinical Decision Support tools were positively viewed as significant resources for the entire clinical team as decision-making tools and training.
Conclusions	Due to the limited resources, the available fields on T6 will be customized. The medical staff is interested in further AIS training and values the implementation of the decision-making tools for all the team in emergency and trauma departments. The communication between the pre-hospital and hospital teams needs internal work within the institution and will not be in the adaptation. In conclusion, the implementation of the T6 platform in the institution is possible but will take considerable time, effort, and a clinical champion. If it can be accomplished, it has the potential to facilitate real-time decision-making, improve patient outcomes, and strengthen the clinical capacity of the physician.
Acknowledgements	This work was funded by Dr. Elaine Kohler Summer Academy of Global Health Research and Department of Surgery
Reference 1	[1] Bickler SN, Weiser TG, Kassebaum N, et al. Global Burden of Surgical Conditions; 2015 Apr 2. Chapter 2./ doi: 10.1596/978-1-4648-0346-8_ch2
Reference 2	[2] Hoque DME, Kumari V, Hoque M, Ruseckaite R, Romero L, Evans SM. Impact of clinical registries on quality of patient care and clinical outcomes: A systematic review. PLoS One. 2017 Sep 8;12(9):e0183667. doi: 10.1371/journal.pone.0183667. PMID: 28886607; PMCID: PMC5591016.
Reference 3	[3] Shanthakumar D, Payne A, Leitch T, Alfa-Wali M. Trauma Care in Low- and Middle-Income Countries. Surg J (N Y). 2021 Oct 22;7(4):e281-e285. doi: 10.1055/s-0041-1732351. PMID: 34703885; PMCID: PMC8536645.

Category	Surgery, #90
Primary Author	Brian J Conway, BS
Secondary Authors	Alexandra O Polovneff, Conner J McMains, Liliana E Pezzin, Kate B Krucoff
Title	The Cost-Effectiveness of Gender Affirming Mastectomy
Introduction	Despite increased visibility and acceptance in recent years, the transgender community continues to experience profound morbidity and mortality partially due to health care barriers, especially limited access to gender affirming medical and surgical care. Examples of these health disparities include increased rates of HIV and sexually transmitted infections (STI's), cancers caused by HPV (anorectal, cervical, penile), depression, anxiety, substance use disorder (SUD), and suicide. Although gender affirming surgery (GAS) is associated with enhanced physical and mental health for transgender individuals, limited surgical resources and lack of insurance coverage remain impactful barriers to GAS. The objective of this study was to demonstrate the cost-effectiveness of gender-affirming mastectomy.
Methods	A cost-effectiveness analysis was performed using a Markov model with a willingness to pay (WTP) threshold of $50,000/Quality Adjusted Life Year (QALY). The two main arms of the Markov model used were access to top surgery or lack thereof with additional sub-arms of negative or positive health events, such as post-operative complications and adverse mental health or successful surgery and access to hormone therapy. Data on health event probability, quality of life, and cost were extracted from the 2015 US Trans Survey (USTS), the Froedtert & Medical College of Wisconsin Health Network, and available literature. Analysis was performed using TreeAge Pro Healthcare (2022).
Results	Compared to lack of access ($3,316.25, 0.47 QALY's), gender-affirming mastectomy results in a greater annual cost but an overall greater effectiveness ($9,047.31, 0.93 QALY's) with an incremental cost-effectiveness ratio (ICER) of $12,458.83/QALY within the first year. Moreover, this model predicts the ICER gradually decreasing to $11052.05/QALY at five years, $9262.93/QALY at ten years, and $8,128.20/QALY at fifteen years.
Conclusions	We are one of the first groups utilizing the 2015 USTS to establish gender-affirming mastectomy and gender-affirming hormone therapy for transgender patients is cost-effective as demonstrated by an ICER less than the WTP threshold. These findings suggest hormonal and surgical gender affirming care should be provided by health institutions and covered by insurance as the health of transgender individuals is enhanced by offering these health services. Other studies have demonstrated associations between gender-affirming care and improved physical and mental, and new findings presented here demonstrate the economic societal benefit of providing care to patients.
Reference 1	US Trans Survey, 2015
Reference 2	Almazan et al., 2021
Reference 3	Padula et al., 2016

Category	Surgery, #91
Primary Author	Bryce B Patin, BS
Secondary Authors	Abdul Hafiz Al Tannir MD, Elise A. Biesboer MD, Morgan Tentis BS, Morgan Maring BS, Patrick B. Murphy MD, Daniel Holena MD, Colleen Trevino MD, Jacob Peschman MD, Christopher J. Tignanelli MD, David Milia MD, Marc A. de Moya MD, Rachel S. Morris MD
Title	VTE chemoprophylaxis within 24 hours of stable TBI: safe and effective
Introduction	Despite existing practice management guidelines recommending the initiation of venous thromboembolism (VTE) prophylaxis within 24-hours of stable head computed tomography (CT) in non-operative traumatic brain injury (TBI), delays in VTE prophylaxis occur out of concern for exacerbating intracranial hemorrhage. We hypothesized that early prophylaxis decreases VTE events with no increase in bleeding complications.
Methods	This is a single-center retrospective review of all TBI patients admitted to a Level 1 trauma center before (2015-2016, early) and after (2019-2020, contemporary) the expansion of the Trauma Program Performance Improvement (PI) team and creation of trauma process and outcome dashboards. Exclusion criteria included discharge or death within 48 hours of admission, expanding hematomas, and a craniotomy prior to chemoprophylaxis initiation.
Results	A total of 1,272 patients met the inclusion criteria, of which 54% (n=682) were admitted after PI expansion. Following the addition of a dedicated PI nurse within the trauma program and creation of process dashboards, the time from stable CT to VTE prophylaxis initiation was shorter (38 vs 56 hours; p <0.001) and more patients received chemoprophylaxis within 24 hours (30% vs 10%; p<0.001) of stable head CT (Figure 1). There was no significant difference in time from first head CT to stable CT (17 vs 18 hours; p=0.11). The contemporary group had a lower rate of VTE events (1% vs 4%; p-value<0.001) with no increase in bleeding events (3% vs 4%; p-value=0.25). On multivariable analysis, the early cohort was an independent predictor of VTE events (Odd's ratio: 3.74; 95%CI:1.45-9.69; p-value<0.001).
Conclusions	A collaborative multidisciplinary trauma PI team improves guideline compliance. Initiation of VTE chemoprophylaxis within 24-hours of stable head CT is safe and effective.
Acknowledgements	Research grant from Focused Ultrasound Foundation supported this work.
Ancillary Materials	VIEW MY POSTER

Category	Surgery, #92
Primary Author	Elise A Biesboer, MD
Secondary Authors	Courtney Pokrzywa, MD, Abdul Hafiz Al Tannir, MD, Juan Figueroa, MD, Rachel S Morris, MD, Thomas Carver, MD, Marc A de Moya, MD, Patrick B Murphy, MD
Title	An Estimated Blood Volume-Based Enoxaparin Dosing Protocol Improves Venous Thromboembolism Prophylaxis in Emergency General Surgery Patients
Introduction	Fixed-dose enoxaparin regimens do not provide adequate Xa inhibition in many surgical populations, and low Anti Factor Xa (AFXa) levels are associated with venous thromboembolism. We aimed to assess an individualized, estimated blood volume (EBV) based enoxaparin dosing protocol on AFXa levels in emergency general surgery (EGS) patients.
Methods	We performed a prospective observational trial of EGS patients admitted to an urban tertiary center. Adult patients without end-stage renal disease and who were otherwise eligible for VTE prophylaxis with enoxaparin were dosed with an EBV-based protocol (Fig 1A). The primary outcome was peak AFXa level obtained 2.5-6hrs at enoxaparin steady state. Accepted AFXa range was 0.2-0.4 IU/mL. Dose adjustment and AFXa re-evaluation was performed when appropriate. Secondary outcomes included bleeding and VTE events. The prospective cohort was compared to a historical cohort of EGS patients dosed with a fixed, BMI-based protocol.
Results	100 consecutive patients with properly timed, steady state AFXa levels were included in the study. The majority of patients were female (55%), the mean age was 57 years, and the most common admission diagnosis was small bowel obstruction (23%). A total of 62% of patients required an operation. Initial AFXa was in-range in 61% of patients on EBV dosing and was significantly more likely to be in-range compared to the historical BMI-based cohort (Fig 1B, 1C, p =.0002). There were four patients who required a blood transfusion. Two of those patients had AFXa levels above 0.4. There were no VTE events on index admission.
Conclusions	An EBV-based enoxaparin dosing protocol improves VTE prophylaxis in EGS patients by increasing rates of in-range initial Anti Factor Xa levels.
Ancillary Materials	VIEW MY POSTER

Category	Surgery, #93
Primary Author	Hope M Reecher, BSc
Secondary Authors	Jennifer L. Koop PhD, Ahmed Awad MD, Andrew Foy MD, Irene Kim MD, Bruce Kaufman MD, Sean Lew MD
Title	Awake Craniotomy for Supratentorial Tumors and Epileptogenic Lesions in the Pediatric Population: A Case Series
Introduction	Awake craniotomy with intraoperative functional mapping is the widely accepted procedure for adult patients (>21 years) undergoing supratentorial tumor or epilepsy lesion resection in areas near eloquent cortex, such as primary motor cortex or dominant hemisphere language regions. In children, awake craniotomies are notably less common due to concerns for compliance and potential emotional or psychological repercussions. Despite concerns, successfully tolerated awake craniotomies have been reported in patients as young as 8 years old, and success rates are comparable to those of adult patients. Aims: This report describes Children's Wisconsin's 17-year experience with pediatric awake craniotomy with insight regarding feasibility and surgical outcomes.
Methods	Retrospective chart review was completed for all pediatric (<21 years) patients at Children's Wisconsin for whom an awake craniotomy was attempted from January 2004 until March 2020. IRB approval was granted.
Results	Candidate patients had intact verbal ability, cognitive profile, and no considerable anxiety concerns during Neuropsychology assessment. 14 awake procedures were attempted in 13 patients. 13 procedures were completed (92.9%) with one procedure aborted due to intraoperative bleeding from the sagittal sinus prior to awakening. One patient had a repeat awake procedure approximately one year after. The average patient age was 15.9 years (range: 11.5 â€“ 19.3 years). Ten patients (76.9%) presented with seizure. Five (76.9%) patients were diagnosed with tumor and secondary epilepsy, four with tumor only, and four with epilepsy only. Beginning in 2010, all patients successfully underwent pre-operative fMRI. Eleven procedures (79%) were performed in the left hemisphere. Average total anesthesia time was 5 hours 41 minutes, total skin-to-skin time was 3 hours 50 minutes. All patients returned to or maintained baseline motor and speech functions by latest follow-up (range: 14 â€“ 130 months). Temporary deficits (resolved by discharge or 1-year follow-up) included transient speech errors, mild decline in working memory, mild decline in visuospatial reasoning, leg numbness, and expected hemiparesis. One patient had a permanent, anticipated quadrantanopia. Of the ten patients with pre-operative seizures, eight patients (80%) achieved seizure freedom (Engel Class 1) at 1-year follow-up, seven remained Class 1 at latest follow-up. Of the six patients with 1-year Karnofsky scores, five were scored 100 at 1-year and latest follow-up, the other was scored 90.
Conclusions	This study presents one of the largest case series of pediatric patients who underwent awake craniotomy for maximal safe resection of tumor or epileptogenic lesions. For candidate pediatric patients, the awake craniotomy technique is safe, feasible and effective in carefully-selected patients.
Reference 1	Alcaraz García-Tejedor G., Echániz G., Strantzas S., et al. Feasibility of awake craniotomy in the pediatric population. Pediatric Anesthesia. 30, 480-489 (2020). doi.org/10.1111/pan.13833
Reference 2	Riquin, E., Martin, P., Duverger, P. et al. A case of awake craniotomy surgery in an 8-year-old girl. Childs Nervous System 33, 1039–1042 (2017). doi.org/10.1007/s00381-017-3463-5
Reference 3	Szántó, D., Gál, J., Tankó, B. et al. Pediatric Neuroanesthesia — a Review of the Recent Literature. Current Anesthesiology Reports 12, 467–475 (2022). doi.org/10.1007/s40140-022-00540-2

Category	Surgery, #94
Primary Author	Jacob Lindemann
Secondary Authors	Benjamin Seadler MD, Ali Syed, Hossein Almassi MD, David Joyce MD/MBA, Stefano Schena MD/PhD, Mario Gasparri MD
Title	Robotic-Assisted Left Atrial Appendage Exclusion After Prior Sternotomy in Patients with Long-Standing Atrial Fibrillation
Introduction	Concomitant left atrial appendage (LAA) occlusion during cardiac surgery is proven to reduce risk of ischemic stroke or systemic embolism in atrial fibrillation (AF) patients. For patients without concomitant LAA management, surgical LAA exclusion is relatively contraindicated after prior sternotomy. However, for those who cannot tolerate oral anticoagulation (OAC) and are not candidates for a percutaneous LAA occlusive device (PLAAOD), the only option for LAA management remains high-risk surgery. We present a case series of robotic-assisted LAA exclusion in patients with prior sternotomy.
Methods	Included were all adult patients with persistent AF and history of prior median sternotomy. A robotic platform was utilized for external LAA clip application. Adequacy of exclusion was measured by intra-operative transesophageal echocardiography (TEE, <1 cm residual stump) and follow-up TEE or cardiac CT scan to measure residual patency at 3 months.
Results	Six male patients (mean age: 70.8 Â± 5.8 years), met inclusion criteria. Prior operations included valvular surgery, coronary artery bypass grafts, and ASD repair. Two patients had contraindications to OAC, two required a concomitant procedure (epicardial ablation and LV lead placement), one had anatomy unsuitable for PLAAOD, and one had concern for LAA thrombus which was not confirmed with intraoperative TEE. There were no conversions to thoracotomy or intraoperative complications. Five patients, 4 of whom already discontinued OAC, returned for LAA evaluation 3 months postoperatively, confirming exclusion in 4 (80%) cases. No stroke, systemic embolism or mortality were observed at 30 days.
Conclusions	LAA exclusion can be performed in selected patients with persistent AF and prior sternotomy. The robotic platform is less morbid than thoracotomy or redo sternotomy, and its enhanced visualization and dexterity increases the likelihood of a successful operation. Although previously considered a contraindication, robotic-assisted LAA exclusion after prior sternotomy can be performed with acceptable risk and better patient tolerance.
Ancillary Materials	VIEW MY POSTER

Category	Surgery, #95
Primary Author	Jacob M Welsch
Secondary Authors	Bryce B Patin, Christopher S Davis
Title	Evidence-Based Guidelines for the Management of Acute Cholecystitis
Introduction	Aim: This review aims to highlight the current evidence-based guidelines for acute cholecystitis. Background: Laparoscopic cholecystectomy is the procedure of choice for acute cholecystitis. The severity of cholecystitis and the patient's clinical status is heterogeneous. Many guidelines have been established to guide the preoperative and intraoperative management of acute cholecystitis. We provide an up-to-date appraisal of these guidelines and expert consensus recommendations. Clinical significance: The management of acute cholecystitis should never be viewed as routine, particularly regarding the heterogeneity of the patient's clinical status and severity of the disease process. Adherence to up-to-date, evidence-based, and expert consensus practice is critical to optimal outcomes for these patients.
Results	Many preoperative considerations exist, including patient health status/risk stratification, the severity of cholecystitis, choice of antibiotics, etiology of cholecystitis, considerations for gravid mothers, and utilization of cholecystostomy tubes. Intraoperative considerations are similarly paramount, including the surgical approach, adjuncts, and grading of the severity of cholecystitis once in the operating room.
Reference 1	Keywords: Acute cholecystitis, Cholecystectomy, Evidence-based management, Literature review
Ancillary Materials	VIEW MY POSTER WATCH MY PRESENTATION

Category	Surgery, #96
Primary Author	Jeffrey Ai
Secondary Authors	Sameer Shakir, Cleo Yi, Kristen Klement, Robert Havlik, Kant Lin
Title	A Comparative Assessment of Midterm Outcomes following Mandibular Distraction and Tongue-Lip Adhesion in the Treatment of Robin Sequence
Introduction	The purpose of this study was to assess early and midterm outcomes of tongue-lip adhesion (TLA) and mandibular distraction osteogenesis (MDO) to resolve obstructive sleep apnea and subsequent feeding difficulties in patients with Robin Sequence (RS).
Methods	A retrospective cohort study was performed of subjects presenting to a tertiary care pediatric center who underwent either primary MDO or TLA for the treatment of RS between 2004 and 2020. Exclusion criteria included subjects without preoperative and postoperative polysomnography (PSG). Study variables included apnea-hyponea indices (AHI), surgery-specific postoperative complications, feeding status, and dental relationships at last follow-up.
Results	In total, n=59 subjects met inclusion (n=34 MDO, n=25 TLA) with a median length of follow-up of 8.8 and 6.7 years (MDO v. TLA, $p<0.27$). There were no significant differences in preoperative patient characteristics including enteral access and respiratory status, other than age at surgery (MDO 31 days v. TLA 17 days, $p<0.05$). Preoperative AHI was similar between cohorts (33.9 and 46.7, $p<0.38$). Subjects undergoing MDO demonstrated improved AHI on initial postoperative PSG performed at 2 weeks (3.4 v. 11.6, $p<0.01$), however AHI at the second postoperative timepoint (270 v. 142 days, $p<0.007$) was no different between cohorts (2.8 v. 2.6, $p<0.89$). Using linear mixed modeling, MDO resulted in a statistically insignificant AHI improvement of 4.3 [-3.5, 12.1] ($p<0.24$). Postoperatively, 14.7% of subjects undergoing MDO required repeat distraction while 20% of subjects required TLA revision or conversion to MDO ($p<0.43$). In subjects undergoing MDO, 3% demonstrated decreased mouth opening and 14.7% demonstrated asymmetric marginal mandibular function. Preoperatively, 68% of subjects in each cohort required enteral nutrition, with only a minority of subjects requiring enteral nutrition at last follow-up (MDO 5.4% v. TLA 9.1%, $p<0.59$). No subjects required supplemental oxygen at last follow-up. Median overjet in the period of mixed dentition was 3 mm in both cohorts ($p<0.88$).
Conclusions	MDO and TLA ultimately achieve similar correction of OSA and associated feeding difficulties in patients with Robin Sequence. While MDO offers a more immediate airway improvement, the procedure carries a nonzero risk of neurosensory and temporomandibular joint dysfunction when compared to TLA.

Category	Surgery, #97
Primary Author	Jessica Ziccarello, BS
Secondary Authors	Melissa Drezdzon MD; Jed Calata MD
Title	Academic Inbreeding: Internal Hiring Bias Among Academic Surgical Faculty at Top Hospitals
Introduction	It is a widely held belief among medical students that matching to a top-ranked residency program can pave the way for future opportunities, especially if they hope to pursue a career in academia. However, little research has been done on the actual influence of residency or fellowship placement in the hiring practices of surgical faculty at academic hospitals. We aimed to identify how often academic faculty are employed at the same institution where they completed their training, and if this phenomenon is disproportionally practiced among top tier institutions.
Methods	The 2022 Newsweek World's Best Hospitals report[1] was used to identify the top twenty hospitals in the United States, and a database of surgical faculty employed at each hospital was created. A regionally matched database of surgical faculty was compiled in the same fashion using hospitals that fell between rankings #22 and #200. Physician's hospital profiles were used to identify the medical school, residency, and fellowship of each surgeon. Medical school rank was determined using the Best Medical Schools report from U.S. News & World Report [2] and residency rank was determined using Doximity Residency Navigator[3]. Additional information collected included if residency and/or fellowship were completed at the institution at which the surgeon was currently employed. A survey Wilcox test was performed on the Medical School and Residency Tier variables, and a survey chi-squared test was performed to compare the differences between groups.
Results	26% of surgical faculty at top hospitals attended residency at the same hospital at which they are employed, and 29% attended fellowship at the same hospital at which they are employed. This was significantly higher than the matched cohort ($p = 0.024$, $p = 0.026$). Surgeons had a lower odds of being employed at a top hospital if they attended a medical school or residency ranked below the Top 20, though this did not reach statistical significance for all tiers. Surgeons who attended residency at the hospital where they are currently employed had a higher odds of being employed by a top 20 hospital (OR 1.47). Similarly, surgeons who attended fellowship at the hospital where they are currently employed had a higher odds of being employed by a top 20 hospital (OR 1.47). On multivariate analysis, tier of residency attended and completing a fellowship at the same institution as current employment were both statistically significant ($p < 0.0001$, $p = 0.009$).
Conclusions	This study suggests that "academic inbreeding" occurs regularly when surgical faculty are hired at academic hospitals, and statistically more often at top-ranked institutions. The most predictive factors in attaining a faculty position at a top hospital in our analysis include matching to a top-tier residency program and attending a fellowship at that same institution.
Reference 1	World's Best Hospitals 2022 - United States. 2022; Available from: https://www.newsweek.com/worlds-best-hospitals-2022/united-states.
Reference 2	2023 Best Medical Schools (Research) - U.S. News Rankings. Best Grad Schools: U.S. News & World Report Rankings 2023; Available from: https://www.usnews.com/best-graduate-schools/top-medical-schools/research-rankings.
Reference 3	Doximity Residency Navigator - Your Specialty: Surgery. 2022; Available from: https://www.doximity.com/residency/programs?specialtyKey=070775e2-4244-4247-a93a-efd863eb83df-surgery&sortByKey=reputation&trainingEnvironmentKey=&intendedFellowshipKey=.
Ancillary Materials	VIEW MY POSTER

Category	Surgery, #98
Primary Author	Jessica Zhou, MS
Secondary Authors	Joseph Lankford, MD, Alejandro M Rivas, Jay I Sandlow MD
Title	HYDROCELE RISK WITH TUNICA VAGINALIS CLOSURE IN SCROTAL SURGERY
Introduction	Scrotal trauma, including scrotal surgery, is a known risk factor for development of hydrocele formation. It has been suggested that the risk of hydrocele formation can be mitigated by either excising or plicating the tunica vaginalis at the time of surgery to obviate any potential space for hydrocele formation. However, to the best of our knowledge the risk of hydrocele formation with tunica vaginalis re-approximation has not been formally evaluated. Our study aims to report on the rate of hydrocele formation after spermatocele treatment in cases with tunica vaginalis re-approximation to better understand this risk and further guide clinical practice.
Methods	All patients undergoing spermatocelectomy or epididymectomy by a single surgeon between December 2008 and December 2021 were reviewed. Procedures involving tunica vaginalis plication or excision were excluded from the study, while procedures with tunica vaginalis re-approximation were included. The rates of hydrocele formation and subsequent management were recorded.
Results	Tunica vaginalis was closed with running 3-0 chromic suture in 56/100 patients undergoing epididymal surgery. Indications for treatment included pain (52%), nuisance (39%), solid epididymal mass (5%), and post-vasectomy congestive epididymitis (4%). The overall hydrocele rate in this population was 3.6% (n=2), with one case resolving spontaneously at 10 months follow up and one case electing to undergo early hydrocele aspiration at 2 months with lasting resolution.
Conclusions	In appropriately selected patients, tunica vaginalis re-approximation following epididymal surgery demonstrated minimal risk for clinically significant hydrocele development.
Reference 1	Agrawal K. Cleft palate repair and variations. Indian J Plast Surg. 2009;42 Suppl(Suppl):S102-S109.

Category	Surgery, #99
Primary Author	Kaila Herold, MS
Secondary Authors	Timothy Stoddard, MD; Nelson-Rodriguez-Unda, MD; John LoGiudice, MD; Rana M Higgins, MD; Erin Doren, MD, MPH
Title	Robotic-assisted surgical repair of rectus diastasis and abdominal bulge following abdominal based breast reconstruction
Introduction	The DIEP flap is the gold standard in autologous breast reconstruction. Despite advances in perforator dissection, abdominal donor site morbidity still occurs. Traditional rectus diastasis (RD), bulge, and hernia repair with open techniques and onlay mesh have high complication rates. We present a case series of delayed robotic repair of symptomatic RD and bulge following abdominally based breast reconstruction.
Methods	A single-center, retrospective review was conducted of patients who underwent DIEP flap breast reconstruction and subsequent robotic-assisted repair of RD and bulge. Pre-operative demographics and post-operative clinical and patient-reported outcomes were reviewed. RD up to 5 cm and any ventral/umbilical hernias were repaired by a single general surgeon via plication with running suture and reinforcement with macroporous mesh.
Results	Ten patients with an average age of 49 years (range 41-63) and BMI of 31 kg/m2 (range 26-44) were included in the study. The average DIEP flap size was 664.95 g (range 315-1197), the average number of perforators harvested was 2.5 (range 1-4). RD and hernia sizes were 2.9 cm (1.5-4.2) and 5.8 cm2 (<1-15), respectively. One patient (10%) experienced post-operative surgical site complications including seroma and wound infection. Two patients (20%) reported a post-operative bulge but CT scan showed no evidence of hernia recurrence. Five patients completed a post-op survey which demonstrated that in general, oneâ€™s abdominal wall affects their health and mental well-being. At 30 days post-op, most patients felt that their abdominal wall does not interfere with activities of daily living.
Conclusions	In a small percentage of patients, abdominal free flap-based breast reconstruction is associated with symptomatic rectus diastasis and abdominal bulge. Minimally invasive robotic repair of rectus diastasis up to 5 cm can be performed with mesh reinforcement. This technique is effective with low complication rates and improvement in quality of life.

Category	Surgery, #100
Primary Author	Kayleigh Cook, BA
Secondary Authors	Andualem Beyene, MD, Zebenay Bitew Zeleke, MD, Ephrem Gebrehana, MD, Yoseph Tediso, Katie Iverson, MD
Title	Strengthening Surgical Systems in Ethiopia: An Assessment of Sustainability in Data Practices
Introduction	In December 2015, the Ethiopian Federal Ministry of Health (FMOH) developed the Saving Lives through Safe Surgery (SaLTS) initiative to improve the quality of and access to surgical care across the country. This project aims to support the objectives of the eighth strategic pillar of SaLTS, “Excellence in Monitoring and Evaluation” by evaluating current surgical data collection practices. Previous work led to the development and implementation of standardized data practices including the monthly analysis of 15 key performance indicators (KPIs) related to surgery. By studying how these indicators are currently collected and reported, data quality and accuracy can be improved and contribute to a better understanding of surgical capabilities throughout the country. Specific Aims: (I) Evaluate the consistency and validity of current surgical indicator collection and reporting practices at the hospital level. (II) Determine facilitators and barriers to accurate surgical data acquisition in these facilities by assessing the flow of surgical data collection and recording.
Methods	Document and observe the data collection process at 10 hospitals across 2 different regions in Ethiopia starting from the initial data recording in registries, to indicator reports, to the regional and national online data collection system (DHIS2). (II) Determine method of collection, documents used, and effectiveness. (III) Collect data for each KPI of focus [1. Surgical Volume, 2. Perioperative Mortality Rate (POMR), 3. Adverse Anesthetic Outcome (AAO), 4. Surgical Site Infection (SSI), and 5. Safe Surgery Checklist (SSC) Utilization] at each “checkpoint” for the previous 6 months (Jan. 2022 to June 2022) and verify for consistency and completeness.
Results	In general, data collection flow involved the following: hospital staff recording data elements in registries, quality officers completing monthly KPI reporting forms and calculating KPIs, and submitting the DHIS2 monthly report to RHBs. For all hospitals, average monthly surgical volume was 47 and SSC utilization was 93%. Total POMR was 0.38% (13/3399), SSI was 0.79% (27/3399), and AAO was 0.15% (5/3399). Verifications revealed inconsistencies at all hospitals, commonly surgical volume (10/10), SSI (6/10), and SSC (3/10). Five hospitals demonstrated incomplete registry data, commonly AAO, SSC, and SSI. All hospitals had complete electronic data, except one hospital missing POMR, AAO, and SSI. Inconsistent KPI reporting forms across different hospitals contributed significantly to the findings.
Conclusions	Marked strengths at individual institutions included continued use of registries from previous data interventions, and use of a separate logbook to document key KPIs. Common barriers to quality data collection include inconsistent recording practices, failure of event capture due to reporting period, inadequate data elements in registries, and lack of standardized monthly KPI reporting forms. Creating better mechanisms for quality surgical data capture will aid in the next phase of Ethiopia’ s surgical system development.
Acknowledgements	This project was accomplished thanks to Dr. Elaine Kohler Summer Academy of Global Health Research and the Medical College of Wisconsin Department of Surgery.
Reference 1	Bari, S., Incorvia, J., Iverson, K.R., et al (2020). Surgical data strengthening in Ethiopia: results of a Kirkpatrick framework evaluation of a data quality intervention. Global Health Action, 14(1), p.1855808.
Reference 2	Blair, K.J., Paladino, L., Shaw, P.L., Shapiro, M.B., Nwomeh, B.C. and Swaroop, M. (2017). Surgical and trauma care in low- and middle-income countries: a review of capacity assessments. Journal of Surgical Research, 210, pp.139â€“151.
Reference 3	Iverson, K.R., Ahearn, O., Citron, I., et al (2020). Development of a surgical assessment tool for national policy monitoring & evaluation in Ethiopia: A quality improvement study. International Journal of Surgery, 80, pp.231â€“240.
Ancillary Materials	VIEW MY POSTER

Category	Surgery, #101
Primary Author	Maddie Rundell, BS
Secondary Authors	Rachel Bailey, BS, Amy Wagner, MD
Title	Enrollment Challenges in a Multi-center Clinical Trial of a Rare Disease: As seen in the Gastroschisis Outcomes of Delivery (GOOD) study
Introduction	The Gastroschisis Outcomes of Delivery (GOOD) Study is a national, multi-site, randomized controlled trial designed to evaluate delivery timing of infants diagnosed with gastroschisis and provide evidence of optimal delivery timing. The recruitment goal for the study is 800 mother-fetus pairs by 2026. The trial has two intervention arms, a 35-week delivery group and an expectant management group with a goal of 38 weeks. Our hypothesis is that delivery at 35 0/7 - 35 6/7 weeks gestation in stable mothers and fetuses with gastroschisis will be superior to expectant management of the pregnancy with a goal of 38 0/7 - 38 6/7 weeks gestation. The primary aim of the study is to compare risk of mortality and major morbidity for infants with gastroschisis between the early and late delivery arms. Throughout the life of the trial the main challenge experienced has been enrollment. This can be broken into two categories: enrollment of centers and enrollment of patients. In the first category, enrollment of centers, we have identified four unique difficulties experienced through the study. (1) this study spans three different disciplines (Pediatric Surgery, Maternal Fetal Medicine, and Neonatology), all of whom need to be on board to participate, (2) visibility of the study doesn't permeate all centers across the nation, leaving researchers unaware of the opportunity, (3) researchers frequently experience staffing shortages and turnover making it hard to join new trials, and (4) communication between the Data Coordinating Center and participating centers can be inconsistent. In the second category, enrollment of patients, we have identified four unique difficulties experienced throughout the study. (1) there is a lack of eligible gastroschisis patients due to a decrease in case numbers across the nation and institutional referral patterns, (2) keeping centers engaged in research activities has been challenging considering many are managing large portfolios of studies, (3) the anticipated exclusion rate based on criteria designed for patient safety was significantly underestimated, and (4) there is no discernable pattern or predictability as to who will or will not enroll in the trial. The GOOD Study DCC Staff has developed an infrastructure, put in place processes, and continued to adapt procedures to the shifting landscape of the study.
Ancillary Materials	

Category	Surgery, #102
Primary Author	Mark Ehioghae
Secondary Authors	Mark C. Lawlor, Addisu Mesfin
Title	Decompression of Pseudogout Attacks through Cervical Laminectomy
Introduction	Calcium pyrophosphate dihydrate (CPPD) deposition, also known as pseudogout, in the cervical ligamentum flavum (CLF), is a rare disease which can cause spinal cord signaling changes leading to rapid deterioration in function. The natural history of cervical myelopathy as a result of CPPD deposition within the CLF is not well understood. Our objective is to describe the presentation, imaging findings, and treatment options of CPPD deposition or pseudogout of the cervical spine.
Methods	Using PubMed, we analyzed studies published from 1978 to 2022. Key words used were “pseudogout,” “CPPD deposit disease,” “cervical yellow ligament,” “CLF,” and “cervical spine.” We excluded “crowned dense syndrome” and “ossification of ligament flavum.” Using a department database, we queried for patients treated for CPPD of the cervical spine.
Results	Twenty clinical studies on CPPD of the cervical spine with 69 patients aged between 15 and 92 years (mean = 72) were identified. Neck pain and numbness of the hands were the most common symptoms. Diabetes mellitus and hypertension were the most common comorbidities. Males and females were affected at equal rates. C4-C5 and C5-C6 were the most affected segments. Earlier surgical treatment produced better outcomes. A laminectomy and fusion or laminoplasty were the most common procedures performed with most patients experiencing some return of neurologic function.
Conclusions	Although rare, CPPD deposit disease in the CLF should be readily considered as a differential diagnosis due to the continuously aging population. CPPD’s progressively worsening nature makes an early diagnosis and treatment important in improving the patient’s overall quality of life.
Ancillary Materials	VIEW MY POSTER

Category	Surgery, #103
Primary Author	Melissa K Drezdzon, MD
Secondary Authors	Sherman, K; Calata, J; Peterson, C; Ludwig, K; Ridolfi, T
Title	Association between BMI and Early-Onset Colorectal Cancer
Introduction	Since 1990, the rates of colorectal cancer (CRC) diagnosis and death have been in decline. However, the incidence of Early-Onset Colorectal Cancer (EOCRC) in adults, ages 18-49 is rising, and rates of diagnosis almost tripled in this population between 2001 and 2017. Retrospective studies have demonstrated a linear association between obesity and colorectal cancer diagnosis, with greatest increase in CRC diagnoses in obese patients aged 18-49. Our study seeks to determine the association between BMI and EOCRC in the Veteran population.
Methods	In this retrospective study, patients diagnosed with EOCRC between January 2001 and March 2020were identified in the VHA Corporate Data Warehouse (CDW). They were each age- and sex-matched to four controls. Demographic variables, BMI, history of diabetes, smoking, and family history of CRC were collected over the 10 years prior to EOCRC diagnosis. Univariable analyses were performed using Chi-Square/Fisher's Exact Test and one-way ANOVA. Stepwise logistic regression models were formed with race, DM, and BMI eligible for inclusion, and stratified by age- and sex-matched clusters. Analyses were performed among subjects with data available at 1, 2, 5, 7, and 10 years (Â± 6 months) prior to EOCRC diagnosis.
Results	A total of 5,560 EOCRC patients were identified (1,497 or 27% had rectal cancer; there were 20,485 controls). EOCRC was associated with a BMI of ≥30 at one and two years prior to diagnosis (OR 1.16 and 1.30, respectively). Colon cancer, when evaluated alone, was associated with a BMI of ≥30 at 1, 2, 5, and 7 years prior to diagnosis (OR 1.29, 1.49, 1.31, and 1.48 respectively). Rectal cancer alone was not related to BMI ≥30. A comorbid diagnosis of diabetes was found to decrease the likelihood of early-onset colon and rectal cancer (OR 0.66 and 0.47, respectively). Additionally, diabetes was found to have a protective effect against early onset colon and rectal cancer.
Conclusions	BMI ≥30 was associated with an increased risk of early-onset colon cancer, but not early-onset rectal cancer. Additionally, diabetes had a protective effect against EOCRC, however, further investigation is warranted to determine possible confounding elements.
Acknowledgments	This project was accomplished thanks to Dr. Elaine Kohler Summer Academy of Global Health Research and the Medical College of Wisconsin Department of Surgery.
Reference 1	Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer Statistics, 2021. CA: A Cancer Journal for Clinicians. 2021;71(1):7-33. doi:https://doi.org/10.3322/caac.21654
Reference 2	mans-Kropp HA, Umar A. Increasing Incidence of Colorectal Cancer in Young Adults. Journal of cancer epidemiology. 2019;2019:9841295. doi:10.1155/2019/9841295
Reference 3	Liu PH, Wu K, Ng K, et al. Association of Obesity With Risk of Early-Onset Colorectal Cancer Among Women. JAMA Oncology. 2019;5(1):37-44. doi:10.1001/jamaoncol.2018.4280
Ancillary Materials	VIEW MY POSTER

Category	Surgery, #104
Primary Author	Micah Rubin BA
Secondary Authors	Nalani Wakinekona BA, Bethany Canales MPH, Neel Mansukhani MD
Title	Examining Sex Bias in Vascular Surgery Research
Introduction	It is unknown if sex bias exists in vascular surgery research. Sex bias is defined as unequal inclusion and analysis of male and female subjects in clinical research. Indications for surgery, postoperative outcomes, complication rates, and readmission rates for vascular illness differ in men and women9,10. Due to these sex differences, it is critical that vascular surgery research equitably include women and analyze sex as an independent variable. Our aims are to determine if sex bias exists in human vascular surgical clinical research, to determine if data are reported and analyzed using sex as an independent variable, and to identify the vascular diseases investigated (e.g. aortic, cerebrovascular, peripheral vascular, venous, dialysis access etc.) in which the greatest and least sex bias exist.
Methods	All original manuscripts published in the European Journal of Vascular and Endovascular Surgery (IF = 5.328), Journal of Vascular Surgery (IF = 3.405), JVS: Venous and Lymphatic Disorders (IF=3.137), Journal of Endovascular Therapy (IF = 3.102), Annals of Vascular Surgery (IF=1.1250) from January 1, 2018 to December 31, 2020 were reviewed for inclusion by two abstractors.
Results	A total of 2936 articles were reviewed across the 5 journals published in a 3-year window. 2710 articles were reviewed that included human participants. Of those, we included the 2558 articles that stated the sex of their participants, while not reporting on a sex-specific disease, in our final analysis. Overall, 22.6% of articles included a discussion of sex, 38.4% analyzed sex, 22.2% included sex in multivariable analysis, and only 4.1% included sex as an independent variable (Table 2). 82% of articles had more men than women. When analyzing these 4 sex variables, there are no statistical differences between the year (P 0.08 – 0.37) (Table 3). The Journal of Vascular Surgery is significantly the highest scoring journal sex analysis and multivariable analysis (P <.001 for both) (Table 3). Furthermore, The Journal of Vascular Surgery: Venous and Lymphatics is the highest scoring journal for the remaining 2 variables: sex discussed and independent analysis of sex with 30% and 7% respectively (P<.001 & <.003)(Table 3). Multicenter studies significantly had higher rates of independent analysis of sex over single center studies 6.3% vs 2.9% (P<.001)(Table 3). There was no statistical difference in independent analysis of sex between domestic and international studies. However, domestic studies were significantly higher in the remaining 3 sex variables over international studies.
Conclusions	Marked strengths at individual institutions included continued use of registries from previous data interventions, and use of a separate logbook to document key KPIs. Common barriers to quality data collection include inconsistent recording practices, failure of event capture due to reporting period, inadequate data elements in registries, and lack of standardized monthly KPI reporting forms. Creating better mechanisms for quality surgical data capture will aid in the next phase of Ethiopia’ s surgical system development.
Ancillary Materials	

Category	Surgery, #105
Primary Author	Monet Woolfolk
Secondary Authors	Elise A. Biesboer, MD, Amber Brandolino, MS, Carissa W. Tomas, PhD, Terri A. deRoon-Cassini, PhD, Mary E. Schroeder, MD, Marc A. de Moya, MD, Colleen M. Trevino, PhD
Title	Early Post-Discharge Self-Reported Mental and Physical Health Outcomes in Gunshot Wound Survivors
Introduction	Survivors of traumatic injury are susceptible to adverse mental health outcomes, which are associated with worse functional outcomes. Up to 20-40% of survivors of any traumatic injury go on to develop PTSD or depression post-injury. Gunshot wound (GSW) survivors in particular may have a higher risk for increased pain, posttraumatic stress disorder (PTSD), and depression post-injury. We hypothesized that on mental and physical health assessment, GSW survivors would have high rates of PTSD and depression symptoms, continued pain, and decreased physical function at their first follow up visit after hospital discharge.
Methods	GSW survivors seen in outpatient follow up approximately 1-2 weeks after discharge were invited to participate in a questionnaire assessing both mental and physical health outcomes. The questionnaire included the Brief Pain Inventory (BPI), the Injured Trauma Survivor Screen (ITSS), the PTSD Checklist for DSM-5 (PCL-5), and the SF-12 Mental and Physical Health components.
Results	A total of 306 patients were seen in clinic, and 193 responded to the survey. The mean age was 34 years (SD=13.3), 80.8% were male, and 78.8 % were Black/African American. The average pain severity score on the BPI was 5.76 (SD 2.58), indicating moderate pain. GSW survivors scored > 2 SD below the US national average on the SF-12 for physical quality of life (M=29.1). Using the ITSS screen, 72% of patients screened risk positive for PTSD, and 45% screened risk positive for depression. Similarly, when assessing PTSD symptoms with the PCL-5, the average score was 42.0 (SD=12.7) indicating considerable symptom burden.
Conclusions	At 1-2 weeks post-discharge, over 2/3 of GSW survivors were at risk for development of PTSD, approximately half were at risk of depression, and physical function was greatly decreased compared to the US national average.

Category	Surgery, #106
Primary Author	Monica Seadler, MD
Secondary Authors	Seadler, Monica MD; Zhang, Youjie ME; Ferraresso, Francesca BS; Robertson, Madelaine BS; Cau, Massimo, BSc; Badior, Katherine PhD; Ketelboeter, Laura PhD; de Moya, Marc MD; Dyer, Mitch MD; Kastrup, Christian PhD
Title	FEASIBILITY OF siRNA BASED APPROACHES FOR KNOCKING DOWN BLOOD PROTEINS IN SWINE
Introduction	Genetic knockout is used extensively in animals models for research, but do not exist for the large animals models used in trauma research. For example, there is no approach available to remove fibrinogen, a key protein in the regulation of hemostasis and thrombosis. Fibrinogen has successfully been knocked down in mice via siRNA encapsulated in lipid nanoparticles (LNP), however pigs are susceptible to infusion related reactions and completement activation-related pseudoallergy (CARPA) when given nanoparticles. We hypothesize that the creation of porcine knockout models is feasible using siRNA encapsulated in state-of-the-art LNP developed for the mRNA-based COVID vaccines
Methods	Knockdown in pig hepatocytes was tested in vitro utilizing 5 siRNA sequences. In vivo safety testing was completed in 6 pigs. Baseline blood samples were collected prior to infusion of LNP containing siRNA (n=4) or saline control (n=2) and then collected again after one week. These samples were analyzed for evidence of organ dysfunction and complement activation. Clinical chemistry analysis included complete blood counts, complete metabolic panels, coagulation studies, and creatinine kinase. Immunoblots were used to assess for complement activation.
Results	We identified one siRNA sequence that knocked down fibrinogen to 20% of normal. Pigs remained hemodynamically normal without physiologic evidence of infusion related reactions. No evidence of significant end organ damage or dysfunction was found in laboratory analysis. No significant complement activation was found by immunoblot.
Conclusions	Administration of siRNA via optimized LNP was safe in porcine models without adverse events. Advancing these studies will enable both improved animal models of trauma and potentially the development of RNA-based therapies against unwanted thrombosis following injury.

Category	Surgery, #107
Primary Author	Morgan Maring
Secondary Authors	Abdul Hafiz Al Tannir MD1, Elise A. Biesboer MD1, Patrick B. Murphy MD MSc FACS1, Lucian A. Durham MD PhD2, Adam Ubert MD FACS2, Marc A. de Moya MD FACS1, Nicholas E. Ingraham MD3, Jeffrey Chipman MD FACS4, Anthony Charles MD FACS5, Rachel S. Morris MD FACS1
Title	ECMO for COVID-19 related Acute Hypoxic Respiratory Failure: The Association between Age and Mortality Outcome
Introduction	Throughout the COVID-19 pandemic, extracorporeal membrane oxygenation (ECMO) has been proposed as a supportive adjunct to COVID-19-associated refractory acute respiratory distress syndrome (ARDS). However, ECMO is associated with high morbidity and mortality rates. This study aims to determine an age threshold associated with higher mortality rates.
Methods	This is a single-center retrospective study of all patients requiring ECMO for COVID-19-associated ARDS from January 1st, 2020, to June 30th, 2022. Electronic medical records were used to retrieve demographics, comorbidities, ventilator settings, ECMO settings, complications, and mortality. Overall missing data-points were low (<5%). Several thresholds of age were chosen: ≤30, ≤40, ≤50, ≤60, and ≤70 years. The relationships between each threshold of age and mortality were explored. The estimation of the receiver operating curve was conducted to predict mortality based on age category.
Results	A total of 99 patients were included in the analysis. The majority were males (65%), and the mean age was 50 years. An overall mortality rate of 44% was observed. Higher age and lower pre-cannulation PaO2 were associated with a higher mortality rate (Table1). On discrimination analysis, the area under the receiver operating characteristic curve (AuROC) was 0.69. The sum of sensitivity and specificity was maximized at the age of 48 years (Figure 1). On curve estimation, the mortality rate increased when age was greater than 50 years old.
Conclusions	COVID-19 ECMO patients have a significantly higher mortality inflection point of 50 years of age.
Ancillary Materials	VIEW MY POSTER

Category	Surgery, #108
Primary Author	Morgan Tentis
Secondary Authors	Abdul Hafiz Al Tannir MD, Elise A. Biesboer MD, Bryce B. Patin, Morgan Maring, Patrick B. Murphy MD, Rachel S. Morris, Jacob Peschman MD, Mary Schroeder MD, Lewis Somberg MD, Thomas W. Carver MD, Marc A. de Moya MD
Title	Implementation of the 300cc-rule Safely Decreases Chest Tube Placement in Traumatic Hemothorax
Introduction	Traumatic hemothorax (HTX) is effectively managed with a tube thoracostomy (TT); however, TT may carry a high complication rate. In 2017, a guideline was implemented at a Level I trauma center to observe any traumatic HTX â‰¤300cc in hemodynamically normal patients. We hypothesized that this guideline would decrease TT placement with no increase in failure rates.
Methods	This is a single-center retrospective review of all adult patients admitted with a HTX on computed tomography (CT) before (2015-2016) and after (2018-2019) the guideline implementation. Exclusion criteria were TT placement prior to CT scan, absence of CT scan, death within 5 days of admission, and a concurrent pneumothorax >20mm. HTX volume was calculated using Mergo's formula: V=d2xL (V: volume; d: depth; L: length). The primary outcomes included observation rates, TT placement, and observation failure, defined as the need for TT, video-assisted thoracoscopic surgery, or thoracotomy â‰¥24 hours after admission.
Results	A total of 391 patients met the inclusion criteria, of which 59% (n=230) were admitted after guideline implementation. There were no significant differences in demographics, comorbidities, or injury characteristics across both cohorts. After guideline implementation, there was a significant increase in observation rate (71% vs 52%; p-value<0.001) and a decrease in TT placement (42% vs 61%; p-value<0.001). A higher percentage of patients with a HTX â‰¤300cc (80% vs 60%; p-value<0.001) were observed. On multivariate analysis, the post-implementation cohort were more than twice as likely to be observed (AOR: 2.39; 95%CI: 1.56-3.62; p-value<0.001). There were no significant differences in observation failure (18% vs 24%; p-value=0.34), pulmonary complications (20% vs 25%; p-value=0.34), 30-day readmission (7% vs 6%; p-value=0.22), or 30-day mortality (3% vs 5%; p-value=0.22) rates. The post-implementation group had a shorter hospital (10 vs 13 days; p-value=0.04) and intensive care unit (4 vs 6 days; p-value=0.04) length of stay (LOS).
Conclusions	The implementation of the 300cc guideline led to a decrease in TT placement correlating with a decreased LOS with no increase in failure or complication rates.
Ancillary Materials	VIEW MY POSTER

Category	Surgery, #109
Primary Author	Nalani A. Wakinekona, BA
Secondary Authors	Micah J. Rubin BA, Neel A. Mansukhani MD
Title	Reporting and Analysis of Race in Vascular Surgery Research
Introduction	Non-White patients experience disproportionately higher morbidity and mortality associated with common vascular pathologies. Despite these known disparities, the inclusion of non-White races varies greatly within vascular surgery research, and the frequency and quality of race-based reporting and analysis is not well characterized. We aimed to describe the frequency and quality of race-based inclusion, analysis, and reporting in vascular surgery original research.
Methods	Bibliographic review of all original manuscripts published in European Journal of Vascular and Endovascular Surgery, Journal of Vascular Surgery, Journal of Vascular Surgery: Venous and Lymphatic Disorders, Journal of Endovascular Therapy, and Annals of Vascular Surgery from January 1, 2018 to December 21, 2020. Letters to the Editors, review articles, editorials, historic manuscripts, and manuscripts with unspecified number of participants were excluded. Data abstracted included inclusion of race-reporting and inclusion of race-based analyses (ie, race included in any analysis, race included in multivariate analysis, results reported separately by race, and racial differences included in discussion section).
Results	Of the 2936 articles reviewed, 2723 (92.7%) included human participants. After excluding 219 articles due to exclusion criteria, 2717 articles remained: 622 (22.8%) reported the race of participants and 2101 (77.1%) did not. US-based articles were more likely to include race in any statistical analysis compared to non-US-based articles (51% vs 18%, P <0.001). Of the 622 articles that reported race, 298 (48%) included race in any statistical analysis, 212 (34%) included race in a multivariable analysis, 34 (6%) reported results separately by race and 150 (24%) discussed the racial differences in the discussion section. During analysis of the different disease processes and anatomic locations studied, there was wide variation in race-based analysis and discussion. Articles investigating arterial occlusive and thoracoabdominal aorta pathologies performed the highest overall at including race in any analysis, reporting the data separately by race, including race in a multivariate analysis, and discussing racial differences (54%, 41%, 5%, and 26%; 57%, 36%, 7%, and 36%, respectively). Articles investigating strokes/transient ischemic attacks (TIA) and mesenteric/renal arterial pathologies comprised over 5 articles per topic and performed the lowest overall in any analysis, reporting the data separately by race, including race in a multivariate analysis, and discussing racial differences (20%, 20%, 0%, and 0%; 11%, 11%, 0%, and 0%, respectively).
Conclusions	The rate of race-based inclusion and reporting in vascular surgery literature is low with less than one-third of articles evaluated reporting race. Among articles that do report race, race-based analysis is low and variable. Race-based inclusion, reporting, and analysis is imperative to improve the generalizability of clinical research and develop evidence-based guidelines.
Reference 1	Deery SE, O'Donnell TFX, Shean KE, et al. Racial disparities in outcomes after intact abdominal aortic aneurysm repair. J Vasc Surg. 2018;67(4):1059-1067. doi:10.1016/j.jvs.2017.07.138
Reference 2	Oddone EZ, Horner RD, Sloane R, et al. Race, Presenting Signs and Symptoms, Use of Carotid Artery Imaging, and Appropriateness of Carotid Endarterectomy. Stroke. Published online July 1999. doi:10.1161/01.STR.30.7.1350
Reference 3	Jaramillo EA, Smith EJT, Matthay ZA, et al. Racial and ethnic disparities in major adverse limb events persist for chronic limb threatening ischemia despite presenting limb threat severity after peripheral vascular intervention. J Vasc Surg. Published online November 2, 2022. doi:10.1016/j.jvs.2022.10.043

Category	Surgery, #110
Primary Author	Tariq Saleh
Secondary Authors	Jordanne Ford, Tammy Kindel, Rana Higgins, Kathleen Lak, Jon Gould, Wen Hui Tan
Title	Inpatient Opioid Utilization and Pain Control Following Robotic versus Laparoscopic Sleeve Gastrectomy
Introduction	Over the last decade, the proportion of bariatric surgery that is performed robotically has been rising. However, the clinical benefits of the robotic approach over traditional laparoscopy are uncertain. One area in need of further investigation is pain control following robotic versus laparoscopic bariatric surgery. We evaluated inpatient opioid utilization and pain control following robotic versus laparoscopic sleeve gastrectomy.
Methods	A retrospective cohort study was conducted of bariatric surgery patients undergoing laparoscopic or robotic sleeve gastrectomy at a single academic institution from October 2019 to August 2022, following the implementation of a standardized postoperative opioid-sparing pain management protocol. Inpatient opioid utilization was measured in morphine milliequivalents (MME). Pain scores were collected by nursing staff.
Results	A total of 368 patients were included: 286 laparoscopic and 82 robotic surgery patients. Patients in both groups shared similar demographic characteristics. For the entire study cohort, mean age was 42 years, BMI 50 kg/m2, 79% were female, and 11% were taking opioids preoperatively. Mean operative time was significantly lower for the laparoscopic group [87.5Â±47.3 min vs 109.3Â±30.3 min (p<0.01)]. The total inpatient MME utilized was similar for both groups: 56.4Â±32.9 for the laparoscopic group vs 53.2Â±39.7 for robotic (p=0.13). Mean postoperative pain scores (scale out of 10) were not statistically significantly different between groups: 5.2Â±1.7 (postoperative day 0) and 4.5Â±1.7 (day 1) for laparoscopic patients vs 5.1Â±2.0 (day 0) and 4.4Â±1.8 (day 1) for robotic. Though there was no difference in inpatient opioid utilization or postoperative inpatient pain scores, the proportion of patients prescribed opioids at discharge was significantly higher for the laparoscopic group [75.2% vs 62.2% (p=0.02)]. Other clinical outcomes including length of stay, 30-day readmissions, and visits to the emergency department were not statistically significantly different between groups.
Conclusions	There is no difference in inpatient opioid utilization or pain scores between patients undergoing laparoscopic and robotic sleeve gastrectomy.

Category	Technology, Imaging & Engineering, #111
Primary Author	Abhishek Janardan
Secondary Authors	Alexandra Polovneff, BS; Neemit Shah, BA; Maie Zagloul, BS; Bradley Crotty, MD, MPH
Title	Human Efficiency of a Post Discharge Digital Engagement Program
Introduction	Patient check-ins outside the hospital following hospital discharge offer tremendous opportunities for health outcome improvement. Telephonic check-ins remain the predominant form of post-discharge check-in yet are labor intensive. Digital applications for remote patient monitoring are gaining popularity and offer patients increased autonomy in out-of-hospital symptom management and communication with the care team. Here, we implemented a post-discharge digital engagement (PDDE) platform alongside traditional telephonic-based outreach for discharged patients to increase accessibility and scale care efforts. We hypothesize that the addition of the PDDE platform could improve the human efficiency of post-discharge care.
Methods	A pragmatic, stepped-wedge cluster randomization trial with five implementation waves based on primary care clinic region was performed. All inpatient hospital discharges between March 2020 - November 2020 were stratified by readmission risk (low, medium, high). Inclusionary criteria required a patient to be admitted to an inpatient unit, have a primary care provider within the Froedtert Health System, and have an insurance payor that is a part of the risk-based payment program within the Froedtert system. Exclusionary criteria included patients with a discharge diagnosis of Covid-19, heart failure, and patients who were admitted for observation, not treatment. Low-risk patients were solely offered access to the PDDE platform, while moderate-risk and high-risk patients were offered access to the PDDE platform and care coordination. Patient outreach encounters were compared. Patient outreach encounters (POE) are defined as the number of outreach encounters attempted between a care-coordination staff member and a patient during the post-discharge period. Primary care clinic regions were randomized to one of five implementation waves. An "intention to treat" primary analysis was conducted at the hospitalization level.
Results	We evaluated 5,490 patient discharges (2,735 control; 2,755 intervention) 1949 patients were classified as high-risk, 2,032 medium-risk, and 1,509 low-risk. A statistically significant increase in POE counts was seen in the PDDE-eligible cohort and medium-risk patient populations that were eligible for PDDE. ($p < 0.001$, $p < 0.001$). Further, sub-analysis via activation of the PDDE displayed statistically significant increases in POE counts for medium and high-risk patients who activated the PDDE app vs. those that did not ($p < 0.001$, $p = 0.023$).
Conclusions	Our findings indicate that utilization of a post-discharge digital engagement application in concert with standard telephonic care outreach can increase patient contact with the medical system. This can be leveraged to further refine care coordination outside the hospital setting and provide patients with additional personalized care. Further analysis needs to be done regarding the meaningfulness of these increased patient interactions alongside its impact on the organizational workflow of healthcare professionals that engage in telephonic outreach and PDDE communication with patients.
Ancillary Materials	VIEW MY POSTER

Category	Technology, Imaging & Engineering, #112
Primary Author	Angela Mathison
Secondary Authors	Jaime Wendt Andrae, Michael Tschannen, Michael Zimmermann, Victor Jin, Raul Urrutia
Title	The Spatial Biology Revolution: Revealing new Layers of Transcriptional Changes in Tissues
Introduction	Spatial biology is the study of transcripts and molecules in a two-dimensional context that overlays with the pathophysiological structures of the tissue. Using spatial biology techniques, researchers can now visualize molecules in their unique contexts to include regions of the tissue and associated cell-cell interactions. Spatial transcriptomics, a sub-category of spatial biology, is a molecular profiling method that measures gene expression in tissue samples and maps where that activity is located. Thus, this technology allows for a greater understanding of the relationship between gene expression, normal tissue development, and disease pathology. To facilitate spatial biology at MCW, the Mellowes Center (MC) has implemented the 10x Genomics Visium protocol with the CytAssist platform. To complete a Spatial Transcriptomics project, samples proceed through the following methods, 1- unstained tissues are hybridized with probes for mRNA detection, 2- using the CytAssist, probes are transferred to the barcoded grid of a Visium slide, 3- libraries are prepared and sequenced, and 4- identity and level of transcripts are mapped back to the tissue location and image. Furthermore, iterative evaluation of transcriptional changes that associate with tissue structures can be completed among samples with different experimental states (for example: considering how cellular infiltration changes in a tumor with a gene knockout). The MC has bioinformatic support available to analyze, develop new strategies to interpret, and integrate the spatial transcriptomic data with phenotypic and translational data sources. Ultimately, the Visium spatial biology workflow maps the whole transcriptome with morphological context of FFPE or fresh frozen tissues in order to discover novel insights into normal tissue development, disease pathology, and much more for clinical translational research. The MC's vision is to establish and develop this type of cutting-edge technology to help MCW investigators advance the mechanistic understanding of disease etiology, pathophysiology, and potential therapeutics with the goal of increasing the knowledge base in translational, personalized medicine research. To learn more about how the Mellowes Center spatial biology platform can support your research and to schedule a consultation, please contact us.

Category	Technology, Imaging & Engineering, #113
Primary Author	Dayeong An
Secondary Authors	El-Sayed Ibrahim
Title	Myocardial displacement fields generation from cine MR images by deep learning network
Introduction	Cardiac MRI cine and tagging sequences are commonly used for evaluating global and regional cardiac functions, respectively. However, the requirement of acquiring additional tagged images and the need for specific software for analyzing these images make the MRI exam longer and more expensive. To address this issue, the cardiac MR feature tracking technique was developed to calculate regional cardiac function from cine images. This method, however, has limitations due to the lack of intramyocardial markers compared to conventional tagging method. In this study, we have developed a deep neural network algorithm that can extract regional cardiac function parameters from cine images after being trained on corresponding tagged images.
Methods	Our developed algorithm is based on image-to-image translation using a generative adversarial network (GAN) and is used to generate myocardial displacement fields from cine images. For the training phase, the inputs to the network are cine difference images, generated by subtracting consecutive cine images using a fine-tuned segmentation Unet network, and corresponding tagged images of the same slice and cardiac phase. The target image of the network is the gold-standard myocardial displacement field, which is generated by analyzing the tagged image using the SinMod method. This study used a dataset of 1134 images obtained from rats scanned on a 9.4T Bruker MRI scanner, with 1114 images used for training and 20 images used for testing. To compare the generated displacement fields with the gold-standard measurements, Bland-Altman plots, Student's t-test, and correlation analysis were conducted on a segmental basis.
Results	The results showed that the generated output displacement fields had myocardial shapes similar to those in the input images and also had regional bright and dark signal intensities, representing tissue displacements, in the same locations as those in the gold-standard displacement fields. The Bland-Altman analysis showed good agreement between the output measurements and the corresponding gold-standard displacement fields, with almost all the measurement differences lying within the Â±2 standard deviation agreement level. The student's t-test showed that there were no significant differences between the paired measurements ($p>0.05$). Lin's concordance correlation coefficients were 0.96 and 0.89 for x- and y-displacement fields, respectively. The developed method reduced the time required for generating the displacement field by two orders of magnitude to less than one second.
Conclusions	The deep learning-based method developed in this study allows for ultrafast and accurate generation of myocardial tissue displacement fields from conventional cardiac MRI cine images. This eliminates the need for acquiring additional tagged images and using special tagging analysis software, reducing scan time and data analysis time as well as improving cardiac MRI value imaging.

Category	Technology, Imaging & Engineering, #114
Primary Author	Leonard Brasuel, BA
Secondary Authors	Rajiv Kodali, BS; Maie Zagloul, BS; Abhishek Janardan, BA; Alexandra Polovneff, BS; Bradley Crotty, MD, MPH
Title	Provider Perspectives of a Post Discharge Digital Engagement Program
Introduction	Remote patient monitoring (RPM) programs present a transformative opportunity for enhanced patient support in the transition from the hospital back to the home. RPM implementation and utilization accelerated due to the COVID-19 pandemic. As the health landscape continues to evolve, it is important to assess both quantitative and qualitative measures of success amongst ongoing RPM programs. The GetWell Loop (GWL) application is an RPM program implemented within the Froedtert and Medical College of Wisconsin Health Network. The GWL system has the capacity to provide post-discharge telephonic care at scale through patient engagement with the program. GWL and telephonic phone outreach is provided by a centralized care coordination team of medical assistants and nurses. Here, we sought to unearth the organizational effects of implementing GWL within the Froedtert Enterprise Care Coordination system and its impact on efficiency of care.
Methods	Nine GWL providers (1 licensed practical nurse, 2 medical assistants, 6 nurses) at an academic-community medical center in Wisconsin were recruited and participated in semi-structured interviews concerning the impact of the GWL patient engagement program from an organizational workflow perspective. Virtual interviews were recorded and transcribed. Qualitative data was generated and analyzed using an inductive coding approach.
Results	Study participants identified GWL implementation as a source of notable change for provider workload and workflow (Workload, 87.5%) while providing opportunities to clarify misunderstandings and guide patients to appropriate resources and care (Clarification, 62.5%). Participants reported that the GWL strategy of organizing patients by risk level and complexity allows the program interventions to address individual patient needs (Matching Need, 75%). The participants identified patient engagement as the most notable determinant of patient benefit through the GWL program (Rewards Engagement, 62.5%). Participants noted the role GWL plays in connecting patients to health information and education as one of the greatest successes of the program (Connection, 87.5%) alongside the provision of a space for patients to feel heard (Patient Affirmation. 50%).
Conclusions	Members of the GWL care coordination team provided key perspectives about the efficacy of the program and organizational implementation strategies. These perspectives will be further contextualized by ongoing quantitative analysis of patient utilization and outcomes. Critical future work will benefit from identifying the ways that social determinants of health and tech-literacy may create disparities within a program that relies on patient engagement with a digital tool.
Ancillary Materials	VIEW MY POSTER

Category	Other Clinical Specialty, #115
Primary Author	Ashley Pittman
Secondary Authors	Monica Morales, Sri Chinta, Amy Pan, Liyun Zhang, Jonathan S Ellison
Title	Impact of Social Determinants of Health on Delays to Seek Care for Children with Testicular Torsion
Introduction	Testicular torsion is a well-documented pediatric urological emergency that poses a time-sensitive risk to the testicle. Although management and treatment for suspected testicular torsion is standardized across most hospitals, delays may occur in time to presentation or transfer to pediatric specific centers. Several social determinants of health (SDH) have been associated with higher orchiectomy rates for testicular torsion. However, factors associated with time to presentation with testicular torsion are not well characterized. We investigated time from symptom onset to presentation patterns from a single pediatric center, hypothesizing an association between SDHs and prolonged time to presentation.
Methods	A retrospective chart review of children â‰¤ 17 years of age presenting with testicular torsion at a single tertiary pediatric center from 2013-2022 was performed. Children who were < 1 month of age, no documented time of symptom onset, or did not receive surgery were excluded. Demographics, symptom onset, time course of care, and surgical outcomes were extracted from the electronic medical records. The primary outcome measure of the study was time from symptom onset to ED presentation. SDHs such as interpreter utilization, race, zip code, area deprivation index, and insurance status were compared and analyzed using univariate analyses.
Results	In total 253 children met inclusion criteria. The essential demographic variables include utilization of interpreter 22 (8.7%), public insurance 168 (66.4%), and Hispanic or Latino ethnicity 43 (17.0%). Racial make-up of the cohort was White 144 (56.9%), Black 79 (31.2%), Other 12 (4.7%), and Unknown 18 (7.1%). No difference was noted on univariate analysis of time to presentation between ethnicity, race, or interpreter usage. However, public insurance had a statistically significant greater time to presentation (Median 11.5 IQR 3.9-49.3 vs 4.9, 2.7-26.2) (P=0.004) shown in Figure 1. A logistic regression analysis found ethnicity to have a higher association with adverse orchiectomy outcomes.
Conclusions	Children with public insurance had significantly longer time intervals from reported symptom onset to presentation. Additionally, ethnicity was associated with higher orchiectomy rates. Further exploring barriers to seek care for testicular torsion serves as a foundation to reduce health disparities.

Category	Other Clinical Specialty, #116
Primary Author	Brendan Waldoch, MD
Secondary Authors	Danyon Anderson, Sydney Newton, David Charles, R. Corey O'Connor, Michael Guralnick
Title	Does Anesthesia Type During Stage 1 Testing for Sacral Neuromodulation for Urge Urinary Incontinence Influence Outcomes?
Introduction	For sacral neuromodulation (SNM), staged testing produces the highest rate of progression to permanent implantation. Stage 1 lead placement (SNM-I) can be done under monitored anesthesia care (MAC), allowing for assessment of sensory and motor responses to optimize lead placement, or general anesthesia (GA) that only allows for motor assessment. Factors specific to MAC including patient discomfort and movement can make lead placement challenging. Additionally, there is evidence that reliance on motor responses alone is adequate for lead placement. Herein we evaluate whether the anesthesia type impacts the progression rate to permanent implantation (SNM-II).
Methods	Retrospective chart review was performed for patients who underwent SNM-I in the operating room for overactive bladder with incontinence between 2001-2021 at our institution. Subjects were divided into two groups, those who underwent SNM-I with MAC vs GA. Clinical variables and progression to SNM-II were compared between groups. Progression to SNM-II was based on â‰¥50% symptomatic improvement during a 1-2 week trial period following SNM-I.
Results	Of 118 patients included in the study, 95 (81%) underwent MAC and 23 (19%) GA for SNM-I. Significantly fewer females (MAC 91%, GA 70%, p=0.01) and more patients with neurologic disease composed the GA group (MAC 37%, GA 65%, p=0.01). There was no difference in the rate of progression to SNM-II between groups (MAC â€“ 67/95 patients, 71%; GA â€“ 17/23 patients, 74%; p=0.75).
Conclusions	Types of anesthesia for SNM-I did not affect rate of progression to SNM-II. The result lends support to the reliance on motor responses alone for lead placement during SNM-I.

Category	Other Clinical Specialty, #117
Primary Author	Carolyn Hammen, PA-C, RT
Secondary Authors	Amanda R. Smolock, MD, PhD, Michelle Back, BS, RT, Sandra Slowik, Janet Ste Marie, BSN, RN, Julie Aguilar, BSN, RN, Tracy Puttre, MSN, APNP, AGNP-C, Holly Dembny, RT, Katy Unferth, RN, Michelle Weithaus, RT, Eric J. Hohenwalter, MD
Title	Increasing Efficiency in Interventional Radiology: A QI Project focused on First Case Start Times
Introduction	Delays in first cases of the day not only set a trend toward a late day but can negatively impact institutional efficiency and revenue. The purpose of this project was to improve on-time start to 85% of cases by identifying causes of pre-procedure delays.
Methods	The PDSA QI method was used for this project. Data was collected from 2018- present and included scheduled arrival time, patient check-in time, patient room time, scheduled procedure time, time of signed consent, time labs sent, time labs resulted, reason for delay and whether or not it was avoidable. The two main reasons for delay were identified and calculated as a percentage of total delays for the month. The study team meets monthly to discuss the data.
Results	The average on-time start was 39% in 2018 when this project commenced. The two main reasons for delay were identified to be: lab delays and vague plan for patients not previously seen in IR clinic. The intervention for this project was to have the APP team evaluate patient charts 2-3 days ahead of the scheduled procedure to clarify the plan and alert nurses to needed labs upon patient arrival. Additionally, a vascular access RN was utilized to start IVs for difficult stick patients, and a dedicated phlebotomist was utilized if there was a delay in IV start and labs were needed. After these changes, the percentage of patient procedures starting on time for the first case of the day improved to at or near goal of 85%. More importantly, the two targeted reasons for delays both decreased from about 5% to 0%.

Category	Other Clinical Specialty, #118
Primary Author	David Cao, MS
Secondary Authors	Jose Lucas Zepeda BS, Morgan Lucero BS, Sameer Shakir MD, Kristen Klement MD, Robert Havlik MD, Kant Lin MD
Title	Comparative Outcomes Assessment of Velopharyngeal Insufficiency and Oronasal Fistula Following Modified Furlow versus Straight Line Palatoplasty—What Modifiable Factors Affect Outcomes?
Introduction	Controversy persists regarding postoperative speech outcomes and complications of different "straight-line" repair techniques such as the Bardach Two-Flap (BTF) and von Langenbeck (VL) palatoplasties with or without Intravelar Veloplasty (IVVP).1-2 We hypothesized that levator muscle repair in the BTF with IVVP demonstrates similar rates of postoperative oronasal fistula (ONF) with decreased rates of velopharyngeal insufficiency (VPI) and secondary VPI surgery as compared to VL palatoplasty.
Methods	A retrospective cohort study was performed of non-syndromic subjects undergoing primary palatoplasty at a tertiary care pediatric hospital over a 20-year period. The VF procedure involved joining two mucoperiosteal flaps with minimal levator muscle dissection. The BTF procedure with IVVP incorporated a pushback technique with retropositioning of the levator musculature with an end-to-end repair while lengthening the soft palate. Subjects underwent palatoplasty by one of three fellowship-trained craniofacial surgeons prior to 20 months of age and had >2 years of postoperative speech evaluations. Speech evaluations were performed by a team of speech language pathologists using the Velopharyngeal Function Assessment Scale (VFAS) scoring system; a VFAS score >5 and subsequent need for secondary speech surgery indicated clinically significant VPI. Patient characteristics and postoperative outcomes related to ONF and speech surgery were collected. Predictors of postoperative complications were assessed, with $p<0.05$ denoting significance.
Results	In total, n=80 subjects underwent BTF with IVVP repair at mean age of 12.4 months and n=47 subjects underwent VL repair at mean age of 12.8 months ($p<0.25$). There was an increased proportion of Veau II clefts in the BTF cohort (8.5% VL v. 26.3% BTF, $p<0.03$). The mean length of follow-up was 10.5 years in BTF and 7.7 years in VL ($p<0.001$). Mean age at initial postoperative speech assessment was 3.1 and 3.7 years in the BTF and VL cohorts, respectively ($p<0.03$). VFAS scores at initial assessment were not significantly different between cohorts (4.4 BTF versus 5.6 VL, $p<0.09$). The rate of postoperative ONF was significantly greater in the VL cohort (22% BTF v. 66% VL, $p<0.001$). The rate of secondary VPI speech surgery was significantly greater in the SL cohort (33% v. 57%, $p<0.01$). Veau classification did not correlate with postoperative ONF or VPI. On multivariate regression, VL repair type correlated with the development of postoperative ONF complications and need for speech surgery (Odds Ratio 8.4, $p<0.001$).
Conclusions	When compared to von Langenbeck palatoplasty, Bardach Two-Flap Palatoplasty with Intravelar Veloplasty may be associated with decreased rates of speech surgery without increased rates of ONF. With either technique, degree of muscle overlap and tension potentially serve as confounding variables for the occurrence of ONF, VPI, and need for speech surgery. Future directions include comparing this cohort to subjects undergoing modified Furlow palatoplasty.
Reference 1	Sommerlad BC. A technique for cleft palate repair. Plast Reconstr Surg. 2003;112(6):1542-1548.
Reference 2	Agrawal K. Cleft palate repair and variations. Indian J Plast Surg. 2009;42 Suppl(Suppl):S102-S109.
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Category	Other Clinical Specialty, #119
Primary Author	Jessica Zhou, MS
Secondary Authors	Amanda Smolock, MD, PhD, Mustafa Haddad, MD, Brandon Key, MD, Parag Patel, MD, MS, Sarah White, MD, MS, Mircea Cristescu, MD, MBA, Matthew Scheidt, MD
Title	Prostate Artery Embolization: Anatomy, Imaging, and Tips for Success
Introduction	Prostate artery embolization (PAE) is a growing interest for many interventional radiologists and requires a high degree of familiarity with the anatomy of the internal iliac artery (IIA). The IIA is complex, highly branched, and has tremendous anatomic variability. Its branches supply important structures in the pelvic walls, pelvic viscera, and gluteal region. Therefore, to achieve successful PAE, it is crucial to study the highly variable IIA branching patterns based on real-world imaging data. The goal of this project is to help familiarize the audience with the imaging features of male IIA anatomy and provide guidance for pelvic endovascular procedures. Learning Objectives 1. General anatomic review of IIA. 2. Imaging modalities used for male pelvic procedures & diagnostics. 3. Angiographic anatomy relevant to PAE. 4. Tips and tricks when performing PAE. 5. Case examples.
Methods	This exhibit will provide a review of the IIA anatomy relevant for PAE. The 4 types of IIA anatomical branching pattern variants will be introduced along with their relative prevalence. Options for pre-PAE imaging modalities will be reviewed along with their pertinent findings and advantages/disadvantages. Intra-procedure angiographic anatomy will also be reviewed. Tips for procedural success including access and approach, catheter and wire selection, and intra-procedural medications will also be discussed.
Conclusions	By reviewing the IIA anatomy and imaging as well as procedural tips, the audience will be familiarized with the imaging features of male pelvic arterial anatomy and procedural considerations for successful implementation of PAE

Category	Other Clinical Specialty, #120
Primary Author	Kaila Redifer-Tremblay, MD
Secondary Authors	Jessica Zhou, MS, Eric J. Hohenwalter, MD, Parag Patel, MD, MS, Brandon Key, MD, William S. Rilling, MD, Matthew Scheidt, MD, Robert Hieb, MD, Sarah B. White, MD, MS, Amanda R. Smolock, MD, PhD
Title	Impact of ICU management of elevated right atrial pressure following TIPS
Introduction	The purpose of this study was to evaluate outcomes in patients with elevated right heart pressure measurements post-TIPS procedure.
Methods	This was a single center IRB-approved retrospective review of TIPS from 2019-2022. In March of 2019, our center instituted a new workflow wherein patients with elevated right atrial pressures (RAPs) (> 15 mmHg) or those with large changes to RAPs (ï€¾ 10 mmHg) had a Swan-Ganz catheter placed status post TIPS and were transferred to the ICU for aggressive cardiac monitoring. Database query yielded a total of 99 TIPS, of which 27 had elevated RAPs managed in the ICU. EMR was reviewed for patient demographics, diagnosis, procedure indication, cardiac and portal pressure measurements, laboratory values, pre and post-TIPS transthoracic echocardiogram (TTE), complications, and post-TIPS management. Clinical outcomes were reviewed for ICU and total length of stay (LOS) and post-operative mortality. Student's t test was used.
Results	Etiology of cirrhosis (21M, mean age 55 ï‚± 12.2 y) was NASH (n=6), alcohol (n=14), cryptogenic (n=2), chronic viral hepatitis (n=2), and multifactorial (n=3). TIPS indications were refractory ascites/hepatic hydrothorax (n=14) and refractory variceal bleeding (n=13). Mean RAP on pre-TIPS TTE was not elevated (6.0 ï‚± 43.6 mmHg). 9 patients had additional cardiac risk factors prior to TIPS. 100% (27/27) had high absolute RAP (mean 21 ï‚± 5.9 mmHg) post-TIPS. Aggressive diuretic therapy was used to manage 23/27 (85%) of patients. No patients required vasopressor or inotropic support. Mean RAP upon arrival to the ICU was 9.8 ï‚± 4.6 mmHg, and the maximum RAP at 24 hours post procedure averaged 15.1 ï‚± 7.2mmHg. Mean ICU LOS was 4 ï‚± 4 d, and mean total LOS was 9 ï‚± 8 d. One patient died during the index hospitalization related to complications of cirrhosis. No TIPS were revised for heart failure.
Conclusions	Prior studies have shown post-TIPS elevation in RAP correlates with poor outcomes. This study demonstrates that early aggressive management of elevated RAP post-TIPS may be critical in improving outcomes and avoiding complications such as acute right heart failure.

Category	Other Clinical Specialty, #121
Primary Author	Maie Zagloul
Secondary Authors	Jonathon Bock MD, FACS
Title	Evaluation of social and clinical determinants of health on dysphagia care pathways at a tertiary care facility
Introduction	Limited research exists evaluating the impact of social and clinical determinants of health in influencing care pathways for patients with dysphagia. A better understanding of whether these determinants correlate to altered care and resource utilization is essential as it relates to patient outcomes.
Methods	All patients seen at a tertiary midwestern hospital were screened for ICD codes of dysphagia diagnoses from 2009-2019. Demographic information was collected from these dysphagia patients including sex, race, ethnicity, and insurance status. Subgroup analysis was performed to assess referral pattern rates and types of diagnostic interventions ordered (none, videofluoroscopic swallow study, esophagram, esophagogastroduodenoscopy).
Results	A total of 31,858 dysphagia patients were seen at our institution during the study period, with a majority being female (56.36%), Caucasian (79.83%), and publicly insured (63.16%), with a median age of 60.35 yrs. There were no detectable significant care delivery pattern differences based on geography/zip code analysis. African American patients were significantly more likely to have imaging or interventions performed (OR 1.463, P=0.005). Patients with public insurance also had higher rates of diagnostic study utilization (OR 1.53, P=0.01). Only 3% of all dysphagia patients were seen by laryngologists.
Conclusions	No significant differences were seen in dysphagia evaluation modalities based on zip code analysis surrounding this tertiary care facility. African American patients and those with public insurance had significantly higher utilization of subsequent testing and intervention for dysphagia care. Further studies are necessary to delineate causes and outcome differences for these measurable differences in dysphagia care pathways.
Acknowledgements	Key Words: disparity; dysphagia; laryngology; social determinants; utilization

Category	Other Clinical Specialty, #122
Primary Author	Marcus Jones, MD
Secondary Authors	Amanda R. Smolock, MD, PhD, Matthew J. Scheidt MD, Brandon Key, MD, Eric J. Hohenwalter MD, Parag J. Patel, MD, Robert A. Hieb, MD, Sarah B. White MD MS
Title	Comparison of Partial Distal Splenic Embolization with Glue versus Other Embolics
Introduction	Distal partial splenic embolization is used as an alternative to surgery in the setting of thrombocytopenia, portal hypertension or trauma. The safety and efficacy of n-butyl cyanoacrylate (n-BCA) glue embolization compared to other embolic agents is not well understood. The purpose of this study was to evaluate our single-center experience with partial splenic embolization using glue compared to our previous institutional standard of particles and coils
Methods	A retrospective review of patients who underwent distal partial splenic embolization between July 2020 and June 2022 was performed. Indication for procedure and embolic used were recorded. Pre- and post-procedure platelet counts (recorded at baseline, 1 month, & 6 months) were recorded. Clinical notes, length of hospital stay, narcotic usage, and complications were reviewed.
Results	A total of 33 patients underwent partial distal splenic embolization in the 2-year period reviewed. Indications for procedure were thrombocytopenia (12/33, 36.4%), trauma (12/33, 36.4%), and portal hypertension (9/33, 27.3%). Glue was used in the majority of cases (66.7%, 22/33). Embolics used in the other cases included permanent and temporary particles, coils, and plugs. PCA pumps were initiated post-procedure for 4/33 (12%), all of whom received glue embolization. A single dose of intravenous narcotic analgesia was administered in 7/22 (31.8%) glue embolization patients and 4/11 (36.3%) of the various embolic group. 26/33 (78.8%) patients had available labs to record up to the six-month period. Platelet counts increased in 17/26 (65.4%) patients who underwent partial distal splenic embolization and 13/22 (59.1%) who received glue embolization over the 6-month period. No post-procedure abscess occurred.
Conclusions	Distal partial splenic embolization can be performed with a variety of agents. In this analysis, there were no significant differences between glue embolization and other methods with regard to safety or efficacy.

Category	Other Clinical Specialty, #123
Primary Author	Marie C Luebke, MHS
Secondary Authors	Emily Schmitt BA, Emily RW Davidson MD, R Corey O'Connor MD, Joanna Balza BS, Joan M Neuner MD, Kathryn E Flynn PhD
Title	DEVELOPING A URINARY INCONTINENCE CARE PATHWAY: A MIXED METHODS STUDY
Introduction	While nearly 50% of adult women report at least one episode of urinary incontinence (UI), most never receive treatment. We sought to understand how primary care providers diagnosed and treated patients to inform a pilot UI care pathway which better integrated primary and specialty care. Herein we describe our 1) interviews with primary care providers to understand current behaviors and barriers to care and 2) results from the pilot UI care pathway intervention.
Methods	Provider interviews: Primary care physicians and advanced practice providers (APPs) within the Medical College of Wisconsin (MCW) network were recruited by email to participate in an interview using a semi-structured guide covering current practices and perceived barriers to UI care. Interviews were audio recorded, transcribed, and coded for emergent themes. Pilot study: Patients who screened positive to a clinical UI question asked by their provider were invited to participate. Baseline data on UI symptoms and treatment history were self-reported via REDCap and participants were given a website link created by the research team that included education about UI, local classes, and a link to a smartphone app of self-treatments to manage UI. A follow-up questionnaire at 8 weeks collected data on UI symptoms, treatments, and the pilot intervention process.
Results	We conducted 5 interviews with providers at 5 clinics within the MCW network. Providers described barriers to completing almost all the steps of diagnosis and treatment strategies for UI suggested in American Urological Association guidelines. The most persistent barrier was lack of time during clinic visits which was noted for every step of diagnosis. Providers also endorsed a lack of training for several steps including physical exam, post-void residual urine volume assessment, bladder diary, and lifestyle modification treatment strategies. Another recurring barrier was the lack of personal relationships with specialists. Providers prefer having a specific specialist physician to refer to rather than referring patients to a department within the health system. Fifteen patients participated in the pilot study and reported several self-treatment strategies including avoiding bladder irritants (7/15), performing Kegel exercises (4/15), and watching a video on bladder health (3/15). After 8 weeks, patients reported small improvements in UI Symptoms (on the ICIQ-UI and LURN-SI patient-reported outcome measures). The PROMIS Ability to Participate Social score improved by 4.6 points. Other patient-reported measures showed no change, including in physical function. At 8-weeks, 3 of 11 patients were interested in a referral to a specialist physician.
Conclusions	This mixed methods pilot revealed several barriers to providing guideline-recommended UI screening, diagnosis, and treatment within primary care. Promising results from a novel UI care pathway pilot indicate that streamlining UI care may assist primary care providers in the diagnosis and first-line treatment of UI to improve patient outcomes.

Category	Other Clinical Specialty, #124
Primary Author	Michael P. Kozuch, MPH
Secondary Authors	Amanda R. Smolock, MD, PhD, Sarah B. White, MD, MS, Matthew J. Scheidt, MD, Brandon M. Key, MD
Title	Standardized Vertebral Compression Fracture Management Pathway Implementation and Associated Database Development
Introduction	Percutaneous vertebral augmentation (PVA) is effective for treating VCFs and has been shown to decrease hospital length of stay, time to ambulation following a procedure, and analgesic requirements. However, PVA has been traditionally reserved for those failing to respond to conventional management. A standardized VCF management pathway developed by a multidisciplinary group at a single institution aims to improve resource efficiency by streamlining care amid changing treatment paradigms. Learning Objectives 1. To describe the introduction and implementation of a standardized vertebral compression fracture (VCF) management pathway in the multidisciplinary setting. 2. To demonstrate creation of a data capture infrastructure for evaluation of the impact of a VCF management pathway on patient outcomes and healthcare resource utilization.
Methods	A multidisciplinary group including representatives from interventional radiology (IR), emergency medicine, neurosurgery, orthopedic surgery, and anesthesia/pain medicine convened at regular intervals to refine a treatment algorithm prior to implementation. Patient selection for entry into the pathway begins with presentation to the emergency department (ED) with vertebral fracture. An order panel distributed across the ED details standardized labs, imaging studies, and initial pain treatment options prior to initiating consults with neurosurgery/orthopedic spine or IR. Inclusion of IR treatment options in this clinical care pathway provides earlier access to PVA for patients. Follow-up with an institutional Bone Health Clinic is also arranged for all pathway entrants. A database was developed to retrospectively evaluate the impact of implementation of this standardized pathway by quantifying changes to healthcare resource utilization and characterizing analgesic prescribing patterns surrounding PVA procedures.
Results	This exhibit reviews the VCF management pathway and its implementation along with database development with a focus on data collection methodology, including parameter determination, establishing timelines for care, and data capture permitting novel analyses related to early percutaneous intervention.
Conclusions	This multimodal treatment pathway identifies opportunities for IR to use highly efficacious, minimally invasive procedures that leverage the impact of PVA against trends of increasing disability adjusted life-years.

Category	Other Clinical Specialty, #125
Primary Author	Michael White
Secondary Authors	Brendan Waldoch, Jonathan Ellison, John Kryger
Title	MANAGEMENT OF ENCRUSTED PYELITIS OF RENAL TRANSPLANT IN A PATIENT WITH EAGLE-BARRETT SYNDROME
Introduction	Encrusted pyelitis secondary to infection with Corynebacterium urealyticum is a known complication following renal transplantation. C. urealyticum, a urease splitting organism, alkalinizes urine and creates a setting in which encrustations can form on mucosal lesions of the pelvicalyceal system. This rare complication can lead to urinary symptoms, obstructive uropathy, and graft loss. Herein we present the case of a pediatric patient with Eagle-Barrett syndrome and a renal transplant who developed severe encrusted pyelitis leading to graft loss despite multimodal management.
Methods	A 5 year old boy with a history of Eagle-Barrett syndrome and renal transplant presented with symptomatic nephrolithiasis and rising creatinine concerning for graft failure. His urologic history was significant for neonatal bladder rupture with urinary ascites that was managed with a vesicostomy created at birth. He subsequently developed end stage renal disease leading to cadaveric renal transplantation at age 4. Ten months post-transplant the patient was admitted for workup of elevated creatinine (5.21 mg/dL on admission). At that time he had symptoms of hematuria and dysuria, and urine culture was positive for Corynebacterium urealyticum. Computed tomography imaging showed diffuse calcification along the entire urothelial lining of the transplanted urinary tract, consistent with encrusted pyelitis.
Results	Initial management consisted of intravenous linezolid, serial percutaneous endoscopic stone debulking, and urinary acidification with continuous infusion of RenacidinÂ® via nephrostomy tube. Retrograde ureteroscopy was attempted prior to percutaneous access but ureteral encrustation precluded this approach. Creatinine initially improved to <1 mg/dL and repeat urine cultures were sterile, but encrustation persisted and creatinine progressively worsened. Two months after presentation the patient underwent unsuccessful debulking of encrustation via open pyelolithotomy. One month later he underwent transplant nephrectomy.
Conclusions	Urinary tract infection with C. urealyticum can cause severe consequences in the immunocompromised renal transplant patient. In our patient presenting with encrusted pyelitis secondary to C. urealyticum infection, earlier identification and aggressive management of this infection may have led to graft preservation.

Category	Other Clinical Specialty, #126
Primary Author	Morgan Briggs, MD
Secondary Authors	Benjamin Beran, MD
Title	Assessment of Uterine Fibroid Knowledge and Education Interests Amongst Healthcare Professionals.
Introduction	Uterine fibroid diagnosis and management is a public health concern due to the significant negative health outcomes experienced by individuals with uterine fibroids and associated high health care costs.1,2 The negative outcomes are compounded by many patients reporting a delay in diagnosis and care.3 Qualitative studies report a barrier to care being a lack of an accessible and trusted health professional. To combat this barrier, this study aimed to determine gaps in health care professionals' knowledge regarding uterine fibroids and investigate areas of educational interest. Currently, there is no literature investigating health professionals' knowledge or education programs regarding uterine fibroids.
Methods	Obstetrics-gynecology, family medicine, and internal medicine physicians, residents, physician assistants, nurse practitioners, and nurses at an urban academic institution received an electronic survey via RedCap. The survey investigated current knowledge and educational areas of interest regarding uterine fibroids. Descriptive statistics were performed using Minitab.
Results	78 of the 415 participants (18.8%) who received the survey (85% (n=65) physicians, 10% (n=8) nurse practitioners, 8% (n=3) nurses, 1% (n=1) physician assistants) completed at least one question. A majority of participants answered questions regarding diagnosis timing, instruments for validated reported outcomes, and risk factors incorrectly. 72% (n=65) of physicians and 100% of nurse practitioners (n=8) and nurses (n=3) desired more education about treatment options and guidelines. A majority of nurses desired education on patient reported outcomes, general disease state education, risk factors, and signs and symptoms of uterine fibroids.
Conclusions	This study provides insight regarding current knowledge of uterine fibroids and areas of education interest amongst different health care professionals. The study team plans to develop targeted education programs for the different healthcare professionals with the goal of improving participants knowledge and confidence when caring for individuals with uterine fibroids.
Acknowledgements	Pfizer: Survey creation and data analysis.
Reference 1	Borah B, Nicholson W, Bradley L, Stewart E. The impact of uterine leiomyomas: A national survey of affected women. American Journal Obstetrics Gynecology. 2013;209:319 e1–e20.8.
Reference 2	Cardozo E, Clark A, Banks N, Henne M, Stegmann B, Segars J. The estimated annual cost of uterine leiomyomata in the United States. American Journal Obstetrics Gynecology 2012;206 (3):211.e1–211.e9
Reference 3	Henry C, Elkeroma A, Filoche S. Barriers to seeking consultation for abnormal uterine bleeding: systematic review of qualitative research. BMC Women's Health. 2020; 20(123): 1-9.

Category	Other Clinical Specialty, #127
Primary Author	Muhammad Khokhar
Secondary Authors	Nader Shammout, Rachel Cutlan, Saman Shabani, Brian D. Stemper
Title	The Effects of Spinal Orientation on Lumbar Spine Fractures
Introduction	Members of the military are consistently exposed to conditions predisposing them to lumbar spine fractures. Studies report the majority of spinal injuries in military members occur between T12 to L5. The type of fracture depends on the characteristics of the loading environment at the time of injury, such as acceleration, applied force, and alignment of the spine. Understanding the factors leading to spinal fractures can aid in decreasing the severity of spinal injuries or prevent them altogether. Aims: 1. Quantitatively investigate spinal orientation at the time of loading and correlate it with the type of injury observed.
Methods	Lumbar spines (levels T12-L5) from post-mortem donors were pre-flexed (5 Nm flexion) and dynamically compressed at different forces and accelerations using a biofidelic loading apparatus. Imaging (X-rays/Pre- & Post-test CT) was used to assess injuries. The spines were classified according to the AO spine classification system. Lastly, flexion/extension was determined by the average Cobb and absolute rotation angles (ARA). These measurements were compared for trends to explain how orientation of the spine affected the injury outcome.
Results	A total of 23 specimens were used for 38 tests. Currently, 9 specimens have been categorized by fracture type: 1 hyperextension, 3 wedge, 2 burst, and 3 chance. All fractures occurred between T12-L1 except for one burst fracture. The largest cobb angle (55.4 degrees) and largest ARA (51 degrees) were seen with the hyperextension fracture. The chance fractures had the smallest Cobb angle of 17.2 degrees and smallest ARA 14.2 degrees. These tended to occur when the spine was more flexed (82.5 degrees), opposite to the orientation of hyperextension fractures (hyperextension: 95.3 degrees). Burst and wedge fracture orientations were in between hyperextension and chance fractures (wedge: 90 degrees, burst: 98 degrees). The average Cobb angle and ARA for wedge fractures were 27 degrees and 21.8 degrees, respectively. L1 Burst fractures had an average Cobb angle of 29 degrees and an ARA of 30.3 degrees. The lone L3 burst fracture was more extended compared to the L1 burst fracture with a Cobb angle of 27.7 degrees and an ARA of 30.3 degrees.
Conclusions	With an ongoing investigation, the current data suggests lumbar spine orientation affects the resulting fracture type. When the spine was in a neutral position with minor pre-flexion, burst and wedge fractures tended to occur in the anterior and middle columns. Burst fractures tended to occur in more extended lumbar spines, while wedge fractures occurred in spines that were more flexed. Chance fractures occurred with extreme flexion. Posterior column hyperextension injuries occurred with pre-extension. This analysis suggests that the position of the military member at time of aircraft ejection or aircraft crash can influence the type of resulting lumbar spine injuries.
Acknowledgements	This study was supported by the Incapacitation Prediction for Readiness in Expeditionary Domains: An Integrated Computational Tool (I-PREDICT) program supported by the Office of Naval Research (ONR) through the Medical Technology Enterprise Corporation (MTEC) and Southwest Research Institute (SwRI). Support was also provided by Department of Veterans Affairs Medical Research.
Reference 1	Edwards M. Anthropometric measurements and ejection injuries. Aviat Space Environ Med. 1996;67(12):1144-1147.
Reference 2	Lehman RA, Paik H, Eckel TT, Helgeson MD, Cooper PB, Bellabarba C. Low lumbar burst fractures: A unique fracture mechanism sustained in our current overseas conflicts. The Spine Journal. 2012;12(9):784-790. doi:10.1016/j.spinee.2011.09.005
Reference 3	Stemper BD, Chirvi S, Doan N, et al. Biomechanical tolerance of whole lumbar spines in straightened posture subjected to axial acceleration. Journal of Orthopaedic Research. 2017;36(6):1747-1756. doi:10.1002/jor.23826

Category	Other Clinical Specialty, #128
Primary Author	Mukul Sharda
Secondary Authors	Megan G. Paradzinsky, Jay I. Sandlow, Peter N. Dietrich
Title	Patient Perceptions of In-Office versus Virtual Consultations Prior to Vasectomy
Introduction	The 2015 AUA Guidelines on vasectomy include a statement that preoperative consultation should preferably be conducted in person. However, virtual vasectomy consultations have become more commonplace, particularly following the COVID-19 pandemic. We sought to understand patient perceptions of in-person versus virtual consultations prior to their vasectomy.
Methods	All patients scheduling an appointment for vasectomy consultation between October 1, 2022 to December 29, 2022 were given the option of an in-person or virtual visit. They were asked to complete a seven-item survey assessing their satisfaction with their consultation, their procedure, as well as their preferred modality for the consultation. Questionnaires were completed following both the consult and their vasectomy. Data regarding patient age at vasectomy and distance travelled to vasectomy site were collected via chart review. Statistical analyses were performed using R Core Team (2022). 68 total patients were included in this study.
Results	The average age of patients undergoing vasectomy was 37.6 years (SD=4.2). The average distance travelled to the clinic was 13.5 miles (SD = 9.4). All patients (68/68) chose in-person consultations. 100% of participants were satisfied with an in-person method of counseling. However, 7% of patients (5/68) reported they would have preferred a virtual consult. Preference for virtual consultation was not influenced by age (p=0.97) or distance required to travel to the procedure site (p=0.71).
Conclusions	In conclusion, despite the accessibility of virtual visits, most patients prefer and are satisfied with in-person consultation prior to their vasectomy.
Ancillary Materials	VIEW MY POSTER

Category	Other Clinical Specialty, #129
Primary Author	Patrick Moran, MD
Title	Plaque Modification Strategies
Introduction	Purpose: 1. Understand when plaque modification strategies need to be used. 2. Understand angioplasty related plaque modification strategies. 3. Understand atherectomy related plaque modification strategies. 4. Understand current data, complications, and limitations of these strategies.
Methods	Chronically calcified atherosclerotic lesions cause challenges in the endovascular treatment of peripheral arterial disease. These challenges include impaired device delivery, decreased luminal revascularization, impaired stent expansion, increased risk of in-stent stenosis and thrombosis, and increased procedural time and cost in addition to increased overall radiation dose. Plaque modification or vessel prep is a strategy that can mitigate issues caused by chronically calcified lesions. There are a variety of balloons and atherectomy devices that can be used for vessel prep as detailed in this review. Operators should have an understanding of when to use these devices and what their limitations are.
Results	Devices for vessel prep can be categorized as balloon and atherectomy devices. Balloons that can be used include plain old angioplasty balloons, high-pressure non-compliant balloons, cutting balloons, scoring balloons, Chocolate© balloon, Serranator© balloon, and intravascular lithotripsy/Shockwave©. Atherectomy devices include rotational, directional, orbital, and laser atherectomy. Data regarding best use of these devices remains limited but will also be discussed. Finally, understanding complications and limitations of these devices is imperative.
Conclusions	There are a variety of balloon and atherectomy devices that can be used for vessel prep. Proper use of these devices can provide a means for improved outcomes for endovascular management of chronically calcified lesions

Category	Other Clinical Specialty, #130
Primary Author	Rana Aliani, M.D.
Secondary Authors	Vienne Seitz, Shirng-Wern Tsaih, ScD, Benjamin D. Beran, M.D., & Emily R.W. Davidson, M.D.
Title	Impact of Race, Insurance, and Procedural Timing on Sterilization Method
Introduction	Ovarian cancer is the fifth leading cause of cancer deaths in women. Removing the entirety of the tubes appears more effective in reducing ovarian cancer development compared to other sterilization methods. It is thus recommended to perform salpingectomy (SL) rather than tubal ligation (TL) for cancer risk reduction. Minority women are disproportionately affected by both ovarian cancer and disparities in healthcare access. Pregnancy is a period where un- or underinsured women may have improved access to health coverage. This makes the postpartum period an ideal time to provide sterilization if desired. Given the interplay of these factors on sterilization, our study sought to assess if race, insurance status, and procedural timing impacted the method of sterilization.
Methods	This was a retrospective case control study. The study population included women who underwent an elective sterilization procedure at a single academic institution from 1/2010 to 12/2020. Women were excluded if salpingectomy was performed with any procedure other than cesarean section, if the procedure was not a SL or TL, or if race or insurance status was not listed. Race groups were Asian, Black, Hispanic, or White. The medical record, including operative note, was reviewed to obtain age, race, procedure type and timing, and insurance status. Timing was divided into peripartum, which included intrapartum or postpartum, or interval procedures. Cases were defined as patients who underwent SL, and controls underwent TL. All statistical analysis was carried out using R. Categorical data is presented as percent (n). A multivariate logistic regression was performed to assess the association of types of procedure with race, insurance status, and procedure timing. This is reported as odds ratios (OR) with 95% confidence intervals (CI).
Results	A sample of 2041 patients received sterilization procedures between 2010 and 2020. 962 were included in the analysis. Most exclusions were due to concurrent gynecologic or other abdominal procedures. 72% (695) of patients underwent TL, and 28% (267) underwent SL. 52% (503) of patients were White, 32% (309) Black, 13% (121) Hispanic, and 3% (29) Asian. 73% (702) of sterilizations were performed during the peripartum period. 61% (584) of patients had public insurance. On multivariate logistic regression, public insurance (OR 0.68 95% CI 0.5-0.9) and peripartum timing (OR 0.03 95%CI 0.02-0.04) were associated with less SL than TL while increased age (OR 1.1 95%CI 1.04-1.1) was associated with more SL. Race was not associated with procedure type on either bivariate or multivariate analysis.
Conclusions	Despite the recommendation for salpingectomy, tubal ligation is more commonly performed in our health system. We found that while race was not associated with the type of sterilization, insurance status, procedural timing, and patient age were factors influencing the method of sterilization.

Category	Other Clinical Specialty, #131
Primary Author	Sean P. Farrell, BS
Secondary Authors	Amanda R. Smolock, MD, PhD, Brandon Key, MD, Mustafa Haddad, MD, Mircea Cristescu, MD, MBA, Sarah B. White, MD, MS, Jayshil Patel, MD, Stephanie Dybul, MBA, RT, Matthew Scheidt, MD
Title	Timing of Catheter Directed Intervention in the Treatment of Intermediate-High-Risk Pulmonary Embolism
Introduction	The impact of time-to-catheter directed intervention (CDI) in patients with intermediate high-risk pulmonary embolism (PE) is unknown. The purpose of this study was to describe time-to-CDI, procedure length, and associated outcomes in intermediate-high risk PE.
Methods	This was an IRB-approved single-center retrospective review of a clinical case log of consecutive Pulmonary Embolism Response Team (PERT) calls between 2018 and 2022. A total of 472 cases were reviewed for intermediate-high risk PE who underwent CDI yielding a total of 27 patients included in the study cohort. CDI type (mechanical, pharmacological, or pharmacomechanical), time-to-CDI from initial PE diagnosis, and CDI procedure length were recorded. ICU and hospital length of stay (LOS) and 30-day mortality were recorded and analyzed. ANOVA and Student's t-test were used to analyze continuous variables, and Chi-square and Fischer's exact tests were used for categorical variables.
Results	The study cohort included 13 mechanical, 12 pharmacological, and 2 pharmacomechanical CDIs. There were no differences in ICU or hospital LOS between CDI types. Median procedure length for all interventions was 37 minutes (range: 16-138 minutes). Cases with procedure length less than or equal to 37 minutes (n=15) had a significantly shorter mean ICU LOS compared to cases (n=12) with procedures longer than 37 minutes (1.5Â±1.4 vs 3.4Â±2.9 days, p=0.034). Procedure length did not appear to correlate with hospital LOS. Median time-to-CDI after PE diagnosis was 17.2 hours (range: 2.3-102.6 hours). Cases where CDI occurred within 17.5 hours of presentation(n=14) trended toward shorter mean ICU LOS, compared to cases (n=13) where CDI was greater than 17.5 hours after presentation (1.6Â±0.6 vs 3.2Â±3.0 days, p=0.062). Time-to-CDI did not appear to be associated with hospital LOS. Overall 30-day mortality rate for the entire study cohort was 7.4% (2/27), but 30-day mortality rate varied by type of CDI (p=0.044).
Conclusions	Appropriate timing of CDI in relation to patient presentation and duration of procedure are important factors which may influence patient outcomes and need for ICU stay. Prospective studies evaluating the impact of time-to-CDI on intermediate high-risk patient outcomes are warranted.

Category	Other Clinical Specialty, #132
Primary Author	Simon Blaine-Sauer BS
Secondary Authors	Tina L. Samuels MS, Pawjai Khampang MS, Ke Yan PhD, Michael E. McCormick MD, Robert H. Chun MD, Steven A. Harvey MD, David R. Friedland MD PhD, Nikki Johnston PhD, Joseph E. Kerschner MD
Title	Novel pediatric middle ear cell lines for studying otitis media
Introduction	Otitis media (OM) is the most frequently diagnosed pediatric disease in the US. Despite the significant public health burden of OM and the contribution research in culture models has made to understanding its pathobiology, a single immortalized human middle ear epithelial (MEE) cell line exists (HMEEC-1, adult-derived). We previously developed MEE cultures from pediatric patients with non-inflamed MEE (PCI), with recurrent OM (ROM), or with OM with effusion (OME) and demonstrated differences in their baseline inflammatory cytokine expression and response to stimulation with an OM-relevant pathogen and cytokines. Herein, we sought to immortalize these cultures and assess retention of their phenotypes.
Methods	MEE cultures were immortalized via lentivirus encoding temperature-sensitive SV40 T antigen. Immortalized MEE lines and HMEEC-1 grown in monolayer were stimulated with non-typeable Haemophilus influenzae (NTHi) lysate. Gene expression (TNFA, IL1B, IL6, IL8, MUC5AC, and MUC5B) was assessed by qPCR. Similar to parental cultures, baseline cytokine expressions were higher in pediatric OM lines than in HMEEC-1 and PCI, and HMEEC-1 cells were less responsive to stimulation than pediatric lines.
Results	Immortalized MEE lines retained the cytokine expression and responsiveness of their tissues of origin and differences between non-OM versus OM and pediatric versus adult cultures, supporting their value as novel in vitro culture models for OM.
Conclusions	Work is currently underway using these lines to investigate factors contributing to pathogen colonization and production of effusion.

Category	Other Pre-Clinical/Laboratory Science, #133
Primary Author	Alexandra Lesnick, BS
Secondary Authors	Tina L. Samuels MS1, Donna Seabloom BS2, Beverly Wuertz BS2, Abhilash Ojha, MS3, Davis Seelig DVM PhD DACVP4, Frank Ondrey MD2, Timothy S. Wiedmann PhD5, Chris Hogan PhD3, Nikki Johnston PhD1
Title	Toxicology of Inhaled Fosamprenavir as a Dry Powder for Laryngopharyngeal Reflux
Introduction	10-30% of the US population suffer from laryngopharyngeal reflux (LPR) with no effective medical therapy. Pepsin is a predominant source of damage during LPR and is a key therapeutic target. Fosamprenavir (an FDA-approved HIV protease inhibitor) has been shown to bind to and inhibit pepsin and prevent damage in an in vivo LPR mouse model. A pre-Good Lab Practice (GLP) inhalation toxicity study was performed to assess safety of inhaled fosamprenavir for use in a dry powder inhaler for the treatment of LPR.
Methods	A small-scale powder disperser was used to generate aerosols of fosamprenivir and the mass distribution measured optically. A preliminary toxicity study was conducted in mice at inhaled dose levels of 0.5X, X, and 2X, where X represents the inhaled dose that was used to achieve efficacy in an earlier study (0.93mg/kg/day). Aerosolized fosamprenavir was provided 5days/week in a previously described LPR mouse model (laryngeal scratch performed weeks 1 and 2 including controls; 300ug/ml pepsin pH7 or solvent instilled 3days/week for 4week). Six mice were used per group. Organ pathology was documented and bronchoalveolar lavage (BAL) and plasma were harvested for Luminex assay.
Results	A particle size range of 2-9µm represents the best choice in terms of higher deposition fraction in the larynx and lower deposition elsewhere in the respiratory tract. No pathology was seen in the nasal cavity, larynx, esophagus, trachea, lung, liver, heart, and kidney tissues from either control or fosamprenavir exposed mice. Neither inflammatory cytokines (GM-CSF, IFNγ, IL-1α, IL-1β, IL-2, IL-4, IL-5, IL-6, IL-7, IL-10, IL-12p70, IL-13, IL-17A, KC/CXCL1, LIX, MCP-1, MIP-2, TNFα) nor cardiotoxicity markers (CXCL16, Endocan-1, Light, Follistatin, Oncostatin M, sCD40L, PIGF-2, Troponin I, Troponin T) were significantly elevated (<p 0.05) in BAL or plasma, respectively, by fosamprenavir relative to control mice receiving only scratch wound and solvent instillation.
Conclusions	Given the benefits of local treatment direct to the site of injury (allowing lower dosing limiting systemic side effects), these preliminary toxicology safety data justify GLP inhalation toxicology necessary for phase I clinical trial of a fosamprenavir dry powder inhaler.
Acknowledgements	1Department of Otolaryngology and Communication Sciences, Medical College of Wisconsin, Milwaukee, Wisconsin. 2 Department of Otolaryngology Head and Neck Surgery, University of Minnesota, Minneapolis, Minnesota. 3Department of Mechanical Engineering, University of Minnesota, Minneapolis, Minnesota. 4Department of Pathology, University of Minnesota, Minneapolis, Minnesota. 5Department of Pharmaceutics, University of Minnesota, Minneapolis, Minnesota. Disclosures: NJ is co-founder, CSO, and shareholder of N-Zyme Biomedical Inc. TS is a shareholder of N-Zyme Biomedical Inc. VC investment in N-Zyme Biomedical is funding drug reformulation and clinical trials of fosamprenavir. Correspondence may be directed to Ally Lesnick (alesnick@mcw.edu), Tina Samuels (tsamuels@mcw.edu) or Nikki Johnston (njohnston@mcw.edu).
Reference 1	Johnston, N., et.al. (2023), Oral and Inhaled Fosamprenavir Reverses Pepsin-Induced Damage in a Laryngopharyngeal Reflux Mouse Model. The Laryngoscope, 133: S1-S11
Reference 2	Modeling Laryngeal Biology, Madison, WI, USA, July 7, 2016. Computational Fluid Dynamics Analysis of Laryngeal Particle Deposition from Inhaled Corticosteroids, Garcia G.J.M., Leschke T.M., Blumin J.H., Bock J.M.
Reference 3	PATENT: PCT/US2021/027758, Aerosolized formulations of HIV protease inhibitors for the treatment of airway reflux.
Ancillary Materials	VIEW MY POSTER

Category	Other Research Related Topics, #134
Primary Author	Andrew L DeGroot, BS
Secondary Authors	Paige E Naylor, PhD, Michelle Loman, PhD, and Elisabeth Vogt, PhD
Title	Utilizing Area Deprivation Index to Predict Pediatric Brain Injury Characteristics.
Introduction	The Area Deprivation Index (ADI) is a tool used to characterize influences of socioeconomic status on healthcare outcomes. ADI seeks to estimate the degree of socioeconomic advantage/disadvantage that exists at the state and national level. Recent studies have indicated a relationship between ADI and health outcomes for multiple conditions, such as morbidity in pediatric acute lymphoblastic leukemia and rate of pediatric pedestrian versus motor vehicle collisions. However, there is limited data available regarding the relationship between ADI and types of pediatric acquired brain injuries (ABI). As such, the current study sought to understand the relationship between ADI and types of pediatric ABI.
Methods	Participants included N = 408 pediatric patients from a Level 1 Pediatric Trauma center referred for the inpatient neuropsychological consultation service from January 2019 to September of 2022. Non-parametric (Kruskal Wallace) ANOVA were conducted to explore the relationships between types of pediatric ABI and ADI.
Results	The ADI converted to a 10 point scale. Mean sample ADI was 6.21 with a standard deviation of 3.19. Approximately 30% of individuals within the current sample were within the lowest two SES deciles. Findings suggest that children with lower ADI are at higher risk for obtaining certain ABI, such as non-traumatic brain injury n=41), penetrating TBI secondary to gunshot wounds (n=11), seizure emergency (n=9), as well as presentations related to illness or infections (i.e., empyema; N=33). Nonparametric ANOVA identified differences in ADI based on injury type [$H(12)=38.63$, $p<.001$)].
Conclusions	Our findings underscore the relationships between ADI and injury characteristics within a pediatric ABI population. Results of the current study suggest that lower socioeconomic status acts as a risk factor for non-accidental trauma, penetrating TBI, seizure emergencies, and illness or infections (e.g., empyema). Consistent with previous literature, children who present with ABI secondary to non-accidental injury, gun violence, and seizure/complex illness are at higher risk for adverse social determinants of health or who are currently experiencing complex psychosocial stressors. The relationship between penetrating TBI and ADI in the current sample is also highly concerning given the increase in firearm related violence in the catchment area of the hospital at which this study was conducted. Given that socioeconomic status has also been related to medical complications in children who have sustained ABI as well as increased risk for unrecognized/unmet needs post-discharge, it is our goal to expand upon these preliminary results in order to identify additional risk factors that may influence follow-up with medical care and identify unrecognized/unmet needs in vulnerable populations.
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Category	Other Research Related Topics, #135
Primary Author	Danica Vendiola, B.S.
Secondary Authors	Amy Pan, PhD, Jennifer Andres, MBA, BSN, Nicole Fabus, B.S. Nutritional Science, Melissa M. Froh, BA, MS, Rebeccsa Heisler, Dietetics, Miranda R. Privatt, BS, Mary R C Seidl, MSN, Martin K. Wakeham, MD, Theresa Mikhailov, MD, PhD
Title	Improved Caloric Goal Documentation in the Pediatric Intensive Care Unit through Modification of Standardized Documentation
Introduction	Nutrition is an important aspect of care when treating critically ill children, with malnutrition prevalent among children admitted to the pediatric intensive care unit (PICU). Studies show worsened clinical outcomes for patients who suffer from malnutrition. Previous research states that early enteral nutrition within 48 hours of admission is associated with better health outcomes. Additionally, research shows that an early estimation and documentation of caloric goals in the electronic health record (EHR) is associated with higher daily energy intake. Establishing early caloric goals is often missing in medical charts due to various reasons, including the availability of a registered dietitian (RD). One approach to increase caloric goal documentation is to standardize the EHR with system prompts. By revising critical care progress notes to prompt providers to estimate a caloric goal when no caloric goal has already been documented by a RD within the first 48 hours, we expect an increased rate of goal documentation. Increase documentation of a caloric goal within 48 hours of PICU admission for all children by 20%.
Methods	The Plan-Do-Study-Act (PDSA) quality improvement method was used. We obtained de-identified data from the Children's Wisconsin PICU through the local Virtual Pediatric Systems, LLC database (VPS). Between May 2020 and April 2021, we obtained baseline data of the frequency of estimated caloric goal documentation within the first 48 hours of PICU admission. A smart link prompt was developed and incorporated into the EHR progress notes templates in May 2021 (see Figures 1 and 2). We monitored the monthly rate of documentation of caloric goals within 48 hours of admission by critical care providers up to April 2022. To analyze and monitor the results, we used a statistical control (p-chart).
Results	The baseline rate of documentation of an estimated caloric goal within 48 hours of admission was 44% (May 2020-April 2021). Upon adding standardized prompts to the EHR system, the rate of documented caloric goal intake within 48 hours of admission by critical care providers was greater than 90% (see Figure 3).
Conclusions	Utilizing automated systems-based prompting in EHRs resulted in an increased frequency of caloric goal documentation exceeding 90% monthly. Establishing a standardized prompting system within the EHR directly led to an overall increased frequency of caloric goal documentation. Future steps are to analyze if the increased documentation led to a direct increase in initiation of enteral nutrition and caloric intake as well as improved health outcomes.

Category	Other Research Related Topics, #136
Primary Author	Eve Prodoehl
Secondary Authors	Adam J. Kanack, PhD Nancy Dahms, PhD
Title	Platelet and Myeloid Cell Phenotypes in a Rat Model of Fabry Disease and the Role of Glycosphingolipids in Sensitizing Platelets to Agonist-induced Activation
Introduction	Fabry disease is an X-linked lysosomal storage disorder caused by deficiency of the lysosomal enzyme â•º-Galactosidase-A (â•º-GalA). Fabry disease results from the widespread accumulation of the glycosphingolipids (GSLs) globotriaosylceramide (Gb3), and globotriaosylsphingosine (lyso-Gb3), impacts multiple organ systems and leads to impaired quality of life. Thrombotic events are common, with strokes and heart attacks contributing to a shortened lifespan for male and female Fabry patients. Previously we showed GSL accumulations in the bone marrow, circulation, and platelets from male â•º-Gal A-deficient rats contribute to increased platelet activation in response to agonists. However, the extent that these GSLs accumulate in the female Fabry population and the mechanisms by which Gb3 and lyso-Gb3 increase thrombotic risk are incompletely defined.
Methods	Using a rat model of Fabry disease, we aim to improve our understanding of GSL accumulation among female animals and define the mechanisms linking GSL accumulation to thrombotic disease. Using a flow cytometric assay quantifying fibrinogen binding to the integrin GPIIb/IIIa, we assessed the activatability of platelets after treatment with the platelet agonist ADP.
Results	In contrast to Fabry male rats, we found that â•º-GalA-deficient female rats do not present with an increased platelet activation response to ADP. Notably, in the bone marrow of 52-week-old female Fabry rats, histological staining of femur sections with Griffonia simplicifolia isolectin B4 (IB4), a lectin with high affinity for terminal Î±-galactose, revealed striking accumulations of GSLs. Further staining with CD68 and CD3 showed elevated levels of monocytes and lymphocytes, consistent with what is seen in the circulation. Additionally, complete blood counts (CBCs) revealed that at 15 weeks, homozygous Fabry female rats had significant increases in lymphocyte and monocyte counts compared to wild-type (WT) females. This trend is seen from 15-75 weeks of age and indicates that homozygous Fabry females have chronically high levels of white blood cells in their circulation. Additional CBC data showed a significant difference in the mean platelet count of WT and homozygous Fabry females at 50-75 weeks. Lastly, we assessed the ability of â•º-GalA substrates to sensitize platelets to activation using WT male and female platelets from 50â€“75-week animals by incubating WT platelets with various GSLs and concentration ranges. WT platelets incubated with 10 ÂµM Gb3 and 2 ÂµM lyso-Gb3, GSLs that accumulate in Fabry patients, as opposed to 10 ÂµM glucocerebroside and 2 ÂµM lyso-glucocerebroside, significantly increased platelet activation and binding to fibrinogen, even without ADP.
Conclusions	Together, these data suggest that chronically high concentrations of the Fabry-associated GSL, Gb3 directly contribute to an increased level of baseline platelet activation even in the absence of exogenous platelet agonists.(NIH K12HL141954 to AK and NMD, R01DK042667 to NMD)
Acknowledgements	We thank the Children's Research Institute Histology Core at the Medical College of Wisconsin for providing technical assistance with slide preparation, staining and imaging. We also thank the Flow Cytometry Core at Versiti Blood Research institute for assistance with machine use and data acquisition. This work was supported by NIH K12HL141954 to AK and NMD, and by R01DK042667 to NMD.
Reference 1	Germain DP. Fabry disease. Orphanet J Rare Dis. 2010 Nov 22;5:30. doi: 10.1186/1750-1172-5-30. PMID: 21092187; PMCID: PMC3009617
Reference 2	Kanack AJ, Aoki K, Tiemeyer M, Dahms NM. Platelet and myeloid cell phenotypes in a rat model of Fabry disease. FASEB J. 2021 Aug;35(8):e21818. doi: 10.1096/fj.202001727RR. PMID: 34320241; PMCID: PMC8341388
Reference 3	Schindelin, J., Arganda-Carreras, I., Frise, E., Kaynig, V., Longair, M., Pietzsch, T., â€¦ Cardona, A. (2012). Fiji: an open-source platform for biological-image analysis. Nature Methods, 9(7), 676â€“682. doi:10.1038/nmeth.2019

Category	Other Research Related Topics, #137
Primary Author	Iaong Vang, BS.
Secondary Authors	Owen Bowie, BS, MPH, Angel Li, BS, MSE, Kajua Lor, Pharm D, BCACP
Title	Evaluation of a Health Equity Curriculum to Improve Cultural Competence with Asian American Native Hawaiian Pacific Islanders (AANHPI)
Introduction	AANHPIs (Asian Americans, Native Hawaiians, and Pacific Islanders) make up 6.1% of the United States population. Cultural competence training is needed with healthcare providers to deliver quality care. This study evaluated the impact of the Health Advancement for Asian Pacific Islanders through Education (HAAPIE) Initiative, a health equity curriculum.
Methods	An online self-paced learning curriculum with 6 modules was developed and available to Medical College of Wisconsin affiliates. Participants completed an electronic pre- and post-survey which contained 5 domains and 69 items. The pre-survey questions were adapted from the Clinical Cultural Competency Questionnaire, a validated survey tool that measures cultural competency. Survey results were evaluated using paired T-tests.
Results	Out of 77 interested participants and pre-surveys, 60 enrolled in the curriculum (77.9%) and 22 completed post-surveys (28.6%). On a 5-point Likert scale, pre-survey results showed supportive attitudes towards the AANHPI population (mean=4.17, SD=0.99) and the importance of learning about this population and their health disparities (mean=4.73, SD=0.7). However, results also indicated a lack of training in cultural diversity (mean=1.9, SD=1.17), little educational experience in AANHPI health (mean=2.62, SD=1.07), cultural awareness, knowledge (mean = 2.98, SD = 1.14), comfort in complex situations (mean=2.61, SD=1.22), and skills (mean=2.32, SD=1.08). Evaluation of the impact of the pilot curriculum showed statistically significant improvements in all fields ($p<0.05$).
Conclusions	The HAAPIE initiative highlighted and addressed the need for training on AANHPI health. This novel curriculum improved attitudes, knowledge, and skills working with AANHPI populations. Future directions include analyzing the impact of curriculum modules and expanding HAAPIE nationwide.

Category	Other Research Related Topics, #138
Primary Author	Salomao Doria Jorge
Secondary Authors	Young-In Chi, Jose Lizarraga Mazaba, Thiago Milech De Assuncao, Angela J. Mathison, Gwen Lomberk, Michael T. Zimmermann and Raul Urrutia
Title	Integrative Modeling, Molecular Mechanics, and Molecular Dynamics Evaluation of Genomics Variants in KMT2C (MLL3), a Gene Involved in Kleefstra Syndrome II
Introduction	Kleefstra Syndrome (KS) is a genetic, neurodevelopmental disorder characterized by intellectual disability, infantile hypotonia, severe expressive language delay, and characteristic facial appearance, with a spectrum of other distinct clinical manifestations. Pathogenic mutations in the epigenetic modifier type 2 lysine methyltransferase KMT2C have been identified to be causative in KS individuals that are EHMT1 mutation-negative, but with a phenotype resembling the core features of KS. These individuals are designated as having KS type 2.
Methods	In this study, we made use of multidimensional approaches, including standard variant annotation, paralog annotation analyses, molecular mechanics, and molecular dynamics simulations, to understand and to enhance the annotation and potential mechanisms by which the variants can affect the KMT2C function.
Results	We developed a scoring system based on statistical integration and modeling of data derived from the structure and dynamics of KMT2C, to classify variants into SV (Structural Variants), DV (Dynamic Variants), SDV (Structural and Dynamic Variant), and VUS (Variant of Uncertain Significance). These variants showed values reflecting alterations in molecular fitness when compared with control tolerated ones. In addition, our study shows that further investigation, including molecular dynamics, provides us with data that is more refined compared to current annotation tools used in human genomics databases. Our built 3D models for variants presented in the ordered domain regions suggested distinct mechanisms that lead to their imbalance and are likely not predictable from sequence alone.
Conclusions	Collectively, our data demonstrate that the missense variants studied here are damaging to KMT2C function by different mechanisms. This new knowledge extends our understanding of molecular mechanism underlying the dysfunction of KS type 2-associated genomic mutations. The identification of KMT2C mutation-specific druggable conformations may pave the way to the future development of small molecules to ameliorate the symptoms of this disease.
Acknowledgements	This study was supported in part by the Linda T. and John A Mellowes Endowed Innovation and Discovery Fund

Biochemistry

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

Research Facilities

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

Applications include:

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

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

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

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

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

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

Richard Bohnsack, MS
414-955-4699 | bohnsack@mcw.edu

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

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

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

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

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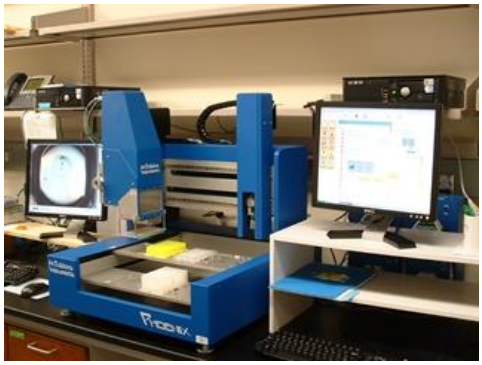
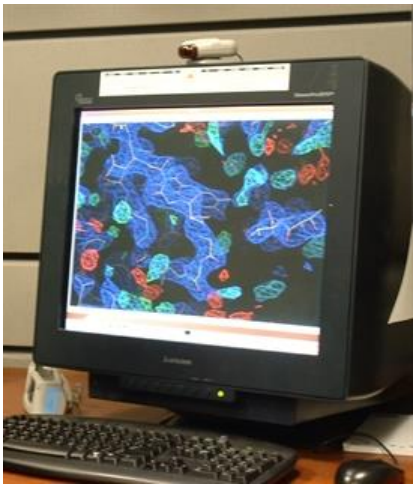
Francis Peterson, PhD
fpeterson@mcw.edu | (414) 955-5777

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



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

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

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

Linda Olson, PhD
lolson@mcw.edu | 955-8545

Shared Research Instrumentation

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

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

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

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

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

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

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

Program in Chemical Biology

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

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

For more information or discussion contact:

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

Biomedical Engineering

DEPARTMENT OF BIOMEDICAL ENGINEERING

MARQUETTE UNIVERSITY

MEDICAL COLLEGE OF WISCONSIN

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

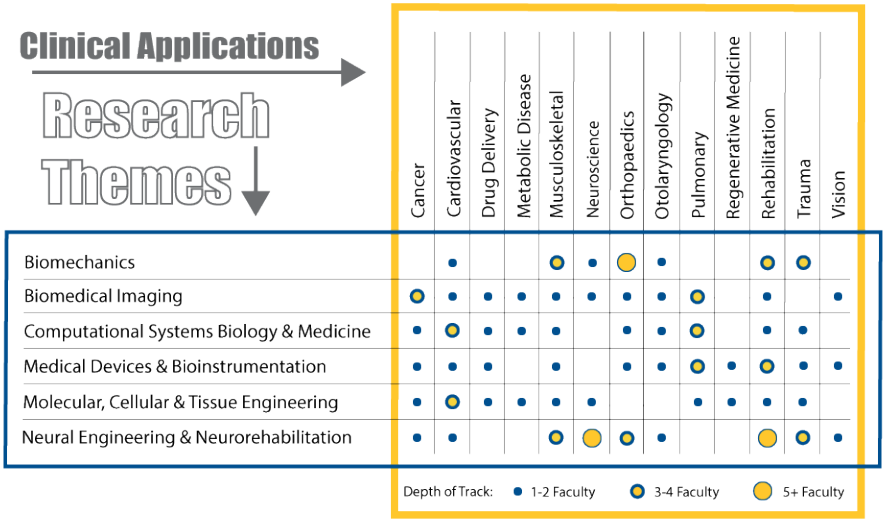
Mission

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

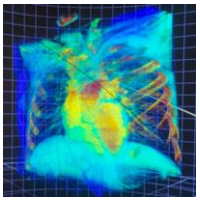
Goals

- 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

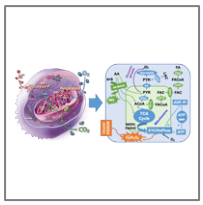
Research in the Joint Department is led by our team of world-class researchers and can be described by our six research themes and thirteen featured clinical applications. Where research themes indicate a specialization as it relates to the field of engineering, clinical applications reveal the biological or medical utility of various lines of inquiry. The grid, in its entirety, demonstrates the immense depth and breadth of the research projects currently underway in our laboratories, with opportunities for collaboration, innovation and education intrinsically tied to each.



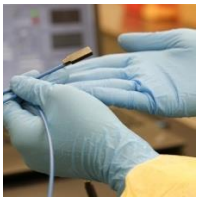
Biomechanics & Rehabilitation Bioengineering
Simply put, Biomechanics is the study of the structure, function and motion of the mechanical aspects of biological systems. When applied to the human body, biomechanics describes how muscles, bones, tendons, and ligaments work together to produce movement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



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

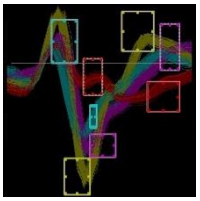


Computational Systems Biology & Medicine
Computational Modeling is the practice of using computer models and systems to simulate complex biological processes. Computational modeling has many applications in medicine, which include improving our understanding of human physiology, visualizing and interpreting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



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

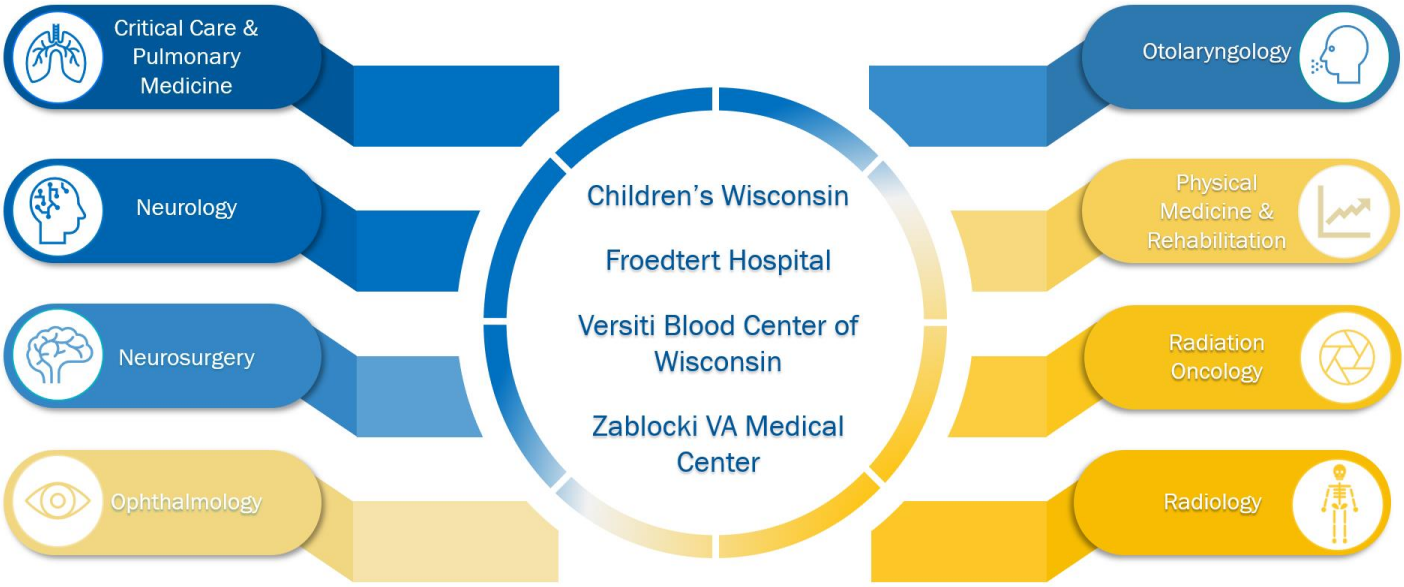
Molecular, Cellular & Tissue Engineering
Tissues may become damaged due to injury or disease. Molecular, Cellular, and Tissue Engineering is a research specialization in Biomedical Engineering which seeks to repair or replace damaged tissues—such as heart valves, blood vessels, skin, cartilage, or bone—by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



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

Clinical Collaborations

The Joint Department provides tremendous opportunities to conduct research involving MCW clinical partner locations throughout the region. This exposure is second to none among biomedical engineering programs around the country, offering an amazing array of research opportunities in close proximity to campus.



Educational Opportunities

The Joint Department remains committed to creating educational opportunities for the next generation of physicians, researchers, and engineers. In addition to our already robust program of undergraduate and graduate research opportunities, the Joint Department has recently launched a new graduate certificate program that provides clinical immersion experiences for professionals working in the medical device design industry. Students seeking the *Clinical Immersion in Medical Device Design* certificate will master the etiquette and skills of successful clinical immersion and develop observational research techniques that are used to uncover new design opportunities.

For more information about this new program, including application requirements and deadlines, **visit the Marquette University Graduate School website**.

People

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

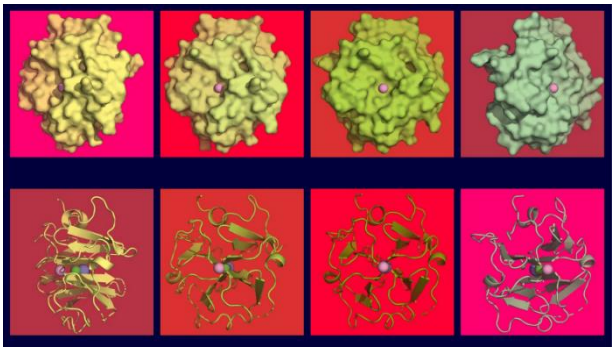
Biophysics

The Department of Biophysics at MCW has a rich history of innovative research focused on questions related to protein structure and function, biomedical imaging, membrane biology, and redox biology. Our unique expertise in technology development spans the range of magnetic resonance technology, computational methods for biophysics and image analysis, and chemical biology.

Our state-of-the-art research resources support molecular biophysics, structural biology, biomedical imaging, and high-performance computing. They are supported by an engineering complex that includes a microwave lab and a machine shop. The Department is committed to research excellence and dedicated to training the next generation of graduate and postdoctoral scientists in a hands-on, informal atmosphere.

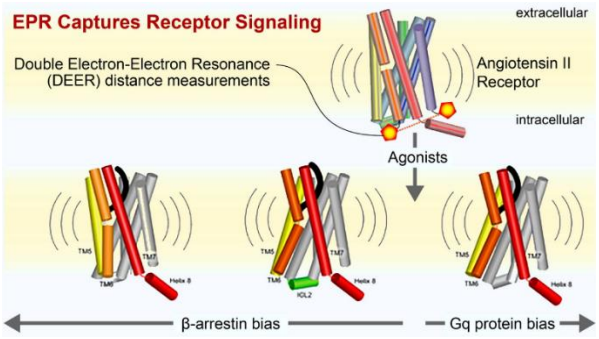
Structural Biology

Knowing the structures, dynamics, and interactions of biological molecules is essential for understanding how they function in human health or misfunction in disease. Faculty, staff, and students in the Department of Biophysics develop and use a wide array of technologies to gain insights about biomolecular structures and functions. Research projects focus on receptor signaling, drug resistance, microbial pathogenesis, redox biology, and diseases of aging. State-of-the-art resources are available for electron paramagnetic resonance (EPR), nuclear magnetic resonance (NMR), X-ray crystallography, molecular dynamics simulations, and cryo-electron microscopy.



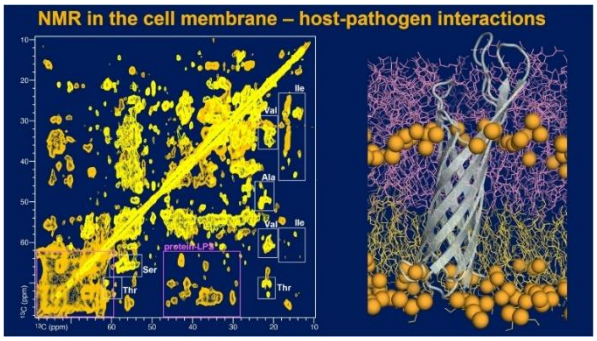
Biomedical Electron Paramagnetic Resonance

EPR is a powerful technology for characterizing the structures and dynamics of biomolecules *in vitro*, in cells, and in many other biological specimens. We are home to the National Biomedical EPR Center, the most extensive EPR resource in the nation. Research focuses on developing and applying new EPR technologies to address biological questions related to receptor signaling in cancer and vascular diseases, drug resistance, microbial pathogenesis, redox biology, and diseases of aging. The EPR Center houses an array of internally developed and commercial state-of-the-art instrumentation.



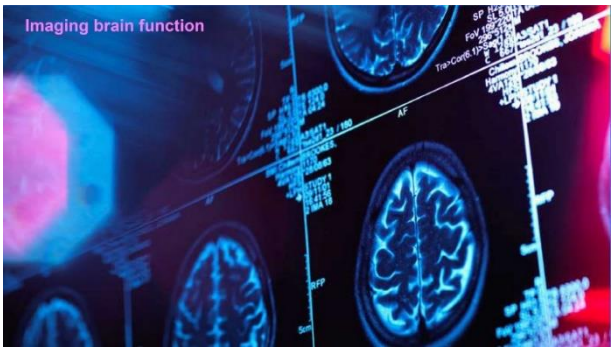
Biomedical Nuclear Magnetic Resonance

Understanding the mechanisms of protein function is critical for gaining biomedical insights about human health and for therapeutic drug development. NMR is ideally suited for this because it is capable of reporting on very small structural changes, very weak intermolecular interactions, and multiple scales of dynamics. Our state-of-art NMR laboratory allows us to examine the structures, dynamics, and interactions of biomolecules in complex multi-component assemblies, including cells and other types of native samples to address problems in cancer, microbial pathogenesis, and diseases of aging.



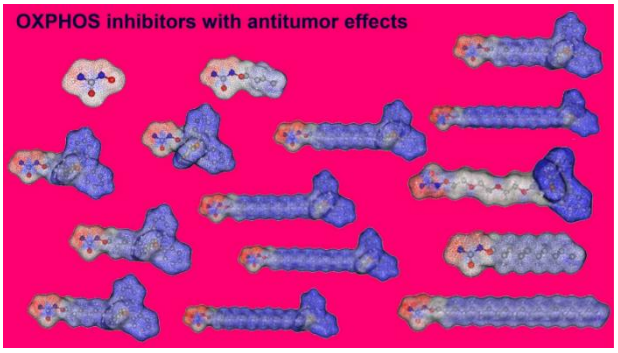
Biomedical Magnetic Resonance Imaging

We are pioneers in functional MRI (fMRI). MCW students and faculty published the first papers on fMRI and resting-state fMRI in 1992 and 1995, respectively. Today, MCW continues to be at the forefront of MRI research, with extensive focus on both technology development and clinical applications, including coil design, MRI methods, image analysis, and clinical applications of MRI to early disease detection and treatment efficacy in neurological and psychiatric disorders, Alzheimer's disease, cancer, chronic pain mechanisms, psychiatric depression, and other fields in neuroscience.



Redox Biophysics

We are recognized internationally for our contributions to free radical and redox biology. Research focuses on understanding the roles of free radicals and oxidants in health and conditions like cardiovascular diseases, neurodegeneration, and cancer. We develop novel molecular tools that allow us to probe the generation of free radicals in cells and *in vivo*, using fluorescence, bioluminescence, and EPR detection. Collaborations with clinicians provide insights about the roles of oxidants in human disease and advance the development of therapeutic drugs for treating neurodegeneration and cancer.



Biophysics Graduate Program

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

Centers

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

More Information

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

National Biomedical EPR Center

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

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

staff with broad experience across many fields."

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

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

Cell Biology, Neurobiology, and Anatomy

Cell Biology, Neurobiology, and Anatomy Cell Biology, Neurobiology & Anatomy (CBNA) is one of the seven 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 Fusion Curriculum courses. We have recently welcomed several new Faculty to MCW, who will enhance collaborative projects across our basic and clinical enterprise and bring new technologies and capabilities to campus. These Faculty provide expertise in neuronal signaling, high resolution microscopy and drug discovery. For further information, please visit our department website: http://www.mcw.edu/cellbiology.htm

Microbiology & Immunology

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

Microbiology & Immunology

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

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

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

Center for Immunology

The Center for Immunology Program consists of a highly collaborative and integrated group of scientists from the Medical College of Wisconsin, Blood Research Institute and Children's Research Institute whose goal is to promote immunological education and research on campus at both the basic and clinical level. the Center for Immunology is composed of research laboratories focused on the immunological aspects of autoimmunity, infectious disease, allergy, immunodeficiency and cancer and is forging new links to physician colleagues at Froedtert Hospital and the Children's Hospital of Wisconsin. Graduate research training in immunology is offered through the Microbiology and Immunology graduate program. The Immunology Group sponsors a number of campus wide events offering additional training in immunology including a weekly journal club and Work-in-Progress.

Faculty Research Expertise:

John Kirby, PhD: Chair. 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 Associate Director for the Medical Scientist Training Program (MSTP).

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

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

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

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

Amy Hudson, PhD: 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.

Many viruses, including all known members of the Herpesvirus family, target antigen presentation by class I MHC molecules as a means of undermining the anti-viral immune response. We focus on two recently discovered human herpesviruses, HHV-6 and -7. Little is known about the immunobiology of these two beta-herpesviruses. They are most closely related to human cytomegalovirus (HCMV), and like all other herpesviruses, HHV-6 and -7 remain latent or establish persistent infections. Thus, it seemed likely that HHV-6 and -7 would also encode unique mechanisms of immune evasion. Because so many of the viral immunoevasins affect trafficking or stability of class I MHC molecules, we took a biochemical approach to examine the maturation and stability of class I molecules in HHV-7-infected T cells.

Christopher Kristich, PhD: Dr. Kristich uses genetic, molecular, biochemical, and genomic experimental approaches to understand (1) the mechanisms by which Gram-positive bacteria sense internal and external stimuli (the input), (2) how these signaling systems control cellular processes in response to environmental conditions (signal processing); and (3) the biochemical mechanisms of antimicrobial resistance and gut colonization (the output). His goal is to understand all aspects of the sensory process: to define the signals that are sensed, to understand the signal transduction processes mechanistically, to identify the corresponding physiological or behavioral output, and to elucidate how that output – the product of the signal transduction processes – enhances the ability of

the bacteria to survive and proliferate in their natural settings. He approaches problems of bacterial signal transduction in the context of basic bacterial physiology, host-microbe interactions, and microbial pathogenesis, with the goal of understanding how fundamental bacterial signaling processes serve to shape the outcome of interactions with human hosts and the environment.

Robert Lochhead, PhD: The Lochhead Lab focuses on mechanisms of arthritis pathogenesis, using animal models of Lyme arthritis and clinical samples collected from patients with various types of arthritis. Much of our research focuses on Lyme disease, caused by infection with the tick-borne pathogen *Borrelia burgdorferi* (Bb). Lyme disease is the most common vector-borne disease in the U.S., and is reaching epidemic levels in many regions, including the Upper Midwest. Lyme disease is an infection-induced multi-system disorder affecting skin (erythema migrans), heart (carditis), joints (arthritis) or neurologic tissue (neuro-borreliosis). Lyme arthritis (LA) is the most common late-stage manifestation of Lyme disease. Although most patients are effectively treated with antibiotics, 10-20% of treated patients develop post-infectious Lyme arthritis, potentially resulting in months or years of disability. Identifying immune factors that contribute to variability in disease severity and treatment outcome is critically important for public health in Lyme-endemic communities such as Wisconsin. By studying LA, we hope to gain important insights into how infection may trigger immune dysregulation, leading to tissue damage, arthritis, and autoimmunity.

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

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

Scott Terhune, PhD: Our research focuses on determining the molecular functions of human cytomegalovirus (HCMV) proteins during infection and disease. HCMV is a member of the beta-herpesvirus family of viruses which includes HHV-6 and 7. Infection occurs upon exposure to virus-containing body fluids, is life-long and generally asymptomatic in healthy children and adults. However, during pregnancy, HCMV infection may result in congenital birth defects including hearing loss and neurological damage. In immunologically immature or compromised children and adults, infection often results in life threatening diseases. And, increasing evidence suggestions that persistent life-long HCMV infection is associated with numerous chronic diseases including atherosclerosis, immuno-senescence, cancer and possibly Alzheimer's Disease.

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

Renren Wen, PhD: The Wen lab has two different but interconnected research focuses. One focus of the Wen lab is aimed at understanding the signaling pathways that govern proper T and B cell activation and communications and how aberrant signaling in T and B cells will lead to human diseases. The lab has studied the mechanisms by which molecules in antigen receptor signaling pathways, such as phospholypase C gamma (PLCγ) and B-cell lymphoma 10 (Bcl10) and molecules in cytokine signaling pathways, including Grb2-associated binding (Gab) proteins in controlling and modulating T and B cell development and activation and how aberrant functions of these molecules lead to lymphopenia and autoimmunity. Studies are performed primarily in gene edited mouse models. The second and the current major focus of the Wen lab is to understand the interplay between immune system and coagulation system in healthy and disease states. Currently, the lab is studying how antibodies regulate the function of platelets and other cells involved in the coagulation system, and the prevalence, ontogeny, activation, and regulation of B cells that make such antibodies in healthy people and in patients with heparin-induced thrombocytopenia and thrombosis (HIT) or COVID-19. Studies will

be performed in both human and mouse systems with the goal of understanding the molecular pathogenesis underlying antibody mediated thrombotic complications in HIT and COVID-19 and developing new diagnostic and therapeutic tools for these conditions.

Xue-Zhong Yu, MBA, MS, MD: The research scope of Dr. Yu's laboratory (Yu Lab) is in tumor immunology and cancer immunotherapy. The researchers in Yu's Lab have been focusing on two lines of basic and translational studies: (1)Allogeneic Hematopoietic Cell Transplantation (allo-HCT). Acting through donor lymphocyte-mediated mechanisms termed the graft-versus-leukemia (GVL) effect, allo-HCT is an effective therapy for hematological malignancies such as leukemia. However, graft-versus-host disease (GVHD) remains a prominent cause of transplant-related morbidity and mortality after allo-HCT. The Yu Lab focuses on defining the cellular and molecular mechanisms that regulate the pathogenicity of allogeneic T and B cells in GVHD, and on developing new and effective therapies to prevent and treat GVHD. (2) Adoptive T-cell Therapy (ACT). The adaptive immune system has the capacity to recognize and kill malignant cells. However, immune tolerant mechanisms that normally protect healthy tissues from autoimmune attack prevent the development of effective anti-tumor immunity. Aiming at understanding T-cell response against tumor and promoting anti-tumor activity, Yu Lab is interested in investigating T-cell activation, differentiation, persistence, migration, and metabolism in immunotherapy against cancer.

Pharmacology and Toxicology

The **Department of Pharmacology & Toxicology** at MCW has a long history of research excellence. Our departmental research culture is highly collaborative, supportive of faculty and trainees, and encourages impactful and creative science focused on advancing our understanding of potential drug targets and guiding therapeutics. Supported by the Cancer, Cardiovascular, and Neuroscience Research Centers of Excellence at MCW, the department has established three major areas of research strength focused on cancer pharmacology, cardiovascular pharmacology, and neuropharmacology. Departmental themes, such as signaling, structural biology, and therapeutics, provide connections among these research areas and support collaboration among labs. Translational efforts in the department involve medication development, including projects supported by our Therapeutic Accelerator Program (TAP), and community-engaged research focused on health disparities, cancer, opioid overdose, and mental health. The department's research culture is growing with the goal of maintaining its status as a leader in pharmacological research and as a destination department for outstanding researchers and trainees. Overviews of our departmental research themes are provided below:

Cancer Research

Our faculty members are discovering more effective methods of preventing, diagnosing, and treating cancer by conducting research that defines the biochemical, metabolic, and genetic abnormalities that cause cancer. The majority of these research programs focus on breast, pancreas, lung, and prostate cancers, which are among the most common or deadly cancers. Cancer research is expanding in the department, aligning with the strategic goals of the MCW Cancer Center to grow strengths in precision oncology, structural and chemical biology, immuno-oncology, and cancer metabolomics. Primary faculty researchers include Drs. Guan Chen, Wei Liu, Carol Williams, and Lan Zhu.

Cardiovascular Research

Heart disease remains the leading cause of death in the United States despite many advances. A number of faculty within the MCW Department of Pharmacology and Toxicology conduct research aimed at understanding the underlying drivers of cardiovascular disease and are focused on elucidating its root causes. To investigate the many features of this complex disease, research within the Department spans all major scientific areas of the MCW Cardiovascular Center, including atherosclerosis, thrombosis, vascular biology, cardiac biology and heart failure, and hypertension. Primary faculty researchers include Drs. John Auchampach, William Campbell, Sandra Pfister, and Michael Thomas.

Neuroscience Research

Neuroscience research in Pharmacology & Toxicology is focused on understanding healthy and pathological brain function with the goal of guiding pharmacotherapeutic interventions for neurological and neuropsychiatric diseases. Departmental strengths include research focused on the neurobiology of addiction and motivated behavior, the impact of stress on the brain, processes that contribute to traumatic brain injury, synaptic biology/physiology as it relates to brain disease, and endocannabinoid systems. Neuroscience research is expanding in the department in partnership with the Neuroscience Research Center with recent emphasis on neuroinflammation, neuroimmunology and neurodevelopment. Primary faculty researchers include Drs. Coti Garcia-Keller, Cecilia Hillard, Sang Lee, Qing-song Liu, Christopher Olsen, and John Mantsch.

Physiology

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

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

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

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

Summary of Faculty Research Programs:

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

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

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

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

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

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

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

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

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

- Mouradian GC Jr., Alvarez-Argote S, Gorzek R, Thuku G, Michkalkiewiz T, Wong-Riley MTT, Konduri GC, Hodges MR. Acute and chronic changes in the control of breathing in a rat model of bronchopulmonary dysplasia. *Am J Physiol Lung Cell Mol Physiol* 316: L506-L518, 2019.
- Burgraff NJ, Neumueller SE, Buchholz K, Hodges MR, Pan P, Forster HV. Glutamate receptor plasticity in brainstem respiratory nuclei following chronic hypercapnia in goats. *Physiol Rep*, 7: e14035, 2019.

- Puissant MM, Muere C, Levchenko V, Manis AD, Martino P, Forster HV, Palygin O, Staruschenko A, Hodges MR. Genetic mutation of Kcnj16 identifies Kir5.1-containing channels as key regulators of acute and chronic pH homeostasis. *FASEB J* 33:5067-5075, 2019.

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

- Chuppa S, Liang M, Liu P, Liu Y, Casati MC, Cowley AW, Patullo L, Kriegel AJ. MicroRNA-21 regulates peroxisome proliferator-activated receptor alpha, a molecular mechanism of cardiac pathology in Cardiorenal Syndrome Type 4. *Kidney International* 93:375-389, 2018.

- Kriegel AJ, Terhune SS, Greene AS, Noon KR, Pereckas MS, Liang M. Isomer-specific effect of microRNA miR-29b on nuclear morphology. *J Biol Chem* 293:14080-14088, 2018.

- Nasci VL, Chuppa S, Griswold L, Goodreau KA, Dash RK, Kriegel AJ. miR-21-5p regulates mitochondrial respiration and lipid content in H9C2 cells. *Am J Physiol Heart Circ Physiol* 316:H710-H721, 2019.

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

- Mansilla AM, Sompallae RR, Nishimura CJ, Kwitek AE, Kimble MJ, Armstrong ME, Campbell CA, Smith RJ, Thomas CP, Targeted Broad-Based Genetic Testing by Next Generation Sequencing Informs Diagnosis and Facilitates Management in Patients with Kidney Diseases. *Nephrology Dialysis Transplantation* (in press) 2019.

- Ma MCJ, Pettus JM, Jakoubek JA, Mennie AK, Kwitek AE, Contribution of Independent and Pleiotropic Genetic Effects in the Metabolic Syndrome in a Hypertensive Rat. *PLoS One* 12:e0182650, 2017.

- Wang J, Ma MCJ, Mennie AK, Pettus JM, Xu Y, Lin L, Traxler MG, Jakoubek J, Atanur SS, Aitman TJ, Xing Y, Kwitek AE, Systems Biology with high-throughput sequencing revealed genetic mechanisms underlying the metabolic syndrome in the Lyon Hypertensive Rat. *Circ Cardiovasc Genet* 8:316-326, 2015.

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

- Xue H, Geurts AM, Usa K, Wang F, Lin Y, Phillips J, Henderson L, Baker MA, Tian Z, Liang M. Fumarase Overexpression Abolishes Hypertension Attributable to endothelial NO synthase Haploinsufficiency in Dahl Salt-Sensitive Rats. *Hypertension* 74:313-322, 2019.

- Liang M. Epigenetic Mechanisms and Hypertension. *Hypertension* 72:1244-1254, 2018.

- Widlansky ME, Jensen DM, Wang J, Liu Y, Geurts AM, Kriegel AJ, Liu P, Ying R, Zhang G, Casati M, Chu C, Malik M, Branum A, Tanner MJ, Tyagi S, Usa K, Liang M. miR-29 contributes to normal endothelial function and can restore it in cardiometabolic disorders. *EMBO Mol Med* 10: e8046, 2018.

Ziqing Liu, PhD: The long-term goal of the Liu lab is to develop novel strategies for cardiovascular regeneration. To achieve this goal, Dr. Liu explores new approaches of making cardiomyocytes and blood vessels by elucidating the molecular mechanisms of direct cardiac reprogramming and vascular development and repair. She investigates these questions by combining state-of-the-art omics approaches with genetic mouse models and human cell culture systems.

- Liu Z, Wang L, Welch JD, Ma H, Zhou Y, Vaseghi HR, Yu S, Wall JB, Alimohamadi S, Zheng M, Yin CY, Shen WN, Prins JF, Liu JD, Qian L (2017). Single Cell Transcriptomics Reconstructs Lineage Conversion from Fibroblast to Cardiomyocyte. *Nature* 551, 100-104.

- Zhou Y*, Liu Z*, Welch JD, Gao X, Wang L, Garbutt T, Keepers B, Ma H, Prins JF, Shen WN, Liu JD, Qian L (2019). Single-Cell Transcriptomic Analyses of Cell Fate Transitions during Human Cardiac Reprogramming. *Cell Stem Cell* 25 (1), 149-164. *co-first author.

- Liu Z, Ruter DL, Quigley KM, Tanke N, Jiang Y, Bautch VL (2021). Single-Cell RNA Sequencing Reveals Endothelial Cell Transcriptome Heterogeneity under Homeostatic Laminar Flow. *Arteriosclerosis, Thrombosis, and Vascular Biology*. 2021 Aug 26: ATVBAHA121316797. Featured article of the issue.

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

- Wodsedalek DJ, Paddock SJ, Wan TC, Auchampach JA, Kenarsary A, Tsaih SW, Flister MJ, O'Meara CC. IL13 Promotes in vivo neonatal cardiomyocyte cell cycle activity and heart regeneration *Am J Physiol Heart Circ Physiol* 316:H24-H34, 2019.

- Flinn MA, Jeffery BE, O'Meara CC, Link BA. Yap is required for scar formation but not myocyte proliferation during heart regeneration in zebrafish. *Cardiovasc Res* 115:570-577, 2019.

- O'Meara CC, Wamstad JA, Gladstone RA, Fomovsky GM, Butty VL, Shrikumar A, Gannon JB, Boyer LA, Lee RT. Transcriptional reversion of cardiac myocyte fate during mammalian cardiac regeneration. *Circ Res* 116:804-815, 2015.

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

- Mukohda M, Fang S, Wu J, Agbor LN, Nair AR, Ibeawuchi SC, Hu C, Liu X, Lu KT, Guo DF, Davis DR, Keen HL, Quelle FW, Sigmund CD. RhoBTB1 protects against hypertension and arterial stiffness by restraining phosphodiesterase 5 activity. *J Clin Invest* 130:2318-2332, 2019.

- Agbor LN, Nair AR, Wu J, Lu KT, Davis DR, Keen HL, Quelle FW, McCormick JA, Singer JD, Sigmund CD. Conditional deletion of smooth muscle Cullin-3 causes severe progressive hypertension. *JCI Insight* 5: e129793, 2019.

- Nair AR, Silva SD Jr, Agbor LN, Wu J, Nakagawa P, Mukohda M, Lu KT, Sandgren JA, Pierce GL, Santillan MK, Grobe JL, Sigmund CD. Endothelial PPARγ (Peroxisome Proliferator-Activated Receptor-γ) Protects From Angiotensin II-Induced Endothelial Dysfunction in Adult Offspring Born From Pregnancies Complicated by Hypertension. *Hypertension* 74:173-183, 2019.

Physiology Biochemical Analytical Lab

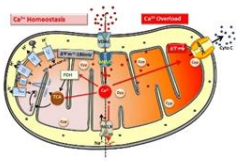
The Physiological Biochemical Analytical Laboratory (Biochemical Assay Lab) provides a consolidated, highly specialized, well equipped and professionally staffed analytical laboratory capable of performing a wide variety of immunoassays, HPLC based assays, clinical chemistry and biochemical analyses.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

Anesthesiology

The Department of Anesthesiology's commitment to the evolution of Anesthesiology and advancement of patient care is led by our Research Division, which continues to push the boundaries of modern science in clinically relevant areas. The Division boasts a historically strong basic science program and expanding translational and clinical research programs. Areas of research excellence within the Department include mitochondrial function, cardiovascular physiology, neurobiology of pain and its interactions with mood and autonomic function, pediatric pain care, and central control of breathing.

The Research Division's outstanding success is driven by the strength of our faculty, staff, and trainees, with collaborative or "team-based" science serving as the backbone of our mission and priorities. Our research footprint includes MCW, Froedtert, Children's Wisconsin, and the Milwaukee VA Medical Center. Faculty are also dedicated to advancing the Education mission of the Department and MCW by providing approximately 50 lecture-hours of instruction to MSA, graduate and medical students. Our Department is one of only 16 Anesthesiology Departments across the U.S.to have an actively funded T32 grant. Consistently ranked amongst the top 30 Anesthesiology Departments in the nation in NIH funding, our research is also funded through extramural grants from non-profit organizations, pharmaceutical and medical device companies, and the VA.

Amadou Camara, PhD examines 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.

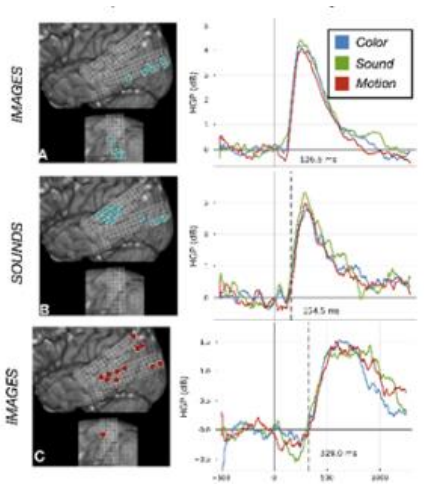


Caron Dean-Bernhoft, PhD investigates, using acute and chronic animal studies and human studies to address the role of endocannabinoid signaling in the integration of sympatho-sensory responses and the transition from acute to chronic pain.

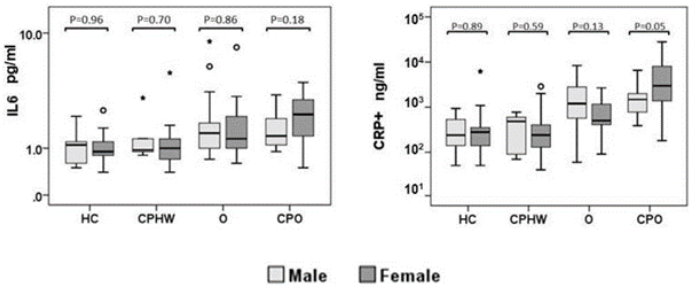
Thomas Ebert, MD, PhD investigates the effects of anesthesia on the cardiovascular, autonomic nervous systems and neuromuscular junction. His research has been supported by the National Institutes of Health, the Veterans Administration, the American Heart Association, other granting organizations as well as pharmaceutical and medical instrument companies over the past twenty-five years

Julie Freed, MD, PhD examines the role that sphingolipids have in the development of endothelial dysfunction in the human microcirculation. Elevated plasma levels of ceramide, a prototypical sphingolipid, is now considered an independent risk factor for major adverse cardiovascular events in otherwise healthy people. The Freed lab is currently investigating how these bioactive lipids are regulated in human endothelial cells.

William Gross, MD, PhD investigates the neurobiological mechanisms of language and memory, and how to translate basic neuroscience research findings to improve the safety and outcomes of neurosurgical procedures. His lab is developing methods to monitor specific language systems by analyzing the dynamics of electrical signals in the brain. His lab is particularly interested in developing Brain Computer Interface (BCI) devices for people with aphasia to assist with communication.

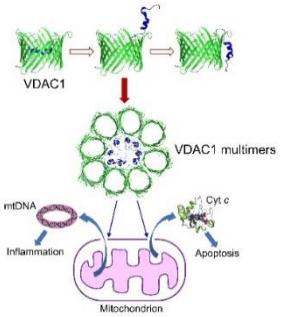


Keri Hainsworth, PhD examines the interrelationships between chronic pain and obesity in children and adolescents. Current research is focused on elucidating the mechanisms underlying pain in this population, including research on the benefits of a probiotic to reduce systemic inflammation and pain. As an expert in pain research, Dr. Hainsworth works with teams to study pain in adults with prolonged grief disorder, and chronic pain in military pilots.



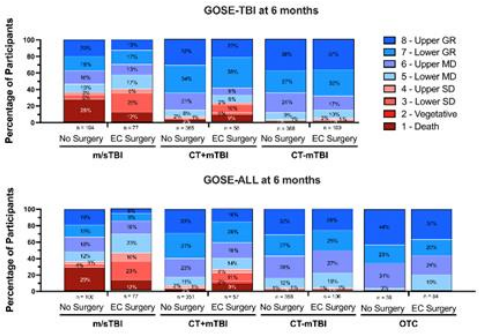
Quinn Hogan, MD examines how injury disrupts function of sensory neurons, exploring novel therapies for chronic pain, and adapting new technologies for evaluating animal behavior.

Wai-Meng Kwok, PhD investigates the roles of ion channels in mitochondrial dysfunction, and electrophysiological characterization of cardiomyocytes derived from induced pluripotent stem cells. His current project uses a highly orchestrated approach that includes electrophysiology, molecular biology, mitochondrial biology, biochemical assays, and proteomics to investigate how functional and structural changes in VDAC1 tip the balance between cell survival and cell death.



Bin Pan, MD, PhD explores the organization of brain function at the network and synaptic level, focusing on the mechanisms of neuropathic pain and chronic pain induced depression, and the role of cannabinoid signaling in the control of these pathways.

Christopher Roberts, MD, PhD investigates the pathophysiology of stress responses, using basic translational research (whole animal models, systems level neurobiology, and the mechanisms that drive them), as well as human studies (volunteers and observational data). Stress affects multiple systems and is pervasive in patients hospitalized for an illness or undergoing surgery, especially when requiring ICU care. His research is relevant to the surgical stress response, brain frailty, anesthetic neurotoxicity, disorders of consciousness, traumatic brain injury, and critical illness.



David Stowe, MD, PhD Investigates how mitochondria utilize and regulate the movement of cations and substrates across its membranes to generate energy and interchange with its host cells to utilize the energy provided for cell function in both normal and stressed cells.

Astrid Stucke, MD studies 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.

Hongwei Yu, MD focuses on gene therapy targeting periphery nervous system for chronic pain. His specific interests are in developing gene and molecular therapy tools for painful conditions. Towards this, he has established design, cloning, and production of AAV vectors to manipulate genes of interests in vivo, anatomically targeting specific pain pathways in the peripheral sensory nervous system via delivery of these vectors into the dorsal root ganglia (DRG). This allows highly specific and effective control of the pain signaling pathways for studying molecular mechanisms of pain and for future translational development.

Dermatology

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

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

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

Emergency Medicine

The Department of Emergency Medicine at the Medical College of Wisconsin is at the forefront of cutting-edge, innovative, and impactful emergency medicine-related research. Our faculty lead a wide range of scholarly programs cutting across disciplinary boundaries and taking place in clinical, educational, and community spaces.

Our scholarship spans the gamut of translational research to generate new knowledge that impacts clinical practice, health education, and healthcare delivery both locally and globally. Particular areas of departmental strength include clinical resuscitation research, substance abuse and injury-related epidemiological and intervention studies, community-based health education and disparities reduction programs, global emergency medicine education and ethics research, as well as research on diversity, equity and inclusion programming. The diversity of our scholarship is mirrored by the diversity of our extramural sponsors; our faculty are supported by diverse sources including the National Institute of Health, the U.S. Department of Health and Human Services, Substance Abuse and Mental Health Services Administration, the Advancing Healthier Wisconsin Endowments, the State of Wisconsin Department of Corrections, the Patient-Centered Outcomes Research Institute, among other agencies. Most notably, our department is among the top 30 emergency medicine departments in the country according to rankings based on funding from the National Institutes of Health.

Our core research infrastructure includes a full-time research faculty member, a faculty director of Research Training and Education, a PhD research associate, a research program manager, a grants operations coordinator, a part-time biostatistician, and a research administrative assistant.

Our department is also home to the NIH-Funded Resuscitation Research Center (RRC), consisting of a faculty director, clinical research manager, and four clinical research coordinators. The RRC employs 24/7/365 research coverage and collaborates closely with the EMS Division and other MCW departments to implement a diverse clinical trials portfolio.
We also host a multidisciplinary acute research team (MART) consisting of a program manager, a clinical research coordinator and three trained research assistants that participate in patient enrollment and data collection from the clinical space. The MART operates seven days a week from 8am to 12am. The department, in collaboration with other MCW departments, also has a grants submission/management team (which include a financial analyst, grant coordinator and administrator) and a part-time biostatistician to assist faculty with statistical planning and analysis.

Medicine

The Department of Medicine is nationally and internationally known for research and scholarship. Department of Medicine faculty members are active in more than 600 clinical trials and are primary or collaborating investigators on a number of NIH, Foundation and Industry grants. In total, the Department has over $35,000,000 in annual research funding, with all Divisions represented. Research efforts are based at the Medical College of Wisconsin campus, the Blood Research Institute/Versiti, and the Clement J. Zablocki VA Medical Center. Through investments and active recruitments, the Department continues to be poised for significant growth in research during the next several years.

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

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

Division of Cardiovascular Medicine

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

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

Active research-intensive faculty members include the following:

- **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. He also is focused on the role of heat-shock proteins dysregulation and its predictive value in patient with COVID-19 infection.
- **Marcie Berger, MD** and **Stacey Gardiner, MD** are studying how an educational intervention could improve cardiometabolic health in individuals living in the city of Milwaukee.
- **Andreas Beyer, PhD** studies the metabolic effects of aging, hyperglycemia, and oxidative stress on the peripheral microcirculation.
- **Scott Cohen, MD** is interested in the impact of vascular dysfunction on exercise tolerance in patients with hypertrophic cardiomyopathy.
- **Jacquelyn Kulinski, MD** is interested in understanding the physiological mechanisms between sedentary behavior and endothelial dysfunction, as well as the physiology of endothelial dysfunction in gestational diseases.
- **Divyanshu Mohananey, MD** is interested in the use of imaging to better predict outcomes in patients with valvular heart disease.

- **Sarah Thordsen, MD** is interested in interventions to reduce racial disparities associated with poor outcomes for patients who develop cardiac diseases during pregnancy, including pre-eclampsia and cardiomyopathies.
- **Michael Widlansky, MD** has efforts focused on the relationship between altered mitochondrial bioenergetics and endothelial dysfunction. In addition, he studies the impact probiotic supplementation on vascular endothelial function in humans with coronary artery disease.
- **David Zhang, MD, PhD** seeks to identify cellular mechanisms by which the endothelium regulates blood vessel tone in both normal physiological conditions and disease states, such as ischemic heart disease and hypertension.

In addition, the Division boasts a robust clinical trials portfolio, including over 40 clinical trials involving all aspects of cardiovascular care including advanced structural heart disease, electrophysiology, advanced heart failure, and secondary prevention of cardiovascular events. In addition, the clinical trials group supports multiple investigator-initiated human translational research studies with the goal of eventually applying knowledge from these initial studies to improve the health of our patients.

Division of Endocrinology & Molecular Medicine

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

- **Ty Carroll, MD, Associate Professor of Medicine**, is interested in novel diagnostic strategies and treatments for cortisol excess (Cushing syndrome). He has been an investigator in multiple clinical trials for the treatment of cortisol excess. He is also interested in the relationship of thyroid disease in different disease states.

- **Yiliang Chen, PhD, Assistant Professor of Medicine**, has worked on the functions of a scavenger receptor CD36 and its role in chronic inflammation and atherosclerosis. Dr. Chen has a life-long passion in the study of metabolic diseases that are often associated with oxidative stress, abnormal lipid metabolism and chronic inflammation.

- **Carol Everson, PhD, Professor of Medicine**, is investigating the ways in which long-term sleep deficiency is physically harmful and increases morbidity and mortality. The laboratory has shown that long-term sleep deficiency in the animal model results in unique metabolic, immune, and hormonal abnormalities. Current studies are investigating the mediation of decreased bone remodeling and impaired bone quality resulting from chronic sleep deficiency. Other organ systems—liver, lung, and intestine—show increased DNA damage; this provides potential biological linkage to epidemiological findings of cancer risk associated with chronic sleep deficiency. In a third area of concentration, sleep and sleep restriction, as well as other agents that affect cerebral blood flow and metabolism, are being studied as interventions in mild concussive injury. The interventions represent practical and low-cost means amenable to field implementation to improve outcomes from concussive injury, determined by changes to brain functional connectivity, hormone status, and behavior.

- **James Findling, MD, FACP, Professor of Medicine and Surgery** is interested in novel tools to diagnose and treat Cushing syndrome. He discovered the importance of inferior petrosal sinus sampling for the differential diagnosis of Cushing syndrome and introduced late-night salivary cortisol as a simple screening test for Cushing syndrome. He has been the PI of clinical trials for treatment and diagnosis of Cushing syndrome.

- **Benjamin Gantner, Assistant Professor of Medicine**, studies how innate immune cells generate early inflammation and what the impact of different types of inflammatory responses is on the mobilization of essential antimicrobial protections as well as the collateral damage that this activation causes to host tissues. To identify pathways that could promote protection with minimal injury, the laboratory studies animal models of bacterial pneumonia and sepsis using both in vitro analyses of macrophages and neutrophils and in vivo analyses including intravital imaging.

- **Srividya (Vidya) Kidambi, MD, MS, Professor of Medicine**, is interested in the role of adiposity distribution and resting metabolic rate in obesity pathogenesis, epigenetic modifications in chronic diseases such as hypertension & cardiovascular outcomes.

- **Bradley Javorsky, MD, Associate Professor of Medicine**, is interested in clinical research related to disorders of adipose tissue and the hypothalamic-pituitary-adrenal axis.

- **Paul Knudson, MD, Associate Professor of Medicine**, is interested in evaluating outcomes of inpatient diabetes management team. He works with information technology for people with diabetes mellitus.

- **Lisa Morselli, PhD, MD, Assistant Professor of Medicine**, is interested in metabolic adaptation to weight loss, resting metabolic rate control and the impact of food insecurity on metabolic outcomes. She has received funding from the Advancing Healthy Wisconsin initiative and the Froedtert Foundation to investigate circulating Agouti-related peptide as a marker of metabolic adaptation to weight loss.

- **Hershel Raff, PhD, FAAAS, FAPS, Professor of Medicine**, is interested in three main research areas of interest. His basic research on the hypothalamic-pituitary-adrenal axis focuses on the short- and long-term consequences of neonatal hypoxia and interventional pain. His translational research evaluates the intersection of obesity and pain in adolescence. His clinical research focuses on the development of diagnostic endocrine tests and, in particular, using the measurement of salivary cortisol to evaluate the hypothalamic-pituitary-adrenal axis in a variety of human diseases and stress models.

- **Daisy Sahoo, PhD, Professor of Medicine**, is interested in the role of scavenger receptors in cardiovascular disease, diabetes and obesity. Specifically, she relies on state-of-the-art biophysical and biochemical techniques to understand how the structural organization of SR-BI, the most physiologically relevant HDL receptor, facilitates HDL-cholesterol delivery to the liver for disposal. In other studies, she is trying to define the underlying mechanisms by which FFAR4 triggers pathways to prevent lipid accumulation in macrophages, how oxidized HDL promotes atherogenesis and how SR-BI modulates metabolic pathways in adipocytes. She also has a collaborative project to study the relationship between dyslipidemia and gammaherpesvirus infection. Dr. Sahoo is currently funded by the NIH.

- **Jenna Sarvaideo, DO, Assistant Professor of Medicine**, is interested in optimal hormonal treatment for transgender patients in line with her clinical interest. She has received funding from the Endocrine Society, DOM Faculty Development Funds and MCW Research Affairs Committee. She was accepted into the Clinical Research Scholars Program for 2019-2021.

- **Joseph Shaker, MD, Professor of Medicine**, his interests include high or low blood calcium and parathyroid disorders, osteoporosis associated with intestinal disease or surgery, and calcium and bone disorders.

- **Mary Sorci-Thomas, PhD, Professor of Medicine**, The major goal of our research program is to determine the mechanism by which Pcpe2 regulates adipose tissue expansion and remodeling. Adipose expansion, in response to excess caloric intake, plays a key role in cardiometabolic health. Therefore, understanding healthy fat expansion and remodeling is of utmost significance as the prevalence of obesity in the US continues to climb, driving increased cardiovascular disease and death. Healthy adipose tissue expansion and remodeling involves the differentiation of vascular stromal precursor cells called adipocyte progenitor cells (APCs), which are in turn influenced by the other major progenitor cell, fibroinflammatory adipocyte progenitor cells (FAPs). Together these progenitor cells are found within the connective tissue surrounding mature adipocytes. Since Pcpe2 is most highly expressed in APCs and FAPs our work focuses on Pcpe2 and its role in adipocyte lipid storage and elucidating the mechanism explaining how Pcpe2 enhances TGFb-like signaling in visceral adipose. With that information we will fill a major knowledge gap in our understanding of diet-induced obesity and how it induces a fibrogenesis and inflammation during unhealthy adipose expansion.

- **Catherine Zhang, MD, Assistant Professor of Medicine**, is interested in the evaluation and management of adrenal tumors, including the impact of mild adrenal cortisol excess on clinical outcomes, and recovery following surgical treatment of Cushing syndrome.

- **Ze Zheng, MBBS, PhD, Assistant Professor of Medicine**, is interested in understanding the role of hepatocyte-derived tPA and basal fibrinolysis in hemostasis, and to develop diagnostic/ preventive/ therapeutic strategies that can be used to combat atherosclerosis, thrombosis, and bleeding disorders. Specific areas of research interests include: 1) a new link between reduced fibrinolysis and dyslipidemia, 2) the role of fibrinolytic proteins and lipoproteins in hemostasis and bleeding disorders, 3) circadian regulation of basal fibrinolysis and the morning onset of thrombotic events, 4) the role of hepatocyte tPA in liver injuries, and 5) a timely study of fibrinolysis in COVID-19.

Division of Gastroenterology & Hepatology

As part of the Department of Medicine at the Medical College of Wisconsin, the Division of Gastroenterology and Hepatology contributes to the MCW Research mission in several ways, spanning a variety of interests. The Division's active clinical, translational, and basic science research program involves gastroenterologists, hepatologists, advanced practice providers, research scientists, research fellows, post-doctoral fellows, and a myriad of MCW medical students and Department of Medicine residents. Our division places special emphasis on teaching and mentorship, as well as partnerships throughout the college. Basic, clinical, and translational research efforts are heavily supported by several successfully funded NIH awards, as well as internal funding from the Clinical and Translational Science Institute (CTSI) and Digestive Disease Center (DDC). During the 2019-2020 academic year, the Division of Gastroenterology and Hepatology has been involved in research spanningesophageal motility, IBD diseases including moderately to severely active Crohn's disease or ulcerative colitis, Cyclic Vomiting Syndrome, hepatic encephalopathy and esophageal obstruction caused by intrinsic or extrinsic malignancies, refractory benign esophageal strictures or fistulas/perforations/leaks, and cystitis. This has resulted in many local, national, and international oral presentations and publications of articles and manuscripts. Below is a short highlight of some of our recent accomplishments:

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

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

Division of General Internal Medicine

The Division of General Internal Medicine (GIM), under the leadership of **Dr. Leonard Egede,** Division Chief**,** and **Drs. Barbara Slawski, Kurt Pfeifer, Theodore MacKinney, and Jeffrey Jackson,** Section Chiefs of Hospitalist Medicine, Perioperative & Consultative Medicine, Primary Care and GIM VA, respectively, has an active and nationally recognized research program focused on conducting innovative clinical and outcomes research. Research efforts by GIM are based at the Medical College of Wisconsin campus, the Clement J. Zablocki VA Medical Center, and in the local Milwaukee community. Research infrastructure includes affinity groups focused on building research capacity and mentoring faculty interested in research, statistical and design support to provide consultation and analysis for

unfunded projects, and research conferences in collaboration with the MCW Center for Advancing Population Science (CAPS). Faculty in GIM are actively involved in dissemination of their work through peer-reviewed publications and participation in national and international conferences, including the Society of General Internal Medicine (SGIM) and the Society of Hospital Medicine (SHM). Faculty also conduct collaborative work with other Divisions, Departments, and the College of Pharmacy within MCW and local institutions.

Faculty in GIM incorporate a variety of research designs into their research including randomized controlled trials, community-engaged research, use of large administrative and clinical databases, and health systems based quasi-experimental research. GIM research faculty have expertise in both quantitative and qualitative research, community based participatory research, program evaluation, cost-effectiveness analysis, and implementation science. Research topics range from evaluating policy changes at the national level like the impact of Medicaid regionalization on disparities in breast cancer care, testing novel interventions to improve chronic care such as financial incentives for improving glycemic control, addressing social determinants of health such as food insecurity, and recruiting participants for a national effort to expand the future of precision medicine.

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

- **Robert Hoerner, MD, Assistant Professor,** areas of research focus on diagnostic reasoning, clinical decision support systems, and evaluation of medical evidence.
- **Jeffrey L Jackson, MD, Professor**, has research focusing on Depression, Health Services Research, Meta-Analysis, Somatoform Disorders, Patient Doctor Communication, and Qualitative Methods
- **Kory Koerner, MD, Associate Professor,** research related to quality improvement, rapid response/emergency response team
- **Julie Kolinski, MD, Assistant Professor,** research focusing on high value healthcare, utilization review and appropriate utilization of resources, clinical documentation and care transitions.
- **Geoffrey C. Lamb, Professor:** Current Research focus - Quality Improvement, Quality Metrics, Patient Safety.
- **Sebastian Linde, PhD, Assistant Professor,** Research focus on causality, economics, machine learning, collective bargaining, hospital charges, patient care team, cost-benefit analysis, hospital costs, statistics
- **Amalia Lyons, Assistant Professor,** with focus on outpatient graduate medical teaching and curriculum development.
- **Theresa C. Maatman, MD, Director, Associate Professor**, with research interest and grants from the Kern foundation (and internal grants) in the use of comics and other graphic representations in medicine
- **Theodore MacKinney, MD, Professor**, with (internal) grants and research in QI in developing countries.
- **Jennifer MacKinnon, MD, Associate Professor**, with research interest in the interface of music and medicine, especially
- **Ann Maguire, MD**, **Associate Professor**, with research interest in after care of patients with cancer
- **James McCarthy, MD, Director, Assistant Professor,** research related to medical education for learners at all levels with a focus on developing engaging and innovative ways to deliver curricula.
- **Marty Muntz, MD**, **Vice Chair, Professor**, with research interest in teaching techniques for medical students.
- **Kavita Naik, MD, Assistant Professor,** research focus on quality improvement, medical education and Hospital Medicine
- **Ann B. Nattinger, MD, MPH, Professor,** research focus on breast cancer outcomes and policy
- **Joan Neuner, MD, Professor of Medicine and Georgia Carroll Endowed Chair in Women's Health**, with extensive research in women's health. She is the acting program Leader/Program Leader for the Cancer Prevention and Outcomes Program. She has multiple current grants from NIDDK, NIA, NIH, and DHHS.
- **Kurt Pfeifer, Professor, MD, Section Chief, Professor,** has research focusing on medical education, undergraduate medical education, continuing medical education, perioperative care, and graduate medical education.
- **Joseph Puetz, MD, Assistant Professor** research related to bedside procedures; POCUS, and community health
- **Brian Quinn, MD, Assistant Professor,** research related to Perioperative Medicine, surgical outcomes for patients who have been either seen in our prep clinic or received co-management from medicine consult service.
- **Sushma Raju, MD, Assistant Professor,** research related to clinical medicine
- **Cecilia Scholcoff, Assistant Professor**, research focus in microaggressions, sexual harassment and gender discrimination.
- **Yogita Segon, MD, Professor**, has research focusing on Medical education, and Quality improvement
- **Barbara Slawski, MD, MS, FACP, SFHM, Professor,** research related to Perioperative Medicine
- **Melek Somai, MD, MPH Assistant Professor,** research focused on Informatics
- **Bipin Thapa, MD, Assistant Dean, Associate Professor,** research related to educational intervention, meta analysis

- **Heather Toth, MD, Professor,** research related to medical education, bedside rounding and inpatient care.
- **Corrado Ugolini, MD, Assistant Professor,** clinical research and medical student teaching. Ares of interest include complex patient care and management
- **Adrian Umpierrez. MD,, MPH, Associate Professor,** research related to bedside procedures and patient safety/quality improvement; bedside procedures and education
- **Lara Voigt, MD, Assistant Professor,** clinical research: procedural safety and improvements, such as our rate of post LP headache compared to national average, and education
- **Rebeka Walker, PhD, Assistant Professor,** research focusing on health systems and Type 2 Diabetes
- **Chad Wenzel, MD, Assistant Professor,** has research focusing on perioperative medicine, and medical education
- **Jeff Whittle, Professor,** chronic disease management
- **Joni S. Williams, MD, MPH, Assistant Professor,** research focus in community-based, patient-level interventions to reduce disparities and improve health outcomes among African American adults
- **Alice Yan, MD, PhD, Associate Professor,** research focusing on community-based participatory research, mixed method, qualitative, quantitative, cancer survivorship and quality of life, lifestyle behaviors (physical activity and healthy diet), diabetes self-management, and health disparities.

Division of Geriatric and Palliative Medicine

The Division of Geriatric and Palliative Medicine has been a consolidated division since January 1st, 2021. We are engaged in a variety of clinical and educational research areas which are intended to advance patient care and innovate/optimize geriatric and palliative education.

Many members of the division have been active through the Kern Institute. Recent faculty and Advance Practice Providers who have completed (or will complete) the Kern KinetiC3 Scholars Program are: April Zehm, MD (July 2020-June 2022), Elizabeth Bukowy, DO (July 2021-June 2023), Christine Restivo-Pritzl, APNP (July 2021-June 2022), and Cara O'Brien, MD (July 2020-June 2023). Dr. Peltier is the founding co-editor for the MCW Kern "Transformational Times." The July 2022 issue of the Transformational Times, focused on geriatrics and palliative care. Dr. Adina Kalet remembers what co-starring with her own grandmother in a brand-new curriculum taught her about why we must, and how we might, ensure all physicians are ready to care for the elderly; Dr. Kathryn Denson shares the story of her journey to medicine and the rich intersection of caring for older patients and those nearing the end of life; Dr. Edmund Duthie and Dr. Angela Beckert share the history of the MCW Med-Ger Program; Dr. Cara O'Brien shares her reflections on the Geriatrics Mentorship program; Dr. Elizabeth Bukowy share reflections on nursing home care during a pandemic; Dr. Katherine Recka shows how, as healthcare workers, stories surround us every day; Dr. Adrienne Klement shares lessons she learned through caring for her patients; Dr. Sean Marks reflects on many years of mentorship through the lens of being a Hospice and Palliative Medicine clinician; Dr. Lara India and Dr. Laura Johns discuss how geriatric friendly EDs show that behind every patient in the ED is someone's loved one and Dr. Renee Foutz and Dr. Alexandria Bear discuss best practice models for communication skills training..

- **Alex Bear, MD, Katie Recka, MD, Katy Van Schyndle, APNP, Christine Restivo Pritzl, APNP, and Jake Taxis, Chaplain,** worked to update their Hospice and Palliative Medicine fellowship curriculum and will present "Bringing fellowship training into the 21st century: An interdisciplinary approach to development and implementation of an HPM fellowship antiracism curriculum" at the American Academy of Hospice and Palliative Medicine Annual Assembly in 2023.
- **Angela Beckert, MD**, submitted an Advancing Innovation in Residency Education (AIRE) Proposal for disseminating the Medicine-Geriatrics Integrated Residency and Fellowship Program and received approval in June of 2020. In May of 2022, Dr. Beckert attended the first American Geriatrics Society (AGS) Annual Meeting since the national dissemination and was joined by other program leaders who adopted the Med-Ger Program into their academic institutions.
- **Elizabeth Bukowy, DO and Steven Denson, MD** are Co-Directors for the bi-annual Wisconsin Update in Geriatric Medicine, a co-sponsored CME event between MCW and UW-Madison. This three-and-a-half-day course invites MCW and UW-

Madison speakers who are experts in their fields to present on topics to an interdisciplinary audience of physicians, nurse practitioners, pharmacists, social workers, and all who care for older patients. This conference has expanded from a Board Review-centered course to be inclusive and engaging for our interdisciplinary audience.

- **Kathryn Denson, MD Edmund Duthie, MD and Steven Denson, MD** were awarded an Advancing Healthier Wisconsin (AHW) grant through their community partner Marquette University in May 2021. "Student Champions: Connecting dementia patients/caregivers to essential community resources" combines efforts from MCW and Marquette, as well as the Alzheimer's Association and Advocate Aurora to educate learners to be advocates for their patients with dementia and their caregivers and connect them to resources of the Alzheimer's Association. In 2022, they submitted "Health Professions Students as Champions for Dementia Caregiver Referrals" to be presented at the 2023 American Geriatrics Society Annual Meeting.

- **Kathryn Denson, MD** is the Editor for Geriatric Fast Facts (GFFs) which is an MCW-run website of accessible, concise, and clinically actionable reports on Geriatric topics applicable across medical specialties. As of March 2023, 100 GFFs have been published. In March 2020, the Alliance of Independent Academic Medical Centers (AIAMC) awarded *Geriatric Fast Facts* the Alliance Innovation Award.

- **Renee Foutz, MD and Paul Stellmacher, MD** are Co-Directors for the annual Great Lakes Palliative Care Conference which brings together educators and leaders to explore topics in palliative care and advance the practice of hospice and palliative medicine. This CME event includes a half-day of workshops and a full-day of conference sessions including invited plenary speakers from all of the United States as well as concurrent sessions presented by MCW and UW-Madison speakers. In 2022, we hosted our 10th Annual Great Lakes Palliative Care Conference!

- **Evan Henricks, MD** submitted a Geriatrics Academic Career Award (GACA) in November 2022. If awarded, his project will affect change in educating interprofessional learners on perioperative care of older adults, age-friendly health system principles, and dementia care. His project's goals will be to reduce post-operative complications, length of stay, and readmissions as well as to train family medicine residents in geriatric medicine principals through a Project ECHO model. His project aligns with MCW's expanding use of innovative technologies and our institutional goals of community engagement and commitment to Milwaukee's underserved populations. His mentorship team includes Dr. Kathryn Denson, Dr. Edmund Duthie, Dr. Angela Beckert, Dr. Kurt Pfeifer, and Dr. Steven Denson.

- **Sean Marks, MD** is the Editor for Fast Facts and Concepts along with Associate Editor Dr. Drew A Rosielle from the University of Minnesota Medical School. By March 2023, 460 Fast Facts and Concepts were published to the Palliative Care Network of Wisconsin (PCNOW). Dr. Marks is also a key member of our Congressionally Directed Spending award through HRSA. The purpose of this award is to promote Age-Friendly Health Systems throughout Wisconsin. Dr. Marks has worked with Hospice and Palliative Medicine fellow Jennifer Turpen, DO to connect the fast facts with the 4Ms (Mentation, Medication, Mobility, and what Matters). He will also be working to include these associations to the PCNOW and Fast Facts website. In 2022, Dr. Marks worked with then HPM fellow Divya Patel, MD, to submit "Can an electronic medical record (EMR) clinician prompt safely improve co-prescribing of intranasal (IN) naloxone in a palliative care (PC) clinic?" and will present at the 2023 American Academy of Hospice and Palliative Medicine Annual Assembly. In June 2022, Dr. Marks was awarded the Scholars in Quality Improvement & Patient Safety Program Certificate from the Department of Medicine after completing his one-year QI project. He was accepted into the program while working on a QI project that assesses house-staff's comfort levels, patient care skills, and preparedness in leading code status discussions on patients admitted to the hospital. The desired outcomes were to understand the educational and system-based gaps involved and then design an educational and clinical interventions to improve the care skills of house-staff when called upon to lead these important discussions at the time of admission. .

- **Cara O'Brien, MD**, will be completing her Kern Institute KinetiC3 Scholars Program in June 2023. With the help of mentors Dr. Edmund Duthie, Dr. Kathryn Denson and Dr. Angela Beckert, she is conducting an evaluation of the Med-Ger Residency and Fellowship Program. This evaluation interviews current and previous Med-Gers to help Program Directors interested in adopting the Med-Ger model at their institutions and to promote benefits of going into Med-Ger compared to traditional residency and fellowship programs.

- **Wendy Peltier, MD,** is an active participant in the MCW Kern Institute, striving to transform medical education through a focus on Caring and Character, with service to the Faculty Pillar and Kern National Network (KNN). She is the founding co-editor for the MCW Kern "Transformational Times," a novel Narrative Medicine project which started as a way to feature real-time experiences of the Covid-19 pandemic. The Transformational Times continues to be a weekly electronic newsletter and has expanded to include experiences outside of the pandemic. Through these story submissions, Dr. Peltier helped to publish "Character and Caring: A Pandemic Year in Medical Education" in 2021 and "Character and Caring: Medical Education Emerges from the Pandemic" in 2023. In 2022, Dr. Peltier lead the Division of Geriatric and Palliative Medicine to publish an issue of Transformational Times focus on geriatrics and palliative care.

- **April Zehm, MD, Alex Bear, MD, Maria Olex, PsyD, and Chaplain Jake Taxis** submitted "'We need help!': Reflections from an interdisciplinary team on embedding a clinical psychologist on the inpatient palliative care consult service to be presented at the 2023 American Academy of Hospice and Palliative Medicine Annual Assembly.

- **April Zehm, MD** and external colleagues submitted "#Friendtorship: Cultivating peer mentor relationships in hospice and palliative medicine" and "Yesterday a Child, Today a Grown-Up: Reflections on the Patient, Family and Team Experience of an Abrupt, Non-Linear Transition from Pediatric to Adult Medicine for Young Adults with Serious Illness" to be presented at the 2023 American Academy of Hospice and Palliative Medicine Annual Assembly. She graduated from the Kern Institute KinetiC3 Scholars Program in June 2022. She was then awarded funding from Kern to present at the American Association of Medical Colleges (AAMC) conference in November 2022.

Division of Hematology and Oncology

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

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

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

- **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 neoplasms with special emphases on the treatment of patients with chronic myelogenous leukemia (CML). He is currently the administrative director of the Jean Khoury Cure CML consortium (HJKC3) which is housed at MCW. In addition, he is the clinical basket chair for patients < 60 with AML in the NCI myelomatch precision medicine initiative. He is PI (co-PI Dr. Guru Murthy) of a multisite phase I trial evaluating the role of a bispecific CD3-CD38 antibody in CD38 positive leukemias.

- **Lisa Baumann Kreuziger, MD, MS,** is a clinical and translational researcher with a focus in thrombosis. She has an interest in device and cancer-associated thrombosis. She started the US network for venous thromboembolism research (VENUS, https://www.venusresearch.org/). Her network coordinated three trials of anticoagulation for COVID-19. She serves on the NIH COVID-19 Guideline panel and the ACCP Antithrombotic Therapy for VTE Disease Guideline Panel. Additionally, she is the institutional PI for cancer-associated thrombosis trials. Lastly, she works in collaboration with Alan Mast, MD, PhD, in

the Recipient Epidemiology and Donor evaluation program (REDS-IVP) to understand outcomes of patients receiving transfusion.

- **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, evaluation of several potential biomarkers of treatment response, and cancer care process improvement.

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

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

- **Xiao Chen, MD, PhD's** research focuses on the potential role of dietary and nutritional factors in the pathogenesis and management of GVHD. Specifically, the lab has been investigating how vitamins A and D as well as prebiotics modulate GVHD risk. Since diet is one of the most important factors that shape gut microbiota, recent research in the lab has focused on how nutritional factors influence GVHD by modulating gut microbiota. The lab is using genetic, nutritional, and immunological approaches in combination with next-generation sequencing techniques to study the complex interplay between nutrients, gut microbiota, and mucosal immune responses during GVHD. The potential use of nutritional interventions to correct gut dysbiosis and mitigate GVHD is being explored.

- **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 particularly the triple negative breast cancer or inflammatory breast cancer. Under his leadership, Froedtert Cancer Center/Medical College of Wisconsin has formed a new Inflammatory Breast Cancer (IBC) team which is part of the international IBC Connect organized by MD Anderson Cancer Center in Houston, Texas. Dr Cheng is committed to provide the state-of-the-art management to this rare and aggressive type of breast cancer.

- **Rachel Cusatis, PhD** is an Assistant Professor of Medicine with training in sociology and survey research methods. Her research focuses on the intersection of patient reported outcomes, social determinants of health, and quality of life to understand patient and caregiver health outcomes. Through mixed methods approaches, her research looks at reported outcomes including physical emotional and financial, patient and provider communication, and decisional regret among transplant and cellular therapy patients.

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

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

- **Jing Dong, MD's** is an Assistant Professor with research interests in integrating high throughput "omics" data into epidemiological studies to develop approaches to reduce cancer burden and cancer disparities. Her lab focuses on identifying genetic determinants underlying outcomes of patients undergoing stem cell transplantation, especially genomic alterations on the mitochondrial genome. In addition, she applies genome-wide association study (GWAS) and next generation sequencing (NGS) approaches to identify genetic and non-genetic risk factors of multiple myeloma in racial/ethnic diverse populations.

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

- **Anita D'Souza, MD, MS** conducts outcome research in plasma cell disorders.

- **Mary Eapen, MD, MS's** research interests have focused on use of alternative donors and grafts for allogeneic hematopoietic cell transplantation for leukemia and non-malignant diseases. She leads an NIH funded phase I clinical trial on gene therapy for severe Hemophilia A and an Clinical Trials Platform that is funded by the National Heart Lung and Blood Institute's Cure Sickle Cell Initiative to support multicenter phase I and phase II gene therapy trials in sickle cell disease.

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

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

- **Joshua Field, MD's** research program focuses on of clinical studies in adults with sickle cell disease. Particular areas of interest include acute and chronic pain, pulmonary complications, transfusion, and therapeutic studies.

- **Kathryn Flynn, PhD's** research focuses on the measure development and analysis of patient-reported outcomes as well as mixed methods approaches to understanding and improving patient-provider communication and patient decision making. Currently funded projects are in the areas of leukemia, cellular therapies, breast cancer, maternal health, and lower urinary tract symptoms.

- **Patrick Foy, MD's** current research focuses on management of bleeding in patients with hereditary hemorrhagic telangiectasia with therapy designed to decrease blood vessel growth (VEGF inhibition). He also assists in ongoing clinical trials in hemophilia and thrombosis. He also is actively engaged in educational research designed to improve teaching of medical students, residents, and fellows in hematology and oncology.

- **Kenneth Friedman, MD** is a clinical laboratory investigator who is involved with numerous clinical trials with several academic institutions, Industry and the NIH investigating the role of diagnostic laboratory hemostasis and thrombosis testing in the evaluation of patient cohorts.

- **Ben George, MD's** research focus is on pancreatic and gastro-esophageal cancers. He is interested in experimental therapeutics, specifically, clinical trials targeting putative molecular mechanisms involved in the development and progression of gastrointestinal malignancies. He chairs the Molecular Tumor Board - a monthly meeting that analyzes genomic alterations in tumors to identify appropriate targeted treatment options. Further, he represents Froedtert and Medical College of Wisconsin at the Precision Medicine Exchange Consortium, of which MCW is a founding member. The goal of the consortium is to pool clinically annotated molecular data among member institutions and use that information to develop clinical trials aimed at actionable genomic alterations. He is the institutional Principal Investigator on several clinical trials in both Pancreatic and Gastro-esophageal Cancers.

- **Thomas Giever, DO, MBA's** main research interest is to enroll patients on genitourinary clinical trials. Additionally, he would like to build a robust general oncology clinical trial portfolio at the Drexel Town Square Health Center Cancer Center within the Froedtert Community Cancer Network and Division of Hematology and Oncology.

- **Guru Subramanian Guru Murthy, MD's** clinical and research interests focus on the outcomes of patients with leukemia and stem cell transplantation. He conducts retrospective and prospective clinical studies in patients with leukemia and stem cell transplantation with a goal of improving disease related outcomes"

- **Mehdi Hamadani, MD's** research interest includes lymphoma, GVHD, and alternative donor transplantation. He is the Scientific Director of the CIBMTR's Lymphoma Working Committee, and the Medical Director of MCW BMT and Cell Therapy Program. He has investigated the role of immunomodulation with HMG-CoA reductase inhibitors and TNF-alpha blockers for preventing acute GVHD as well as the role of the novel proteasome inhibitor MLN9708 in preventing chronic GVHD. As part of BMT CTN's Data Coordinating Center, Dr. Hamadani is intricately involved in the development and conduct of several cooperative group trials looking at prevention and treatment of GVHD, and mitigation of post-transplant relapse-risk in acute leukemias.

- **Mary Horowitz, MD, MS** is Deputy Cancer Center Director**.** Her career has focused on assessing clinical outcomes of blood and marrow transplantation (BMT) and other cell therapies through the Center for International Blood and Marrow Transplant Research (CIBMTR). She leads the BMT Clinical Trials Network (CTN), funded by NHLBI and NCI. The BMT CTN conducts large multicenter trials and enrolls patients from more than 100 centers in the US, Canada, France and Germany.

Dr. Horowitz is co-PI, with Dr. Mary Eapen, of a grant from NHLBI for theCIBMTR to participate in NHLBI's Cure Sickle Cell (CureSC) Initiative. The CIBMTR works with the CureSC Data Consortium to build a research data ecosystem designed to support investigator-initiated collaborative research. The CIBMTR also supports the design and launch of gene therapy sickle cell disease clinical trials using the infrastructure of the BMT CTN.

- **Siegfried Janz, MD, DSc** performs translational research on new therapeutic approaches to 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 chromosomal translocations, he recapitulates important features of human plasma cell neoplasms, such as multiple myeloma, plasmacytoma and light-chain amyloidosis. His laboratory takes advantage of mouse models of this sort to evaluate emerging immunotherapies of cancer including armored CAR (chimeric antigen receptor) T cells. The long-term goal of Dr. Janz' work, which is supported by a generous grant from the Paula and Rodger Riney Foundation, is to improve the outcome of patients with myeloma and related blood cancers. To that end, he collaborates with fellow investigators from HemOnc, the Department of Medicine, and the MCW Cancer Center.

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

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

- **Mandana Kamgar, MD, MPH's** research focus is on pancreatic ductal adenocarcinoma, clinical trial development and translational research. Dr Kamgar and his collaborations are studying how different KRAS mutations lead to different treatment susceptibilities. She is principal investigator of a phase I study looking at the role of CPI-613, an inhibitor of Krebs cycle in tumor cell, as radiosensitizer (NCT05325281). She also works as part of the precision oncology team to deliver personalized targeted therapies to patients with pancreatic cancer.

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

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

- **Emily Lemke, DNP** research interests center around genitourinary cancers including symptom management and real world outcomes. She is also the co-director of the APP Hem/Onc Fellowship program and has additional research interests studying metrics and outcomes for APP post graduate education.

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

- **Subramaniam Malarkannan, PhD's** research interests include signaling cascades that regulate the development and functions of human Natural Killer cells (NK) patients with malignancies, inherited diseases and infections, and developing

translational models to improve the anti-tumor efficacy of human NK cells. His team uses cellular, biochemical, and transcriptomic (single-cell RNA-seq) approaches. Research in his laboratory is supported by NCI, NIH, MACC Fund, Nicholas Family Foundation, and Gardetto Family Endowed Chair.

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

- **Robert Taylor, MD's** research interest is in head and neck cancers and malignant hematology.
- **James Thomas, MD, PhD's** research interest is in oncology drug development and the role of reactive oxygen species in cancer development and treatment.
- **Jonathan Thompson, MD, MS,** has interest in clinical and translational research related to thoracic malignancies, particularly regarding the use of immunotherapy and novel agents for the treatment of lung cancer. He also focuses on early drug development through phase I clinical trials, solid tumor cellular therapy, and studying cancer immunotherapy toxicity.
- **Li-Shu Wang**, **PhD,** conducts pre-clinical and clinical studies to investigate the mechanisms of nutritional-based approaches to prevent cancer through immunity and gut microbiome modulations.
- **Stuart Wong, MD,** conducts clinical research evaluating novel therapies for head and neck cancer, and in particular, agents that are used concurrently with radiation therapy. His research efforts include NCI funded clinical trials. His research also focuses on national patterns of care for head and neck cancer treatment, and mitigation of toxicity from head and neck cancer treatment, and cancer prevention. Dr. Wong is the lead investigator for the Lead Academic Participating Site (LAPS) of the NCI's National Clinical Trial Network at MCW. MCW is one of the top 32 institutions in the country to receive a LAPS award. He also received an RO1 NIH grant with Ming You, MD. PhD, to study a new agent in patients with oral cancer. Dr. Wong is the Co-PI of the NCI-NCTN study NRG HN004 and the follow-up study, NRG HN 012.
- **Anthony Zamora, PhD's** research spans the fields of viral and cancer immunology, with a special focus on identifying ways to modulate the immune system to more effectively target and eliminate virally infected or cancerous cells. Along these lines, the lab utilizes cellular-based engineering approaches that aim to increase the specificity of immune cells for their targets and at the same time decrease the likelihood of off-target toxicities. A longstanding goal in the lab has also been to help address the current disparities in cancer research by developing reagents, assays, and tools that provide a deeper understanding of the underlying mechanisms that govern antitumor immunity across diverse demographic groups. Current research in the Zamora lab focuses on: (1) discovering tumor antigens that serve as immunogenic targets, (2) identifying the mechanisms involved in the immune system's ability to generate antitumor specificities, (3) characterizing the phenotypic, functional, and receptor repertoires of NK cells and neoantigen-specific T cells, and (4) exploring ways to translate these findings in order to expand on the current therapeutic options used to treat cancer.

Division of Infectious Diseases

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

Primary research investigators include the following:

- **Dr. Bilal Abid's** research interest intersects in areas of both Oncology and Infectious Diseases. He heads projects dealing with immunotherapy, cytokine release syndrome, CAR T-cells, malaria, as well as the gut microbiome. He analyses haploHCT patients at MCW to study the association between CRS and infections. He spearheads a study in genomic profiling of a case of tumor hyper progression with pre-existing Li Fraumeni Syndrome that spans across both the Division of Infectious Diseases and Hematology and Oncology.
- **Dr. Sol Aldrete** is currently working on project in which the Retrospective observational study of patients who received BCG vaccination seeking to identify patient factors associated with Mycobacterium bovis infection after instillation of the

vaccine for bladder cancer. This is a study in the VA along with Dr. Gundacker. Second project is looking at HIV Preexposure prophylaxis initiation and retention in care at an HIV health care system in Wisconsin.

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

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

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

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

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

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

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

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

- **Dr. Sheran Mahatme** is involved in a variety of quality improvement and clinical research projects at ZVAMC. She has partnered with Allergy/Immunology, Emergency Medicine, and ID Pharmacy in reassessing beta lactam allergy listings and has supported ID Pharmacy in conjunction with Geriatric Medicine and Nursing in developing an algorithm to reduce the acquisition and unnecessary antimicrobial use in asymptomatic bacteriuria. Dr. Mahatme has worked with Inpatient Internal Medicine, Radiology and Nursing to initiate a Venous Access Team to provide a standardization process for long term venous access placement and has collaborated with ID Pharmacy in assisting the Department of Surgery's reassessment and update of antimicrobial surgical prophylaxis. She has spearheaded implementation of the ANNIE Program on a local level to improve the medical adherence, retention and linkage of care of people living with HIV and those on pre-exposure prophylaxis. Finally, Dr. Mahatme is involved in two clinical studies, one looking at developing an improved interferon release gamma assay using specific T cell stimulation for the detection of *M. tuberculosis,* and the second as a site co-investigator for a National VA Cooperative Study assessing the optimal treatment for recurrent *C. difficile* infection by comparing the efficacy of oral Vancomycin, oral Vancomycin (taper and pulse) and Fidaxomicin.

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

Division of Nephrology

The main research priorities of the Division of Nephrology include:

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

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

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

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

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

Division of Pulmonary & Critical Care

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

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

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

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

Pulmonary & Critical Care Medicine has over 84 active projects, 66 industry, 12 IIT, 6 grants; 1 $1.73M 3-year award through NCATS in collaboration with CTSI and 3 CF Foundation awards. Our research trials are primarily led by: J Biller MD, M Barash MD, A Betensley MD, V Bonne MD, R Franco MD, K Hu MD, D Ishizawar MD, E Jacobs MD, D Kogan MD, J Kurman MD, R Lipchik MD, MD, R Nanchal MD, J Patel MD, K Presberg MD, S Sultan MD & A Taneja MD. Supported by; Ashley Wuerl RM, Alexander Beale CRC I, Christian Campbell CRC II, Monserrat Dondeigo CRC I, Erin Hubertz CRC II, Alyssa Ruediger CRC I, Samantha Servi CRC I, Kiley Timler CRC I, Kiran Sehgal CRC I, along with active recruitment for 1 additional team member; CRA III.

Last year has enlightened us with new challenges along with many new opportunities of research and collaboration for our department, we look forward to the many new endeavors we have in store for 2023.

Division of Rheumatology

The Rheumatology Division at the Medical College of Wisconsin has a strong history of research, largely in crystal-related arthritis, and has continued this focus, while simultaneously pursuing work in Systemic Lupus Erythematosus (SLE) and scleroderma, and participating in clinical trials of SLE and scleroderma. We are always interested in collaborations and have expertise that spans bench

research, industry-sponsored clinical trials and investigator-initiated human studies. We have assistance from a clinical research coordinator in the department of medicine and expert laboratory personnel at the VA.

- **Ann Rosenthal, MD** continues to work on crystal arthritis, with a focus on calcium pyrophosphate deposition disease (CPPD). She runs a federally-funded research program at the Zablocki VA where she is delineating mechanisms of calcium crystal formation in articular cartilage. Dr. Rosenthal's current work focuses on the role of the multipass membrane protein known as ANKH, which was described as a novel mediator of ATP efflux in chondrocytes. She also has a project to explore the role of osteoprotegerin mutations in CPPD which involves studies of osteoclastogenesis and bone metabolism. Current local collaborators at MCW include Brian Volkman, Ph.D. Dr. Rosenthal is a standing member of the Skeletal Biology Development and Disease study section at the NIH, and a mentor for the US/Canada Bone and Joint Initiative Young Investigators Workshop. Additionally, she has published work on musculoskeletal complications of diabetes, osteoarthritis, and gout. She was the site PI for two clinical trials of cardiovascular risk in gout and osteoarthritis patients at the Zablocki VAMC, where she is Associate Chief of Staff for Research and Development.

- **Mary-Ellen Csuka, MD** is an expert in scleroderma and participates in many research initiatives with this rare disease at the national and international level. She has received funding with Dr. Kirkwood Pritchard to study IRE5 in scleroderma patient samples and currently collaborates with Dr. Polly Ryan on an NIH-funded study of health behaviors in osteoporosis patients. She has active clinical trials in scleroderma, Raynaud's and autoimmune overlap syndromes.

- **David Gazeley, MD** continues collaboration with UW Health Rheumatology regarding lupus retention in care and adherence in high risk SLE patients. He completed a pilot study assessing apathy in a cohort of lupus patients. Lupus clinic remains a site for an active lupus nephritis clinical trial and additionally negotiations underway for a systemic lupus erythematosus (SLE) trial.

- **Michael Putman, MD** is developing a research program related to vasculitis, with a particular focus on giant cell arteritis. He has received funding from the Rheumatology Research Foundation for multiple projects relating to GCA research.

Neurology

Research to improve health care for neurological illness is a major mission of the Department of Neurology, which maintains a wide range of basic and clinical research programs. Below is a list of 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.

Neurodegenerative and Memory Disorders Research Program: Members of the Neurodegenerative Translational Research Program (NTRP) conduct a variety of studies including grant funded and investigator-initiated research projects and pharmaceutical sponsored clinical trials. This research team is led by Dr. Malgorzata Franczak (director) and Dr. Laura Umfleet (co-director. Dr. Umfleet currently has several grants that are funding research with collaborators at MCW as well as outside collaborators, including her multi-PI R21 is examining the gut microbiome and its effects on brain connectivity and her multi-PI CTSI award that is examining related neurobiological underpinnings of subjective cognitive decline using advanced multimodal neuroimaging techniques. Dr. Umfleet is the PI for a community-based research project funded by AHW to examine and address barriers and needs in the aging Black community to improve equity in health care and research in a collaborative project with Greater New Birth Church called The Black American Neurodegenerative Discovery (Band) – Together Initiative. There are several pharmaceutical sponsored clinical trials that are also ongoing using a variety of new therapeutics. These clinical trials include the use of drugs like Aducanumab, a recent FDA approved drug, and Lecanemab which was recently granted accelerated approval. This clinical trial work is led by Dr. Malgorzata Franczak and Dr. Elias Granadillo.

Neuromuscular Research Program: The neuromuscular research group has 13 clinical trials open to enrollment or in the start-up process. Most of these trials are for Amyotrophic Lateral Sclerosis (ALS), studying various oral and IV medications that are thought to help slow disease progression. Notably, MCW is a site for the HEALEY ALS Platform Trial, which is a first-of-its-kind trial in ALS research that accelerates the path to new ALS therapies by testing multiple treatments at once. In addition to ALS research, the neuromuscular research team is running a clinical trial for primary mitochondrial disease, with a first-in-class mitochondrial protective agent that has been shown to improve cell viability and organ function. The team will open its first trial for Inclusion Body Myositis later this year and are also managing a new trial for Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) and Myotonic Dystrophy Type 1.

NIH R21 Grant - High-Density Surface EMG Based CMAP Scan for Motor Unit Number Estimation: Dr. Xiaoyan Li's R21 grant aims to improve diagnostic & therapeutic efficacy through new EMG techniques in patients with ALS. Specifically, this project combines HD-EMG and CMAP scan to create a novel technique that will help minimize the limitations of standard MUNE (electrophysiological) techniques. This study has enrolled about 40 healthy control subjects and patients with ALS.

Movement Disorders Research Program: The movement disorders group currently has 4 clinical trials open to enrollment or in the start-up process for Parkinson's Disease (PD) and Essential Tremor (ET). The trial for ET is studying a calcium channel blocker that is thought to help decrease tremor and improve motor function. The PD trials are studying various oral medications that aim to slow disease progression, improve motor function, or do both. Notably, the movement disorders research team will soon be opening a trial involving a novel translational inhibitor thought to reduces several neurotoxic aggregating proteins (α-Synuclein, Amyloid Precursor Protein, and tau) and therefore improve motor function and cognitive functioning.

The Effect of External Pharyngeal Exercise on treating Dysphagia associated with Parkinson's Disease: In collaboration with the MCW GI department, the neurology team is working on a local project to evaluate the biomechanical effect of a novel resistance exercise program in strengthening the striated muscles involved with swallowing in patients with Parkinson's disease. The neurology team helps to recruit patients and complete the non-motor/motor function rating scales.

Neuroimmunology & MS Research Program:
Drs. Staley Brod, Ahmed Obeidat and Sam Hooshmand have been actively growing the research portfolio year after year. Numerous studies have been actively recruiting in our center, many in collaboration with researchers at Marquette University and Versiti. The topics include but are not limited to studies examining changes in the composition of T cell and B cells in people with MS before and after treatment with certain disease modifying therapies, integration of technology-based measures to quantify functional disability in people with MS, balance training in people with MS, survey based studies, and laboratory based animal research. In addition, the team has been very active with numerous interventional therapeutic studies and large international registry research. The study team investigates new drug therapies for patients diagnosed with multiple sclerosis and other neuroimmune disorders (e.g., neuromyelitis optica spectrum disorders, myelin

oligodendrocyte glycoprotein associated disease, and autoimmune encephalitis). The team also gathers rich clinical data to support registries and future research. The team currently has approximately active 15 clinical trials and 10 observational clinical studies. The team members include Sam O'Dell, Hope Campbell, Alexis Micale, DeAnna Finnessy, Kaylan Fenton, Rebecca Rehborg and Lynn Wheeler.

Stroke Research Program: The Stroke Team has expanded its participation in clinical trials, investigator-initiated studies, and continues to participate in the NIH StrokeNet Consortium. Ann Helms, MD has recently joined a new study with Bayer Pharmaceuticals, Inc. testing the safety and effectiveness of an oral FXIa inhibitor compound for the prevention of ischemic stroke. Marek Cierny, MD was awarded an Advancing a Healthier Wisconsin Seed Grant Award to evaluate the racial and geographic inequalities in inpatient mortality and processes of care among a multi-year cohort of persons with ischemic stroke to promote advocacy within the healthcare system and reduce health inequalities. Xiaoyan Li, PhD will collaborate with the Stroke Team to examine the development of muscle weakness, specifically neural and muscle components affecting force generation, in acute and subacute stroke population. The Stroke Team will open two new StrokeNet Studies over the next several months including: A biomarker study to validate the relationship of TMS and MRI biomarkers of corticomotor system integrity after stroke in patients with upper extremity motor impairment; and a study comparing the use of anti-coagulation and anti-platelet therapies in subjects with stroke attributed to intracranial atherosclerotic stenosis.

Headache Research Program: The Headache Program welcomes new Principal Investigator, James Murtha, MD. Dr. Murtha and the Headache Team are participating in a clinical trial to evaluate the efficacy and safety of eptinezumab for episodic cluster headache (eCH). In addition, the team are exploring the effectiveness of the combination of CGRP mAB and small molecule CGRP antagonist for treatment of chronic migraine.

Epilepsy Research Program: The Epilepsy Team are exploring the use of Near-Infrared Spectroscopy (NIRS) cerebral oximetry as an alternative, non-invasive test to MRI by demonstrating fMRI data correlation to NIRS data in cohort of healthy adults and a cohort of epileptic patients who have focal and/or frequent interictal spike activity. The Epilepsy Team are retrospectively evaluating the surgical approach, efficacy, and safety in patients who have been treated in the thalamus with the RNS system. Additionally, the Adult Epilepsy Team will collaborate with the Pediatric Epilepsy Team to evaluate the safety and efficacy of the RNS System for the reduction of generalized seizures.

Child Neurology Research Program : Child Neurology has 16 current and incoming clinical interventional trials including gene therapies, cellular therapies, novel anti-myostatin therapies, monoclonal antibodies for conditions affecting the pediatric and young adult populations including Duchenne Muscular Dystrophy, Spinal Muscular Atrophy, Migraine, and Multiple Sclerosis. The Child Neurology division has 37 current and incoming observational, registry, bank, and chart review studies – including some NIH and other grant funded research – all on a variety of conditions including NORSE, Epilepsy, Traumatic Brain Injury, Neuropsych, Spina Bifida, Biomarkers, and Community Health.

Beardsley Lab: Scott Beardsley, Ph.D. (Associate Professor, Director of Undergraduate Studies, Joint Department of Biomedical Engineering, Marquette University and the Medical College of Wisconsin) continues to conduct functional near-infrared (fNIRS) research in the lab following Dr. Harry Whelan's retirement and shift to Professor Emeritus. The Lab continues to test this technology with aims of translational diagnostic use in the clinical setting. Dr. Beardsley's research interests include neuroengineering, neuroplasticity and learning, human visuo-motor processing, and functional neuroimaging. https://mcw.marquette.edu/biomedical-engineering/directory/scott-beardsley.php

Language Imaging Laboratory: This lab is directed by Dr. Jeffrey Binder in collaboration with Drs. Lisa Conant, Leo Fernandino, Bill Gross, Sara Pillay, and Priyanka Shah-Basak. The lab has long been at the forefront of neuroimaging research on basic mechanisms of language processing in the human brain and has had continuous NIH funding for over 25 years. We conduct research with healthy participants, people with aphasia, and people with epilepsy. We use a range of methodological approaches, including cognitive and psychophysical measures, computational modeling, fMRI and structural MRI, magnetoencephalography (MEG), voxel-based lesion-symptom mapping in people with stroke and epilepsy, intracranial EEG obtained during brain surgery, transcranial magnetic stimulation (TMS), and transcranial electrical stimulation (TES). Our recent work focuses on understanding how concepts are stored in the brain and development of computational methods for decoding brain signals associated with concept retrieval. Our aphasia studies build on the insights resulting from this foundational research and focus on using TES methods to accelerate neural plasticity after damage to language networks. The Language Imaging Laboratory is funded by grants from the NIH, the Advancing a Healthier Wisconsin Endowment, the Clinical and Translational Science Institute, the Neuroscience Research Center, and the WE Energies Foundation.

Magnetoencephalography (MEG) laboratory: The MEG Program at Froedtert & The Medical College of Wisconsin is conducting research on MEG responses from both patients and healthy control participants with the goal of improving presurgical evaluations of epilepsy

surgery. The primary objective is to aid in the localization and characterization of the epileptogenic zone and language function. In pursuit of this objective, they have recently begun collaborating with scientists at MEGIN to comprehensively investigate language mapping approaches and establish standard guidelines for clinical language mapping that will benefit clinical sites worldwide.

The group has a long-standing history of studying neural oscillatory patterns related to language processing functions. They collaborated with the Epilepsy Connectome Project to demonstrate that beta-band oscillations are linked to semantic processing of story-listening responses. Their findings, published in the Journal of NeuroImage in 2022, revealed right hemisphere dominance towards the end of the comprehension process, likely related to social and pragmatic inference processing.

The group is also collaborating on other research projects, including developing a MEG-based brain-computer interface for significant upper-limb impairment with the University of Chicago. Their goal is to develop decoding strategies that enable patients to control movements and convey tactile feedback through intracortical microstimulation of the somatosensory cortex. Additionally, they collaborated with the University of Ulster, UK, and the University of Aalto, Finland, to demonstrate the use of beta-band oscillations for mapping and decoding motor imagery and mental processes of a BCI task. Their work has been accepted for publication in the Journal of Human Brain Mapping.

Obstetrics & Gynecology

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

Notable accomplishments include:

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

Other key programmatic initiatives include:

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

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

Where are we heading?

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

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

Ophthalmology & Visual Sciences

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

Significant accomplishments from the past year include:

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

Dennis P. Han, MD Advanced Ocular Imaging Program

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

Ocular Gene Therapy Lab

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

Orthopaedic Surgery

Biomaterials and Histopathology Laboratory

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

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

Biomechanical Laboratory

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

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

- Studies of the stability of total-joint replacement
- Acetabular cup and hip stem micromotion
- Joint mechanics
- Biomechanical analysis of subtalar motion
- Spine mechanics
- Experimental and computational evaluation of spinal instrumentation
- Bracing in scoliosis and spine fractures
- Planned projects include:
- Three-dimensional finite element modeling of the pelvis
- Strain measurement in the pelvis and ankle ligaments
- A study of femoral neck fractures

Cell Biology Laboratory

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

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

Musculoskeletal Functional Assessment Center: Pediatric Orthopaedic Research Lab

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

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

Center for Motion Analysis

The Center for Motion Analysis (CMA) is designed to support a broad scope of both clinical and research oriented projects. Clinically, the center can provide gait analyses for both pediatric and adult patients, which enhance diagnoses and improve functional outcomes for neuromuscular and orthopaedic impairments as well as dysfunction caused by other deformities. Motion abnormalities include

complex alterations imposed by the musculoskeletal and neuromuscular systems, as well as secondary adaptations that the patient makes in order to function. Identification of these patterns is extremely difficult, even for the trained clinician. Quantitative motion assessment includes specialty models for the distal extremities (foot and ankle, upper extremity, hand and wrist, trunk) sports applications and higher speed analysis capability, and rehabilitation (assistive devices, prosthetics and orthotics.) Educational support through clinical training and research project participation is provided for research fellows, orthopaedic residents, medical students and engineering students. Numerous technical development projects are supported through close collaboration with the Department of Biomedical Engineering at Marquette University. The center also collaborates with Children's Hospital of Wisconsin, Froedtert Hospital, and other institutions (MSOE, UWM and CUW). Research applications include studies of surgical interventions, orthotic and prosthetic treatments, and therapy upon upper and lower extremity motion and control. Motion analysis provides a frame-by-frame analysis of the three-dimensional joint motion, limb kinematics, kinetics, and muscular activity. While changes from activity patterns of age-matched normals are used to formulate a clinical treatment plan, research studies of pathological motion and muscular control patterns are designed to increase our understanding and ultimately our ability to improve future diagnosis, treatment and injury prevention.

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

Sports Medicine Motion Analysis Laboratory

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

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

Otolaryngology and Communication Sciences

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

The primary research platform for our department is OTO Clinomics, a comprehensive platform for investigating clinical outcomes, treatment pathways, and disparities in healthcare delivery for the spectrum of otolaryngologic disorders. This platform is ideal for resident and medical student projects to gain experience with basic research techniques including study design, data collection and validation, statistics, abstract and manuscript writing, and presentation. Projects in OTO Clinomics have encompassed all our divisions including otology, rhinology, sleep medicine, pediatrics, plastics, head and neck oncology, and laryngology.

The Department of Otolaryngology and Communication Sciences also has a robust basic science research program with laboratory space within the Department of Microbiology and Immunology and within the Biomedical Engineering program of Marquette and MCW. Studies include molecular biological aspects of otitis media, drug discovery for treatment of laryngopharyngeal reflux, and computational fluid dynamics modeling of upper airway obstruction.

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:

Jazzmyne A. Adams MPH
Director, OTO Clinomics
jaadams@mcw.edu

Pathology

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

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

Core Values

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

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

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

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

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

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

In recent years biomedical research has tremendously expanded our understanding of the molecular and genetic mechanisms of disease. Modern science has exponentially advanced in terms of its ability to perform assay for molecular and genetic abnormalities that underlie most human disorders. Newer techniques such as DNA in-situ hybridization, polymerase chain reaction, fluorescence in-situ hybridization and molecular profiling have revolutionized the field of medical research. Pathologists are uniquely positioned to

apply these techniques for the study of human tissues and, as such, to translate the knowledge gained from basic science to the bedside. As such, pathologists are the original and quintessential “translational researchers”.

Funded Research

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

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

Pediatrics

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

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

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

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

responses that might otherwise limit its efficacy. Other investigators focused on hemostasis include **Dr. Veronica Flood**, who also has R01 funding from the NHLBI to study the interaction between Von Willebrand Factor and type 4 collagen.

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

Physical Medicine and Rehabilitation

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

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

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

Research Administration Committee (PM&R)

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

Orthopedic Rehabilitation & Engineering Center

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

Human Motion Analysis Laboratory (Gait Lab)

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

Rehabilitation Robotic Research and Design Lab (RRRD)

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

The lab is focused on:

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

Plastic Surgery

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

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

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

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

Psychiatry and Behavioral Medicine

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

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

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

Alan Nyitray, Ph.D., Associate Professor of Epidemiology
Dr. Nyitray's research has focused on the natural history of anal human papillomavirus (HPV) infection and, most recently, anal cancer screening. The anal HPV epidemiology research has included studies with gay, bisexual, and other men who have sex with men, heterosexual couples, and heterosexual men. He has published more the 90 peer-reviewed papers on these topics and is funded by the National Cancer Institute (NCI). Prior to his HPV research, Dr. Nyitray delivered HIV prevention in a service capacity for 15 years.

His current NCI-funded research assesses equity-based protocols for anal precancer and cancer screening including determining engagement with annual HPV DNA self-screening among HIV-positive and HIV-negative gay and bisexual men (both cis and trans) and transgender women, assessment of molecular biomarkers for anal cancer screening, and assessing the sensitivity and specificity of self- and partner palpation for anal abnormalities. Men who have sex with men (MSM), especially MSM with HIV, have increased risk for anal cancer; however, screening for either anal precancers or anal cancers is not widely recommended.

The Prevent Anal Cancer (PAC) Self-Swab Study: The PAC Self-Swab Study recruited MSM and transpersons, aged ≥25 years in Milwaukee, Wisconsin into a clinical trial to assess screening for anal precancers. The study, (7R01CA215403, PI Nyitray), is a randomized clinical trial (NCT03489707) to evaluate engagement with annual home-based (self) vs clinic-based HPV DNA specimen collection among HIV+ and HIV- persons. Secondary objectives determine factors associated with annual screening compliance; estimate the influence that home-based vs clinic-based screening has on the uptake of high-resolution anoscopy; estimate the association between high-risk HPV persistence and anal high-grade squamous intraepithelial lesions (HSIL); and estimate the association between HPV-16/host DNA methylation and anal HSIL. The study partners with five geographically dispersed clinics in Milwaukee, both community clinics and Froedtert/MCW clinics. Nine clinicians in these clinics have been trained in digital anal rectal examination and anal swabbing techniques.
With community advisory board support, the project consented 253 Milwaukeeans and randomized 240 of these to receive a home-based self-swabbing kit for anal cancer screening or to go to a clinic for screening. At baseline, home-based screening resulted in greater screening engagement overall compared to clinic screening, especially among Black persons and people with HIV, groups with increased vulnerability to anal cancer. These results will support development of
equity-based anal cancer screening programs. Participants in this longitudinal study will continue to attend study visits through August 23, 2023.

The PAC Palpation Study: The PAC Palpation Study is recruiting MSM and transpersons who have sex with men, aged ≥25 years in Chicago and Houston to test anal self-exams (ASE) and anal companion exams (ACE) that seek to reduce morbidity and mortality from anal cancer. The PAC Palpation Study tests the ability of ASE and ACE to detect early anal cancer tumors when they are much more treatable. Results could propel the development of a low-resource screening for rapid dissemination to populations with high anal cancer risk and no currently proven screening options.

The study (1R01CA232892, PI Nyitray) consented 926 HIV+ and HIV- persons with oversampling of Black MSM given their underrepresentation in HPV research and high risk for HIV. A total of 727 participants were randomized, all of whom were taught about anal anatomy, pathology, and the procedure for an ASE or ACE. Then, they received a digital anal rectal examination (DARE) by a clinician after which they conducted the exam in private and recorded a result of either abnormal or normal. The primary objective is to compare the participant's ASE or ACE result at baseline with the clinician's gold-standard DARE to determine concordance, sensitivity, and specificity. The secondary objectives are to test the effect of practice on concordance after six months, and, using mathematical modeling, estimate the cost-effectiveness of ASE, ACE, and DARE and their impact on survival and health-related quality of life.

Jeffrey A. Kelly, Ph.D., Professor and Director, CAIR/HISG
Katherine Quinn, Ph.D., Associate Professor and Associate Director, CAIR/HISG
Center for AIDS Intervention Research (CAIR) / Health Intervention Sciences Group (HISG)
CAIR is a multidisciplinary Center dedicated to advancing scientific and public health knowledge concerning high-impact HIV prevention that integrates behavioral and biomedical modalities and that accelerates the implementation of these approaches by providers in the field. CAIR's mission is to conceptualize, conduct, and scientifically evaluate the effectiveness and community impact of interventions to prevent HIV infection and prevent adverse health outcomes among persons living with HIV infection. Drawing upon more than 25 years of HIV prevention research experience, the Center's research mission has been expanded to now also apply lessons learned from successful

HIV interventions to other new, emerging, and existing health threats. Current research projects, their CAIR/HISG Principal Investigators, and their funding sources are:

Principal Investigator(s)	Funding Source	Study Title
Yuri Amirkhanian & Jeffrey Kelly	NIMH	Mobilizing Social Network Resources for HIV Care Support: Development and Testing of an Intervention for HIV-Positive MSM
Michelle Broaddus	Advancing a Healthier Wisconsin Endowment	Phase III Implementation: HWPP Strategic Component of Wisconsin Community Coalitions Behavioral Health Initiative
Michelle Broaddus	Advancing a Healthier Wisconsin Endowment	Behavioral Crisis Response Transformation in Douglas County
Michelle Broaddus	Advancing a Healthier Wisconsin Endowment	CA:tCH—Expanding Shared Data Systems for Coordinated Community Crisis Response
Carol Galletly	Advancing a Healthier Wisconsin Endowment	Integration of Hepatitis C Diagnosis and Treatment into a Mobile Harm Reduction Unit
Laura Glasman	NIMH	Regular HIV Testing and HIV Prevention Among At-Risk Latino Men in the Heartland
Steven John	NIMH	Optimizing an IMB-guided intervention to support HIV self-testing and PrEP uptake among YMSM: A pilot factorial RCT
Steven John & Randolph Hubach	NIMH	3T-Prevent: Piloting a Multi-Level, Combination Intervention Strategy to Expand HIV and Bacterial STI Prevention
Jeffrey Kelly & Yuri Amirkhanian	NINR	Increasing PrEP Use in High-Risk Social Networks of African American MSM in Underserved Low-Uptake Cities

Jeffrey Kelly, Yuri Amirkhanian, & Katherine Quinn	NIMHD	Behavioral and Social Science Research to Optimize SARS-CoV-2 Protective Vaccine Uptake in Racial Minority Communities with High Rates of COVID-19
Katherine Quinn & Dexter Voisin	NIMH	Continuous Traumatic Violence and the HIV Continuum of Care Outcomes Among BMSM
Katherine Quinn & Dexter Voisin	NIMH	The Impact of Violence and Systemic Racism on COVID-19 Testing Outcomes Among Black Residents of Chicago
Jennifer Walsh	NIMH	Longitudinal Predictors of PrEP Use and Adherence Among Young Black MSM

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

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

Dr. Knight's research program aims to investigate biological risk and interventions – both pharmacologic and behavioral – for social health disparities in cancer, specifically among hematopoietic stem cell transplant (HCT) and cellular therapy recipients. Our lab does this by investigating how variations in immune function based on socioeconomic status (SES) – among other social health variables including depression, stress, sleep quality, and anxiety – contribute to differential patient responses and outcomes following HCT and cellular therapy. Reciprocally, we also investigate how these cancer therapies affect central nervous system function.
To accomplish these goals, we study biobehavioral mechanisms of cancer progression. Candidate mechanisms include the conserved transcriptional response to adversity (CTRA) transcriptome profile and associated molecular changes, inflammation, sympathetic nervous system activation, neurotoxic metabolites, and the endocannabinoid system, among others. These pathways are investigated as potential mediators of social health disparities among HCT recipients.

Dr. Knight's group has identified a potential effective candidate pharmacologic intervention for such social health disparities – propranolol. They have identified propranolol as an effective pharmacologic mitigator of CTRA gene expression among a cohort of patients with multiple myeloma undergoing HCT. Subsequent future research goals involve investigating whether propranolol is effective in ameliorating adverse clinical outcomes associated with reduced expression of these potential biomarkers. We have also recently confirmed preliminary findings that these CTRA-related transcriptome dynamics are associated with adverse clinical outcomes among HCT recipients. Examples of ongoing and future work include investigating the following:
- Bidirectional neuroimmune effects of tocilizumab, an IL-6 antagonist used to treat
- Biobehavioral implications of chimeric antigen receptor (CAR) T cell therapy
- Mindfulness to improve sleep and related symptomatology and inflammatory markers among hospitalized HCT recipients
- Effect of donor SES on recipient HCT outcomes
- Propranolol as an intervention to reduce cancer progression

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

Kelly E. Rentscher, PhD

Kelly E. Rentscher, PhD, is a clinical and health psychologist, an Assistant Professor of Psychiatry and Behavioral Medicine, and an MCW Cancer Center Scholar. Prior to joining the faculty at MCW, she obtained her Ph.D. from the University of Arizona, completed a pre-doctoral internship at the University of Wisconsin-Madison and a post-doctoral fellowship in psychoneuroimmunology at UCLA, and held an Assistant Professor appointment, also at UCLA.

Dr. Rentscher's research program examines biobehavioral factors that contribute to accelerated aging in midlife adults and cancer survivors, with a focus on transplant and cellular therapy. She has a particular interest in understanding how experiences of stress and adversity may increase risk for accelerated aging and age-related disease, and how social relationships may protect against the negative effects of stress on these outcomes. Dr. Rentscher's research integrates cutting-edge behavioral (e.g., naturalistic observation) and genomics (e.g., whole-genome RNA and DNA methylation profiling) methods, with a focus on molecular biomarkers of aging (e.g., cellular senescence, epigenetic age acceleration). One of her longer-term goals is to translate findings from this research to develop behavioral interventions that can prevent or slow accelerated aging in cancer survivors to improve their quality of life and extend their healthspan and lifespan.

Dr. Rentscher has received several intramural and extramural grants to support her research, including an NIH Mentored Research Scientist Development Award (K01) to examine the influence of social processes on accelerated biological and phenotypic aging in hematopoietic cell transplant survivors during the first year of recovery, and a Junior Faculty Career Development Award from the Childhood Cancer Survivor Study at St. Jude Children's Research Hospital to examine accelerated aging in adult survivors of childhood cancer.

Radiation Oncology

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

Radiation Oncology Committee to Advance Knowledge and Education Through Clinical Trials (ROCKET) program
ROCKET supports the mission of the Froedtert & Medical College of Wisconsin Cancer Network through the demonstration of national scientific leadership while providing meaningful contributions to the Cancer Center interventional clinical trials portfolio.
ROCKET develops and supports innovative early phase radiation clinical trials. The goal is to provide pilot data for extramural funding, develop therapies for National Clinical Trials Network (NCTN) or other multisite trials, and test novel treatment approaches to establish new standards of care and improve outcomes for cancer patients.

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

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

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

Radiology

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

The Department of Radiology continues to grow a robust administrative research infrastructure to support research and the team is led by Co-Vice Chairs of Radiology Research Kevin Koch PhD, the Director of the Center for Imaging Research, and Sarah White, MD, MS. Due to the large volume of clinical research currently being performed, Kelly Salinas and Helena Zaldivar Alcantara were recently hired as VIR Clinical Research Coordinators. In their roles they recruit, consent, and manage follow-up of clinical trial patients. In addition to her part-time IR research RN position, Kelly is a Froedtert Operating Room Operations Coordinator Charge Nurse. Helena comes to us with a background as a nephrologist as well as past pharmaceutical clinical research experience. Continuing in their roles as Clinical Research Manager and Radiology Program Manager are Elizabeth Weil and Jodi Nicolai-Johnson respectively. Elizabeth navigates the regulatory processes for all VIR research as well as patient related research activities. Jodi is an expert in grant submission and post grant award follow-up. After the grant is awarded, Jodi tracks the budget and timelines for the follow-up of deliverables with the assistance of new Grants Operations Coordinator Madeline Kornbeck. Additionally, Jodi, Helena and Elizabeth have been involved in the OnCore Financials pilot program.

Together Drs. Koch and White have obtained MCW IRB approval for an umbrella protocol that can be used by all radiology faculty. This radiology umbrella protocol was modeled after the VIR umbrella protocol. It allows research (retrospective chart review) of all imaging studies and their comparators to be reviewed. So far, 54 sub-studies have utilized this umbrella protocol. The investigative teams (under this protocol) have presented their research findings as oral presentations (2) & posters (2) at radiology-related conferences and abstracts (12) & publications (8) in high-impact journals. To better accommodate the research needs of our active sections, we've added two MCW IRB-approved umbrella protocols (for the Breast and Neuro radiology sections) to our portfolio. In addition, Dr. Andrew Nencka is the PI of another umbrella MRI protocol that allows for clinical and research technology investigations. This protocol can be used for investigations of new sequences and processing applications on consenting volunteers and clinical subjects.

In August 2022, the VIR division welcomed VIR research fellow Arun Kamireddy. Arun assisted with manuscript preparation for many of the sub-studies developed from IR umbrella protocol. Two junior faculty members, Azadeh Sharafti, Ph.D., and Nikolai Mickevicius, Ph.D., joined the research core last year - 2022. Both lend invaluable support to the scientific programs and departmental infrastructure support led by senior technical faculty members Dr. Kevin Koch and Dr. Andrew Nencka. Together, our core technology faculty members seek to develop programs that can open extramural funding opportunities and support existing funded research programs. Our approach is to leverage interdepartmental and inter-institutional collaborations to position the department strategically for these opportunities.

The benefits of an increased and strengthened research support staff are already apparent with many process innovations and new opportunities. Dr. Peter LaViolette received an R01 for his study titled “Prostate Cancer Radio-Pathomics for Differentiating Clinically Significant Disease” and Dr. Yang Wang was awarded an R21 for his “Neurovascular Uncoupling and Cognitive Impairments of Long COVID in Aging” project. The Radiology Pilot program is functional and has assisted (and continues to support) our clinicians/faculties/fellows with their research ideas, design, and execution. Among other things, through the support pilot program, we have successfully secured grant funding from the Research Affairs Committee for one of our Medical Physicists and recently obtained MCW IRB approval for one of the radiology fellows for an observational study using MCWAH trainees.

The overall research activity within the Department of Radiology continues to grow. Within the past year, the Department has submitted approximately 33 grant applications, and has collaborate on over 33 other grant applications. Current fiscal year research revenue includes $1M NIH funding, we also have a couple of multi-PI Federal Grants submitted with other institutions.

Other Extramural revenue stayed strong at $600K which is an increase from the previous year. Sponsors with recognizable names such as Radiological Society of North America, Siemens, CR BARD, Cook Medical, Penumbra, DFINE, W.L. Gore and Associates, Medtronic

GE Healthcare, Histosonics, Vesper Medical, Instylla, Neuwave Medical have new and ongoing collaborations with the Department of Radiology.

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

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

For the 2022-2023 academic year, the MCW Division of VIR continued to expand its clinical and translational research activities. The VIR Faculty are serving as sub-investigators on at least 10 protocols for other department's clinical trials (e.g. oncology, nephrology, GI, vascular surgery). Drs. White and Smolock's translational Interventional Oncology (IO) lab published 3 papers (and 2 in progress), 7 abstracts, 6 ongoing grants, awards from JVIR and SIO and 3 invited lectures. The Division plans to open 3 new clinical trials, completed and closed 2 trials and continues research activities in 4 clinical trials. Their research endeavors have resulted in 4 publications, 3 grants, 16 abstracts, 2 oral presentations and 8 poster presentations at national and international meetings. Herein we will highlight some of the pivotal trials our faculty have been involved with over the past year:

- **Vice-chair, Clinical Operations-Image Guided Procedures, William S. Rilling, MD, FSIR** continues to build his research interests, which are focused on image guided therapy for cancer. He continues to provide research mentorship to trainees and medical students. Dr. Rilling served as national PI for an embolic device trial MONARCH that was completed in 2022. He is also working on opening new trials evaluating new radiation therapies for primary and secondar liver cancer. As a testament to his illustrious career, Dr. Rilling delivered the 2023 SIR Annual Dr. Charles T. Dotter Lecture, the highest award bestowed upon an IR in the US.

- **VIR Division Chief, Eric J. Hohenwalter, MD, FSIR** is serving as PI, and actively recruiting for, the C-TACT trial which is a NIH-funded randomized controlled trial that is examining new treatments for damage to veins caused by blood clots (DVT). Dr. Hohenwalter as serves as PI and continues to enroll patients in an investigator-initiated trial in collaboration with cardiology and GI physicians. Funded by the Radiological Society of North America (RSNA), the study will determine the impact of the transjugular intrahepatic portosystemic shunt (TIPS) procedure on cardiac function.

- **Parag J. Patel, MD, MS, FSIR** serves as PI for several clinical trials. A liquid embolic multi-center clinical trial, LAVA, was completed in late 2022. Dr. Patel is PI for 2 venous stent device trials, VIVID and VIAFORT, for treatment of iliofemoral obstruction; VIVID has completed enrollment and patients are in follow-up while VIAFORT is anticipated to begin enrollment in Q2 2023. Dr. Patel is also collaborating with the Department of Surgery/Trauma Critical Care on their We Care Funded investigator initiated splenic embolization trial. Dr. Patel just completed his tenure as President for the Society of Interventional Radiology (SIR).

Co-Vice Chair, Radiology Research, Sarah B. White, MD, MS, FSIR, FCIRSE continues work in her translational research laboratory at MCW with an emphasis on interventional oncology. Dr. White is also very involved in student programs such as the Medical Student Summer Research Program, SIR sponsored summer research students, and the SPARCC (Student-Centered Pipeline to Advance Research in Cancer Careers) program where undergraduate students observe and learn about interventional and diagnostic radiology and the research done in the department. Dr. White is the PI for the currently enrolling Histosonics #HOPE4LIVER clinical trial. Dr. White was the PI for an embolic device trial MONARCH that was completed in 2022 and will be PI in an upcoming embolic device trial, HALT, with enrollment anticipated for Q2 2023.

- **Matthew J. Scheidt, MD, FSIR** is the PI for the STRIKE_PE multicenter clinical trial; using real world long term functional outcomes the trial is evaluating safety and performance of the Indigo Aspiration System for the treatment of pulmonary embolism (PE) in acute high and intermediate risk PE patients. Dr. Scheidt will also be the PI for the upcoming NIH-funded, multi-center randomized trial PE-TRACT. PE-TRACT seeks to determine whether patients with submassive PE who are treated with catheter-directed therapy (CDT) (includes catheter mechanical thrombectomy (MT) and catheter directed lysis (CDL)) plus medical therapy (CDT group) have better cardiopulmonary health in the year following PE than patients treated with medical therapy alone (No-CDT). Dr. Scheidt continues to provide research mentorship to trainees and medical students.

- **Amanda Smolock, MD, PhD** joined the division of VIR in 2020. She has been a research mentor for several trainees and students. Dr. Smolock is a pioneer in histotripsy research and is part of the #HOPE4LIVER and in June 2022 made the news

for MCW's unique participation in this trial for treating the third patient in the country with the device. MCW is one of only 8 sites in the country participating, largely due to Dr. Smolock's involvement. Our participation in this study was picked up by the institution's media with featured articles in both MCW Magazine and Froedtert Today. A link to the Spectrum News 1 video is below: https://spectrumnews1.com/wi/milwaukee/news/2022/06/01/sound-waves--new-clinical-trial-in-wisconsin-uses-technology-to-treat-liver-cancer#. Dr. Smolock will be the PI for ACCLAIM; a prospective multi-center trial of microwave ablation as curative treatment for metastatic colorectal cancer. Enrollment is anticipated to begin Q2 of 2023. She will also be Co-I (Dr. Shreenivas PI) on PERIO-02 which seeks to test an immuno-stimulatory drug with the potential to overcome the intra-tumoral pressure and immunosuppressive barriers within HCC and ICC tumors delivered via hepatic arterial infusion with a pressure-enabled delivery device. The goal is IRB approval later in 2023. Dr. Smolock also has work in the animal translational research lab. In 2022 she received 2 year funding for the prestigious RSNA Research Scholar Application for her proposal entitled *"Understanding the Effect of Histotripsy on Tumor Hypoxia in a Pancreatic Cancer Model".*

- **Brandon Key, MD** joined the division of VIR in 2020 after completing his IR Fellowship at MCW. Dr. Key's interests lie in technique for image guided orthopedic applications. Dr. Key is the PI for a vertebral compression fracture (VCF) registry that is collecting real world data regarding current clinical practice to assess patterns of care and outcomes.
- **Mircea Cristescu, MD** joined the division of VIR in 2022. He has been instrumental as a Sub-Investigator and enhanced enrollment for the VIR clinical trials.

Surgery

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

The department received $6.3 million in research funding in FY2021 and jumped 20 spots in the Blue Ridge Institute rankings to #45 with over $2.7 million in NIH funding. In 2022 the department had over 380 active human subject research projects in a variety of fields.

Surgery faculty worked one-on-one with 25 medical students as part of the SAMS Medical Student Summer Research Program (MSSRP) in 2022. 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. Department faculty also engage General Surgery Residents in research with 9 residents electing to take research rotations in this last year.

Division of Research

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

Strategic Goals – E^4:

Empower: **Train tomorrow's surgeon scientists**

Elevate: **Facilitate research beyond support**

Engage: **Foster intentional research development**

Excel: **Focus on our strengths as a differentiator**

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

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

Division faculty and their research interests:

Gwen Lomberk, PhD, serves as the Chief for the Division of Research, Director of Basic Research and Associate Professor of Surgery and Pharmacology & Toxicology. Dr. Lomberk's research program is broadly focused on the epigenetic landscapes that characterize subtypes of pancreatic cancer (PDAC) and refining the utility of epigenetic inhibitors for treatment and re-sensitization to conventional therapies. Epigenomic-based pharmacology has the potential to serve as a robust tool to improve the treatment of PDAC. Her laboratory seeks to contribute to the field of experimental therapeutics through combined inhibition of genetic-to-epigenetic pathways, as an important and provocative consideration for harnessing the capacity of cell cycle inhibitors in efforts to enhance future use of epigenetic inhibitors.

Young-In Chi, PhD, Assistant Professor, joined us from Kyongpook National University Medical Center in Daegu, Korea where he was a Research Professor in the Center for Drug Discovery and Development for Diabetes and Metabolic Disease. Dr. Chi is a member of Dr. Raul Urrutia's team in the Genomic Sciences and Precision Medicine Center and conducts basic science research in the areas of molecular modeling, variant analysis, and precision medicine of pancreatic cancer.

Angela Mathison, PhD, Assistant Professor, joined the Department of Surgery in August 2018 from the Genomic Sciences and Precision Medicine Center where she is the Technology Development Director. Dr. Mathison's research focuses on the role epigenetics play in the development and progression of pancreatic cancer and the potential to target these cellular mechanisms for novel therapies.

Raul Urrutia, MD, serves as the Director of the Genomic Sciences and Precision Medicine Center, Warren P. Knowles Professor of Genomics and Precision Medicine and Professor in the Department of Surgery. Dr. Urrutia's laboratory focuses on precision medicine as it applies to pancreatic cancer, as well as other diseases. Precision Medicine is a clinical discipline that was born from basic science in genetics, as well as engineering, representing a translational science "par excellence" with an actual marriage of basic science with clinical science. Through the combination of three innovative tools of Cancer Precision Medicine, namely multi-omics, computational modeling, and patient-derived models, his research program seeks to identify new mechanisms, diagnostic markers, and therapeutic targets for pancreatic cancer. His laboratory has been focused on investigating how epigenomic regulators work as nuclear effectors of common mutations (e.g. KRAS) associated with human pancreatic diseases.

Division of Cardiothoracic Surgery, Adult

Paul Pearson, MD, PhD is the chief of Cardiothoracic Surgery and has dedicated the majority of his career to clinical trial participation and device development, largely in the field of cardiac valve replacement and repair. He is looking forward to his upcoming left atrial appendage occlusion trial during cardiac surgery in addition to the development of our pre-clinical studies to evaluate a new mitral valve annuloplasty ring of his own design. His research interests include the use of new and innovative valve repair devices in addition to his interest in increasing patient accessibility to cardiac valve repair centers.

Lyle Joyce, MD, PhD has been practicing in the field of cardiothoracic surgery for more than 40 years, focusing on heart transplantation and the surgical treatment of heart failure. He is world-renowned in the field of cardiothoracic surgery having been on the team that implanted the first permanent artificial heart in a man and was the first surgeon ever to use a total artificial heart in a woman. He recently implanted the first ever regenerative synthetic coronary artery bypass graft in a human and is still seeking ways to improve coronary artery bypass grafting in high risk patients through the use of intraoperative cardiac support devices.

G Hossein Almassi, MD is the chief of Cardiothoracic Surgery at the Clement J. Zablocki Veterans Affairs Medical Center. He was a key investigator in the ROOBY trial, a randomized trial of on-pump vs off-pump coronary artery bypass surgery. He is involved in continued analysis of data related to the ROOBY trial and has a keen interest in post-operative atrial fibrillation in this population. In addition, he was an investigator in the REGROUP trial, a large multicenter study which randomized patients to endoscopic versus open saphenous vein harvest during coronary artery bypass.

Nilto De Oliveira, MD is the surgical director of the lung transplant program and performs a variety of surgical procedures such as aortic valve surgery, mitral valve repair and reconstruction, aortic arch aneurysms, total aortic arch replacement, and redo-cardiac

operations in addition to lung transplants. His interests and expansive expertise allow him to participate in various clinical trials throughout the division.

Lucian Durham, MD, PhD is the head of our ECMO program which is one of the busiest in the Midwest. He currently serves as the primary investigator on numerous clinical trials involving heart & lung transplants and hemofiltration devices to remove unwanted medications during surgery. His research interests involve the development and growth of ambulatory ECMO, durable LVAD technology in pediactric and adult populations, improving outcomes in ECMO patients, AI in healthcare, and expanding the use of hemofiltration devices to remove inflammatory mediators during surgery.

Mario Gasparri, MD is a thoracic and robotic cardiac surgeon currently serving as the principal investigator of the cryo nerve block technique to reduce postoperative pain following robotic lung resections. He is also one of the leading physicians of our atrial fibrillation research group and pioneered a minimally invasive robotic ablation technique for atrial fibrillation modified from the traditional CONVERGENT procedure.

David Johnstone, MD is a thoracic surgeon interested in comparing patient outcomes and procedural costs of robotic assisted, video assisted, and traditional open thoracic surgeries. He pioneered the Transcervical Endoscopic Esophageal Mobilization (TEEM) technique for patients with esophageal cancer, participated in studies utilizing molecular diagnostic techniques to improve targeted oncologic therapies, and devoted his career to improve the outcomes and qualify of life of cancer patients through interdisciplinary collaboration with oncologists and other specialties.

Takushi Kohmoto, MD, PhD, MBA is primarily interested in research surrounding patient outcomes related to heart transplantation, cardiac revascularization, and limiting inflammation during cardiac surgery. His research interests include regenerative cardiac techniques such as stem cell therapy for patients in severe heart failure or patients with cardiac damage as a result of a previous infarct and techniques to increase cardiac viability of heart transplant donors.

Paul Linsky, MD is interested in blood based biomarkers for early detection of recurrent lung cancer and nutrient deficiency/replacement for esophageal cancer patients to improve their quality of life. Additionally, he is currently seeking approval to become a diaphragmatic stimulation implant center for ventilator dependent spinal injury patients to not only improve their quality of life but also decrease their overall healthcare expenses. He is interested in collaborating with the VA moving forward evaluating outcomes and utilization of large databases.

James Mace, MD is involved in numerous clinical trials in our division including the use of mechanical support devices during coronary artery bypass surgery as well as his interest in the use of hemofiltration devices to remove unwanted drugs during emergent procedures. His interests include the risk-benefit ratio of cardiac procedures along with his ability to critically assess patients maximal improvement to ensure patients have the best quality of life even if that means surgery isn't the best option. His past research evaluated cardiac surgery in transplant recipients with minimal perioperative risk demonstrating his interests and continual contributions towards cardiothoracic surgery.

Stefano Schena, MD, PhD is interested in the development of new therapies and procedures such as transcatheter treatment options through interdisciplinary collaboration. He is one of the contributing members that developed the robotic iteration of the convergent plus procedure and is actively involved in the surgical/hybrid treatment of atrial fibrillation research group. His other research interests include minimally invasive management of the left atrial appendage in atrial fibrillation, identification of perioperative risk factors determining severe post-operative bleeding in cardiac surgery, and cardiac surgery outcomes research focusing on HIT, post-operative bleeding and early intervention, and bicuspid aortic valve patients with concomitant aortopathy.

H. Adam Ubert, MD is actively seeking to develop and improve our ambulatory ECMO program with a specialized interest in the optimization of anticoagulation in these patients. He plans to continue to participate in the growth and development of the ECMO outpatient clinic, the ambulatory ECMO program, and he is actively seeking funding for ECMO & MCS immunoprofiling.

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.

Michael E. Mitchell, MD and **Aoy Tomita-Mitchell, PhD** collaborate closely with the multidisciplinary Herma Heart Institute (HHI) research team and prioritizes mentoring students and trainees in research. Dr. Michael Mitchell is PI of the Congenital Heart Disease (CHD) Tissue Bank, and member of the HHI Cord Blood Bank which is aimed at advancing the science and practice of cell-based clinical therapies for high-risk patients with CHD. He is Co-PI of a Children's Research Institute grant to investigate the role of cell-free DNA as a predictor of clinical outcomes in patients undergoing pediatric cardiac surgery. Dr. Tomita-Mitchell and her collaborators are investigating the role of genetic variants in CHD etiology using patient-specific induced Pluripotent Stem Cells (iPSCs) differentiated into cardiomyocytes to model CHD. The team has been investigating therapeutic strategies including gene editing, cell signaling modifications and other molecular approaches through funding from AHW and TAP program. In collaboration with Biomedical Engineering, the Mitchell team has been exploring using bioprinted patient-specific cardiac cells in a 3D tissue construct in a study funded through the AHA. The Mitchell lab has also studied the science of cell-free DNA extensively and continues to explore numerous applications in cardiac transplantation, cardiac surgery, and during infection with collaborators through studies currently funded through NIH, CRI, CTSI, and industry.

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. He is the site PI for 2 large multicenter studies and has organized a multicenter registry to evaluate mechanical circulatory support in single-ventricle patients. He regularly mentors medical students on clinical projects which often lead to podium presentations and publications. Additionally, Dr. Woods is actively engaged in innovation to develop new technology to improve the quality and safety of surgical care.

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

Tracy Geoffrion, MD, MPH has published over 50 articles, abstracts, original papers, book chapters and reviews to date. Her primary interests include clinical outcomes after surgery for congenital heart disease, quality improvement initiatives to improve care delivery in CHD, and quality of life in CHD patients. Her published research includes studies on clinical outcomes after heart and lung surgery, quality improvement, unique surgical case reports, and translational research for cardiac surgery using animal models. Her previously funded research projects include studies of mitochondrial adaptation to chronic hypoxemia, mitochondrial function post cardiopulmonary bypass, the impact of genetic variation on outcomes following congenital heart surgery, and hemodynamic patterns in bidirectional Glenn patients during CPR. She is a principal investigator on a developing clinical trial studying novel medical treatments for congenital heart disease patients with heart failure. She has also initiated collaborative efforts with the Divisions of Bioethics, Critical Care, and Palliative Care to study medical decision-making in complex congenital heart disease patients. Dr. Geoffrion also serves as an investigator for the NIH NHLBI funded Multi-Institutional Neurocognitive Discovery Study in Adult Congenital Heart Disease (ACHD-MINDS). Her ultimate research goal is to improve quality of life and high-quality longevity in these patients with a combination of medical and surgical therapies.

John Baker, PhD. Dr. Baker's research program serves as a nexus to translate basic science discoveries into clinical applications. He is currently focused on several areas of study. One such area is investigating why survivors of childhood cancer who have been treated with radiation therapy are at increased risk for heart disease. Another area of focus funded by NASA is determining the increased risk for developing degenerative cardiovascular disease from exposure to components of space radiation using a ground-based rat model. Additionally, and in collaboration with Dr. Aoy Tomita-Mitchell, Dr. Baker is looking at cell free DNA as a biomarker for assessing DNA damage from radiation exposure during cardiac catheterization. This research will fulfill an unmet need in children with congenital heart disease who require cardiac catheterization by monitoring damage to DNA from medical radiation and potentially mitigating diseases later in life.

Division of Colorectal Surgery

The research efforts within the Division of Colorectal Surgery remain robust. **Dr. Kirk Ludwig** continues as the institutional principal investigator (PI) for a Cooperative Group Colorectal Cancer Trial at the Froedtert and MCW Cancer Center. The purpose of the trial is to explore the use of neoadjuvant chemotherapy for treatment of locally advanced rectal cancer. Dr. Ludwig is also involved in two

early-stage clinical trials studying the safety and efficacy profile of each new product. One study drug is to be used in conjunction with an enhanced recovery pathway for gastrointestinal recovery on the resolution of postoperative ileus following bowel resection. The objectives of the other study are to determine the safety and effectiveness of the SFM Anastomosis Device when used to create a small bowel anastomosis for patients undergoing ileostomy reversal as compared with a propensity-matched historic control group of patients who underwent ileostomy reversal using a conventional closure technique (sutures or stapler). Dr. Ludwig also serves as the Division Chief and holds the Vernon O. Underwood Endowed Chair. Under his supervision, the Division has begun to carefully track functional outcomes in those undergoing resections for rectal cancer and the treatment of anal cancer. Dr. Ludwig has a national reputation as an expert in the surgical treatment of rectal cancer with special emphasis on sphincter sparing techniques.

Dr. Jed Calata recently joined the division and leads several active research studies focused on physician social media content effect on patients' physician preference, housing affordability for residents, and influence of residency or fellowship placement in the hiring practices of surgical faculty at academic hospitals. An upcoming study will aim to determine if the availability of a skin-tone congruent ostomy appliance would impact the patient-experience of living with an ostomy, and if so, how.

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

Dr. Carrie Peterson is the site PI for the rectal cancer surgical collaboration study, aimed at enhancing our understanding of the use and outcomes of neoadjuvant therapy for rectal cancer across the US. Dr. Peterson collaborates with Dr. Bill Hall on the MRI-Guided Adaptive Radiation Therapy for Organ Preservation in Rectal Cancer study. Dr. Peterson also continues to pursue her research interests in minimally invasive colorectal surgery and surgical outcomes. She is heavily involved in several research projects evaluating improvements in quality and perioperative process improvements.

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

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

Division of Minimally Invasive Gastrointestinal Surgery

The Division of Minimally Invasive Gastrointestinal Surgery supports the Department's commitment to excellence in education and research. Over the 2022-2023 academic year, faculty and research staff collaborated to develop 6 new research protocols and showcased the institution's innovative efforts through virtual presentations at local, regional, and national meetings. Additionally, Tammy Kindel, MD, PhD received an R01 from the NIH National Heart, Lung, and Blood Institute for her project titled "*Identifying Gut Microbiome Mediated Mechanisms for Diastolic Dysfunction Improvement After Bariatric Surgery.*" Throughout the academic year the division faculty mentored 12 medical students and 4 general surgery residents. Our research is focused in the domains of foregut surgery, bariatric surgery, and hernia surgery.

Bariatric Surgery

The bariatric surgery program at Froedtert and the Medical College of Wisconsin is accredited as a Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program (MBSAQIP) Comprehensive Center with Adolescent Qualifications. A current quality improvement project is focused on understanding the impact of VTE prophylaxis on bariatric surgery outcomes, led by Dr. Kindel. Additionally, Dr. Higgins is evaluating the sociodemographic factors leading to preventable emergency department visits after bariatric surgery. The division published multiple peer-reviewed bariatric surgery manuscripts in journals that including *Surgery for Obesity and Related Diseases, JAMA Surgery, Surgical Endoscopy, Obesity Surgery, the American Journal of Surgery,* and *Surgery.*

Foregut Surgery

In the 2022-2023 academic year, the division participated in several multi-institutional sponsored trials on gastroesophageal reflux disease (GERD) surgical outcomes using implantable medical devices. We continued to review long-term outcomes for patients following surgery that received an implanted magnetic sphincter augmentation device (LINX). Faculty continued to examine long-term patient experiences following implantation of a gastric electrical stimulation device (Enterra) in patients with medically refractory gastroparesis. In addition, the Tailored Myotomy to Reduce the Incidence of Post-Procedure Reflux after Peroral Endoscopic Myotomy (POEM) trial was approved for enrollment. The Division presented findings in foregut surgery outcomes at Wisconsin Surgical Society, Academic Surgical Congress, and Society of American Gastrointestinal and Endoscopic Surgeons (SAGES). Peer-reviewed manuscripts were accepted to *Surgical Endoscopy, the Journal of Gastrointestinal Surgery,* and *Surgery.*

Hernia Surgery

Sponsored and investigator-initiated studies in the hernia domain included studies designed to evaluate quality and recovery outcomes following implantation of various types of mesh. Dr. Kastenmeier is PI for a multisite study assessing the clinical safety and performance of the Dextile anatomical mesh when used as intended in a real-world setting. Dr. Goldblatt is PI of a study evaluating the ENFORM Biomaterial product in hernia repair. The Division continues to participate in the Americas Hernia Society Quality Collaborative, a national quality improvement effort aimed at improving the quality of care provided to hernia patients. The Division's hernia research efforts were presented at MCW, the *Wisconsin Surgical Society*, and nationally at *Academic Surgical Congress, Southwest Surgical Association,* and the *International Hernia Congress*.

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 2023-2024 and beyond.

Division of Pediatric General and Thoracic Surgery

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

Kirkwood Pritchard, Jr., PhD leads a successful bench research lab focused on vascular function in sickle cell disease and bronchopulmonary dysplasia. Dr. Pritchard has an NIH R01 grant to research mechanisms of oxidative stress and inflammation in sickle cell disease. In addition, he has a We Care grant to study how H1N1 seasonal flu injures the lung and increases the risk of acute respiratory distress syndrome (ARDS), and explore novel therapies for reducing the risk of complications resulting from severe seasonal flu. Dr. Pritchard established the licensing agreement for MCW startup ReNeuroGen, LLC to develop and test a novel treatment for secondary brain injury after stroke. ReNeuroGen has been funded by the NIH SBIR program.

Brian Craig, MD bench research program is focused on understanding the role that perioperative factors, such as tissue injury and inflammation, play in enabling progression of metastatic disease in neuroblastoma. He is developing a pre-clinical model to enable mechanistic investigations of the immune response to surgery and how that immune response may either suppress antitumor immunity and/or directly support tumor growth. The lab's long term goal is to identify novel therapeutic opportunities that would be unique to the perioperative window, and ultimately to translate these findings to children who undergo major surgery as a part of their therapy for neuroblastoma. Dr. Brain Craig has been awarded grants from the Children's Research Institute, the American Pediatric Surgical Association Foundation, and most recently, an NIH KL2 through the CTSI.

Jose Salazar Osuna, MD bench research focuses on prematurity and the artificial placenta in a sheep model. He is investigating a model of extracorporeal support of a premature sheep fetus with preservation of the placenta. This model could address limitations of the artificial placenta by avoiding fetal exposure to heparin and modulating blood flow before it reaches the fetus. Dr. Salazar

Osuna's initial experience and design of the model was presented at the International Fetal Medicine and Surgery Society 2022 meeting.

Amy Wagner, MD is the national PI for the Gastroschisis Outcomes of Delivery (GOOD) Study. The GOOD Study is a national, multi-site, randomized controlled trial designed to evaluate delivery timing of infants diagnosed with gastroschisis and provide evidence of optimal delivery timing. This study also aims to establish a national clinical data registry and bio-bank comprised of gastroschisis patients. Currently, 34 centers across the country, including MCW as the coordinating center, are participating in the study. This trial is federally funded by an NIH R01 and has received financial support from the We Care Fund, the Melitta S. Pick and Joan M. Pick Charitable Trust, the Ruth St. John and John Dunham West Foundation, the North American Fetal Therapy Network, and the Stanek Fund.

The majority of the clinical research in Pediatric Surgery is through multi-institutional collaboration. The Midwest Pediatric Surgery Consortium (MWPSC) is comprised of 11 children's hospitals that collaborate on groundbreaking research projects by enabling institutions to combine data on diagnoses and anomalies with low incidence rates to generate meaningful results that impact the greater community. **Dave Lal, MD, MPH** spearheaded multiple MWPSC projects including two that have directly impacted the current care of pediatric patients including 1) creating evidence-based clinical practice guidelines to standardize management for patients with esophageal atresia/tracheoesophageal fistula, leading to an over 80% reduction in strictures and 2) development of a standardized preoperative algorithm for patients with ovarian masses to increase ovarian preservation. **Katherine Flynn-O'Brien, MD, MPH** recently designed and led a MWPSC study that examined the effect of the COVID-19 pandemic on the distribution, injury pattern, and severity of pediatric trauma. This study alone contributed seven publications, five national presentations, and one regional presentation highlighting burns, gunshot wounds, non-accidental trauma, and socioeconomic status variability in pediatric trauma during the pandemic. **David Gourlay, MD** developed and implemented a protocol through the MWPSC to prospectively study venous thromboembolism prophylaxis in pediatric trauma patients.

The Pediatric Colorectal and Pelvic Learning Consortium (PCPLC) consists of 17 clinical sites across the United States with a focus on anorectal malformations (ARM), Hirschsprung disease, and other colorectal and pelvic disorders. **Casey Calkins, MD** is the acting Documentation Sub-committee Chair on the Steering Committee, providing direction and assigning priorities for the consortium. **Jack Schneider, MD** is a member of the Documentation Sub-Committee. The primary study of the PCPLC is the creation and maintenance of a comprehensive registry of subjects with Hirschsprung disease, ARM, and idiopathic constipation. A supplemental study, Patient- and Parent-Reported Outcome Measures (PROMs), collects validated quality of life surveys from subjects and families, adding lived experience and perspective that can be linked to the surgical and medical data in the registry to study the relationship between treatment options and outcomes/quality of life.

The Pediatric Surgical Oncology Research Collaborative (PSORC) is a multi-institutional collaborative effort to improve surgical care for children with cancer with representation from 33 major children's hospitals. Drs. Dave Lal and Brian Craig have been an integral members of PSORC from its inception, and continue to drive innovation within this collaborative network. We are currently finishing co-leading a project to identify which patients with Ewing sarcoma with lung metastases may benefit from surgery. Upcoming studies include a rare renal tumor study and a unified neuroblastoma study with six sub-studies, one of which will be led by Dr. Craig examining chemotherapy delays in this surgical population.

Access to quality pediatric surgical care in underserved communities is the focus of **Kyle Van Arendonk, MD, PhD** current research. Dr. Van Arendonk is a skilled data scientist who works with large national databases to understand disparities in pediatric surgical care. He is also the leader of the division's ERAS initiative and leads the division's participation in projects through the national Pediatric Surgical Research Consortium (PedSRC).

John Densmore, MD has a strong clinical interest in Congenital Chest Wall Malformations. His research works to identify variability that impacts the cost of pediatric surgical care. Dr. Densmore is also spearheading groundbreaking innovations in treatment of tracheal agenesis, with emphasis on studying the impact of embryology on development of this rare diagnosis.

Division of Transplant Surgery

Introduction

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

Basic Science Research

While a significant number of patients awaiting liver transplantation die each year due to lack of suitable donor organs, similar number of donated livers are being discarded because of poor organ function caused by ischemia and reperfusion injury (IRI). The primary goal of our basic science research program is to develop novel bench to bedside therapies that would circumvent IRI. These therapies would expand the organ donor pool by converting high-risk liver organs (currently being discarded) to normal-risk transplantable organs and thus, saving more human lives.

The primary area of study is on the mechanisms of liver IRI as it relates to transplantation immunobiology. Our research laboratory utilizes experimental rat model to study the physiologic, immunologic, metabolic, and transcriptomic profiles of liver IRI.

Clinical and Translational Science Research

Current ongoing studies involving Divisional Faculty in academic year 2022-2023

1) Assessment and Treatment of Hepatic IRI in Rats
2) Clinical Outcomes According to Race Among Heart Failure Patients Evaluated for Advanced Therapies
3) The Effect of Early Mobility on Outcomes of Critically Ill Patients in a Transplant Intensive Care Unit
4) Quantification of the pathologic impact of inflammation and fibrosis on outcomes following orthotopic liver transplantation for severe acute alcoholic hepatitis
5) Pancreatitis in Liver Transplant Patients
6) Incidence and Effect of Cardiomyopathy in Liver Transplant Recipients
7) The Role of Everolimus in Liver Transplantation. Safety and Efficacy Assessment
8) The Effect of Early Post Liver Transplant Hypercalcemia on Transplant Outcomes
9) Candidates Removal from the Kidney Transplant Waiting List for Cardiovascular Reasons: A Single Center Experience
10) Neurocognition in Heart Failure and Relationships with Mechanical Circulatory Support and Transplant Outcomes
11) The effect of race on Liver Transplant Outcomes. A single center experience
12) Impact of an Active Feedback Protocol to Reduce Liver Allograft Cold Ischemia Time for High-Acuity and High MELD Recipients
13) Bronchoscopy in End Stage Liver Disease

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 2022/2023 academic year, we have had internal and external funding, including from non-profit, government and industry sources.

Marc de Moya, MD, Chief of Trauma & Acute Care Surgery, is funded to support his research focus in prospective controlled trials for improving surgical outcomes in trauma, acute care surgery, and surgical critical care patients. In addition, he is growing his research experience in Global Surgery.

Tom Carver, MD's research focuses on non-opioid pain medications in trauma, thoracic trauma and the treatment of chest injuries, splenic injury diagnosis and management, ultrasound use in trauma and surgical education.

Terri deRoon-Cassini, MS, PhD is funded to focus on developing acute neurobiological risk factors and treatment targets for PTSD and depression in adult injured trauma survivors.

Christopher Davis, MD, MPH's research focuses on comprehensive injury prevention including but not limited to injury from violence, falls, and motor vehicle crashes. He is also Chair of the Bleeding Control Initiative of Wisconsin which aims to train all of Wisconsin's citizens how to stop life-threatening hemorrhage through the American College of Surgeons' "Stop the Bleed" course.

Chris Dodgion MD, MSPH, MBA's research focus involves work to strengthen trauma systems, expand quality improvement initiatives in low resource settings and address the global surgical workforce shortage through education innovation. He is currently involved in collaborative projects in Haiti, Ghana, and Ethiopia.

Anu Elegbede, MD is studying the impact of a dedicated Geriatric Trauma co-management program with internal medicine. She is also studying penetrating injury in the Geriatric population, as well as mentorship of medical students and surgical residents.

Daniel Holena, MD's research interests include trauma systems, the use of audiovisual recordings to improve processes of care in trauma resuscitation, and the application of the Failure to Rescue (FTR) metric to trauma populations. Dr. Holena currently serves as the Director of Research for the Division of Trauma and Acute Care Surgery.

Katie Iverson, MD's research focuses on global surgery, violence intervention and prevention, and trauma system development in low-resource settings.

David Milia, MD's research focus includes both primary and secondary prevention of urban firearm violence as well as real-time mapping and geospatial analysis of foci or violence in and around Milwaukee.

Jacob Peschman, MD, MSPE's research focuses on medical education, system and protocol development in trauma and acute care surgery, and management of rib fractures.

Mary Elizabeth "Libby" Schroeder, MD's research interests focus on the development of curriculum to teach surgeons in LMIC's how to perform basic clinical research, and evaluation of barriers to accessing trauma care in Ethiopia. She is also funded to focus on improvement of post-injury care management for prevention of PTSD in adult injured trauma survivors.

Todd Neideen, MD's research focuses on improvement of patient care and emergency general surgery practice management guidelines through data collection and registry development.

Colleen Trevino, RN, NP, PhD leads research focused on understanding the transition from acute to chronic pain in adult injured patients and developing novel models of holistic multidisciplinary care to prevent chronic pain and psychological distress.

Rachel Morris, MD is funded to focus on developing a prediction model for the triage of the severely injured trauma patients and outcomes in geriatric trauma patients. She currently serves as the Associate Director of Research for the Division of Trauma and Acute Care Surgery.

Andrew Schramm, PhD's research focus includes sociocultural influences on recovery from traumatic injury, posttraumatic stress disorder, and suicide prevention.

Patrick Murphy, MD, MPH, MSc's research focus is to understand the perspective of patients diagnosed with emergency general surgical conditions and define and measure high-quality of care using traditional and non-traditional outcomes.

Division of Vascular Surgery

The MCW Division of Vascular and Endovascular Surgery has continued to expand its research activities throughout the Academic Year 2022-2023, with multiple aortic device trials in various stages of data collection. Additionally, the division participated in several retrospective studies, vascular device registries, a surgical preparation trial, and other device trials.

Peter Rossi, MD, Chief of the Division of Vascular and Endovascular Surgery, as site principal investigator (PI) at Froedtert Hospital (FH), led the division to be the top enroller nationally for "A Prospective, Multicenter, Non-Blinded, Non-Randomized Study of the RelayPro® Thoracic Stent-Graft in Subjects with Traumatic Injury of the Descending Thoracic Aorta" with Terumo Aortic. He is also the national PI for the Terumo Relay Pro-D trial for the use of the RelayPro endograft for acute complicated type B aortic dissections. Dr.

Rossi oversees local data collection for the GREAT Registry (Global Registry for Endovascular Aortic Treatment Outcomes Evaluation). This registry, sponsored by WL Gore, collects data on Gore endovascular aortic grafts utilized by surgeons throughout the world. Dr. Rossi is also the US secretary for the Aortic Trauma Foundation, the world's largest prospective registry for the management of aortic injuries, and is the co-PI for a basic science project investigating the development of an amniotic membrane-derived vascular graft.

Dr. Mitchell Dyer joined the Division in September 2022 and has since started his basic science laboratory at the Versiti Blood Research Institute in collaboration with Christian Kastrup, Ph.D. His projects include ex vivo transfection of platelets with mRNA to enhance the coagulability of transfused platelets, investigating the role of fibrinogen in chronic thrombosis by targeted reduction of plasma fibrinogen using siRNA, and understanding the role of plasminogen in swine models of hemorrhagic shock. He was awarded an Advancing a Healthier Wisconsin seed grant for the project to enhance platelet coagulability. He will submit another internal grant for the fibrinogen project through the We Care Foundation. Finally, Dr. Dyer is involved in several clinical projects with his former colleagues at the University of Pittsburgh.

Dr. Joseph Hart, recently named Director of Dialysis Access, is our regional representative to the Arterial Research Advisory Committee for the Society for Vascular Surgery Vascular Quality Initiative (SVS-VQI) at MCW. Our division utilizes the VQI data for several research projects.

Additionally, MCW has a standing relationship with The University of Kathmandu, Nepal, as **Michael Malinowski, MD, MEHP**, has been collaborating and researching Content Transfer for International Educator-based lectures for vascular disease among medical students in Nepal.

Dean Klinger, MD, who recently joined Vascular Surgery along with Christopher Johnson, MD, has recently submitted two projects in collaboration with Kathmandu University School of Medical Sciences. These projects study the prevalence of abdominal aortic aneurysms and peripheral arterial disease in the general population of Nepal.

Vascular surgeons **Brian Lewis, MD, Kellie Brown, MD, Shahriar Alizadegan, MD, Abby Rothstein, MD, and Nathan Kugler, MD,** are co-investigators on open and accruing Vascular and Endovascular Surgery protocols and continue to author and co-author articles, book chapters and presentations with other division faculty including emeritus Division Chief, Dr. Gary Seabrook and Charles Edmiston, Ph.D. Several of our faculty are also involved in research at the Clement J Zablocki VA Medical Center, where they have surgical privileges and conduct research trials.

Contributions to the division's research efforts have also been made by MCW 2022/2023 Vascular/Endovascular Surgery fellows, **W. Sheaffer Sorrells, MD and Mohammad Rajaei, MD**. Finally, our research Nurse Coordinator, Beth Weseman, RN, and several medical students are invaluable and remain critical elements to the success of the Vascular Surgery research program.

Division of Surgical Oncology

Section of Breast Surgery

The Section of Breast Surgery includes Amanda L. Kong, MD, MS (Section Chief), Adrienne N. Cobb, MD, MS, Chandler S. Cortina, MD, MS, Caitlin R. Patten, MD, and Tina W.F. Yen, MD, MS. The group has active clinical outcomes, health services, and translational research programs, addressing the treatment and outcomes of both benign and malignant diseases of the breast. Funded health services research related to breast cancer treatment and outcomes is performed in affiliation with MCW's Center for Advancing Population Science. Our faculty also collaborate with the basic science faculty at the medical school on translational research projects converting science from bench to bedside through NIH funding. In collaboration with the Kern Institute, our faculty are also invested in educational research as well as methods of improving medical education. Health services research on cancer screening and treatment within the LGBTQ+ community is also being performed through collaborative partnerships with community members and the Froedtert and MCW Inclusion Health Clinic, funded by PCORI and Advancing a Healthier Wisconsin.

As active members of the Cancer Center, our faculty participate in numerous clinical trials sponsored by industry and the National Cancer Institute through cooperative groups, including the Alliance for Clinical Trials in Oncology, NRG Oncology, and ECOG-ACRIN cancer research group. 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 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. The Section of Endocrine Surgery maintains three prospectively-collected clinical databases (thyroid, parathyroid, and adrenal) with clinical data from >20 years of a high-volume clinical practice, which serve as the foundation for the research program. The section has had continuous research with students, residents, and fellows over the past fifteen years, with annual oral podium and poster presentations at regional and national surgical meetings.

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

Section of Gastrointestinal (GI) Surgery

The Gastrointestinal (GI) Section of the Division of Surgical Oncology's active clinical, translational, outcomes and basic science research program involves eight 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, bile duct) as well as soft tissue sarcomas, peritoneal surface malignancies, gastric and other gastrointestinal cancers, palliative care. In addition, investigators in the GI section have expertise in health services research, data science, machine learning, and health disparities. This has resulted in multiple national oral presentations, high impact publications, and extramural funding.

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

Since its inception the Surgical Oncology Tissue Bank has enrolled over 3700 patients. This bank stores blood throughout a patient's oncologic treatment from the time of diagnosis and throughout treatment. Benign and malignant pancreas, liver and adrenal tissues that would otherwise be discarded at surgery are banked. The bank has been instrumental in a multi-center NIH collaborative examining non-coding RNA for early detection of pancreatic cancer. Specimens have also been utilized the development of a novel platform to perform chemotherapeutic testing on pancreatic cancers ex vivo and to examine the germline variants of uncertain significance in patients with sporadic pancreatic cancer. The bank supports one of five Post-mortem Tumor Donation Program which allows patients to donate their remains for pancreatic cancer research following death. The Tissue Bank collaborates with multiple research collaborations including external collaborations with MIT, Van Andel Institute, University of Wisconsin-Madison, and City of Hope, as well as internal collaborations within MCW.

Clinical databases maintained in GI Surgery Oncology include efforts in gastric, sarcoma, liver, pancreas, neuroendocrine, and peritoneal carcinomatosis. In addition, the GI section houses several national cancer registries and databases. These resources have supported the completion of numerous studies that inform surgical oncologic care nationwide. Additionally, the clinical program supports infrastructure for innovative quality programs including the development of ERAS pathways, longitudinal quality of life measures, assessment of social determinants of health, implementation of universal genetic testing, and precision medicine efforts.

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. Urology faculty current lead research efforts that are funded by internal funds, internal competitive grants, and extramural funding from organizations such as Centers for Disease Control and Patient-Centered Outcomes Research Institute. As well, we have recently begun Uroclinomics, a department wide quality and outcomes initiative with the overall goal to assess outcomes regarding urologic conditions and initiate change to improve the health of the patients we serve. The areas we study include uro oncology, voiding dysfunction, reconstructive urology, urinary tract obstruction, urinary tract infection, urinary stone disease, erectile dysfunction and infertility.

Current research projects within the Department of Urology include:

Erectile dysfunction
- IT MATTERS study- industry sponsored longitudinal prospective data collection on non-standard implants (2 piece and semirigid)
- Multicenter evaluation of infectious outcomes of penile prosthesis as it relates to diabetes and other comorbid conditions

Benign prostate diseases
- Retrospective evaluation on safety/efficacy of Holmium laser enucleation of prostate (HoLEP)
  - risk of bladder neck contracture in small glands
  - efficacy in patients with small gland and atonic bladder
  - efficacy of treatments for post-HoLEP incontinence

Voiding dysfunction
- Outcomes of sacral neuromodulation for voiding dysfunction based on type of anesthesia
- longitudinal evaluation of urinary symptom progression in patients with demyelinating diseases (in conjunction with dept of Neurology)
- Diagnosis and treatment pathways of urinary incontinence in primary care clinics

Reconstructive urology
- Ureteral reconstruction techniques
- Mesh erosion into the ureter after abdominal sacrocolpopexy

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 on characteristics of men undergoing vasectomy
- ADAM trial (a prospective, randomized, double-blind trial for infertility medication).

Urinary stone disease
- Comparison of Thulium fiber lithotripsy vs PCNL for stone burden >2cm
- Identifying Key Proteins in Calcium Oxalate Kidney Stone Formation Using Stone Matrix Proteomics (collaboration with Nephrology)

Prostate cancer
- Underdiagnosis and under treatment of chronic diseases in men with newly diagnosed prostate cancer

Kidney cancer
- Should Chest X-ray be Utilized for pT1a Renal Cell Carcinoma Pulmonary Surveillance After Surgical Resection?

Pediatric Urology
- Multiple projects in pediatric kidney stones including comparative effectiveness of surgical treatments, imaging patterns and radiation exposure from CT scans, and development of a decision aid for surgical options for kidney stones.
- Bladder exstrophy outcomes
- Opioid prescribing patterns in pediatric patients
- Social Determinants of Health and institutional factors affecting management and outcomes of testicular torsion
- Care of infants and children with spina bifida
- Use of intravesical oxybutynin for management of overactive bladder

Cancer Center

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

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

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

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

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

Cardiovascular Center

The Cardiovascular Center (CVC), founded in 1992 at the Medical College of Wisconsin (MCW), is at the forefront of scientific discovery in cardiovascular health and disease, ranking in the top 20 in the U.S. for federal dollars for cardiovascular research in medical schools. Over 32,000 square feet of space is dedicated to over 20 laboratories and housing offices, conference rooms, and equipment cores primarily located on the fourth floors of the Health Research Center (HRC) and Medical Education Building (MEB). The CVC is staffed by full- and part-time personnel who maintain core equipment, coordinate academic research, funding, and community outreach initiatives, and provide support to the more than 170 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 diverse and proficient cardiovascular scientists and physicians, and engaging the community to eliminate disparities in health outcomes.

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

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

Cross-Cutting Affinity Groups:
Cardio-Oncology
Prevention

The CVC is directed by Ivor Benjamin, MD, Professor of Medicine at Froedtert Hospital and MCW, and 2018-2019 President of the American Heart Association, who has over 25 years of experience and expertise leading cardiovascular clinical and research programs. The CVC is also supported by its four Associate Directors: Mary Sorci-Thomas, PhD, Professor of Medicine, who co-directs Training and Education; Curt Sigmund, PhD, James J. Smith & Catherine Welsch Smith Professor and Chair of Physiology, who directs Team Science; Michael Widlansky, MD, MPH, Northwestern Mutual Professor in Cardiology, who directs Adult Translational Science, and Joy Lincoln, PhD, Professor of Pediatrics, who co-directs Training and Education. Moreover, as an MCW "Green Center", the CVC is also guided by an external scientific advisory board, internal scientific advisory board, and institutional leadership.

Along with its exceptional leadership, the CVC receives extensive institutional support in addition to 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. The CVC was awarded a $2.7 million postdoctoral training grant from the National Heart, Lung, and Blood Institute (NHLBI), one of only three T32 postdoctoral training programs on campus and is funded by the American Heart Association to increase diversity of the biomedical workforce through a 10-week undergraduate summer research experience program.

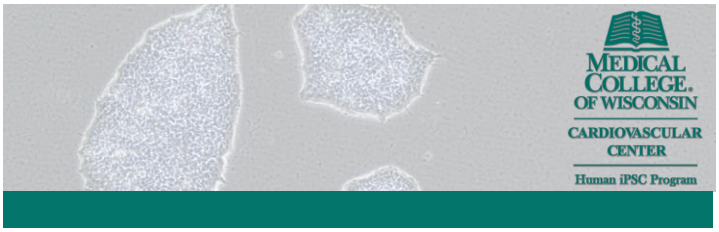
T32 Training Grant for Postdoctoral Fellows:
Building on excellence in cardiovascular research, the CVC's T32 postdoctoral training program, *"Training in Signature Transdisciplinary Cardiovascular Sciences,"* is funded by the NHLBI that provides support for six postdoctoral training slots each year.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

The program, which was recently renewed for funding through 2027, has been highly successful in training 15 postdoctoral fellows, 36% that belong to underrepresented groups, continuing to work toward our ultimate goal of training the next generation of cardiovascular scientists and physicians, including individuals from underrepresented groups, by incorporating broad-based, personalized, diversity-conscious, supportive, and rigorous training opportunities. Our graduates all remain in academia and have obtained subsequent federal funding thus bridging their path to independence.

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

Undergraduate Summer Cardiovascular Research Program:
The Supporting Undergraduate Research Experiences (SURE) Program, sponsored by the American Heart Association, provides mentored summer experiences in cardiovascular research in our research laboratories. For 10 weeks during each summer, undergraduates who identify as Black, African American, Hispanic or Latino, American Indian, Native Hawaiian, Hmong, or Pacific Islander and/or identify as LGBTQ+ receive hands-on training in cardiovascular research under the guidance of the faculty mentor with professional skills development, seminars on cardiovascular-related topics, and social/networking events. Participants are paid a $6,000 stipend and receive free lodging and a free one-time roundtrip airfare to the program if not locally-based. Applications for the summer of 2024 open in November of 2023. Go to www.mcw.edu/sure for more information.

Human Induced Pluripotent Stem Cell (iPSC) Program



To advance translational and precision medicine research, the CVC established the Human Induced Pluripotent Stem Cell (iPSC) Program with funding from the Advancing a Healthier Wisconsin Endowment. Over 600 square feet within the center is dedicated to reprogramming of somatic cells into iPSCs, generation of iPSC-derived macrophages, fibroblasts, cardiac, endothelial, hepatic, smooth muscle, and other cell types, customized organoids/microtissues for investigators campus-wide. Currently, the costs are subsidized significantly thanks to institution's strategic support during FY23 and FY24.

Since its inception, over 20 different projects have benefited from:
•Reprogramming of Fibroblasts (for 2 labs, 2 projects)
•Reprogramming of PBMCs (for 1 lab, 2 projects)
•Cardiomyocyte Differentiation (for 3 labs, 8 projects)
•Endothelial Cells Differentiation (for 2 labs, 6 projects)

The core offers reprogramming of somatic cells into iPSCs (from blood, urine, or skin samples), the production of human iPSC-derived myocardial, endothelial, and other cells, and quality maintenance and differentiation services for investigators campus-wide. For services, go to iLAB or contact Gracious Ross, DVM, PhD at gross@mcw.edu

Specialized Services and Infrastructure
The CVC offers its primary members and their trainees and staff access to core facilities including microscopy, imaging, other core equipment, a quarterly newsletter, weekly seminar notices, funding e-newsletter, conference rooms for meetings and presentations, eligibility for CVC grant awards (approximately $200,000/year in competitive awards offered), Signature Program meetings, and access to the CVC Seminar Series and Trainee Development Seminar Series, which are held on a monthly to quarterly basis, respectively, during the regular school year in the CVC's main conference room on the fourth floor of the HRC. CVC members and their trainees and staff are also given many educational and networking activities throughout the year, including the annual CVC Research Retreat.

Last year, the members of the CVC were awarded more than $90 million in total funding, with $41.5 million being funded by the National Heart, Lung, and Blood Institute (NHLBI) of the National Institutes of Health. MCW ranks in the top 15 medical schools nationally for its funding from the NHLBI in 2021.

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

CVC Core Equipment
Axion Microelectrode Array System
Beckman Coulter DU640 Spectrophotometer
Bio-Rad Cell Counter TC-10
Bio-Rad CFX96 Touch Real-Time PCR Detection System, 2 Units
Bio-Rad CFX384/C1000 PCR Detection System
Bio-Rad ChemiDOC MP Imaging System
BMG Labtech CLARIOstar Microplate Reader
BMG Labtech Fluorstar Omega Microplate Reader
Chemical Hood, Built-in
Chromium 10x Single Cell Sequencing System
Li-COR Odyssey CLx Infrared Imaging System
Protein Simple WES Western Blotting System
Microscopes & Accessories
Nikon C2 Confocal
Nikon Eclipse 55i
Nikon A1R+ Confocal ($25/hr)
Nikon A1R+ Environmental Chamber/Cell Stage
Nikon TE-2000
Computer with Software for Analyzing Nikon Images
Centrifuges & Rotors
Beckman Coulter XPN-100 Ultracentrifuge
Sorvall Superspeed RC 6+ Centrifuge, 2 Units

MEDICAL COLLEGE OF WISCONSIN

CARDIOVASCULAR CENTER

Year in Review

30 YEARS AS A CENTER

#1 IN WI FOR FEDERAL DOLLARS FOR CARDIOVASCULAR RESEARCH

TOP 15 IN THE US FOR FEDERAL DOLLARS FOR CARDIOVASCULAR RESEARCH IN MEDICAL SCHOOLS

177 MEMBERS WHO ARE RESEARCHERS AND DOCTORS

OVER **25** DEPARTMENTS/INSTITUTES

Schools of Medicine	NHLBI FY21
1. New York Univ School of Medicine	$483.0M
2. Univ of Pennsylvania	$78.3M
3. Univ of California, San Francisco	$69.1M
4. University of MI at Ann Arbor	$65.3M
5. Columbia University	$63.7M
6. Univ of Pittsburgh at Pittsburg	$59.7M
7. Northwestern Univ at Chicago	$57.6M
8. Stanford University	$56.6M
9. Washington University	$47.5M
10. Yale University	$46.2M
11. Johns Hopkins University	$45.9M
12. Univ of California, San Diego	$43.3M
13. Medical College of Wisconsin	$41.5M

$90M IN FUNDING (TOTAL COSTS)

OVER **500** PUBLICATIONS IN PEER-REVIEWED SCIENTIFIC JOURNALS

196 FUNDED RESEARCH PROPOSALS

OVER **300** RESEARCH PROJECTS

OVER **40** CLINICAL TRIALS

MENTORED OVER **100** TRAINEES

NIH T32 POSTDOCTORAL TRAINING INVESTING **$500,000** IN TRAINING EACH YEAR

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

Center for Advancing Population Science

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

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

CAPS Strategic Goals

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

Center Units

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

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

Health Systems Consulting Service Center – The Health Systems Consulting Service Center aids in the development, design, analysis, and interpretation of quantitative study results. Investigators throughout MCW, Froedtert, University of Wisconsin – Milwaukee, and Marquette University can use this service to obtain biostatistical support. This service supports CTSI mini-grant population health projects and investigator-initiated projects billed to MCW departments.

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

Areas of research focus for the center include:

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

Center for Advancing Population Science (CAPS)
(414) 955-8801 | capsmbx@mcw.edu
Medical College of Wisconsin
8701 Watertown Plank Road
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Oakwood Office
10361 West Innovation Drive
Milwaukee, WI 53226

Center for the Advancement of Women in Science & Medicine

MCW's Center for the Advancement of Women in Science and Medicine

About MCW's Center for the Advancement of Women in Science and Medicine

At the Medical College of Wisconsin (MCW), we believe that health starts from within and that our institution can cultivate a culture of engagement through wellbeing, professionalism, and inclusion. MCW's Center for the Advancement of Women in Science and Medicine (AWSM) believes that when *all persons* can bring their *whole self* to work, all of us benefit.

MCW's Center for the Advancement of Women in Science and Medicine (AWSM) was created to accelerate the promotion of women to higher levels of their careers.

Our focus areas are:

- Building a culture in which all genders thrive
- Empowering women leaders and expanding women's networks
- Researching and highlighting women in academic medicine

Vision, Mission, Our Why and How

Vision: Our vision is that MCW will cultivate an inclusive and vibrant culture that supports all genders to grow and thrive in the health sciences.

Mission: The mission of MCW's Center for the Advancement of Women in Science and Medicine (AWSM) is to strengthen the culture for women at MCW through data-informed strategic projects that enhance opportunity and improve workplace climate.

Why? We want each person to bring their best every day

How? We do things with evidence. For equity.

Focus Areas

Gender Equity Campaign

MCW's IWill gender equity campaign began in October 2018 at AWSM's launch, when Dr. Cheryl Maurana called each of us to pledge to do our part to create gender equity. It has grown from the initial individual-action campaign in 2019 to include WeWill and MCWill initiatives that support gender equity at the individual, departmental and institutional levels.

Women's Leadership Learning Collaborative: Building on previous research and results from MCW's engagement surveys and succession-planning tools, AWSM planned a Women's Leadership Pilot (WLP)designed to remove barriers and provide development strategies for mid-level women leaders. WLP 1.0 ran from Feb 2020 through March 2021 (interrupted by COVID). The first cohort of the fully realized program will run Jan-Oct 2023.

Center for Biomedical Mass Spectrometry Research

Scope & Mission

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

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

MEDICAL COLLEGE OF WISCONSIN

Center for Biomedical Mass Spectrometry Research

Center for Healthy Communities and Research

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

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

The CHCR has the following major areas of research activity:

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

CHCR faculty and staff develop, implement and evaluate educational courses across the continuum of medical education, graduate and post graduate education. This includes support of primary care research. CHCR faculty 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 and graduate students in MCW's programs in Public and Community Health.

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

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 2 research-dedicated MRI systems, one being the newest generation 3.0T GE Healthcare Signa Premier, the other being 3.0T GE Healthcare Advantage Workstation with VolumeShare 7.0, both of which are located in the MRI annex to the MACC Fund Building, and a pre-clinical 9.4T Bruker Biospec located in the MRI annex.

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

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

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

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

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

Center for Immunology

The Center for Immunology was established in 2018 and combines expertise in basic and clinical immunology to accomplish two goals across MCW:

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

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

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

Center for Infectious Disease Research

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

Under Director Dr. Chris Kristich, CIDR is 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

CIBMTR (Center for International Blood and Marrow Transplant Research) collaborates with the worldwide scientific community to advance the field of cellular therapy, which includes hematopoietic cell transplantation (HCT), chimeric antigen receptor T cells (CAR-T), and other cellular therapies. A research collaboration between MCW and the National Marrow Donor Program/Be The Match, CIBMTR facilitates important clinical research to increase survival and enrich the quality of life for thousands of patients.

CIBMTR's research arises from a base of collaborative scientific and statistical expertise, a network of 375 centers across the globe, a clinical database containing information from >630,000 patients, and a biospecimen repository containing >205,000 samples. Information from the database, and the support provided by CIBMTR's 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, CIBMTR has >200 observational studies and >25 prospective studies ongoing. Since inception, the organization has published >1,750 articles and chapters in scientific publications. In 2022, CIBMTR generated 71 peer-reviewed publications and presented 95 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 CIBMTR's clinical outcomes research. Each committee focuses on a specific disease, use of cellular therapy, or complication of therapy. They utilize CIBMTR's clinical database to answer clinically important questions in a timely manner. CIBMTR data and expertise are also used to address other specific questions in a variety of settings, often in collaboration with other research partners.

Clinical Trials. CIBMTR supports prospective research to evaluate new cellular therapies. The Blood and Marrow Transplant Clinical Trials Network conducts multicenter Phase II and III national trials. CIBMTR Clinical Research Organization Services supports Phase I-III trials, providing investigator support services, survey research, and clinical study management.

Immunobiology. 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 cellular therapy.

Health Services. CIBMTR facilitates studies regarding economic and health-related cost analyses, disparities in and barriers to access, treatment decision making and support, health care utilization, quality and value of care, and survey research.

Bioinformatics. CIBMTR analyzes genetic data, particularly the major histocompatibility complex; research activities include improving the transplant match algorithm and data standards as well as conducting donor registry modeling.

Statistical Methodology. In conjunction with the MCW Division of Biostatistics, CIBMTR's Coordinating Center not only provides advice and statistical consultation to researchers writing proposals and developing protocols for cellular therapy studies but also investigates new statistical approaches and techniques for analyzing their data.

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

Resource Publicly Available: Cellular Therapy Datasets. In accordance with the NIH Data Sharing Policy and NCI Cancer Moonshot Public Access and Data Sharing Policy, CIBMTR makes the final datasets from published studies publicly available on the CIBMTR Research Datasets for Secondary Analysis webpage. These datasets are freely available to the public for secondary analysis. Currently there are >100 final datasets from published studies available for download.

Visit our website for more information: https://cibmtr.org/

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.

Benefits:

- Collaboration with MCW, Froedtert, CRI, and VBRI investigators
- Gnotobiotic Core Facility (GCF) resource and expertise
- Training & assistance in microbiota-focused sample collection & processing, and requesting sequencing
- Biannual intramural pilot funding program for highly focused and/or preliminary microbiome-related experiments
- Invited speaker seminar series, journal club, & bioinformatics workshops

Microbiome-Focused Services Offered

- Consultation: Study design and funding applications
- Sample collection and processing methods specific to microbial targets
- Gnotobiotic Core Facility (GCF): Axenic and gnotobiotic rodent husbandry & experiments, including choice of isolators or iso-caging as appropriate for your study
- Bioinformatics and biostatistics analysis services and training

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https://www.mcw.edu/departments/center-for-microbiome-research

Center for Neurotrauma Research

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

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

Spinal Cord Injury Research

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

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

Traumatic Brain Injury Research

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

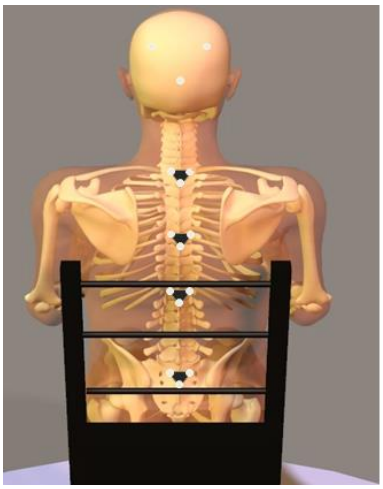
Head and Spine Biomechanics

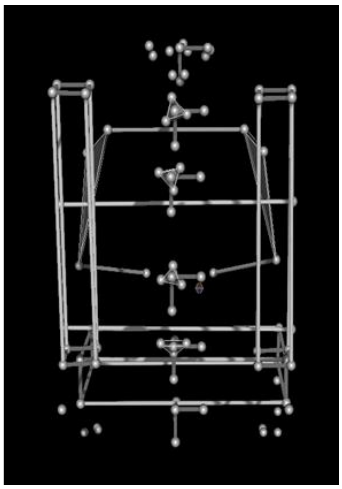
One of the longest running research programs in the Department of Neurosurgery has focused on head and spine biomechanics, with emphasis on trauma and disease. This research area brings together engineering scientists specializing in biomechanics and neurosurgeons to determine how the spine and the head-neck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

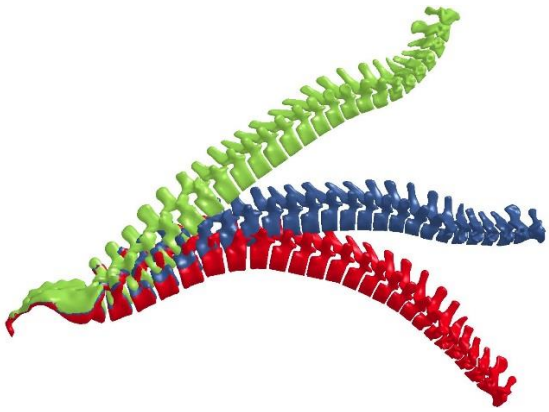
in active military personnel, investigation of head supported mass and the effects of wearing advanced combat helmets for prolonged periods of time, and the development of spine injury criteria for female military personnel.

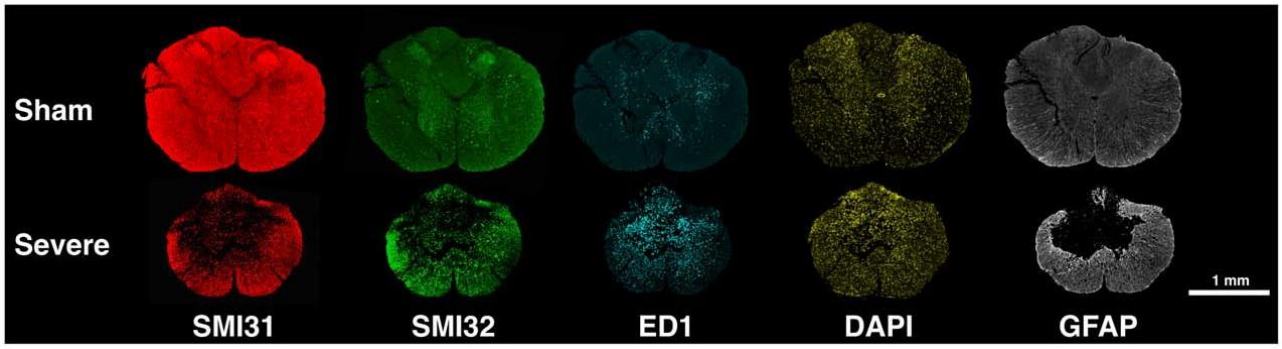
Patient Specific Modeling

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









Center of Systems Molecular Medicine (CoSMM)

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

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

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

CoSMM is the intellectual home to several standing or extramurally funded programs, including Program for Medicine and AI Research (MARs), Dynamic Systems Modeling Program, a recently completed, AHA-funded center program on the basic, clinical, and population sciences of the epigenomics of hypertension, and an NIH-funded Program Project on Genetics and Epigenetics of Blood Pressure Regulation and an RC2 program on genetics and epigenetics of human kidney disease.

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

Children's Research Institute

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

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

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

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

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

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

Examples of research awards for ongoing CRI investigations include:

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

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

Clinical & Translational Science Institute

Clinical & Translational Science Institute
of Southeast Wisconsin

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

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

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

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

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

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

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

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

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

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

Comprehensive Injury Center

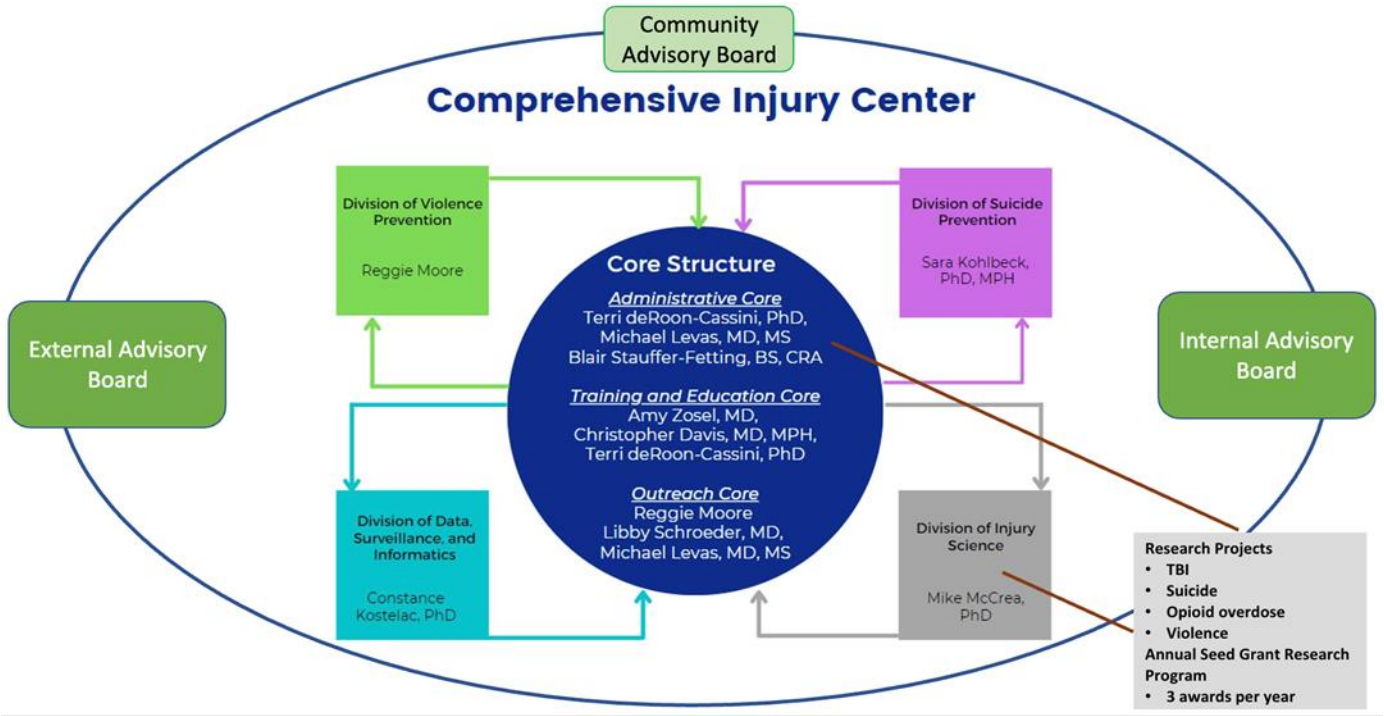
The mission of the Comprehensive Injury Center (CIC) is to create a platform to engage campus and community partners in the advancement of injury control and prevention science. The CIC is particularly focused on the public health model of prevention, focusing on injury, violence, and suicide. The CIC builds 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, particularly in underserved populations.

The goals of the CIC are to:

1. Research: Advance the science of health equity in injury prevention and control by facilitating, conducting, and disseminating interdisciplinary translational research that leads to novel findings across all levels of prevention for populations who experience or are at risk for injury-related health disparities.
2. Education: Develop, implement, and evaluate multi/inter-disciplinary educational opportunities that emphasize health equity to educate and train both current and the next generation of injury prevention researchers, practitioners, and educators, as well as community partners and leaders.
3. Outreach: Maintain, develop, and foster model partnerships for the health and safety of marginalized populations at greatest risk for injury disparities, including partnerships with public health organizations, community groups, as well as other public and private sectors and systems that facilitate, translate, and disseminate evidence-based injury prevention and control 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.

The CIC has four divisions, including community safety, suicide prevention, data surveillance and informatics, and injury science. The model below represents the structure of the CIC.



Genomic Sciences & Precision Medicine Center

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

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

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

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

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

Services:

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

Facilities:

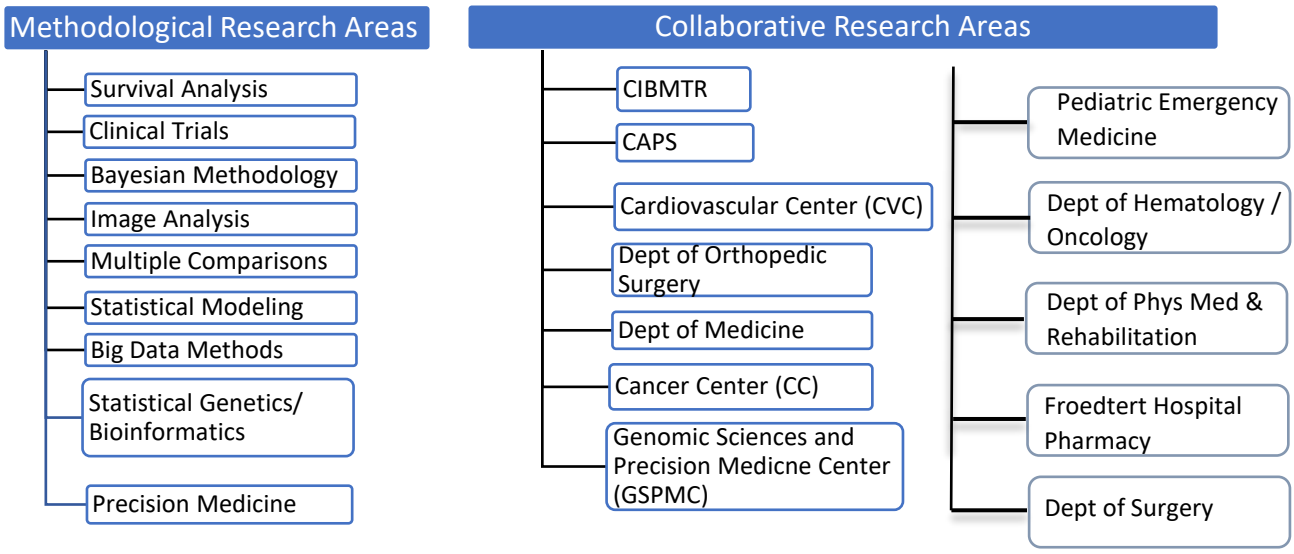
The GSPMC occupies a 20,000 square foot facility on the 5th floor of MCW's Health Research Center. These facilities have modern design, state-of-the-art equipment, and expert personnel to allow the efficient implementation of next generation sequencing methodologies to Cancer Genomics, Non-Cancer Clinical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

Our Technology:

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 2021, the Division of Biostatistics helped bring in over $173 million dollars to the Medical College of Wisconsin from various grants they were included on. In calendar year 2021, the Division published 16 methodological papers that appeared in the statistical literature either online or in print. The Biostatistics Consulting Service collaborated on 265 projects which resulted in 47 Publications.

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

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

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

Contact Us:
McKenna Busse
mbusse@mcw.edu | 414-955-5872

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 1982. 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; comparing clinical consent and research consent; vaccination and objection; and disabling cardiac devices.

Currently, CBMH faculty are engaged in a variety of research and scholarship activities, as described below. CBMH faculty are available to provide research ethics consultation services to investigators before, during, and after engaging in research activities.

Faculty Scholarly Expertise

- **Arthur R. Derse, MD, JD**, *Professor and Director* – Dr. Derse's publications and research focus on emergency medicine and ethics, law and bioethics, informed consent, end-of-life decision making, confidentiality and the doctor-patient relationship. Additional areas of specialization include decision making capacity; medical futility; ethics, humanities and medical education; do not resuscitate orders; exception from informed consent in emergency research; health care ethics committees and clinical ethics case consultation.
- **Annie Friedrich, PhD**, *Assistant Professor* – Dr. Friedrich's research combines theoretical and empirical analyses to explore ethical dimensions of clinical care, family-provider communication, and decision making in pediatric settings. Her work focuses on better understanding the ways technological intervention shape parental decision making in pediatric intensive care.
- **Fabrice Jotterand, PhD, MA**, *Professor* – Dr. Jotterand's scholarship and research focus on issues including neuroethics, ethical issues in psychiatry and mental health, the use of neurotechnologies in psychiatry, the philosophy of medicine, medical professionalism, neurotechnologies and human identity, and moral/political philosophy. Present research examines issues at the intersection of philosophical anthropology, emerging technologies, and medicine, with a particular focus on what should guide the education of future physicians and clinical practice considering the increasing integration of powerful technology in medicine.
- **Garson Leder, PhD**, *Assistant Professor* – Dr. Leder's research focuses on what mental disorders are and how different conceptions of 'mental disorder' affect treatment, attitudes, and patients' understandings of their conditions and recovery. His work also examines theoretical explanations for mental health and how these explanations affect users of mental health services. An additional area of focus is clinical ethics with empirical and conceptual research on decisional capacity, medically inappropriate treatment, and informed consent.
- **Ryan Spellecy, PhD**, *Professor and Assistant Provost for Research* – Dr. Spellecy's research focuses on the area of research ethics, IRBs, the use of clinical data for research, informed consent, ethical issues in psychiatry, community-based research, and community education about research.

Division of Epidemiology

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

- **Laura Cassidy, MS, PhD,** Professor and Director of the Epidemiology Division and Founding Director of the MS Program in Global Health Equity in the Institute for Health and Equity. She has expertise in pediatric trauma, clinical research, community health, health disparities and global health. She is the MCW PI of the Great Lakes Native American Research Center for Health (GLNARCH) - Expanding Community and Academic Partnerships. As part of NARCH she is also the PI of an NIH funded grant, Building a Menominee-Centric Trauma Resilience Model that measures adverse childhood experiences and resilience in middle and high school students at Menominee Indian High School. She is also funded by the Childress

Institute for Pediatric Trauma to lead a national initiative to create a smartphone app, pediatric trauma pre-arrival checklist for trauma centers. As one of the PI's of the AHW Redirect grant, she leads a team that analyzes citywide data on social determinants of health and academic achievement in Milwaukee Public School students. Her global health projects include measuring early childhood development in Uganda using the Malawi Developmental Assessment Tool (MDAT), barriers to immunizations in Ugandan children and depression in young mothers in Uganda.

- **Ronald Anguzu, MBChB, MPH, PhD:** Dr. Anguzu is a Ugandan trained physician, and global health researcher with experience in the maternal and child health epidemiology, infectious diseases epidemiology, behavioral, and mental health. He is an assistant professor in the Division of Epidemiology and Social Sciences, Institute for Health and Equity, at the Medical College of Wisconsin. Dr. Anguzu's research work generally focuses on investigating and addressing disparities in maternal, newborn, and child health risk factors, outcomes, and service utilization in the United States, and Uganda. Specifically, his collaborative research evaluates behavioral risk factors such as violence within families which includes intimate partner violence, and violence in post-war communities, and informal settlements. His research in the US assesses approaches to reduce the impact of high-risk pregnancies such as pre-eclampsia, and gestational diabetes. Dr. Anguzu is a principal investigator (PI) on an Advancing a Healthier Wisconsin (AHW) grant implemented with community-based partners in Milwaukee to address environmental injustice of lead poisoning through household lead water testing and referrals through a network of collaborators for care. Other research expertise includes investigating chronic medical conditions such as perinatal depression, cervical cancer, HIV and Tuberculosis. His current research interests seek to expand the field of prevention of perinatal depression and IPV through use of web-based or mobile health (mHealth) technology to improve providers clinical (screening), management, and referral practices for depression and IPV during pregnancy in rural prenatal care clinics in rural districts of Uganda. He holds degrees in Medicine and Surgery from Makerere University School of Medicine and a Master of Public Health from Makerere University School of Public Health, both in Uganda, and PhD in Public and Community Health from the Medical College of Wisconsin.

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

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

- **Julia Dickson-Gomez, PhD:** Dr. Dickson-Gomez studies HIV prevention among drug users in the United States and El Salvador and is also interested in the influence of structural factors on HIV risk. Her research explores the effects of housing policy on drug users' access to housing, variations in housing status and housing options of drug users, and levels of HIV risk related to these factors. Dr. Dickson-Gomez's work also explores macro- and micro-social contexts of crack use and HIV risk in communities in El Salvador. Her work develops and evaluates the impact of structural and multi-level interventions in the U.S. and Latin America. Currently, Dr. Dickson-Gomez is leading a three-state study that examines the effects of state law

and policy on illicit opioid users and their transition to the use of heroin. She has three international projects in progress, two in Uganda and one in Tanzania, exploring the informal settlements of each county and constructing a buprenorphine intervention for opioid users in Uganda. She's also the MCW lead for the Great Lakes Node of the Clinical Trials Network and has started the Substance Use Working Group.

- **Brian Jackson Chi Ayaabe (Big Buck), MS, Ed.D.** Dr. Jackson joined the MCW January 16, 2023, as assistant professor with a background serving Indian Country with an emphasis on Community Based Participatory Research. He is part of the Great Lakes Native American Research Center for Health (GLNARCH) Community Scientific Advisory Committee serving the Bemidji Area. He has worked extensively with Native American students in student development programs through storytelling and cultural teachings combining academic research and Indigenous ways of being. Furthermore, Dr. Jackson is trained as a Family Circles AODA Prevention Program facilitator; providing instruction in language, traditional cultural practices, history, and culture of Native people will be preserved, thereby restoring pride in the identity of Anishinaabe. With an introspective approach in which family members examine their own behaviors, the curriculum enables individuals to better understand how the process of realizing positive healthy lifestyles within the family begins with self-esteem building, coping skills building through Indian culture, values and lifestyles.

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

- **Liliana E. Pezzin, PhD JD:** Dr. Pezzin is an economist specialized in Econometrics and Public Finance, with a long-standing interest in issues related to healthcare delivery, its measurement, antecedents, and consequences. A significant part of her early work centered on the economics of aging, with a special focus on the interplay between public policy and family decisions regarding living and caregiving arrangements of older persons, a field that enabled her to explore, both theoretically and empirically, the notion of public policy as a means to influence family dynamics and potentially overcome inefficiencies in the provision, cost, and quality of post-acute and long-term care. Through a fascination with economics applied to health, she became interested in outcomes research, particularly the comparative effectiveness of different care settings and medical treatments. Understanding the effectiveness of health care often requires the use of advanced methods of causal inference applied to carefully designed study experiments. Funded by NIA, NCI, NHLBI, VA, and other federal agencies, she has used national surveys, prospectively-collected observational data and health insurance claims to examine the effectiveness and cost-effectiveness of alternative public policies and health care delivery modes.

- **Charles R. Rogers, PhD, MPH, MS, MCHES®:** Dr. Rogers is committed to dismantling systems of oppression to ensure equitable health for all as an Associate Professor of Epidemiology & Social Sciences in the Institute for Health & Equity at MCW. He is also an MCW Cancer Center Research Scholar Endowed Chair and the inaugural Associate Director of Community Outreach & Engagement for MCW's Cancer Center. In addition to being the Founding Director of his Men's Health Inequities Research Lab since 2014, Dr. Rogers is also an Associate Member of the University of Michigan-Mixed Methods Program. since 2018, Dr. Rogers has been awarded over $3.3M from the National Cancer Institute, the Research Foundation of the American Society of Colon and Rectal Surgeons, Exact Sciences, the Medical College of Wisconsin, 5 For The Fight, and the V Foundation for Cancer Research for his community-engaged, mixed-methods research aiming to eradicate inequalities in both colorectal cancer (CRC) screening completion among African-American men and early-onset CRC among individuals younger than the previously recommended CRC screening age of 50. In addition to being a thought leader in the CRC space, his research foci also include cancer health disparities, behavioral & community-based implementation science, mixed methods, and survey methodology.

- **Carissa Tomas, PhD:** Dr. Tomas joined MCW in 2021 as an Assistant Professor of Epidemiology and Social Sciences. She is also the Deputy Directory of the Division of Data Surveillance and Informatics in the Comprehensive Injury Center (CIC) at

MCW. With a background in neuroscience and data science, she is establishing a novel line of research that comprehensively evaluates injury and trauma populations with advanced quantitative techniques. With traumatic injury being a leading cause of hospitalization and financial burden within the US healthcare system, it's imperative to understand pre-injury risk factors and post-injury outcomes in as comprehensive manner as possible. In her unique position across Epidemiology and Social Sciences and the CIC, her work interrogates the biopsychosocial and environmental context from which trauma populations come to understand outcomes after trauma and injury. By applying a more holistic approach, she aims to understand risk and resilience factors of injury and violence that can inform prevention and intervention programming. Her research has identified neural, behavioral, and contextual factors related to negative psychological outcomes after traumatic injury. In her KL2 award, she has applied longitudinal analysis to understand traumatic injury trends in a national database, used forecasting procedures to evaluate the impact of the COVID-19 pandemic on local injury trends, and used geospatial analysis to understand the spatial trends of injury within the Milwaukee community. Through collaborations in the CIC, she has also analyzed trends of suicide in WI, forecasted firearm-related injury in Milwaukee County, and co-led the evaluation design and plan for community- and hospital-based violence interruption programs.

- **Wei Xu, PhD:** Dr. Wei Xu joined MCW in 2023 as a spatial epidemiologist. His work primarily focuses on the relationship between place-based factors, including physical, built, and social environments, and aging over the life course. Through integrating social determinants of health and life course epidemiology frameworks, Dr. Xu's primary research projects leverage the linkage between residential histories of a WI population-representative cohort and long-term neighborhood conditions to examine the effects of dynamic neighborhood structural disadvantage over the life course on epigenetic aging and related inequalities. One of his research areas, funded by NIA, investigates how interactions between health behaviors, particularly physical activity, and neighborhood environments influence one's risk of incident dementias. Recently, Dr. Xu's work has extended to examine the systemic inequities in access to long-term care resources and their consequences for the utilization, quality, and health outcomes among older adults, including those with Alzheimer's disease and related dementias, in WI. Ultimately, Dr. Xu's goal is to conduct research to better understand the role of place in healthy aging and facilitate evidence-based policy interventions to support equitable aging in place.

Community Health Division Research

The IHE Community Health Division includes many research projects and 4 graduate education programs led by 15 community engaged faculty and staff.

- **Jess Olson, PhD, MPH**, research focuses on determining the cause of exercise response variability to tailor lifestyle interventions to individual survivors of breast cancer. Dr. Olson was senior author of "Racial Disparities in Postmastectomy Breast Reconstruction Following Implementation of the Affordable Care Act: Systematic Review Using a Minority Health and Disparities Research Framework" in the *American Journal of Surgery*. She directs the CTSI PhD in Basic and Translational Science program. Dr. Olson serves as Director of Evaluation and Innovation Initiatives in the MCW Office of Diversity and Inclusion. She has been active in the National Lung Cancer Roundtable. She presented the launch of the State-Based Initiative Planning Tool at the National Lung Cancer Roundtable conference.

- **Jamila Kwarteng, PhD,** focuses research on improving wellbeing, quality of life, and survivorship for African American cancer survivors and cancer prevention for African Americans and Latinos. Dr Kwarteng uses a community-engagement approach by partnering with local and state organizations to develop programming. This includes providing resources to address unmet needs of cancer survivors; facilitating education and training for churches to better support cancer survivors within faith-based communities; and providing programs for cancer prevention. She celebrated the Total Wellness project with 62 participants who completed a 2-4 month cancer prevention program. She will present at the Society of Behavioral Medicine this year. Dr. Kwarteng was accepted into the 2023 NIH Summer Institute on Randomized Behavioral and Clinical Interventions.

- **John Meurer, MD, MBA**, is director of the Institute for Health & Equity. With 20 primary care health centers, the faith community, and community agencies, he is co-PI of a major NIH grant to CTSI to study the seroprevalence of COVID among adults in Milwaukee, the individual and neighborhood risk factors for severe illness, and the impact of vaccines. With a decade of CDC funding, Dr Meurer is co-investigator of studies of the effect of variations in state Medicaid expansion on

diabetes outcomes. He is co-PI of AHW-funded research in early childhood development by improving resiliency and equity (REDIRECT). He leads an evaluation of STRY365 trauma-informed coaching and a video game on 5th to 9th graders at 4 schools. He is first author of "Team science criteria and processes for promotion and tenure of health sciences university faculty" in the *Journal of Clinical and Translational Science*.

- **Angelica Delgado Rendón, PhD,** has experience in community research, program evaluation, and public health education. Dr Delgado Rendón currently serves as Instructor. She has worked on various health areas: nutrition, physical activity, depression, Alzheimer's disease, fall prevention, tobacco smoking, marijuana smoking, and chronic disease management. She is analyzing interviews of early childhood educators about the value of shared service networks of childcares. Dr. Rendon significantly revised and directed the MPH courses "Health Promotion & Disease Prevention" and "Theory & Practice."

- **C. Greer Jordan, PhD**, serves as the MCW Chief Diversity and Inclusion Officer and is an Assistant Professor in IHE. Dr. Jordan's research interests include social process of inclusion in organizational settings, diversity and inclusion cultural assessment, institutions as anchors for fostering positive social determinants of health systems change, and whole scale change theories and methods. Dr. Jordan is the PI of two AHW projects: 1) Milwaukee Healthcare Workforce Initiative to create a pipeline to support the region's health care industry through an employer-led training program to create a diverse candidate pool for Advocate Aurora and other health systems across the Milwaukee area; 2) Building a Healthcare Workforce Through Access and Equity in which MATC determines, implements, and assesses systemic changes to its student scholarship and supports programs to create greater opportunity for students from diverse backgrounds to enter healthcare professions. MATC partners with Milwaukee Public Schools, UWM, MCW, regional healthcare systems and providers to recruit, educate and place diverse candidates in the healthcare workforce.

Neuroscience Research Center

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

Overall Goals:

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

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

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

How does this help me?

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

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

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

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

If you are interested in becoming a member of the NRC and receiving email updates of seminars, events and grant opportunities, please contact Hailey Wirtz (hwirtz@mcw.edu).

Versiti Blood Research Institute

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

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

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

Adult Translational Research Unit (A-TRU)

What Do We Do?

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

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

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

Services Offered:

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

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

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

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

All of Us Research Program

What is the *All of Us* Research program?

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

What is the promise for researchers?

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

What do the participants look like?

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

As of March 29– 425,288 people have provided access to EHR, completed 3 core surveys and donated biospecimens

- 46.7% ethnic/racial minorities
- 2,300 non-binary, 1460 transgender
- Median age mid-50's
- All 50 states represented
- Over 24,000 in Wisconsin

What kind of data is available?

https://databrowser.researchallofus.org/

- Electronic health records (n=372,380) – records from recent enrollees have not yet been uploaded and curated
- Vital signs, Body Mass Index, and waist and hip circumference measured by research staff (n=311,300)
- Genomic data (98,560 with WGS online; 165,080 genotyping array – these overlap, so total is 168,080)
- Surveys regarding medical history, family history, health habits, COVID experiences, social determinants of health, etc. https://www.researchallofus.org/data-tools/survey-explorer/

How do I sign up to access this?

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

You need to:

- Be at an institution with a Data Use Agreement – MCW, Marquette, UW-Milwaukee are included in 494 such institutions
- Have an ERA commons account
- Complete All of Us specific humans studies research training – takes 2-3 hours.

FOR HELP

- Everything is in the User Support Hub - https://support.researchallofus.org/hc/en-us
- Video Tutorials/Webinars - https://support.researchallofus.org/hc/en-us/categories/5942794068756-Videos
- Office hour recordings - https://support.researchallofus.org/hc/en-us/sections/6000285700372-Office-Hour-Informational-Sessions

WHY ARE YOU WAITING

- 130 published articles used the All of Us dataset - https://www.researchallofus.org/publications/
- 4312 active projects – see them all https://www.researchallofus.org/research-projects-directory/

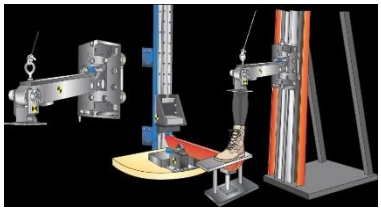
Biomechanics Core

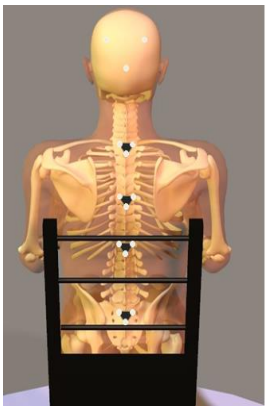
What Do We Do?

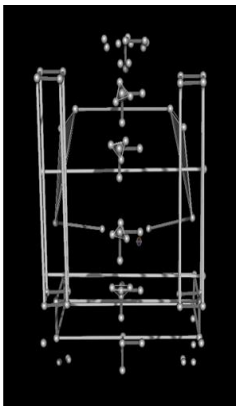
Multiple specialty labs serve as the "Biomechanics Core" facilities. We are equipped with multiple small-animal injury models, including custom-designed equipment to deliver blunt or blast brain injury to rodents and tissue. We also have facilities and equipment for investigators who want to obtain mechanical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

Equipment Available

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







Contact Us:

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Cancer Center Biomedical Imaging Shared Resource

What Do We Do?

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

Equipment Available

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

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

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

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

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Cancer Center Redox & Bioenergetics Shared Resource

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

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

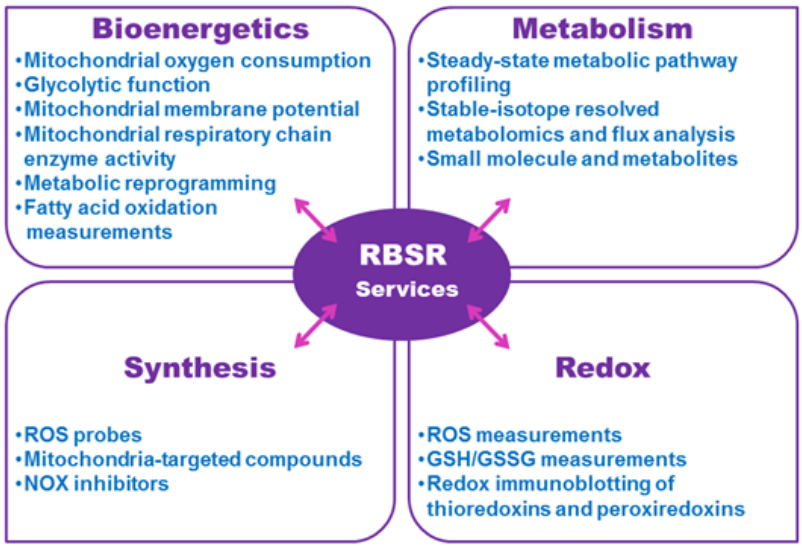

Figure 1. The RBSR promotes the understanding of cancer cell bioenergetics, metabolism, reactive oxygen species, and redox signaling, which are central to several areas of cancer research.

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

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

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

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

1. Cheng G, Hardy M, Topchyan P, Zander R, Volberding P, Cui W, Kalyanaraman B. Potent inhibition of tumour cell proliferation and immunoregulatory function by mitochondria-targeted atovaquone. *Sci Rep*. 2020 Oct 21;10(1):17872.
2. Cheng G, Hardy M, Zielonka J, Weh K, Zielonka M, Boyle KA, Abu Eid M, McAllister D, Bennett B, Kresty LA, Dwinell MB, Kalyanaraman B. Mitochondria-targeted magnolol inhibits OXPHOS, proliferation, and tumor growth via modulation of energetics and autophagy in melanoma cells. *Cancer Treat Res Commun*. 2020 Sep 17;25:100210.
3. Wang F, Qi XM, Wertz R, Mortensen M, Hagen C, Evans J, Sheinin Y, James M, Liu P, Tsai S, Thomas J, Mackinnon A, Dwinell M, Myers CR, Bartrons Bach R, Fu L, Chen G. p38γ MAPK is essential for aerobic glycolysis and pancreatic tumorigenesis. *Cancer Res*. 2020 Aug 15;80(16):3251-3264.
4. Rios N, Radi R, Kalyanaraman B, Zielonka J. Tracking isotopically labeled oxidants using boronate-based redox probes. *J Biol Chem*. 2020 May 8;295(19):6665-6676.

5. Zhang Q, Cheng G, Pan J, Zielonka J, Xiong D, Myers CR, Feng L, Shin SS, Kim YH, Bui D, Hu M, Bennett B, Schmainda K, Wang Y, Kalyanaraman B, You M. Magnolia extract is effective for the chemoprevention of oral cancer through its ability to inhibit mitochondrial respiration at complex I. *Cell Commun Signal*. 2020 Apr 7;18(1):58.
6. Cheng G, Pan J, Podsiadly R, Zielonka J, Garces AM, Dias Duarte Machado LG, Bennett B, McAllister D, Dwinell MB, You M, Kalyanaraman B. Increased formation of reactive oxygen species during tumor growth: Ex vivo low-temperature EPR and in vivo bioluminescence analyses. *Free Radic Biol Med*. 2020 Feb 1;147:167-174.
7. Nasci VL, Chuppa S, Griswold L, Goodreau KA, Dash RK, Kriegel AJ. miR-21-5p regulates mitochondrial respiration and lipid content in H9C2 cells. *Am J Physiol Heart Circ Physiol.* 2019 Mar 1;316(3):H710-H721.
8. Cheng G, Zhang Q, Pan J, Lee Y, Ouari O, Hardy M, Zielonka M, Myers CR, Zielonka J, Weh K, Chang AC, Chen G, Kresty L, Kalyanaraman B, You M. Targeting lonidamine to mitochondria mitigates lung tumorigenesis and brain metastasis. *Nat Commun*. 2019;10(1):2205.
9. Horikoshi Y, Yan Y, Terashvili M, Wells C, Horikoshi H, Fujita S, Bosnjak ZJ, Bai X. Fatty acid-treated induced pluripotent stem cell-derived human cardiomyocytes exhibit adult cardiomyocyte-like energy metabolism phenotypes. *Cells*. 2019 Sep;8(9). pii: E1095.
10. He C, Danes JM, Hart PC, Zhu Y, Huang Y, de Abreu AL, O'Brien J, Mathison AJ, Tang B, Frasor JM, Wakefield LM, Ganini D, Stauder E, Zielonka J, Gantner BN, Urrutia RA, Gius D, Bonini MG. SOD2 acetylation on lysine 68 promotes stem cell reprogramming in breast cancer. *Proc Natl Acad Sci U S A*. 2019 Nov 19;116(47):23534-23541.
11. Chen Y, Yang M, Huang W, Chen W, Zhao Y, Schulte ML, Volberding P, Gerbec Z, Zimmermann MT, Zeighami A, Demos W, Zhang J, Knaack DA, Smith BC, Cui W, Malarkannan S, Sodhi K, Shapiro JI, Xie Z, Sahoo D, Silverstein RL. Mitochondrial metabolic reprogramming by CD36 signaling drives macrophage inflammatory responses. *Circ Res*. 2019 Dec 6;125(12):1087-1102.

For more information, contact Jacek Zielonka, PhD (955-4789 or jzielonk@mcw.edu) or visit the RBSR website (https://www.mcw.edu/departments/redox-and-bioenergetics-shared-resource).

Clinical Research Data Warehouse (CRDW)

What Do We Do?

The CTSI's Clinical Research Data Warehouse (CRDW) provides **no-cost self-service tools** to CITI-trained research teams for project feasibility, cohort discovery and data extraction. CRDW tools include two cohort query tools (i2b2 and TriNetX) and the Honest Broker data extraction tool. We also have a new "big data" environment called Jupyter Hub for experienced programmers and biostatisticians.

Data sources include Epic, GE/IDX (physician billing system), MCW Tissue Bank biospecimens, NAACCR tumor registry, Muse ECG data (in Jupyter Hub only), and genetic testing vendors (Foundation Medicine, Tempus, Ambry, Guardant, Invitae).

Browse our Honest Broker data dictionary: https://ctsi.mcw.edu/images/sites/37/CTSI-Honest-Broker-Data-Dictionary.pdf

The query tools help to answer the question "Does the CRDW contain a cohort of patients with certain characteristics?"
Honest Broker allows teams to extract fully de-identified cohort data from a variety of domains without an IRB protocol. Identified data extraction is also available once a team has an approved IRB protocol that is linked to our CRDW IRB banking protocol.

How Can Investigators and Their Teams Get Access?

1. Join the CTSI at https://ctsi.mcw.edu/about/join-ctsi/
2. Complete MCW's CITI Training Modules for Human Subjects Research (HSR) in Biomedical Research
3. Complete an Access Form at https://redcap.mcw.edu/surveys/?s=3TR398YFTY

Feel free to browse our web site for more information! https://ctsi.mcw.edu/ctri/cda/crdw/

Contact Us:
CRDW@mcw.edu for general biomedical informatics or research data warehouse questions
Chelsea Spangenberg, CTSI Program Manager [cspangenberg@mcw.edu] for intake/access questions
Kristen Osinski, CTSI Business Analyst [kosinski@mcw.edu] for CRDW content/training questions

Comprehensive Rodent Metabolic Phenotyping Core

What Do We Do?

The mission of the Comprehensive Rodent Metabolic Phenotyping Core (CRMPC) is to provide investigators with low barrier and guided access to quantitative and comprehensive assessments of energy flux and fluid homeostasis in rodents to assist in the dissection of complex and integrated mechanisms of cardiometabolic disease.

Services available:

- **Multiplex Metabolic Phenotyping** (16 cage Promethion; Sable Systems International)
  - Data-rich, 24hr continuous assessments of metabolic rate in rodents (mice and rats), food/water intake, physical activity, and behavioral matrices recorded over 5 consecutive days.
- **Body Composition Analysis** via time-domain nuclear magnetic resonance (LF110 NMR; Bruker Biospin)
  - Rapid and non-invasive measurements of fat and lean mass without the need for anesthesia.
  - Tissue biopsy assessment (fat and lean mass) available (10-500mg).
- **Stand-alone O_2/CO_2 Respirometers** (FMS3; Sable Systems International)
  - High resolution measurements of respiratory gas exchange for the assessment of energy expenditure in rodents (mice and rats).
- **Gradient-layer Direct Calorimetry** (Custom fabrication)
  - Measurements of total heat dissipation (both aerobic and anaerobic) and core temperature heat retention in rodents.
- **Metabolic Caging** (Tecniplast and Nalgene)
  - Quantitative collections of food/water intake and fecal/urine outputs for downstream assessments (osmolality, electrolytes, intake behaviors).
- **Sterile Fecal Collections**
  - Provides sterile fecal collections for downstream gut microbiome analysis and fecal material transfer studies.
- **Bomb Calorimetry** (Model 6725; Parr Instruments)
  - High resolution quantification of caloric density of biological samples (food, feces, urine).
- **Bioimpedance Spectroscopy** (ImpediVet)
  - Fast, minimally invasive assessment of body fluid compartmentalization (intracellular versus extracellular reservoirs) combined with whole body electrolyte measurements for osmotically active and inactive cellular stores.
- **Thermal Infrared Imaging** (FLIR)
  - High resolution image capture and temperature measurements in biological models.
- **IACUC Protocol and Study Design Guidance**
- **Statistical Analysis Assistance**
  - Expert statistical consultation for complex metabolic data interpretation.

Contact Information:

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Research Scientist II / Core Manager
jreho@mcw.edu | (414) 955-2124

Justin L. Grobe, Ph.D.
Associate Professor of Physiology & Biomedical Engineering / Core Director
jgrobe@mcw.edu | (414) 955-4981

Useful Links:

https://mcw.ilab.agilent.com/service_center/5692/?tab=about

https://www.frontiersin.org/articles/10.3389/fphys.2022.855054/full

CRI/CC Flow Cytometry Shared Resource

What Do We Do?

The Children's Research Institute and cell b Cytometry Shared Resource is an advanced technology facility primarily serving MCW and CRI investigators. The facility provides secondary support to on-campus colleagues at the BRI, as well as collaborators off campus at institutions in the Upper Midwest. Our facility provides 24/7 access to analytical cytometers and cell sorters for trained users and operator-assisted cell sorting by appointment. In addition to these services, we assist both new and established investigators with protocol and assay development, including sample preparation, selection of antibodies and fluorochromes, proper staining and compensation controls, and selection of appropriate buffers. Assistance with Data analysis using FlowJo, FCS Express, DIVA and SpectroFlo software is also available by appointment.

Equipment Available:

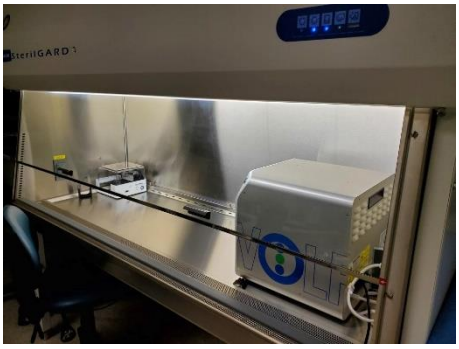
- BD LSRFortessa X20 – 5-laser (18-color, 20-parameter) Flow Cytometer
- 2 Cytek Aurora – 5-laser (64-color, 67-parameter) Flow Cytometers
- BD FACSAria II – CC 4-laser (10-color, 12-parameter) Cell Sorter
- BD FACSAria IIu – CRI 4-laser (12-color, 14-parameter) Cell Sorter
- NanoCellect WOLF-Sorter – 1-laser (3-color, 5-parameter) Cell Sorter
- Miltenyi MACSQuant Tyto – 3-laser (8-color, 10-parameter) Cell Sorter
- HemaVET 950 - CBC Analyzer (24 parameters, including platelets; multi-species)
- FlowJo Software
- FCS Express
- SpectroFlo Software

Contact Us:

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

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

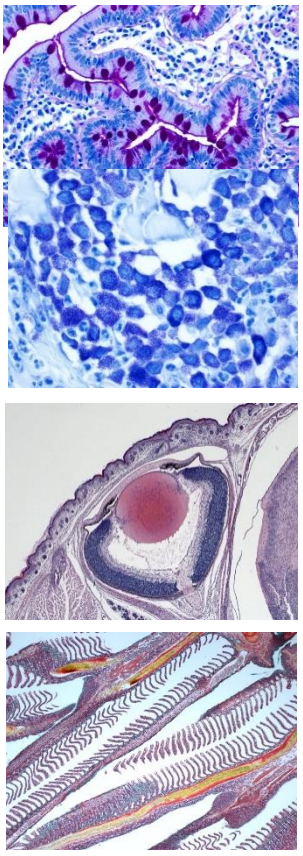
MACC Fund Research Center, 5th Floor, #5052
Monday – Friday, 9:00 a.m. – 5:00 p.m.



CRI Histology Core

What Do We Do?

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



Histology Core Equipment:

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

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

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

Histology Core Staff

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

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

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

Histology Core Directors

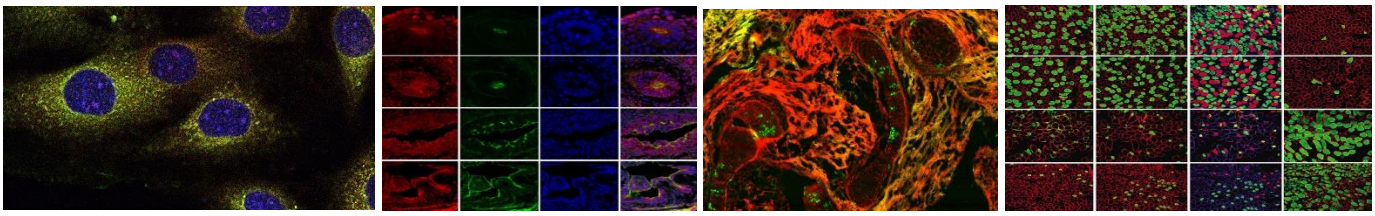
Jason A. Jarzembowski, MD, PhD
Interim Chief Executive Officer, Children's Specialty Group
Vice Chair (Pediatric Pathology) and Professor, Department of Pathology, MCW
Interim Senior Associate Dean of Clinical Affairs, MCW
Medical Director, Pathology and Laboratory Medicine, Children's Wisconsin
Chair,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

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

CRI Imaging Core

What Do We Do?

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



Equipment Available

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

Contact Us:

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

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

Echocardiography Core – Clinical & Small Animal

What Do We Do?

The Echocardiography Core provides expertise, data analysis, and interpretation for cardiac and vascular ultrasound research in animals and humans. The Echo Core supports investigators needs for their specific study protocol. We aim to support researchers in everything from a single analysis study to comprehensive correlative studies. The Echo Core Lab is directed by Dr. Noelle Garster and Dr. Divyanshu Mohananey. For questions or to set up an appointment, please contact Lindsey Kalvin ACS, RDCS (AE & PE), FASE. We are happy to support your research needs.

Small animal imaging services offered:

- Cardiac and vascular imaging
- Data analysis
- Strain left ventricular function data

Human imaging services offered:

- Echocardiograms performed with American Society of Echocardiography (ASE) guidelines.
- Support sponsor-base trials and MCW investigator initiated trials
- Physician interpretation
- Strain data analysis
- Definity contrast available upon request

Electron Microscopy Core Facility

What Do We Do?

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

Equipment Available

- JEOL 2100 electron microscope equipped with a 2K x 2K ultrahigh resolution digital camera
- JEOL 1400 electron microscope equipped with side entry, high resolution digital camera and AMT image processing.
- Leica EMPact 2 high pressure freezing apparatus
- Leica Automated Freeze Substitution Apparatus
- RMC PowerTome & Leica Ultracut UCT ultramicrotomes

Contact Us:

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

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

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

Epidemiology Data Resource Center

What Do We Do?

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

Services Offered

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

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

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

Geospatial Epidemiology & Outcomes (GEO)

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

Geospatial Services

Geographic Information Systems (GIS) and Spatial Analysis Services

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

Epidemiology Services

General epidemiologic information about cancer burden

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

Outcomes Services

Data acquisition, preparation, management and analysis

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

Contact Us:

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

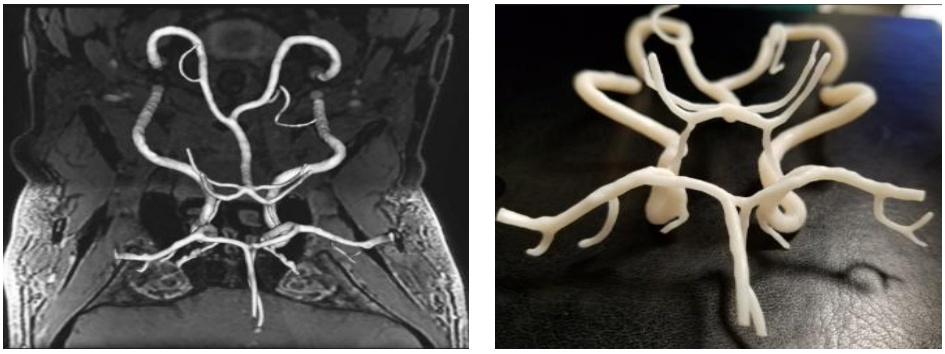
MCW Engineering Core

What Do We Do?

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

Services Offered

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



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

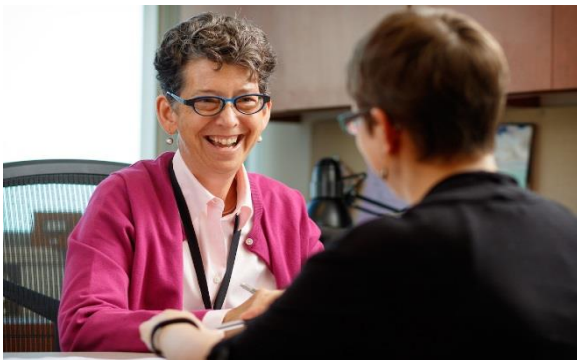
Contact Us:
Bonnie Freudinger, ME
MCW Engineering Lab Supervisor
bfreudinger@mcw.edu | (414) 955-4722

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

MCW Libraries

What Do We Do?

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



Services Offered

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

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

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

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

MCW Tissue Bank

What Do We Do?

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

Services Offered

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

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

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

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

NRC Microscopy Core

What Do We Do?

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

Instruments:

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

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

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

NRC Rodent Behavior Core

What Do We Do?

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

Equipment Available

Mouse (sample listing)

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

Rat (sample listing)

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

Contact Us:

Jennifer Sterrett
414-955-8620

Breanna Glaser
414-955-2226

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

Office of Technology Development

What Do We Do?

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

Services Offered:

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

Contact Us:

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

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

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

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

Pediatric Echocardiography Core

What Do We Do?

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

Equipment Available

Hardware:

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

Software:

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

Ultrasound Equipment:

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

Contact Us:

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

Pediatric Translational Research Unit (P-TRU)

Kids deserve the best.

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

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

The TRU provides a variety of services, including:

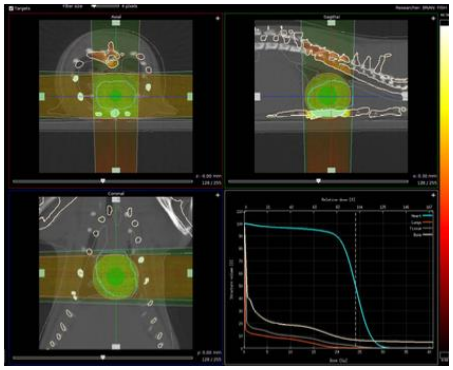
- Research Coordination Training Support
    - EPIC Research Trainer and consultant
    - IRB Navigation (IRBnet) assistance
    - Budget consultation
    - Study monitoring
    - Well versed with FDA Regulations (IND/IDEs/audits)
- Nursing support
    - Nursing study support
    - Nursing coordination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

*Whenever you wish to initiate a study using the TRU or are considering using the TRU, please contact: Cristen Berry (P-TRU Manager) 266-7233 and/or Jeff Crawford 266-7254 (P-TRU Research Operations Specialist) to set up a meeting for initial conversations.

Precision Irradiation Core

Location: TBRC Suite E, MFRC 1005 and MFRC 4072
P.I.: Dr. Heather Himburg
Contact:

- Brian Fish, Core Director
  414-955-4673
  bfish@mcw.edu
- Tracy Gasperetti, Core Manager
  414-955-4686
  tgasperetti@mcw.edu
  Hours: Monday – Friday 7:30am – 3:30pm



Overview
The Precision Irradiation Core houses three X-RAY instruments capable of irradiating small animals and cells. The core can perform whole body irradiations as well as targeted irradiation of small volumes, tumors and cells at various dose rates. Irradiations are available on a fee-for-service basis.
The core also breeds, houses, and sells the only WAG/Rij rat strain in the United States.

Irradiator/Software	Use	
SmART x-ray machine, Precision X-Ray (small animal radiotherapy unit)	Small field targeted radiotherapy with CT imaging and full treatment planning; total body irradiation (TBI) for mice; ability to irradiate mice and rats	
X-RAD 320 kVp X-ray unit, Precision X-Ray	Large field irradiations with motorized turntable and adjustable shelf; total body irradiation (TBI) and partial body irradiation (PBI) on WAG/RijCmcr rats only	
Cell Rad+, Precision X-Ray	Benchtop cell irradiator with integrated dosimeter to irradiate cells and tissues	

*All irradiations are performed by core technicians on behalf of investigators

Qualitative Research Consulting Service

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

Services Offered:

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

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

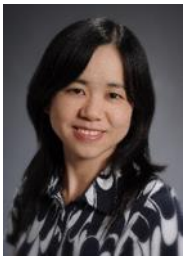
Contact Us:

Staci Young, PhD
Director

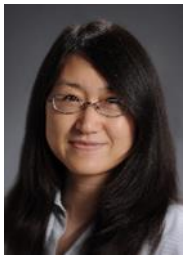
Katinka Hooyer, PhD
Co-Director

Jeanine Schultz-Merrill, Core Administrator
jschultzmerrill@mcw.edu
https://mcw.ilab.agilent.com/service_center/show_external/5073/qualitative_research_consulting_service_core

Quantitative Health Sciences (QHS)



Ke Yan, PhD
Interim Chief, QHS



Amy Pan, PhD
Associate Director

Jody Barbeau, BS
Database Administrator

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

Specialties:

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

Services Offered

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

Contact Us:

Ke Yan, PhD
Interim Chief, QHS
Associate Professor
kyan@mcw.edu

Amy Pan, PhD
Associate Director
Associate Professor
apan@mcw.edu

Jody Barbeau, BS
Database Administrator
jbarbeau@mcw.edu

Cindy Feltz
Consultation Contact
cfeltz@mcw.edu

Pippa Simpson, PhD
Professor Emeritus
psimpson@mcw.edu

CRI/TBRC, 3rd Floor, #C3135; Monday – Friday, 8:30 a.m. – 5 p.m.
Currently meeting by Zoom or in-person if requested.

Redox Biology Program

The mission of the Redox Biology Program is to foster communication and an exchange of expertise among clinicians and basic science researchers in the spirit of collaborative research. To that end, the Redox Biology Program unites a broad, interdisciplinary group of researchers who are interested in the role of redox processes in physiology and pathology. These scientists have extensive research experience and technological skills, and their laboratories contain cutting-edge resources. The goal is that data and novel hypotheses resulting from interdisciplinary collaboration will yield funded grant proposals, published manuscripts, and course curricula.

The Redox Biology Program collaborates and consults with interested faculty around MCW to provide a scholarly scientific environment to conduct redox-related research, and provides training for students, who are the medical and science leaders of tomorrow. Areas of expertise include bioenergetics, cancer, cardiovascular disease, fetal brain injury, nitric oxide and its interactions, reactive oxygen species, thiol biochemistry, free radical chemistry and biochemistry, EPR (electron paramagnetic resonance) spin trapping, and inflammation, infection, and immunity.

To facilitate the exchange of expertise and ideas, the Redox Biology Program delivers high-quality education events for busy physicians and scientific investigators. We have successfully organized three regional symposia with a focus on redox processes in pathology. Learn more about the Redox Biology Program at www.mcw.edu/departments/redox-biology-program.

Research Computing Center

The Research Computing Center (RCC) provides the infrastructure and campus-wide access to high performance computing (HPC) resources required for computationally-intensive biomedical research. RCC is institutionally supported and available to all MCW students, staff, and faculty. RCC services and operations are governed by representatives of the MCW Faculty in partnership with RCC leadership.

Services

HPC:

RCC maintains a Linux-based HPC cluster ideal for both massively parallel and high throughput workloads.

- 50 nodes
- 1200 cores
- 44 GPUs
- 10TB of memory
- Infiniband Interconnect

Storage:

RCC also provides petascale data storage to support both data-intensive computing and long-term retention.

- High-performance parallel file system
- Long-term storage for completed projects
- 10GigE interconnect

Consulting:

RCC provides consulting services for users, groups, and projects regarding a variety of research computing related topics.

- Training on HPC systems
- Software installation and setup
- End-user support and trouble-shooting
- Grant assistance and boilerplate language
- Consulting on IT needs of computational research projects

Staff and Facilities:

RCC has full-time dedicated staff with extensive experience in system administration and computational research. All hardware is housed in professionally managed MCW datacenters. RCC also collaborates with and is supported by MCW's excellent central IT teams.

- 2 Datacenters
    - Redundant power and cooling
    - Biometric access control
- Professional staff
    - Experience in research computing, system administration, network, and security

Shared High-Frequency Ultrasound Imaging Facility

About Us:

- Provide instrumentation for high-resolution in vivo ultrasound imaging
- Managed by the Department of Pharmacology & Toxicology
- Purchased with support by an NIH S10 Shared Instrument grant (acknowledge 1S10 OD025038 in all publications)

Services:

1. Access to instrumentation on a fee-for-use basis
2. User training
3. Use of data analysis using Vevo Lab software

Equipment & Technology:

- VisualSonics Vevo 3100 high-frequency ultrasound imaging unit, small animal imaging station, micro-injection system, anesthesia unit
- Linear array transducers (MX250, MX550D, MX700) providing resolution up to 30 um
- Power Doppler, Tissue Doppler, 3D mode, strain analysis, cardiovascular analysis and 3D imaging software
- Work-station for data analysis

See: https://www.visualsonics.com/product/imaging-systems/vevo-3100

Contact Us:

Tina Wan
Manager, Research Scientist
twan@mcw.edu

John Auchampach, PhD
Principal Investigator
jauchamp@mcw.edu

Shared Mass Spectrometry Facility

What Do We Do?

The MSMS Facility is an interdepartmental research service unit managed on behalf of MCW by the Department of Pharmacology & Toxicology. It provides service and consultation for research projects requiring mass spectrometric analysis. Two mass spectrometers are available to analyze samples. We operate on a fee for service basis. The facility provides quantitation using SRM (MRM) for known compounds. In addition, the facility can identify unknown small molecules using MS/MS techniques. The facility will implement reported procedures for analysis and quantitation and will develop new methods that answer investigator-driven questions.

Equipment Available

Agilent 6460 Triple Quadrupole-LC Mass Spectrometer: LC/MS/MS has Jet Stream source interfaced to a 1290 Infinity liquid chromatograph and autosampler. Mass analyzer uses both positive and negative detection modes with data-sampling rate of up to150 SRM/s. The 6460 routinely achieves fmol sensitivity.

Thermo Scientific Triple Quadrupole-GC Mass Spectrometer: TSQ 8000 (GC/MS/MS) is equipped for electron impact (EI) and chemical ionization (CI). Analyzer has a mass range up to 1100 m/z in both positive and negative ion detection modes. Interfaced to Trace 1310 gas chromatograph equipped with a TriPlus autosampler.

Typical Analyses:

- Complex Lipids
- Smaller, volatile lipids
- Endocannabinoids
- Drugs of Abuse
- Metabolites
- Peptides

Contact Us:
Michael J. Thomas, PhD
Director
mjthomas@mcw.edu | (414) 955-8605

Therapeutic Accelerator Program

What Do We Do?

The Therapeutic Accelerator Program (TAP) in the Department of Pharmacology & Toxicology serves MCW and Clinical & Translational Science Institute of Southeast Wisconsin partner institutions. The process of translating research ideas into technologies that improve human health is many steps and requires the assistance of different teams with diverse expertise. TAP catalyzes the bench to beside journey, bridging the gap between basic research and the development process. TAP provides advising, project-based funding opportunities, and connections to our network of resources to de-risk and advance technologies along the path to commercialization.

- Project-based funding opportunities for therapeutic development
  (Drugs, devices, diagnostics, platform technologies, HealthTech)
- Advising
- Independent scientific review and guidance
- Concept validation and feedback via multidisciplinary panel review
  (Scientific, medical, legal, regulatory, business, technical and clinical development)
- Connection to networked resources
  (Scientific, medical, legal, regulatory, business, technical and clinical development, training in entrepreneurship, funding assistance, venture capital)
- Facilitating collaborations
- Mentoring for proof-of-concept work

Contact Us:

Kristin Ciezki, PhD
Director, Therapeutic Accelerator Program
Department of Pharmacology & Toxicology
kciezki@mcw.edu

Transgenic Core

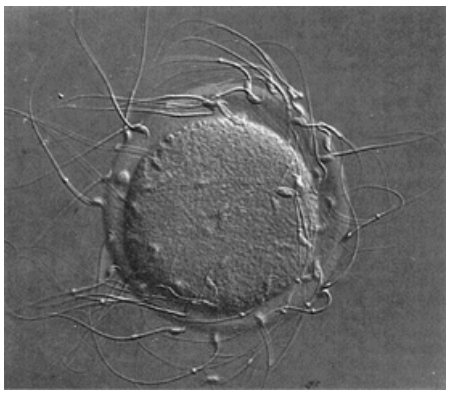
What Do We Do?

The Mouse Transgenic Core assists research staff with procedures involving the production and maintenance of transgenic mouse lines. The Core works primarily with Investigators on campus providing both sperm and embryo cryopreservation/recovery, IVF, strain rederivation, as well as pronuclear microinjection of CRISPR and DNA/BAC constructs. We are also available for consultation involving colony breeding issues. We are able to recover lines from cryopreserved embryos or sperm that were purchased or transferred from another institution. The laboratory is located on the first floor in the vivarium of the Translational and Biomedical Research Center at MCW

Instrumentation includes 2 injection workstations (Nikon inverted phase contrast microscope with Hoffman modulation optics, temperature-controlled injection stage, Eppendorf motor-driven injection system), microforge, needle puller, Nikon stereo zoom microscope, surgical microscopes and multiple dewars for storage of cryopreserved mouse germplasm.

Services Offered

- **Sperm Cryopreservation**
- **In Vitro Fertilization (sperm cryopreservation recovery)**
- **Embryo Cryopreservation and Recovery**
- **Pronuclear Microinjection of CRISPR, DNA constructs**
- **Strain Rederivation to clean lines from pathogens**



VA NODES (Network of Dedicated Enrollment Sites)

Milwaukee VA is now part of VA's Network of Dedicated Enrollment Sites

Membership in the NODES program allows the Zablocki VA Office of Research to support VA investigators who would like to participate in VA funded studies, but do not have experience or staff to help them do so. This assistance can extend to clinical trials funded by other Federal agencies (NIH, PCORI, CDC, etc) or even industry-funded studies. To obtain assistance, reach out to Zablocki NODES leadership – Jeff Whittle, MD, Elizabeth Gore, MD or Julie Rieder, CCRC.

The Network Of Dedicated Enrollment Sites (NODES) is a program to enhance the planning and conduct of large multicenter clinical trials and epidemiological studies in the Department of Veterans Affairs(VA). It is supported by the VA's Cooperative Studies Program (CSP), which has funded studies ranging from the 1960's demonstration that coronary artery bypass surgery improved survival in persons with left main coronary artery disease to multiple studies of COVID interventions and outcomes. NODES supports research by providing infrastructure to help mitigate many of the problems investigators face with study conduct. The CSP funds NODES staff members to assist with key, typically underfunded or unfunded, study activities such as hiring, training and monitoring research staff, securing office space, obtaining IRB approval, and completing close out. In addition to supporting study logistics, NODES works with the VA facilities Research Office to monitor the success of recruitment and retention activities, as well as the quality of data collected. Because of their experience and core funding, NODES staff and leadership can provide both advice ***and*** assistance to help investigators achieve or exceed goals.

NODES staff are led by an Associate Director for Operations (ADO), a VA employee fully funded by CSP; Julie Rieder serves that role at the Zablocki VA. In addition, to be a NODES site the local VA must support 20% of the time of a clinical investigator with extensive experience in clinical trials to serve as the NODES director. Jeff Whittle, MD, MPH is the NODES director for the Zablocki VA. Because of her special expertise in cancer clinical trials and longtime VA leadership role, Elizabeth Gore, MD, MPH was asked to serve as co-Director and has agreed to do so.

While NODES was started to help VA ensure consistency and efficiency in the conduct of CSP funded trials, it is now available to support other clinical research. Currently studies receiving NODES support include MCW faculty researchers from Dermatology, Medicine, Psychiatry and Radiation Oncology, with a couple surgical studies in planning. Topics range from diabetes to dementia and COVID to cancer. Researchers considering the conduct of clinical trials at the Milwaukee VA should contact the NODES ADO at 414-384-2000 ext. 46628 or by emailing julie.rieder@va.gov or jeffrey.whittle@va.gov for more information.

Investigators seeking to develop and lead a clinical trial can work with NODES leaders to access the VA's Cooperative Studies Program, which provides methodologic expertise, access to a number of VA sites and data management and analytic infrastructure. This is briefly described on the following page.

Starting a VA Cooperative Study

The following outlines the process for how a CSP study begins. For specific details, you will need read the detailed guidelines, available from the VA intranet or from NODES program leaders.

1. A Letter of Intent (LOI) (or Planning Request) is submitted to CSP Central Office by an eligible VA investigator (Principal Proponent).
   - Key elements in the LOI include:
     - Objectives of the proposed research
     - Importance of the study to VA and its patients
     - Justification for a multi-site study and the feasibility of conducting it within VA
     - Summary of preliminary research and data to support a large-scale evaluation
     - Proposed study design
     - Anticipated size of the study
   - VA investigators must have a 5/8ths appointment at a VA facility.

- While rare, an investigator may request and be given an eligibility waiver.

2. After an administrative review for appropriateness, the LOI is sent for external review of the scientific/clinical merit and feasibility by independent experts in the field.
3. Based on LOI reviews and recommendations, a decision to fund a study planning meeting is made by the Director, Cooperative Studies Program.
4. If the LOI is approved for planning, a CSP Coordinating Center (CSPCC) is assigned to assist the study proponent in developing a full proposal.
    - If necessary, a clinical research pharmacist and/or health economist is included on the study team.
    - Typically, two planning meetings are required to develop a full proposal.
    - After the first planning meeting, the CSPCC Director submits a request to CSP Central Office for a second planning meeting based on study progress.
5. Upon completion, the full proposal is submitted for peer review to the Cooperative Studies Scientific Evaluation Committee (CSSEC).
    - CSSEC is an independent panel of clinicians, research methodologists, and statisticians who all have expertise in clinical trials.
    - CSSEC meets twice a year, usually in May & October.
6. After a face-to-face review between CSSEC and the study proponent, biostatistician, CSPCC Director, and health economist (if needed), a recommendation and priority score is given to the Director, Cooperative Studies Program. Generally one of the following four recommendation are made:
    - Unconditional Approval *
    - Conditional Approval *
    - Defer consideration of the study with a recommendation for resubmittal
    - Rejection of study

    * Note: Approval by CSSEC does not ensure funding. Funding will be based, in part, on the priority score assigned and CSP budgetary considerations.
7. If a study is funded by CSP Central Office, the study proponent works with the CSPCC to move into a "Study Initiation" phase.

Department of Veterans Affairs
Office of Research and Development
Introduction to Million Veteran Program (MVP) data

For Medical College of Wisconsin researchers seeking to use the rich MVP research data, it is important to know that the VA greatly values team science. It is the expectation that some VA researchers will need to work with experts from outside the VA. These experts will need to apply for “Without Compensation” employee status within the VA, or be contracted by the VA. Only MCW faculty who have at least 5/8 FTEE VA appointments would be able to serve as a principal investigator. More detailed information about the MVP data is available through websites that are located behind the VA firewall.

The **Million Veteran Program (MVP)** is a national genetics research initiative of the Department of Veteran Affairs Office of Research and Development (ORD). The purpose of MVP is to create a longitudinal cohort of at least one million Veterans to understand better how genes, lifestyle behaviors, and military exposures impact health and illness, and to bring personalized medicine to VA health care. Veterans who volunteer to join MVP provide access to their medical records, complete a baseline survey, an optional lifestyle survey, and provide a blood specimen. Currently, MVP has over 930,000 Veterans participating.

MVP data access is open to all VA researchers through Merit Awards. Since 2015, VA has funded over 70 VA research projects using MVP data. These projects represent VA investigators from all four ORD research services and the Cooperative Studies Program. The project teams have helped MVP test the computational infrastructure, and the regulatory and administrative frameworks around data

access in addition to increasing the scientific knowledge regarding the genetics of various chronic illnesses and traits impacting US Veterans.

This guidance document outlines 1) how VA investigators can apply for VA Merit Awards that include aim(s) requiring MVP data across the four ORD research services and 2) the updated data types that will be available to use for VA Merit awards starting in the Spring 2023 review cycle.

Available MVP data and Computing Environment:
All data analysis using MVP data will take place behind the VA firewall in the Genomic Information System for Integrative Sciences (**GENISIS**) research environment. **GENISIS** serves as the MVP informatics and computing platform. In addition, **GENISIS** also supports recruitment and enrollment module, and the Biorepository Laboratory Information Management System (**LIMS**). The MVP data resources include electronic health records extracted from the VA Corporate Data Warehouse (**CDW**) through the Veterans Informatics and Computing Infrastructure (**VINCI**), curated self-reported survey data and genomic data, and a High-Performance Computing (HPC) cluster with analytical tools. Researchers will have access to data, computing resources, and analytical tools within this secure study-specific study mart in **GENISIS**. The Data and Computational Sciences (**DACS**) Core team builds and manages the protected data and computing infrastructure for MVP behind the VA firewall.

Details Of Data Available on MVP Participants.
1) **Electronic Health Records (EHR) data** on ~**930,000 MVP participants,** extracted from the Corporate Data Warehouse (CDW) through the Veterans Informatics and Computing Infrastructure (VINCI). Note that the VA has had structured laboratory and pharmacy data available at the individual patient level for over 2 decades.

2) **Data from two surveys completed by the MVP participants**. The first is a "Baseline Survey" on ~75% of the participants, focusing on demographic characteristics, medical and family history, health status, and lifestyle habits. The second is an optional "Lifestyle Survey" designed to gather detailed military and environmental exposure, dietary habits, and other behavior data, available on ~60% of the MVP participants.

3) **Genotype data on ~650,000 MVP participants** generated by a custom designed Axiom genotyping array designed to maximize genomic coverage of common and rare SNPs as well as markers with clinical significance. There are **~800,000 SNPs** on the MVP Axiom array. More information can be found in GenHub resource.

4) **MVP Nutrition data**— Dietary energy and nutrient intake data were derived from food frequency questionnaire (FFQ) data collected on the **MVP Lifestyle Survey**. This included frequency of 61 food items in addition to questions about added sugar, fried food consumption, and 21 dietary supplements. More information can be found at https://vhacdwdwhweb100.vha.med.va.gov/phenotype/index.php/Nutrient-Level_Data_(MVP_Core_Data)

5) **MVP Whole Genome Sequence (WGS) data**—WGS data from over 100,000 MVP participants will be available in FY23. The WGS data has been generated on the short read Illumina platform with 30X depth of coverage.

6) **Methylation data** – Methylation data on ~40,000 MVP participants will also be available in FY23. The methylation data is generated on the Illumina EPIC array with ~850,000 probes.

7) **COVID-19 Survey data –**surveys from ~255,000 MVP participants on symptoms, diagnosis, hospitalization, behavioral and psychosocial factors physical and psychological impacts of the COVID pandemic--- available for COVID-related aims onl

Researchers will also have access to the Centralized Interactive Phenomics Resource (**CIPHER**), the VA Phenotype library with a catalog of phenotype descriptions and associated metadata.

Versiti BRI Flow Core

What Do We Do?

The Flow Cytometry Core Laboratory provides flow cytometric analysis and cell sorting. An experienced Flow Cytometry Specialist is in charge of the lab and will help with experimental design, data analysis and will train new users. We primarily serve internal investigators on a first-come, first-serve basis, and assist outside users as capacity permits. New users must attend a free training session prior to using the analysis instruments. Sample preparation is always critical to success, therefore we invite researchers to discuss their protocols with us in advance.

Equipment Available

- **BD LSRII Flow Cytometer:** 10 color & 12 parameter acquisition; 4 laser system; BD HTS can be used on this instrument; reads 96 well & 384 well microtiter plates.
- **BD LSRII Special Order System:** 12 color & 14 parameter acquisition; 4 laser system; BD HTS can be used on this instrument; reads 96 well & 384 well microtiter plates.
- **BD FACSAria Cell Sorter:** 10 color & 12 parameter acquisition; 4 laser system.
- **BD FACS Melody Cell Sorter:** 9 color & 10 parameter acquisition; 4 laser system; self-service after training.
- **Accuri C6:** 4 color & 6 parameter acquisition; 2 laser system

Software Available:

- FlowJo
- FCS Express
- FACSDiva
- CFlow Plus
- Miltenyi Biotec Magnetic Cell Separation Workstation also available

Contact Us:

Benedetta Bonacci
Flow Core Lab Operator
(414) 937-3843
Blood Research Institute, West Wing, #269 – 270
https://www.versiti.org/research/blood-research-institute/core-labs/flow-cytometry-core-lab

Versiti BRI Protein Chemistry Core

What Do We Do?

The Protein Core Lab at the Blood Research Institute provides services in the areas of custom FMOC solid phase peptide synthesis, peptide purification, mass spec verification, coupling peptides to carriers for antibody production and labeling peptides. Other core services are consultation on sequence selection for antigenicity, and consultation on project design and feasibility.

Modifications Available:

- C terminal labeling: Amidation
- N terminal labeling: Acetylation; Biotinylation; Fluorophores and Myristylation
- Cyclization: Disulphide; End to End; Hydrocarbon Stapling
- Backbone Modifications: D-enantiomers; N-methylamino acids; Peptoids
- Conjugation and Labeling: Carrier Proteins; Stable Isotope Labeling; Click Chemistry and PEGylation
- Special Amino Acids: Phosphoamino Acids; Dipeptides to Overcome Aggregation; Pseudoproline Derivatives and Non-Natural Amino Acids

Contact Us:

(414) 937-3847
Blood Research Institute, West Wing, Room #273
https://www.versiti.org/research/blood-research-institute/core-labs/protein-chemistry-core-lab

Versiti BRI & MCW Vector GMP Production Facility

What Do We Do?

The Versiti Blood Research Institute & Medical College of Wisconsin Vector Production Facility operates under the direction of Jeffrey Medin, PhD, MACC Fund Professor, Vice Chair of Research Innovation for the Department of Pediatrics, and Research Director of Pediatric Hematology/Oncology at the Medical College of Wisconsin (MCW).

The Vector Production Facility (VPF) provides gene transfer vectors and scientific expertise to investigators interested in conducing pre-clinical research. It is also developing the capacity to provide vectors and expertise to clinicians and scientists interested in acquiring/implementing clinical-grade vectors for early-phase gene therapy trials.

The facility's dual-controlled access space includes independent ISO Class 7 cleanroom suites designed for the bioprocessing of plasmid DNA and the packaging of lentiviral vectors, as well as a quality assurance laboratory and a cold storage ward. The cleanroom environment is temperature- and humidity-monitored; airflow is HEPA-filtered and carefully controlled. All personnel inside the cleanrooms wear full sterile personal protective equipment, and all product manufacturing is conducted under aseptic conditions. The production suites are consistently monitored for sterility and are decontaminated between production runs. All of the equipment used in the manufacture of products is validated.

Likewise, critical production parameters are monitored in real-time and critical computer systems are compliant with 21 CFR part 11.

Services Include:

- Pre-clinical, research-grade lentivector design, construction and production
- Certification testing for both in-house and client research-grade preps (including functional titering of vectors and assessment of transduction efficiency)
- Clinical-grade cGMP lentiviral production and release testing (coming soon)
- cGMP plasmid production (coming soon)
- Quality assurance testing, including sterility, mycoplasma, endotoxin and more, on investigator-supplied laboratory samples (coming soon)

Contact Us:

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https://www.versiti.org/versiti-blood-research-institute/core-facilities-services/gmp-facility-core-lab

Versiti Viral Vector Core Lab

What Do We Do?

The Viral Vector Core is shared between Versiti Blood Research Institute and the Medical College of Wisconsin. Viral vectors systems used by the core include those based on lentivirus, retrovirus, adenovirus and adeno-associated virus.

This core provides services in the areas of viral vector design, viral vector gene silencing and protein expression, including viral vector construction, viral vector amplification, viral vector purification and viral vector titration. Additional services include viral vector cloning, viral vector mutagenesis and plasmid DNA preparation.

Contact Us:

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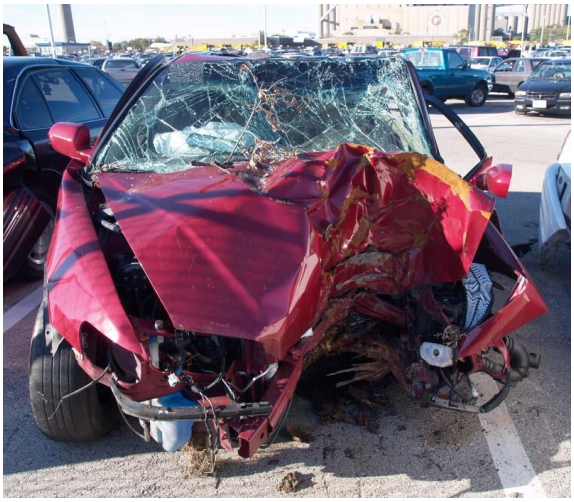
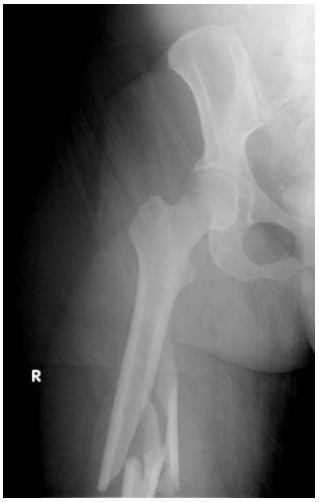
Wisconsin CIREN: Crash Injury Research Engineering Network

Narrative: The CIREN center contributes to the National Highway Traffic Safety Administration's (NHTSA) mission to prevent and reduce deaths, injuries and economic losses resulting from motor vehicle travel on our nation's roadways. The CIREN Center at MCW is one of seven national centers. It conducts crash injury research collecting and analyzing relevant data in the interest of public health. Real-world crashes are investigated to further the following objectives: Reconstruct and understand crash and injury causation, improve prognosis and treatment for crash trauma patients, reduce time of recovery and treatment costs, simulate crash scenarios in laboratory environment, disseminate data to industry, regulatory, and public agencies, develop strategies to reduce fatalities and injuries in automobile accidents, provide information to improve public infrastructure to reduce accidents, develop and disseminate safety messages to the public and train health care providers in vehicular safety and associated care.





Available Equipment: FARO 3D LIDAR scanner

Contact:
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