

Breakthroughs

Feinberg School of Medicine Research Office

October 2023

Understanding How Sex-Based Differences Impact Health Outcomes

*Neurons in the anterior cingulate cortex that project to the dorsomedial striatum.
Courtesy of the Cox laboratory.*

By **Melissa Rohman**

Sex is a major determinant in disease prevalence and treatment response, caused by a vast number of genetic differences between men and women. However, the inclusion of both sexes in clinical and scientific research had not been mandated by federal law until nearly the turn of the century.

In 1993, Congress wrote the Women and Minorities as Subjects in Clinical Research law into the [National Institutes of Health \(NIH\) Revitalization Act of 1993](#), which requires the NIH to include cisgender women and racial and ethnic minority groups as subjects in all clinical trials, and that these trials are designed to allow scientists to determine whether the variables being studied affect these groups differently than other participants.

In response, significant strides in sex-based research have been made over the last three decades, but according to [Barbara Stranger, PhD](#), associate professor of Pharmacology, the work continues

“The simplest thing we [scientists] can do to consider sex as a potential influence on any kind of trait, disease or relationship is to disaggregate our data by male and female study participants. The problem with not doing these kinds of analyses means that you miss the opportunity for a more personalized-by-sex answer to whatever question you may have,” Stranger said.

In a recent editorial [published](#) in the journal *Cell*, Stranger argues that despite the success of genome-wide association studies which explore how genetic variation contributes to the manifestation of complex traits or diseases, the use of data to investigate sex differences in the underlying mechanisms has been scarce.

In her editorial, which outlines best practices for investigators studying and testing for sex-dependent genetic effects, Stranger also asserts that designating sex as a biological variable in clinical and scientific research will accelerate the understanding of disease risk and biology in both sexes and improve precision medicine and equitable care.

“We won’t know if we don’t look... and this really has potential to discover new knowledge and help contribute to a more personalized approach to many aspects of medicine,” Stranger said.

A New Wave of Research

Feinberg investigators across specialties are studying how sex-based differences impact various aspects of health and disease, including behavior, cognitive function in response to stress, and the manifestation of pain.

In the laboratory of [Julia Cox, PhD](#), research assistant professor of [Neuroscience](#), her research aims to understand the neural mechanisms that influence decision-making and how these mechanisms may differ between each sex.

In a recent study [published](#) in *Nature Neuroscience*, Cox’s team studied the activation of a subset of neurons in mice while the mice were tasked with choosing a lever to press in the hopes of receiving a reward.

By performing two different experiments, Cox found that the mice’s motivation to engage in the task was influenced by “action value,” or how likely they were to receive a reward for an action based on their own past experiences. Furthermore, Cox’s team observed that this “action value” behavior was demonstrated more strongly in the female mice than the male mice.

Sex-Based Differences *(continued from cover page)*

Replicated experiments involving human participants had confirmed their findings — female participants were slower to reengage in the task based on what happened in previous trials compared to male participants.

“I think that more broadly, when studying sex differences in laboratory animals, even if the behavioral differences don’t always end up translating to humans, it’s possible that some of the differences in the neural circuits still are consistent across species,” Cox said.

Other Feinberg investigators have also identified sex-based differences at the intercellular level. In a study led by [Murali Prakriya, PhD](#), the Magerstadt Professor of Pharmacology, and [published](#) in *Sciences Advances*, investigators found that specific calcium channels in microglia — the primary immune cells of the brain — regulate sex differences in the functioning of immune cells in response to neuroinflammation and neuropathic pain.

More than a decade ago, Prakriya’s laboratory discovered a class of calcium channels called Orai1 channels. In the current study, his team sought to determine what role Orai1 plays a role in microglial activation and neuropathic pain following nerve injury.

By studying microglial Orai1 knockout mouse models with sciatic nerve injury, they found that the loss of Orai1 mitigated pain hypersensitivity in male mice, but not in female mice. Male mice also had reduced induction of inflammatory cytokines — signaling molecules secreted from immune cells in response to injury — in spinal cord tissue but was not observed in female mice.

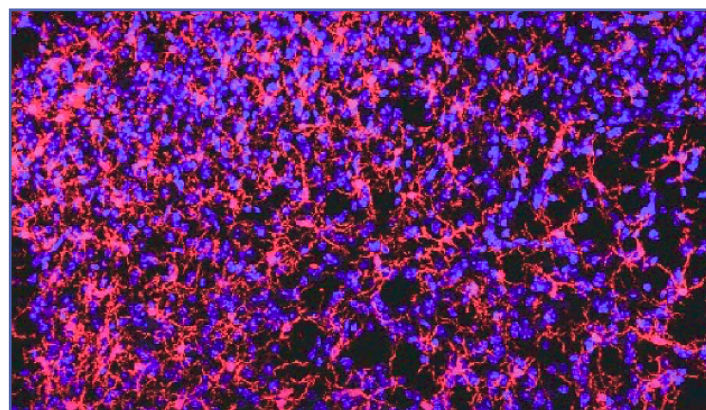


Image showing microglia in the lumbar spinal cord labeled with the microglial marker IBA1 (in red). The blue stain shows nuclei of cells labeled with a nuclear marker. Courtesy of the Prakriya laboratory.

Next, both male and female mice were given a small-molecule Orai1 inhibitor compound called CM4620 and found that the compound mitigated neuropathic pain in male mice but had no effect in the female mice.

“This study points to striking sex differences in the underlying mechanisms mediating pain hypersensitivity between males and females. We are now working on identifying whether Orai1 signaling can be manipulated in other immune cells to provide pain relief in female mice,” Prakriya said.

In addition to understanding how sex impacts the manifestation of pain and behavior, other Feinberg investigators have delved into how sex-based differences influence stress response which translates to the development of mental health disorders, particularly major depressive disorder (MDD).

Recent work led by [Talia Lerner, PhD](#), assistant professor of Neuroscience and of [Psychiatry and Behavioral Sciences](#), discovered how novel sex-specific mechanisms control how stress hormones impact dopamine transmission and motivation.

By studying changes in brains of mice given the stress hormone corticosterone (the rodent equivalent of cortisol), Lerner’s team discovered that chronic dysregulation of corticosterone impaired dopamine transmission in the dorsomedial striatum (DMS), a region of the brain that mediates decision-making and reward-seeking behaviors.

In male mice, corticosterone dysregulation reduced the function of the dopamine transporter in the DMS. In female mice, corticosterone dysregulation decreased the amount of dopamine in the DMS altogether.

The findings, [published](#) in the journal *Neuropsychopharmacology*, underscores that the design of new therapeutic strategies for MDD and other mental health disorders need to account for sex, gender and hormone status.

“We must continue to probe for sex differences at the molecular level if we are to appropriately translate preclinical discoveries into medicines that act at the molecular level,” Lerner said.

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RISE Program Empowers Medical Students Pursuing Research

By **Melissa Rohman**

Now in its second year, Feinberg's Research Intensive Scholarly Emphasis (RISE) program supports medical students engaging in an additional year of research during their medical school career.

"We started RISE to give students the opportunity to spend a year during medical school engaging full-time in research," said [Matt Feinstein, '11 MD, '17 MS](#), associate professor of [Medicine](#) in the Division of [Cardiology](#), director of Student Research and a co-director of RISE, along with [Jacob Sznajder, MD](#), the Ernest S. Bazley Professor of Asthma and Related Disorders and co-director of RISE, and Liza Rivnay, associate director of Student Research.

"This Northwestern-funded program represents a unique offering for aspiring physician-scientists given the current funding landscape, which otherwise offers limited opportunities for medical students to spend a funded year doing research during their training. The response from students and faculty alike has been extraordinary and is reflected in their incredible productivity just one year into the program," Feinstein said.

During this extra, fully funded year, RISE scholars design and implement a research project of their choice while being closely mentored by a Feinberg faculty member.

Tyler Smith, a third-year medical student and a current RISE scholar, is exploring how machine learning models can help better determine the physiology of patients diagnosed with cardiovascular disease. Smith is completing his project under the guidance of his RISE mentor, [James D. Thomas, MD](#), professor of Medicine in the Division of Cardiology.

"In medical school, everything is moving so fast, and we don't often get the chance to sit down and do the things we need to do in research to have a deeper understanding, so I've loved having that opportunity over the last couple months," Smith said.

Smith said once he completes his project, he's looking forward to applying what he's learned to future research that aims to improve patient care and outcomes, and to teaching his peers about the integration of AI and medicine.

Tazim Merchant, a fourth-year medical student and former RISE scholar, completed two research projects during her RISE year, which involved understanding disparities in postpartum pain management and understanding the scope of food insecurity among low-income, pregnant individuals.

"I think the really cool thing about having so many people interested in AI right now is that learning the methodology so deeply this year gives me the opportunity to really teach my peers and bring this work back into the wards and back into the world," Smith said.

Former RISE scholar and fourth-year medical student Tazim Merchant credits her RISE year to validating her interest in becoming a physician-scientist as well as learning first-hand how to design, implement and publish a successful research project.

With her RISE mentor [Lynn Yee, '08 MD, '08 MPH](#), the Thomas J. Watkins Memorial Professor of Obstetrics and Gynecology, Merchant decided to tackle two research projects during her RISE year, one exploring disparities in postpartum pain assessment and management and the other investigating healthcare-based interventions to address food insecurity, as well as the scope of food insecurity among low-income, pregnant individuals.

For her first project, under the guidance of [Nevett Badreldin, MD, MS](#), assistant professor of [Obstetrics and Gynecology](#) in the Division of [Maternal Fetal Medicine](#), Merchant used an implementation science approach — examining evidence-based systems level interventions to impact the community — to learn about healthcare providers' perspectives on postpartum pain management. She conducted interviews probing about potential biases in pain assessment, healthcare providers' views on ways to reduce biases, and views on interventions to optimize opioid use during the postpartum period.

"Reproductive age women are the largest growing demographic that are affected by the opioid epidemic, and given that and the inequities that are already seen and documented in the literature, we wanted to understand from many different provider's perspectives which of these interventions might make the most sense in being able to reduce opioid use and reduce disparities in care," Merchant said.

Findings from Merchant's preliminary work in her second project, examining the scope of healthcare-based interventions to address food insecurity, was recently [published](#) in the *American Journal of Obstetrics & Gynecology – Maternal-Fetal Medicine*.

For Merchant, she said that completing her research was not the only gratifying aspect of her RISE year, but also developing a one-on-one relationship with her mentor and participating in different career-building opportunities.

"I wanted a year of intensive research focus to be able to develop this toolkit where I could design, execute, and publish these implementation science studies. I think working under Dr. Yee has been such a gratifying experience because she gives you the tools and the autonomy and the leadership to be able to do exactly that," Merchant said. The first cohort of RISE scholars published a total of 43 total research publications during the 2022-2023 academic year, 15 of which are first-author publications. The program has since grown from 10 RISE scholars in its first year to 18 in its second year.

Campus Events and Opportunities

13th Annual Les Turner Symposium on ALS

November 6, 8:00 a.m. to 5:00 p.m.

The Les Turner Symposium on ALS has featured presentations from leading ALS scientists and clinicians, as well as people living with ALS; in addition research posters, a Q&A panel and more. The symposium is free to attend, but attendees are encouraged to make a donation to ALS research.

**Northwestern Memorial Hospital Feinberg Pavilion
Krumlovsky Atrium, Third Floor**

251 E. Huron St., Chicago

[More information](#)

Q Founder Series at Chicago | Labor and Employment Issues for Startups

November 13, Noon to 1:00 p.m.

The InQBation Lab's third seminar of the Q Founder Series will focus on issues related to building a startup team. The presentation will focus on key labor and employment legal issues for startups. Topics will include the hiring process and initial hiring paperwork, the legal differences between independent contractors and employees, legal requirements for interns and typical employment challenges such as terminations, common employment litigation, and the use of foreign employees and contractors.

**Robert H. Lurie Medical Research Center
Baldwin Auditorium**

303 E. Superior St., Chicago

[More information](#)

Global Health Experience Information Session

November 15, Noon to 1:00 p.m.

The Robert J. Havey, MD Institute for Global Health invites you to join a Global Health Experience Session. We will explore opportunities to engage in global health, available funding and our network of global partners. The Global Health Experience, coordinated by the Havey Institute for Global Health, refers to both elective and non-elective rotations for Feinberg School of Medicine students. All applicants are strongly encouraged to attend one of these group information sessions. Lunch will be served at the in-person sessions.

**Simpson Querrey Biomedical Research Center
Trienens Conference Room (1M-209)**

303 E. Superior St., Chicago

[More information](#)

SQE Distinguished Lecturer Series: Genomics of B Cell Lymphoma: Role of Super-Enhancer Hypermethylation

November 28, 10:00 to 11:00 a.m.

Riccardo Dalla-Favera, MD, will present "Genomics of B Cell Lymphoma: Role of Super Enhancer Hypermethylation." The Simpson Querrey Institute for Epigenetics is proud to present this lecture. Diffuse large B-cell lymphoma (DLBCL) is the most common B-cell non-Hodgkin lymphoma and remains incurable in around 40 percent of patients. Coding-genome sequencing efforts identified several genes/pathways altered in this disease, including new potential therapeutic targets. However, the non-coding genome of DLBCL remains largely unexplored. We found that active super-enhancers (SEs) are highly and specifically hypermutated in 92 percent of DLBCL samples. Join this event to learn more about their research.

**Simpson Querrey Biomedical Research Center
Simpson Querrey Auditorium**

303 E. Superior St., Chicago

[More information](#)

Research in the News

US News and World Report, September 5

[AI Equals Human Radiologists at Interpreting Breast Cancer Scans](#), Mozziyar Etemadi, MD, PhD, was featured.

Crain's Chicago Business, September 7

[Northwestern Develops Implant Monitor for Transplanted Organs](#), Lorenzo Gallon, MD and John A. Rogers, PhD, were featured.

New York Times, September 12

[Fall Allergies Are Real. And They're Getting Worse.](#) Anju Peters, MD, was featured.

NPR, September 13

[The New COVID Boosters are Coming: Here's What You Need to Know](#), Tina Tan, MD, was featured.

Chicago Tribune, September 18

[With New Spanish-Language Pulmonary-Thoracic Program, Northwestern Doctors Hope to Improve Health Outcomes for Hispanic Patients](#), Daniel Meza, MD, and Diego Mauricio Avella Patino, MD, were featured.

NBC 5 Chicago, September 28

[Northwestern Medicine Doctor Opens Latina Breast Cancer Clinic](#), Claudia Tellez, MD, was featured.

Improving Parental Mental Health and Wellbeing

Sheehan Fisher, PhD, '12 GME, associate professor of Psychiatry and Behavioral Sciences in the Division of Psychology



[Sheehan Fisher, PhD, '12 GME](#), is an associate professor of [Psychiatry and Behavioral Sciences](#) in the Division of [Psychology](#) and associate dean for Diversity and Inclusion for The Graduate School at Northwestern.

His research and clinical interests focus on parental mental health, with an

emphasis on father's mental health during the perinatal period and their impact on the family dynamic and child outcomes. Specifically, his research examines the hormonal and socio-environmental factors that contribute to postpartum depression in fathers and mothers, and his clinical work specializes in behavioral therapies for fathers and couples during the perinatal period.

Fisher is a member of the [Center for Reproductive Science](#), the [Center for Behavior and Health](#), and the Northwestern University Clinical and Translational Sciences ([NUCATS](#)) Institute.

What are your research interests?

My research career focuses on the effects of perinatal and subsequent parental mental health on infant/child health outcomes, with a sub-specialization in the emerging field of father mental health. I want to understand the risk factors for depression, anxiety and other perinatal mental health disorders for birthing and non-birthing parents to inform the design of interventions that help to prevent or treat perinatal mental illness.

What is the ultimate goal of your research?

My aim is to reconceptualize parental mental health research to integrally involve birthing and non-birthing parents to differentiate parents' impact on child medical and mental health. Ultimately, the goal of my research plan is to optimize the health and effectiveness of the parental team to positively influence the child health trajectory starting during pregnancy.

How did you become interested in this area of research?

During undergrad, I was debating about applying to child or adult clinical psychology graduate programs. I was conflicted because I wanted to prevent or provide early intervention for

mental illness in children at an early stage and I also wanted to support adults suffering from mental illness. Perinatal mental health provided an opportunity to both support the mental health of adults during a major life transition while also reducing the risk of children developing mental illness. As a man who wanted to become a parent one day, I wanted to understand the experience of mothers and fathers to support both parents' wellbeing.

What types of collaborations are you engaged in across campus (and beyond)?

Perinatal mental health is an interdisciplinary field, so I have collaborated with psychiatrists, psychologists, social workers, obstetricians, pediatricians, anthropologists and qualitative and quantitative statisticians across the Chicago and Evanston campuses of Northwestern. I also collaborate with perinatal specialists nationally and internationally, along with public health departments, activists, advocacy groups, documentarists and influencers.

How is your research funded?

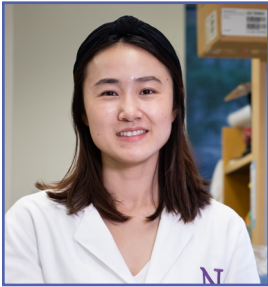
I currently have a National Institute of Mental Health funded R34 randomized controlled trial to prevent postpartum depression in women with high ACE (adverse childhood events) scores and a National Institute on Minority Health and Health Disparities funded R21 randomized controlled trial that trains fathers to support and improve the mental health of African American mothers with depression. I recently received a Friends of Prentice grant to support women with severe nausea and vomiting during pregnancy.

Who inspires you? Or who are your mentors?

[Katherine Wisner, MD](#), is my mentor at the [Asher Center](#). She is a world-renowned perinatal psychiatrist and investigator who is a pioneer in the perinatal mental health field. She takes mentorship very seriously and has been essential in my career development and that of countless other psychiatrists, psychologists, trainees and members of our research team. She also recruited a diverse team of investigators and staff that is exemplary for DEI in the workplace and for creating a highly productive and safe community. I know that excellent mentorship is valuable and rare, so I am very fortunate. I aim to mirror the generous and dedicated mentorship style that she modeled, so that others have the opportunity to reach their academic potential.

Training to Lead in Neuroimmunology and Neuroinflammation

Zhangying (Jennie) Chen, fifth-year PhD-MPH student,
Driskill Graduate Program



An early interest in biology first led Chen to the University of Illinois at Urbana-Champaign, where she completed her bachelor's degree in integrative biology.

Through her work in the laboratory of Steven Schwulst, MD, associate professor of Surgery in the Division of Trauma and Critical Care, Chen has

identified potential cellular culprits for predicting traumatic brain injury outcomes in aged mice.

Where is your hometown?

I was born and raised in Taizhou, located south of Shanghai, China.

What sparked your interest in science or medicine?

I did well in biology at high school, which led me to major in biology in college. I enjoyed taking my biology classes and developed a comprehensive understanding of different fields within biology. When faced with the real question: what am I going to do with my bachelor's degree in biology? I started exploring different career options by working as a research assistant, joining various student clubs, engaging in community and volunteering activities and meeting with different people. In the end, I realized it was the pure biologic questions that intrigued me the most. Still, it wasn't until my first year at Northwestern as a master's student that I realized I was passionate about benchwork and analyzing and interpreting my experimental results. As I am discovering, I have noticed that all my interests converged to a career in scientific discovery. I became dedicated to pursuing a PhD and a lifelong journey through biomedical research.

What are your research interests?

My ultimate research interests are mechanistic and therapeutic discoveries for neurologic disorders, with a focus on neuroinflammation and neuroimmune interactions. Many neurologic disorders, such as Alzheimer's disease, still lack any significant therapeutic options and ultimately result in significant morbidity and mortality.

What are you currently working on?

My PhD research centers around traumatic brain injury (TBI). TBI afflicts about 69 million people worldwide yearly. While TBI affects individuals of all ages, the elderly (65 years and older) experience higher mortality and more severe consequences,

including TBI-related dementia, than younger individuals with similar injury severity. Understanding of the disparate response between elderly and young patients after TBI is still in its infancy. Utilizing a well-established mouse model of TBI in the laboratory of Dr. Steven Schwulst, I have uncovered potential cellular culprits for worse TBI outcomes in aged mice – the disproportionate number of CD8 T-cells within aged brains after TBI. These T-cells come from the peripheral blood and infiltrate the brain as the blood-brain-barrier is damaged after TBI. Inhibiting the infiltration of these CD8 T-cells via an FDA-approved drug called Natalizumab (a monoclonal antibody against the adhesion molecule integrin $\alpha 4$, also known as CD49d) significantly reduces mortality in the aged mice but not young mice post-TBI. This treatment also improved long-term neurocognition and motor outcomes in aged mice post-TBI.

Please tell us about a defining moment in your education at Feinberg thus far.

I did not have a pre-defined project when I first joined my lab. Instead, my thesis advisor, Dr. Schwulst, allowed me to delve into the bioinformatic analyses of our lab's transcriptomics data. I was also encouraged to initiate my own research line and find my research passion. That includes asking an exciting, scientifically testable questions and proposing simple, yet rigorous and well controlled, experiments. Moreover, I was encouraged to ask the "why" and "what if" questions – to be innovative without boundaries. Based on this background, I proposed my thesis based on an observation from our bioinformatics analyses – the T-cell infiltration observed within the aged brains, but not the young brains, of mice after TBI. On top of that, my thesis advisor and lab mates trusted me to be thorough and rigorous in my experiments, devoting their time and resources to my growth and success as a scientist. The training I have received from my current lab constantly motivates me to pursue a career in scientific research and addresses the importance of doing meaningful science.

What do you hope to do with your degree?

With my PhD in integrative life sciences, I hope to continue expanding my knowledge base in neuroinflammation and neuroimmunology and to continue to hone my skills through a post-doctoral fellowship. My ultimate career objective is to become a leader in the field and an independent scientist with my own laboratory investigating important questions at the intersection of neuroscience and immunology.

Leading and Supporting the Facilitation of Ground-breaking Research

William Edwards, manager of Research Administration,
Institute for Public Health and Medicine (IPHAM)



Edwards came to Northwestern from Boston University, where he supported the research enterprise. Now, Edwards works with Northwestern Medicine investigators to prepare proposals, training grants and other efforts to support research within IPHAM.

Where is your hometown?

I was born in a small town in Alabama called Jasper, approximately 45 minutes away from Birmingham. A few years after I was born, my family moved to a small town in Northeast Tennessee, near the Virginia and North Carolina borders.

What led you to Northwestern?

I came to Northwestern from Boston University after relocating to the Chicagoland area a few years ago during the COVID-19 pandemic. I was excited to bring my research administration skills to the medical and clinical setting in Feinberg after previously working with investigators in environmental and sustainability research.

What are you currently working on?

Currently, I'm working with a few cross-disciplinary investigator teams to prepare several upcoming proposal submissions, beginning to work on an institutional training grant application due by end of year and working with the program director to kick off a recently funded T32 training grant. I'm also developing presentations and discussions for ongoing training for our research administration team in IPHAM. Outside of Northwestern, I've recently begun working with a multi-institutional team at the National Council of University Research Administrators (NCURA), on a specialized diversity, equity and inclusion initiative.

How does your work support the research enterprise at Feinberg?

I support investigators at all stages, including students, postdocs, residents and faculty of all ranks, in IPHAM along the entire grant and research lifecycle, from developing and preparing grant budgets and proposals to responding to sponsor requests throughout the review process, working alongside investigators and research teams to keep project spending and budgets on track and compliant and finally liaising between investigators and other Northwestern offices to ensure all grant deliverables have been met so that we can conclude and close out a grant. I, along with my fellow co-manager on the IPHAM research administration team, also work to develop partnerships with crucial research administration offices at Northwestern and to keep our team up to date in the ever-changing landscape of research administration. I've also recently taken on an executive committee role in Northwestern University Research Administration Professionals (NURAP) to help bring together research administrators across Northwestern for meaningful connections and partnerships and training and development opportunities.

Why do you enjoy working at Northwestern?

I enjoy working with the renowned and field-leading investigators here at Northwestern to propel their research forward and help free up their time to focus on their research while our team helps facilitate the day-to-day administrative aspects of their grants and projects. It's extremely rewarding to celebrate the accomplishments and triumphs alongside our investigators, and I also enjoy the opportunities to problem-solve and develop solutions to challenges that our team and investigators face so that our community can continue moving forward with successful and groundbreaking research.

New Faculty

[Joo-Seop Park, PhD](#), joined Feinberg in March as professor of Medicine in the division of Nephrology and Hypertension. His research explores how stem/progenitor cells differentiate into specific cell types using the mouse kidney as a model system. His lab aims to determine the roles of developmental signaling pathways in nephron formation, identify transcription factors that define cell identities for each cell type found in the nephron and elucidate how these transcription factors coordinate with signaling pathways in gene regulatory networks. Previously Park was faculty at Cincinnati Children's Hospital and University of Cincinnati College of Medicine. He completed his doctoral degree at Cornell University Molecular Biology and Genetics and completed a postdoctoral fellowship at Harvard University. He also holds a master's degree in biochemistry and a bachelor's degree in pharmacy from Seoul National University.



NIH News

[NIH Designates People with Disabilities as a Population with Health Disparities](#)

Eliseo J. Perez-Stable, MD, director of the National Institute on Minority Health and Health Disparities (NIMHD), designated people with disabilities as a population with health disparities for research supported by the NIH. The designation is one of several steps NIH is taking to address health disparities faced by people with disabilities and ensure their representation in NIH research. Designated populations experience significant disparities in their rates of illness, morbidity, mortality and survival, driven by social disadvantage, compared to the health status of the general population. "To the disability community, we hear you and thank you for sharing your lived experiences with NIH," said Acting NIH Director Lawrence A. Tabak, D.D.S., Ph.D. "This designation marks an important step in an agency-wide effort to advance health equity for people with disabilities which also includes updating the NIH mission statement to accurately reflect our goal of turning scientific discoveries into better health for all, including people with disabilities."

[NIH Launches Community-led Research Program to Advance Health Equity](#)

The National Institutes of Health is funding a first-of-its-kind community-led research program to study ways to address the underlying structural factors within communities that

affect health, such as access to safe spaces, healthy food, employment, opportunities, transportation and quality healthcare. Through the NIH Common Fund Community Partnerships to Advance Science for Society (ComPASS) program, NIH made 26 awards to community organizations and a coordinating center, totaling approximately \$171 million over five years, pending the availability of funds. Through these awards, ComPASS will enable research into sustainable solutions that promote health equity to create lasting change in communities across the nation.

[Further Clarifying NIH's Foreign Subaward Agreement Policy: Addressing Community Feedback](#)

In response to the feedback received from the research community, Dr. Lawrence Tabak, Acting Director of NIH and Michelle Bulls, Director, Office of Policy for Extramural Research Administration (OPERA) released the final guide notice clarifying NIH's long-standing policy on foreign subaward and consortium written agreements. Based on the feedback, the most recent notice modifies the requirements to state that "subaward agreements must stipulate that foreign subrecipients will provide access to copies of all lab notebooks, all data and all documentation that supports the research outcomes as described in the progress report, to the primary recipient with a frequency of no less than once per year, in alignment with the timing requirements for Research Performance Progress Report submission."



NUCATS Launches Pair of Seminar Series

Faculty are invited to attend two dynamic seminar series hosted by the NUCATS Institute this academic year.

[Navigating the Research Enterprise](#)

Join us for our annual series designed for early-career faculty and postdoctoral fellows who have protected research time. Each one-hour session — which includes a Q&A segment — is designed to provide attendees with needed support to promote development of the key skills young scientists require to progress beyond "just doing good research." Get more information on the NUCATS [website](#).

[The NUCATS Series on Developing and Enhancing Mentoring Relationships](#)

This is a set of monthly 90-minute workshops exclusively for faculty. Registration will be available until the day of a given workshop. View the schedule on the NUCATS [website](#).

Access the NUCATS Resource Directory

The NUCATS Institute [Resource Directory](#) is designed to maximize user experiences and provide more streamlined access to the Institute's services, resources and educational opportunities. The site can be searched by keyword or resource type to make it easier for users at Northwestern and its affiliates to find the information they are looking for.

The Resource Type dropdown menu includes many categories, including:

- Clinical Research Staff
- Research Funding
- Grant Preparation and Consultation
- Recruitment
- REDCap
- Study Tracker

[Search the directory here.](#)

Sponsored Research

PI: [Dong-Hyun Kim, PhD](#), associate professor of Radiology

Sponsor: National Cancer Institute

Title: Local Tumoral Delivered Immune Checkpoint Blockades Immunotherapy and Radioembolization Combination Therapy



Systemic mono- or combination- immune checkpoint blockade (ICB) immunotherapy has been an established therapeutic paradigm. However, a risk of serious autoimmune side effects has been evidenced with non-specific cytotoxic T-cell expansion. Substantial research has investigated how to best harness the antitumor potential of combination immunotherapies and how to direct immunotherapies at the tumor. Hepatocellular carcinoma (HCC) is the fifth most common malignancy in the world and the fourth leading cause of cancer death in the US. Resection and transplantation are the sole potentially curative treatments for HCC, but only 10-15 percent of patients are candidates.

Recent clinical trials demonstrate the potential of ICB antibodies against programmed cell death 1 (PD-1) or its ligand PD-L1 for the treatment of HCC. However, the strong immune suppressive microenvironment and low expression of immune checkpoint molecules within the HCC tumor lead to a resistance to immunotherapy in HCC; thus, the efficacy of ICB immunotherapy may not be sufficient to elicit durable clinical benefits. 90Y-radioembolization (90Y-RE) can precisely deliver high doses of radiation to HCC, protecting healthy tissues and avoiding side effects. 90Y-RE should be an ideal complement to ICB immunotherapy given that 90Y-RE induces immunogenic cell death.

Recently clinical trials have been initiated to evaluate systemic ICB immunotherapy in combination with 90Y-RE in the hope of enhancing overall therapeutic effects. However, one limitation that accounts for the compromised efficacy of combined ICB immunotherapy is off-target binding of the ICBs to normal tissues upon systemic administration. Ideally these ICBs should be delivered selectively to the tumor lesion to avoid systemic non-specific activation of the immune system.

We propose catheter-directed intra-arterial (IA) infusion of anti-PD-L1 (aPD-L1) loaded Au supra-nanostructures (AuSN) in a combination with 90Y-RE. Catheter directed local infusion of aPD-L1 with high surface area and reactive oxygen species responsive degradable AuSN will augment the localization of immunotherapy to the targeted HCC permitting radiation-enhanced activation of the immune system for superior therapeutic outcomes. Our proposed tumoral IA infused anti-PD-L1 loaded AuSN will permit efficient and targeted delivery of immunostimulatory aPD-L1 to allow an increase in the dosage and improved safety profile. The local ICB delivery of AuSN carriers will offer the potential to significantly increase the local immune- stimulating efficacy of 90Y-RE. Our CT visible AuSN and cross-sectional CT and MR image guidance should also permit us to monitor/track/quantify the delivery of aPD-L1-AuSN to the targeted tumor tissues. It should allow early prediction of elicited responses to prompt timely adjustments to individual treatment regimens. Through a collaborative project, we seek to develop a powerful new approach for tumor directed local combinational aPD-L1 immunotherapy and 90Y-RE for the treatment of HCC.

[Learn more about this project.](#)

PI: [Megan McHugh, PhD](#), associate professor of Emergency Medicine

Sponsor: Agency for Healthcare Research and Quality

Title: Healthy Hearts in Manufacturing: Improving Cardiovascular Care in Worksite Health Clinics



Heart disease is the leading cause of death in the United States and contributes to more than \$320 billion annually in health care costs and lost productivity. Manufacturing communities, many of which are rural, have significantly higher rates of smoking, obesity, physical inactivity, diabetes and cardiovascular deaths, compared to other communities. Similarly, manufacturing employment is associated with higher rates of hypertension and smoking. Two-thirds of manufacturing workers are male, and manufacturing workers are, on average, older than workers in other industries. Many large manufacturers provide health services to employees, spouses, dependents and retirees through worksite health clinics, particularly in areas where there are shortages of primary care providers. Given their potential reach into manufacturing communities, worksite health clinics are well positioned to address deficiencies in small and rural communities.

In this study, Healthy Hearts in Manufacturing (HHM), we propose to examine the use of worksite health clinics as a vehicle for improving cardiovascular care in manufacturing communities. We will adapt a package of evidence-based interventions related to hypertension and tobacco cessation, implemented with evidence-based supports, including on-site practice facilitation, health information technology support, and data feedback and benchmarking. In prior grants from AHRQ, our team has successfully implemented these cardiovascular interventions in small primary care physician practices.

The specific aims are to: (1) Contextually adapt, for worksite clinics, evidence-based interventions for cardiovascular disease care, previously designed for implementation in small primary care practices; (2) Implement HHM in 12 randomly selected worksite clinics, identify facilitators and barriers to sustainable maintenance of HHM, and test whether HHM improves hypertension control and tobacco screening and cessation intervention; and (3) Estimate the budget impact of HHM and the potential health care savings to companies and Medicare. This study is innovative in its use of worksite health clinics as a means to improve care for a hard-to-reach, disproportionately rural population with high rates of smoking and chronic illness. It will also be a first effort to report on quality measures from worksite health clinics. Results may reveal an economically sustainable quality improvement strategy to address heart health for an at-risk population. The study will produce findings, tools, materials and lessons that could aid other efforts to implement evidence-based quality improvement in worksite health clinics.

[Learn more about this project.](#)

Funding

The Feinberg School of Medicine has increased seed funding up to \$50,000 for application preparation to initiate new multi-investigator program project or center grant applications involving Feinberg faculty. [Learn more on the website here.](#)

Mental Health Award: Understanding How Anxiety- and Trauma-Related Problems Develop, Persist and Resolve

[More information](#)

Sponsor: Wellcome

Preliminary application deadline: November 14

Full application deadline: March 5

Upper amount: Up to \$4 million over 5 years

Wellcome's mental health strategic aim is to drive a transformative change in our ability to intervene as early as possible in the course of anxiety, depression and psychosis, in ways that reflect the priorities and needs of people who experience these problems. This call will fund research that advances scientific understanding of the causal mechanisms through which brain, body and environment interact over time in the development, persistence and resolution of anxiety- and trauma-related disorders.

Klingenstein-Simons Fellowship Awards in Neuroscience

[More information](#)

Sponsor: Esther A. & Joseph Klingenstein Fund

Deadline: February 15

Upper amount: \$300,000 over 3 years

The Klingenstein-Simons Neuroscience Fellowship supports innovative research by early career investigators. The research should have relevance for understanding the mechanisms underlying any of a wide range of neurological and behavioral disorders, that may lead to improvements in the diagnosis and treatment of these disorders. Several areas within neuroscience are of particular interest including cellular and molecular neuroscience, neural systems and translational research. Investigators must hold a PhD or MD and have completed all research training, including post-doctoral training.

Mechanisms of Alcohol Tolerance (R21/R33 Clinical Trial Optional)

[More information](#)

Sponsor: NIH, National Institute on Alcohol Abuse and Alcoholism (NIAAA)

Deadline: February 16

Upper amount: \$275,000 over two years

While many Americans imbibe in alcohol beverages, for some, drinking becomes problematic, potentially leading to an alcohol use disorder (AUD). The response to the initial alcohol experiences, sometimes known as sensitivity, may predict AUD later in life. Alcohol sensitivity and tolerance vary in the population, yet research on underlying mechanisms is sparse and findings are disparate. The goal of this funding opportunity is to build a framework for the systematic analysis of the factors that contribute to alcohol sensitivity and tolerance and the mechanisms that regulate tolerance and transition to AUD.

Using Innovative Digital Healthcare Solutions to Improve Quality at the Point of Care (R21/R33 Clinical Trial Optional)

[More information](#)

Sponsor: Agency for Healthcare Research and Quality (AHRQ)

Deadline: July 18

Upper amount: \$275,000 over two years

The Agency for Healthcare Research and Quality's (AHRQ) mission is to produce evidence to make healthcare safer, of higher quality, more accessible, equitable and affordable, and to work within the U.S. Department of Health and Human Services and with other partners to make sure that the evidence is understood and used. This funding opportunity invites applications that propose research projects that test promising digital healthcare interventions aimed at improving quality of care and healthcare services delivery at the point of care.

Read more about the highlights of our educational programs, innovative research and discoveries and our outstanding students, faculty and staff in the [Feinberg News Center](#).

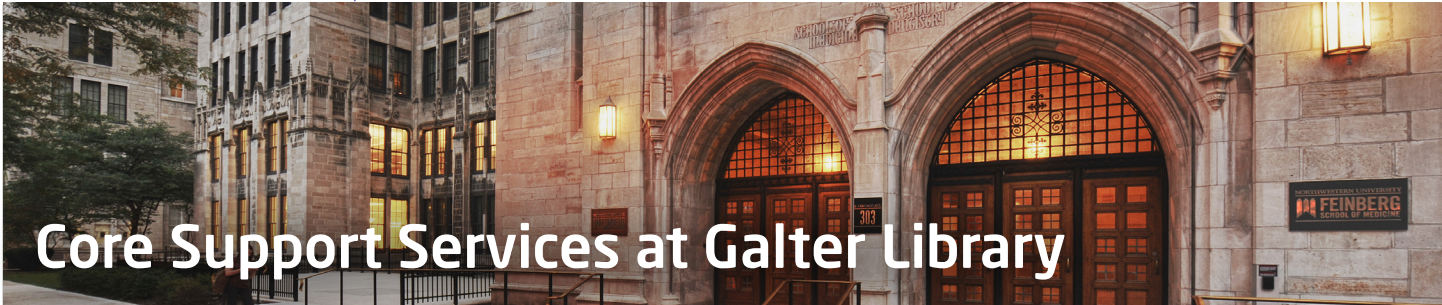
Breakthroughs Podcast

Drinking Alcohol Impacts Aging with Lifang Hou, MD, PhD

Both long-term alcohol consumption and binge drinking can speed up biological aging, according to a Northwestern Medicine study published in the journal *Aging*. [Lifang Hou, MD, PhD](#), chief of Cancer Epidemiology and Prevention in the Department of Preventive Medicine led the study and discusses the link between genetics and lifestyle in the context of preventing disease.

[Tune into hear Hou discuss her research.](#)





Core Support Services at Galter Library

In addition to our physical and online collections, Galter offers specialized support services to meet the research needs of the Feinberg community. Below is a broad overview of some of the services you could add to your research plan to ensure you are utilizing all available resources.

Liaison Librarians

Every department, program, center and institute within the Feinberg School of Medicine is assigned an individual librarian who triages specialized information requests and is available for specific instruction and consultation. Galter's Liaison Librarian program offers collaborative support that takes an integrative approach to all aspects of your research. Connect with your [Liaison Librarian](#).

Systematic and Scoping Reviews

Galter offers support for systematic and scoping reviews by providing consultation and collaboration with varying levels of engagement based on your selected [service model](#). Contact your Liaison Librarian to receive specialized support in question formulation, protocol development and data collection. Our team is also equipped to assist you with citation management systems, capturing data for the PRISMA flow diagram and contributing to the final review process for manuscript submission. Check out our classes on the [review and reporting processes](#), [EndNote](#) and our GalterGuides related to [EndNote and Citation Management](#).

DataLab

Galter's [DataLab](#) provides training and development and facilitates collaborative innovations connecting faculty, staff, and students to data-related resources. Through the DataLab you can connect with our free [DataClinic](#) that offers consultations, training support and expert assistance in resolving technical issues. Our services are centered around best practices related to data management, reproducibility, compliance with data sharing policies, and open science. Check out our classes on [data management](#) and find out how we can best support you throughout all stages of the research data lifecycle. To request a DataClinic consultation fill out this [contact form](#).

Writing and Publication Support

Galter library offers curated instructional content to help you navigate the writing and publication process. In our GalterGuide on [writing, citing and publication](#) you will find information on citation and style guides, copyright-terms and agreements and open access resources. The Galter team is also available to assist in grant preparation with a specific

concentration on the fundamentals of the National Institutes of Health (NIH) grant process and requirements. We have compiled resources to guide you through [NIH BioSketch best practices](#), [NIH Compliance and Public Access Policy and obtaining PMCIDs](#) and [Data Policies from Funding Agencies](#). You can also attend our class on the [NIH Public Access Policy](#) that covers manuscript submission to PubMed Central and managing your bibliographies with MyNCBI's My Bibliography.

Research Impact and Dissemination

Galter's [Research Assessment and Communications](#) (RAC) department is available to assist you through the communication and dissemination of your research. Our RAC team manages [Northwestern Elements](#) which serves as a web-based warehouse of information about scholarly products and helps Feinberg faculty maintain current publications lists and reduce data entry. We offer support for [Open Researcher and Contributor ID \(ORCID\) Integration](#) and best practices to help make your research discoverable. Our [Metrics and Impact Core](#) (MIC) is designed to help you communicate the impact of your work by providing expertise in alternative and bibliometrics, research communication, and preservation.

In addition, Feinberg School of Medicine has a newly available institutional repository called [Prism](#). Prism preserves the intellectual works created by the Feinberg scholarly community and holds articles, conference presentations, preprints and other items created by faculty, staff, and students. Prism helps openness, maximizes reproducibility, and enhances research connections. Email questions to prism@northwestern.edu.

Clinical Informationist Service

Galter Library's clinical informationists can join your team on rounds and bring the resources and services of the library to you. This service answers clinical questions generated as a part of patient care discussions. Our team specializes in rapid support for dissemination of research findings, clinical support services, and collaborations with key constituents on clinically focused projects. To explore options for a clinical informationist to join your team on rounds, email clinicalquestion@northwestern.edu.

Connect with your [Liaison Librarian](#) to ensure you are using all the resources available to you as you navigate your research plan. Whether you are in the planning phases of your research, working towards publication or assessing impact, we are here to support you.

High-Impact Factor Research

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Featured Core

Genomics Compute Cluster on Quest

Northwestern IT provides the [Genomics Compute Cluster](#) (GCC), to foster and empower computational genomics research across Northwestern.

The GCC is a 6,500-core allocation on Quest, consisting of 113 compute nodes, three high-memory nodes, two GPU nodes and 355 TB of dedicated scratch space. The GCC can be used to align sequencing data, run RNA-Seq, ChIP-seq, single-cell analysis, whole genome analysis, custom code, utilize GPUs for machine learning and model training and more.

The GCC is available for all computational genomics investigators at Northwestern and is supported by the Feinberg School of Medicine and the Weinberg College of Arts and Sciences.

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