By Melissa Rohman

Today, more than 50 million adults in the U.S. suffer from chronic pain — pain lasting longer than three months — and it’s the most common reason why people seek medical attention, according to the Centers for Disease Control and Prevention (CDC). For some, the cause of their chronic pain can be pinpointed to an injury site or chronic illness; for others, the causes are elusive and virtually untreatable.

The limited number of therapies for chronic pain is due to major gaps in the understanding of the underlying mechanisms of pain itself. As a result, there are no scientifically validated treatments available for chronic pain. However, recent breakthroughs made by investigators at Northwestern’s Center for Translational Pain Research are moving the field forward and suggest that the brain’s emotional circuitry plays a causal role in chronic pain.

“It is a step away from treating the body part that’s injured into treating the whole organism and the response of the organism to that injury and how the organism is in fact reorganizing their brain circuits, their emotional interpretation of that injury. All of that becomes a critical part of what is the pain stage that they’re living in, so that gives us a whole new window where we can begin to look at components of those circuits and see if we can find new targets to treat pain,” said Apkar Apkarian, PhD, director of the Center for Translational Pain Research and a professor of Neuroscience, of Anesthesiology and of Physical Medicine and Rehabilitation.

The Center for Translational Pain Research was established in 2019 to expand collaborative, cutting-edge research that enhances the understanding of these mechanisms with the ultimate goal of leading to the development of novel non-opioid treatments managing and ameliorating acute pain and chronic pain conditions.
Mechanisms of Pain (continued from cover page)

Since 1999, the number of opioid overdose deaths in the U.S. have quintupled; In 2020, opioids caused nearly 75 percent of all drug overdose deaths. In recent years, the CDC has ramped up its efforts encouraging healthcare providers to implement tapering — gradually decreasing a patient’s dosage — when caring for patients with opioid addiction. However, a recent study found this approach actually increased a patient’s risk of withdrawal and death.

With these findings top-of-mind, and this year marking the center’s five-year anniversary, Apkarian said the center’s commitment to having an impact on the opioid epidemic is stronger than ever.

“Our goals for the next five years are to try to understand the adaptations of the brain circuitry, both in humans and in animal models doing tapering, and to see if we can identify targets within those adaptations that we can then use to develop novel treatments for both chronic pain and also for dependence on opiates,” Apkarian said.

Collaboration at its Core

To accelerate bench-to-bedside research, the center partners with the Department of Anesthesiology, a symbiotic relationship that is fundamental for integrating basic science into clinical care and accelerating the development of novel therapies.

“We want to engage the clinicians within the Anesthesia Pain Center and bring them into our studies and collaborate,” Apkarian said.

For example, a recent study led by Apkarian and Paula Bronco, PhD, assistant professor of Anesthesiology in the Division of Pain Medicine, used machine learning to predict acute pain after mild traumatic brain injury (mTBI). By studying brain structural properties in brain white matter from mTBI patients, the investigators characterized specific neural networks underpinning early acute pain, their findings published in the journal Pain.

Translational pain research also permeates other departments across Feinberg and Northwestern. Investigators led by Talia Lerner, PhD, assistant professor of Neuroscience, discovered that dopamine signaling in the brain’s dorsomedial striatum promotes the development of compulsive behaviors in animal models, their findings published in Current Biology. These circuits are known to control the expression of compulsive behaviors commonly observed in obsessive-compulsive disorder (OCD) and substance misuse disorders and addiction.

“Neurobiological variability is an interesting thing to take advantage of to understand how psychiatric illnesses might result from being on the tail ends of distributions, and looking what circuits control that variability in animal models will be really important for understanding human variability,” Lerner said.

Related work led by Rajeshwar Awatramani, PhD, associate professor in the Ken and Ruth Davee Department of Neurology, discovered that dopamine neurons have distinct projection patterns, expanding the understanding of the clinically important neurotransmitter system. The findings, published in Nature Neuroscience, could also improve the understanding of the cells’ role in different neuropsychiatric disorders, as well as chronic pain and drug addiction.

“Dopamine has been implicated in a spectrum of neuropsychiatric disorders including Parkinson’s disease, ADHD, depression, chronic pain and drug addiction. Our work opens the possibility that distinct dopamine subtypes may be involved in these diverse conditions,” Awatramani said.

Most recently, investigators led by John Rogers, PhD, the Louis Simpson and Kimberly Querrey Professor of Materials Science and Engineering, Biomedical Engineering and Neurological Surgery, developed a small, soft, flexible implant device that relieves pain on demand and without the use of drugs. The first-of-its-kind device, detailed in Science, could provide an alternative to opioids and other highly addictive medications.

“We have many different laboratories bringing in a lot of very rich technology that’s state-of-the-art, all of which is directed towards uncovering new potential targets for changing the whole landscape of both chronic pain and opiate abuse and dependence,” Apkarian said.

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McDermott Honored with AHA Clinical Research Prize

By Olivia Dimmer

Mary McDermott, MD, ’92 GME, the Jeremiah Stamler Professor of Medicine in the Division of General Internal Medicine, has been awarded the American Heart Association 2023 Clinical Research Prize.

This nationally recognized award is presented at the Annual Scientific Sessions conference hosted by the American Heart Association (AHA) to recognize and reward an individual who is making outstanding contributions to the advancement of clinical science and who currently heads an outstanding clinical research program. The prize comes with a $5,000 honorarium.

McDermott, also a professor of Preventive Medicine in the Division of Epidemiology, is an accomplished physician-scientist with extensive expertise in lower extremity peripheral artery disease and has authored hundreds of publications which have furthered scientific knowledge of the symptoms and treatment of the condition.

Peripheral artery disease (PAD) in the legs or lower extremities is characterized by the narrowing or blockage of the vessels that carry blood from the heart to the legs. It is primarily caused by the buildup of fatty plaque in the arteries and affects more than 6.5 million people aged 40 and older in the United States, according to the Centers for Disease Control and Prevention.

McDermott’s initial scientific investigation of PAD demonstrated for the first time that people with PAD had more difficulty with walking distances and greater declines in walking ability over time than people without PAD, and that this phenomenon occurred even in people with PAD who reported no symptoms from their condition.

Following clinical trials on the effectiveness of supervised treadmill walking for improving mobility in patients living with PAD, McDermott’s research has helped to change clinical practice guidelines to recommend home-based exercise as a treatment. McDermott’s findings also played a role in the Centers for Medicare and Medicaid Services’ decision to cover supervised exercise for PAD patients.

“My laboratory’s work changed the understanding of PAD when we used the six-minute walk test to objectively measure the magnitude of walking difficulty in people with PAD and showed that walking difficulty even occurred in people without classic symptoms of PAD, including those who were asymptomatic. Later, my laboratory’s work contributed to changes in clinical practice guidelines by documenting that a six-month home-based exercise program significantly improved walking performance and had durable effects on walking performance in PAD,” McDermott said. Read the full story here.

Chandel Receives Prestigious Lurie Prize

Navdeep Chandel, PhD, the David W. Cugell, MD, Professor of Medicine in the Division of Pulmonary and Critical Care and of Biochemistry and Molecular Genetics, has been named a recipient of the 2023 Lurie Prize in Biomedical Sciences by the Foundation for the National Institutes of Health (FNIH).

Chandel joins Vamsi Mootha, MD, an investigator of the Howard Hughes Medical Institute, who was also named a recipient of this year’s Lurie Prize.

Each scientist has made important and distinct discoveries in the field of mitochondrial science by exploring the characteristics and functions of mitochondria in human physiology and disease.

“Each of this year’s Lurie Prize recipients are breaking new ground in mitochondrial research,” said Dr. Julie Gerberding, President and CEO of the FNIH. “Drs. Chandel and Mootha embody the innovative spirit of the Lurie Prize as they advance our understanding of the many roles these complex structures play in health and disease.”

Chandel’s research team has shown that mitochondria do much more than supply energy to cells. His research team has revealed how mitochondria function as signaling organelles that control the body’s normal functions and impact diseases, including cancer and inflammation.

“Mitochondrial signals are critical regulators and unraveling their complex functions could advance the design of new therapies,” Chandel said. “Receiving the Lurie Prize honors the entire past and present Chandel Lab. It is a celebration of my mentors, collaborators and my mentees, and a recognition of the importance of progress in the mitochondrial field.”

Currently in its 11th year, the Lurie Prize in Biomedical Sciences recognizes outstanding achievement by promising scientists ages 52 years and younger. The prize includes a $50,000 honorarium to each awardee, made possible by a donation to the FNIH by philanthropist Ann Lurie, president of the Ann and Robert H. Lurie Foundation and president of Lurie Holdings, Inc.

The 2023 Lurie Prize will be awarded to both recipients at the FNIH 11th annual awards ceremony on Oct. 18 at the REACH at the Kennedy Center for the Performing Arts in Washington, D.C. The sixth annual Trailblazer Prize for Clinician-Scientists will also be presented during the ceremony, as well as the Charles A. Sanders, M.D., Partnership Award. Read the full story here.
Campus Events and Opportunities

17th Annual Lewis Landsberg Research Day
September 14, 1:00 to 5:00 p.m.
Join us for the 17th Annual Lewis Landsberg Research Day. The keynote speaker is Craig B. Thompson, MD, of the Memorial Sloan Kettering Cancer Center. Research Day offers students and scientists at Feinberg a public forum for presenting their findings and an opportunity to receive valuable feedback from their colleagues. Each year, Research Day participants compete for awards in basic science research, clinical research, public health and social sciences research and women’s health research.

Robert H. Lurie Medical Research Center, Hughes Auditorium
303 E. Superior St., Chicago
More information

Common Metric for Substance Use to Prevent HIV: Psychometric Linking of Substance Use Severity Questions
September 18, Noon to 1:00 p.m.
In this Third Coast Center for AIDS Research seminar, Patrick Janulis, PhD, and Benjamin Schalet, PhD, will present findings from their 2020 CFAR administrative supplement award, “A common metric for substance use to prevent HIV: Psychometric linking of substance use severity questions.”

Online (Webcast Link)
More information

IRB Brown Bag | A Lesson on (New) Streamlined IRB Training Requirements and Records Management
September 20, Noon to 1:00 p.m.
Beginning September 1, 2023, Northwestern IRB training requirements will move from a dual-option course, including Biomedical and Social Behavioral learning tracks, to a streamlined single-track course for all individuals conducting human research within Northwestern University. Join Human Research Protection Program (HRPP) Education and Communication Specialist, Nazneen Ali, as she walks us through these new training requirements along with best practices in affiliating CITI training records from other institutions, troubleshooting eIRB+ records integration issues, and onboarding research team members to Northwestern studies.

Online (Webcast Link)
More information

13th Annual Medical Education Day
September 27, All day
The 13th Annual Medical Education day is an opportunity for all Feinberg educators to celebrate, reflect on and learn about the outstanding education that occurs every day. The day-long event will consist of workshops and lectures focused on medical education. A live poster session is planned in the Simpson Querrey Lobby. The day will conclude with an award ceremony and reception, celebrating the achievements of the past year.

Simpson Querrey Biomedical Research Center
303 E. Superior St., Chicago
More information

Research in the News

The Washington Post, July 1
What You Need to Know About Freezing Your Eggs
Mary Ellen Pavone, MD, was featured.

Associated Press, July 12
Pence Would Ban Abortions When Pregnancies Aren’t Viable. His GOP Rivals Won’t Say if They Agree
Alan Peaceman, MD, was featured.

Chicago Tribune, July 14
Lingering Long COVID Looms Even as Chicago Hospital Admissions Decline, Northwestern Research Shows
Igor Koralnik, MD, and Marc Sala, MD, were featured.

WebMD, July 17
What Young People Should Know About Stroke Risks
Ali Shaibani, MD, was featured.

WBEZ Chicago, July 18
FDA Approves Antibody Drug to Protect Infants Against RSV
Anat Brinkman, MD, was featured.

CBS News, July 30
Hospital Introduces New Dancing Program to Combat Parkinson’s Disease
Danny Bega, MD, was featured.
Improving the Diagnosis and Treatment Related to Maternal-Child Health Outcomes

Jeffrey Goldstein, MD, PhD, assistant professor of Pathology in the Divisions of Perinatal Pathology and Autopsy

Jeffrey Goldstein, MD, PhD, is an assistant professor of Pathology in the Divisions of Perinatal Pathology and Autopsy. For his research and clinical practice, he employs machine learning and bioinformatics to improve the health of pregnant women and their children, primarily through improved diagnosis and fundamental understanding of the placenta. He is also a member of the Center for Reproductive Science, the Institute for Artificial Intelligence in Medicine’s Center for Computational Imaging and Signal Analytics in Medicine and the Northwestern University Clinical and Translational Sciences (NUCATS) Institute.

What are your research interests?
Don’t worry if you’ve never heard of placental pathologists — we’re extremely rare. That causes a lot of problems. Most placentas aren’t looked at by experts, and everyone is stretched thin. One area of my research interests is using machine learning to make it easier to make diagnoses faster and agree on them. The other problem in placental pathology is what you might call the Clue problem. We only look at placentas after the child is delivered and it’s hard to intervene. So, what’s the point? Many people will get pregnant again, so there’s often something we see in this placenta that can help next time. The other thing we think about is this idea of developmental origins of health and disease, which are things that happen when you’re in the womb and will go with you your whole life. There are some very impressive findings, but it’s also hard because you literally have to watch people for years and years to see what happens with them. I’ve also done work on COVID, and I’m interested in other infectious diseases during pregnancy, as well.

What is the goal of your research?
The ultimate goal of my research is to improve pregnancy, birth, and lifelong outcomes for pregnant people and their children. I approach that in a few different ways, one of which is to look at my clinical domain, placental pathology. The placenta is the in-utero life support system for the fetus. Most of the time it works very well, but there can be problems, and investigating it is what a placental pathologist does.

How did you become interested in this area of research?
I like development, genetics and the interaction between maternal and fetal. For machine learning, I’ve always enjoyed computers and I love the way we can put together data in surprising ways.

What types of collaborations are you engaged in across campus (and beyond)?
I work very closely with Lee Cooper in the Department of Pathology. Lee is an engineer and expert in machine learning and extraordinarily helpful in turning ideas into reality. Elisheva Shanes and Leena Mithal have helped with studying COVID and a lot of other things. I’m also working with a group at Penn State on placental machine learning, and another at Mayo Clinic.

How is your research funded?
I have a K08 award from the National Institute of Biomedical Imaging and Bioengineering and, of course, I’m on the hunt for more.

Who inspires you? Or who are your mentors?
David Aronoff at Indiana University has been a long-term mentor and is the kindest person I know. He’s completely devoted to raising people up. It’s easy to be very competitive, and he shows how to be successful in a different and positive way.

New Faculty

Joshua J. Ziarek, PhD, joined Feinberg on July 1 as associate professor of Pharmacology. His research interests are in the characterization of biomolecular interactions, the molecular mechanisms of allosteroy and the rational design of molecular therapeutics and tools with a long-standing interest in G protein-coupled receptors (GPCRs). Previously, Ziarek was assistant professor of Cellular and Molecular Biology at Indiana University. He did his postdoctoral training at Harvard Medical School and earned his PhD from the Medical College of Wisconsin.
Emily Stroup is a fifth-year PhD candidate in the Driskill Graduate Program. She graduated from the University of Notre Dame, where she studied physics in medicine.

In the lab of Zhe Ji, PhD, assistant professor of Pharmacology and McCormick School of Engineering, Stroup combines her data and computational skills with medicine to develop deep learning models to better understand polyadenylation.

Where is your hometown
I was born in Overland Park, Kansas, near Kansas City, but I consider Fort Wayne, Indiana, my hometown. My family moved there when I was ten years old, and it’s where most of the memories and experiences that shaped who I am happened.

What sparked your interest in science or medicine?
As far back as I can remember, I have been extremely curious about the world around me and constantly asked questions about new things I encountered. I wanted to learn as much as possible and was naturally drawn to math and science. My high school physics teacher and math teacher were incredible and sparked my interest in how we could mathematically explain the world and connect what I thought were disparate fields of study. This motivated me to pursue physics in medicine in college, where I worked with a research mentor who used traditional physics research techniques to study cancer cell growth. This experience opened my eyes to the opportunities for interdisciplinary research in science and medicine.

What are your research interests?
My interests are interdisciplinary, bridging biology and human health with math and computational analysis. In particular, I am very passionate about repurposing existing yet underutilized datasets. There is so much data generated or collected but not fully explored, especially with the increased accessibility of sequencing over the past decade. I’ve worked on several projects that utilize published data or large consortium databases to answer new biological questions, and I believe this avenue of research helps maximize the efforts and benefits of biomedical research.

What are you currently working on?
My recent work has been focused on developing deep learning models of polyadenylation regulation in humans and other species. As mRNA are transcribed, there are many potential sites along the gene where the transcript can be cleaved and a polyA tail synthesized as part of the mRNA maturation process. However, the factors that govern site selection are not well understood. I have leveraged previously published sequencing data from dozens of samples to model where polyadenylation sites are found in the genome and to explain the factors that promote site utilization. We hope this work will further our understanding of how polyadenylation activity has been optimized on an evolutionary timescale and provide a resource to characterize disease-associated variants that alter polyadenylation dynamics.

Please tell us about a defining moment in your education at Feinberg thus far.
During my second and third years, I participated in the Biomedical Data Driven Discovery training grant, which helped set the course of both my project and my development as a scientist. Through this program, I took math, statistics and data analytics classes on the Evanston campus, which provided a solid technical foundation for my research. I also regularly interacted with students and faculty across different domains, who brought new perspectives from their respective fields that broadened the way I think about approaching research challenges.

What do you hope to do with your degree?
I want to continue developing new computational techniques to gain insights from biomedical and healthcare data to advance our knowledge of human disease and how we deliver care. My work in the lab has predominantly been focused on dissecting a fundamental process in RNA biology and how it is dysregulated during disease formation. I hope to use the skills I’ve accumulated at Feinberg to translate information uncovered from the vast amount of data available to improve human health and how we provide care to our community.
Developing Center Resources to Support Research

Read the Q & A below.

Carolyn Schafer, MPH, is the center administrator for the Center for Health Services and Outcomes Research (CHSOR) at Feinberg’s Institute of Public Health and Medicine.

Schafer grew up in Cleveland, Ohio and worked in research management in Malawi and Sierra Leone before moving to Chicago. She received her bachelor’s degree in biology from Saint Mary’s College and her master’s of public health from Saint Louis University.

Carolyn Schafer joined the Center for Health Services and Outcomes Research in December 2021 and was recently promoted to her current role empowering investigators and staff to conduct their research.

Where is your hometown?
I am from Cleveland, Ohio. I am a proud alumna of Saint Mary’s College in Notre Dame, Indiana, where I obtained my BS, and St. Louis University where I obtained my MPH.

What led you to Northwestern?
I initially came to Northwestern to work as a Research Project Manager with Dr. Tara Lagu on two NHLBI R01s focused on increasing use of cardiac rehabilitation for patients with heart failure. Dr. Lagu is extremely engaging and full of life; it was an easy draw to come here! Her research is focused on improving health systems and using implementation science techniques, which aligned with my experience with implementation science in developing and under-resourced settings, making it the perfect career move for me. Having spent the beginning of my career in international public health research in Malawi and Sierra Leone, I wanted to gain more experience in the U.S. healthcare system, so joining Dr. Lagu brought a lot of my interests together. Additionally, Northwestern has a breadth of resources and opportunities that I want to explore, and I’m hoping to further my education here.

What are you currently working on?
I was recently promoted to the Center Administrator of the Center for Health Services and Outcomes Research (CHSOR) within the Institute of Public Health and Medicine (IPHAM). My work has shifted from direct project management to center operations, where I am applying my prior research experience and moving my career in a direction I am excited about. First and foremost, I am lucky enough to continue my work with Dr. Lagu, as she is the Center Director. We work together on faculty and staff support via engagement, finances, hiring, etc. Right now, I am focused on filling a couple of open staff positions and creating a research resource repository for CHSOR members. I began my role as a Research Project Manager during the tail end of COVID when office use was inconsistent, making it difficult to know which staff members whom I could turn to for guidance. The goal of the research resource repository is to serve as a starting point for new CHSOR staff and bring together the myriad resources you can find at NU for research operations. I am also trying to reinvigorate our workspace post-COVID with in-person faculty and staff meetings. It has been such a pleasure to work in person with so many colleagues on our floor, which we are lucky enough to share with the Center for Education in Health Services and the newest IPHAM center — the Center for Dissemination and Implementation Science. I am extremely grateful to those Centers and my colleagues who have helped me seamlessly transition into this new role.

How does your work support the research enterprise at Feinberg?
As a center administrator, I work with investigators, research administrators, Institute administrators, human resources, Feinberg department administrators, and CHSOR staff to ensure everyone has what they need to conduct research. This includes allocating working space on our floor, focusing on financial operations, performance excellence, and staff professional development — from payment requisitions to making sure our working space is welcoming. Simply put, I am the hub of administration for CHSOR. This position allows me to work with colleagues to problem solve and celebrate achievements. An overarching theme of my career has been quality improvement. Some examples include improving healthcare delivery via research, standardizing research operations for Dr. Lagu, and implementing standard operating procedures. My focus on quality improvement is something I plan to continue in my new role as Center Administrator. I aim to be a competent and compassionate resource for any of my colleagues at Northwestern.

Why do you enjoy working at Northwestern?
I enjoy working at Northwestern because I can show up as my full authentic self when I come to work. Northwestern has brought me a community of unique colleagues and peers that I am constantly learning from. Everyone I’ve had the opportunity of working with is dedicated to their work and making healthcare more accessible, equitable, and efficient. In my new role as center administrator, I thoroughly enjoy problem solving and learning more about business operations and NU systems. I feel supported in my career development at Northwestern, where I have been able to sharpen my strengths and hone new ones.
NIH News

Strengthening Integrity and Fairness in Peer Review Through New Required Trainings

Beginning for the May 2024 council round, all reviewers will be required to complete trainings related to review integrity and bias awareness prior to serving on NIH peer review groups. These trainings build on NIH’s long-standing commitment to maintain integrity and fairness throughout the review process. In this new process, there are two training modules needed to be completed. The “Review Integrity” module is designed to increase reviewer knowledge and awareness of review integrity throughout the NIH peer review process and provide reviewers with tools to prevent and report integrity breaches. The “Bias Awareness and Mitigation” module is designed to raise reviewer awareness of potential sources of bias in review of grant applications and help reviewers take action to mitigate bias.

Using AI in Peer Review Is a Breach of Confidentiality

AI has been brought to the forefront of the scientific community. However, using AI reviewers are trusted and required to maintain confidentiality throughout the application review process. Thus, using AI to assist in peer review would involve a breach of confidentiality. Reviewers have long been required to certify and sign an agreement that says they will not share applications, proposals or meeting materials with anyone who has not been officially designated to participate in the peer review process. This includes AI platforms. Ensuring confidentiality means that scientists will feel comfortable sharing their candid, well-designed and thorough research ideas with the NIH. Using AI absolutely violates the NIH peer review confidentiality expectations and is thus, not permitted.

Meet Sheila Garrity, the New Director of the HSS Office of Research Integrity

Sheila Garrity, JD, MPH, MBA, began as director of the HSS Office of Research Integrity (ORI) in March. She has over thirty years of experience supporting research integrity efforts within academia and professional societies. She previously led research integrity and responsible conduct of research efforts at John Hopkins University, George Washington University and the Association for Research Integrity Officers. HHSI ORI has the authority and the responsibility to review and monitor investigations of research misconduct allegations involving U.S. Public Health Service funding. When NIH receives an allegation of research misconduct, it is reviewed and referred to ORI as appropriate.

NUCATS Regulatory Team Provides Comprehensive Study Team Support

The Regulatory Unit of the Center for Clinical Research (CCR) can assist investigators with meeting essential regulatory activities and provides training, and general support to Feinberg research staff. Services include:

- New IRB submission of protocols and amendments
- Preparation and negotiation of informed consent documents
- Assistance with the completion of required documentation and for monitor visits
- Oversight of regulatory binders (physical, E-Regulatory Files, and Complion system binders)

Please visit our new resource page, which includes newly added Regulatory Support Guidelines, for additional information.

The Regulatory team is also available for weekly 15 minute drop-in sessions for general questions, or through email.

NuCATS Corner

CCR works closely with local Institutional Review Boards (IRB) at Northwestern University and Ann & Robert H. Lurie Children’s Hospital of Chicago as well as external IRB offices to reduce investigator burden, share best practices, maximize quality and efficiency of all programs and quickly resolve issues when they arise.

If there is another CCR service you would like to use, please complete the CCR intake form. If you are not sure where to start, request a virtual Studio Consultation for an opportunity to learn how CCR services can help with your research project or browse the links below. To learn more about how we can help you, email ccr@northwestern.edu.
Ca2+ signaling mediates many essential roles in the brain including neurotransmitter release, synaptic plasticity and gene transcription. Neurons and glia have an extensive Ca2+ signaling toolkit that includes many types of ion channels and Ca2+ release pathways which can be mixed and matched to create signals with widely different spatial and temporal properties. One of the newest — and least understood — members of this toolkit in the brain is store-operated calcium entry (SOCE). SOCE is mediated by the opening of Orai channels (Orai1-3), which are activated by the endoplasmic reticulum Ca2+ sensors, STIM1 and STIM2. In immune cells where SOCE was first discovered, the pathway mediates critical functions including gene expression and cytokine release, and aberrant Orai/STIM function is implicated in the etiology of several diseases including immunodeficiency, inflammation, and myopathy. However, in the brain where multiple isoforms of Orai and STIM are expressed, the molecular mechanisms and physiological functions of SOCE remain very poorly understood.

Previous work on the molecular choreography of SOCE has revealed that Orai channel opening is triggered by a unique inside-out mechanism where store depletion activates the ER Ca2+ sensors STIM1 and STIM2 which then translocate to ER-plasma membrane contact sites to directly gate Orai1 channels. Our previous mechanistic work has established a strong framework for understanding the gating mechanisms of Orai channels, and using conditional Orai1 and STIM1 knockout mice, we have now begun to discover vital roles for Orai channels in effector functions in the brain such as NFAT-mediated gene expression, synaptic plasticity, and memory. We have learnt that SOCE in neurons exhibits unique specializations, including rapid activation and unusual Ca2+ dependencies whose basis cannot be readily explained easily from existing activation models. In this application, we aim to build an integrated view of the SOCE mechanism in the nervous system, its micro and macro architecture, regulation, and gating, and elucidate how neurotransmitter and receptor signaling through SOCE impacts fundamental processes of synaptic communication, metabolism, learning, and cognition.

To address this goal, we will use a full range of approaches from electrophysiology, structural analysis and molecular dynamics simulations to behavioral analysis of cognition, depression and disease to gain an unprecedented view of the SOCE mechanism in the brain. These studies will address the role of a poorly understood Ca2+ entry pathway in the nervous system with immense relevance for a range of functions from cognition to pain, and ultimately facilitate efforts to target Orai channels for drug discovery for neurological diseases.

Learn more about this project.

Sponsored Research

PI: Murali Prakriya, PhD Magerstadt Professor of Pharmacology, Professor of Pharmacology and Medicine (Allergy and Immunology)

Sponsor: National Institute of Neurological Disorders and Stroke

Title: The Physiology of Store-Operated Channels in the Nervous System

Lymphangioleiomyomatosis (LAM) is a rare disorder with devastating consequences for the young women diagnosed with this disease. We observed occult expression of the glycoprotein gp100 and other melanoma associated antigens in nodular, pulmonary tumor lesions. LAM cells carry a dysfunctional TSC complex and exhibit constitutive mTOR activation. Though rapamycin can provide relief, there is a great need to develop a true cure for women with LAM. We evaluated the expression of suitable antigens and the associated infiltration by immune cells. Here we propose to capitalize on the occult expression of melanoma associated antigens to develop safe and effective, T-cell-based immunotherapy for LAM.

First, we will generate constructs targeting LAM antigens to transduce T-cells and prepare the cells for adoptive transfer. These constructs are equipped or not with a homing receptor to drive the adoptively transferred T-cells to LAM lung, exploiting the consistent overexpression of the chemokine ligand CCL2 within affected tissues, in order to minimize off tumor effects. Transgenic T-cells are generated with stem cell-like attributes to promote longevity and continued functionality. Efficacy and safety comparisons are made between TCR engineered T-cells and PDX implanted mice to explore the treatment potential of adoptively transferred, LAM reactive T-cells. Within PDX mice, the LAM microenvironment is well conserved. Expression of LAM tumor antigens can be maintained over time, while therapeutics can be tested in a statistically and biologically meaningful way. Finally, we will explore the immune microenvironment in LAM and in PDX tissues exposed to adoptive transfer or not, to learn whether T-cells harbored by LAM lung or supplied by adoptive transfer can be taught to clear existing lesions. Next, our collaborative group aims to develop a winning immunotherapeutic approach to treat the devastating disease.

The project will thus cover (1) generating and in vitro testing of transgenic mouse and human T-cells; and (2) measuring the anti-tumor efficacy of adoptively transferred T-cells in immune competent as well as PDX models of LAM as well as (1) in-depth analysis of the immune environment encountered in LAM lesions before and after adoptive transfer. Resulting preclinical data can then serve to design a clinical trial in follow-up studies and test the hypothesis, that benign tumors in LAM are amenable to treatment by adoptive transfer of tissue homing, LAM reactive T-cells.

(Michael Nishimura, PhD, from Loyola University is a co-PI for this award.)

Learn more about this project.

PI: Caroline Le Poole, PhD professor of Dermatology and Microbiology-Immunology

Sponsor: National Heart Lung and Blood Institute

Title: Time to ATTAC: Adoptive Transfer of T-cells Against gp100+ Cells to treat LAM

Lymphangioleiomyomatosis (LAM) is a rare disorder with devastating consequences for the young women diagnosed with this disease. We observed occult expression of the glycoprotein gp100 and other melanoma associated antigens in nodular, pulmonary tumor lesions. LAM cells carry a dysfunctional TSC complex and exhibit constitutive mTOR activation. Though rapamycin can provide relief, there is a great need to develop a true cure for women with LAM. We evaluated the expression of suitable antigens and the associated infiltration by immune cells. Here we propose to capitalize on the occult expression of melanoma associated antigens to develop safe and effective, T-cell-based immunotherapy for LAM.

First, we will generate constructs targeting LAM antigens to transduce T-cells and prepare the cells for adoptive transfer. These constructs are equipped or not with a homing receptor to drive the adoptively transferred T-cells to LAM lung, exploiting the consistent overexpression of the chemokine ligand CCL2 within affected tissues, in order to minimize off tumor effects. Transgenic T-cells are generated with stem cell-like attributes to promote longevity and continued functionality. Efficacy and safety comparisons are made between TCR engineered T-cells and PDX implanted mice to explore the treatment potential of adoptively transferred, LAM reactive T-cells. Within PDX mice, the LAM microenvironment is well conserved. Expression of LAM tumor antigens can be maintained over time, while therapeutics can be tested in a statistically and biologically meaningful way. Finally, we will explore the immune microenvironment in LAM and in PDX tissues exposed to adoptive transfer or not, to learn whether T-cells harbored by LAM lung or supplied by adoptive transfer can be taught to clear existing lesions. Next, our collaborative group aims to develop a winning immunotherapeutic approach to treat the devastating disease.

The project will thus cover (1) generating and in vitro testing of transgenic mouse and human T-cells; and (2) measuring the anti-tumor efficacy of adoptively transferred T-cells in immune competent as well as PDX models of LAM as well as (1) in-depth analysis of the immune environment encountered in LAM lesions before and after adoptive transfer. Resulting preclinical data can then serve to design a clinical trial in follow-up studies and test the hypothesis, that benign tumors in LAM are amenable to treatment by adoptive transfer of tissue homing, LAM reactive T-cells.

(Michael Nishimura, PhD, from Loyola University is a co-PI for this award.)

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.

SQI Launches Seed Funding Program to Spark Nanomedicine Research
More information

Sponsor: Simpson Querrey Institute for BioNanotechnology (SQI)
Deadline: September 1
Upper amount: $50,000

This is a new seed funding program to support early stage, innovative projects in regenerative nanomedicine and connected fields, such as aging, immunology, inflammation, cancer, synthetic biology, and bioelectronics, among others. The SQI Synthesizer Research Grant Program will fund projects up to $50,000 annually for 1-2 years and is open to all Northwestern faculty members.

Analyzing Early Events in TB and TB/HIV Infection for Interventional Targets (R01 Clinical Trial Not Allowed)
More information

Sponsor: National Institutes of Health, National Institute of Allergy and Infectious Diseases
Letter of Intent: September 11
Deadline: October 11
Upper amount: Up to $500,000 over five years

The purpose of this funding opportunity is to support mechanistic studies of the early stage of Mycobacterium tuberculosis (Mtbt) infection, with and without HIV, to identify interventional targets for vaccine and host-directed therapies. The primary focus should be on mechanisms of Mtbt-induced immune evasion/disruption of immunity-related cell functions and interactions among myeloid, lymphoid and non-immune cells within the airway and lung tissue that determine disease progression vs. cessation. Delineating how HIV infection impacts host immunity early in Mtbt infection is also of particular importance.

National Glaucoma Research Program
More information

Sponsor: BrightFocus Foundation
Deadline: October 31 at 5:00 p.m. EST
Upper amount: $200,000 over two years

BrightFocus provides research funds for U.S. and international researchers pursuing pioneering research leading to greater understanding, prevention and treatment of glaucoma. The standard award provides significant funding for researchers who have already generate some amount of preliminary data, but are often required to demonstrate additional, significant progress before they can apply to governmental or industrial funding agencies.

Mechanistic Studies to Investigate the Interrelationship Between Sleep and/or Circadian Rhythms and Substance Use Disorders (R01 Clinical Trials Not Allowed)
More information

Sponsor: National Institutes of Health, National Institute on Drug Abuse
Letter of Intent: October 13
Deadline: November 14
Upper amount: Up to $300,000 over five years

The purpose of this funding opportunity is to support research project applications to expand knowledge on the basic neurobiology of the interrelationship between sleep/circadian rhythms and substance use disorders (SUDs). Sleep dysregulation including insufficient sleep duration, altered sleep architecture, poor sleep quality and irregular circadian rhythm is prevalent in more than 75 percent of individuals with SUDs and represents a challenge to recovery. The NIDA seeks to stimulate research targeted at understanding the mechanisms that underlie the intersection of sleep and/or circadian rhythms and SUDs. These studies will investigate how sleep, alterations in sleep homeostasis, alterations in circadian rhythms and/or sleeping disorders influence substance use, substance dependence, withdrawal, relapse and/or recovery from SUDs.

Exploratory Clinical Trial Grants in Arthritis and Musculoskeletal and Skin Diseases (R21 Clinical Trial Required)
More information

Sponsor: National Institutes of Health, National Institute of Arthritis and Musculoskeletal and Skin Diseases
Deadline: November 3
Upper amount: $400,000 over three years

This funding opportunity is designed to facilitate clinical trials to support research leading to the prevention of reduction of symptoms and improve outcomes and function in patients with rheumatic, musculoskeletal, or skin conditions or diseases. The proposed study should be supported by a strong scientific rationale.
The Power of Open Science

By Kristi Holmes, PhD, Director, Galter Health Sciences Library

The federal government defines open science as “the principle and practice of making research products and processes available to all, while respecting diverse cultures, maintaining security and privacy, and fostering collaborations, reproducibility, and equity.” UNESCO has been an incredible champion for openness, reinforcing open science pillars of knowledge (e.g., publications, software, data, educational resources), infrastructures, engagement and exchange with other knowledge systems. The White House Office of Science and Technology Policy (OSTP) issued guidance in August 2022 on Ensuring Free, Immediate and Equitable Access to Federally Funded Research, asking agencies to accelerate access to data and publications. The OSTP declared 2023 as the Year of Open Science to advance national open science policies across the federal government. This strategic priority area has been reinforced by actions across the federal government to advance national open science policy, provide access to publicly-supported research, accelerate discovery and innovation and achieve equitable outcomes.

The NIH has long been a leader in openness through the NIH Public Access Policy, established in 2009, and most recently through the NIH Policy for Data Management and Sharing (DMS Policy), which became effective earlier this year to promote the management and sharing of scientific data generated from NIH-funded research. The DMS Policy establishes requirements of Data Management and Sharing Plans, emphasizes the importance of good data management practices, and communicates the expectation for prioritizing the appropriate sharing of data. NIH has developed several resources to support consistent processes and compliance, while minimizing researcher burden including elements of an NIH data management and sharing plan, allowable costs for data management and sharing and desirable characteristics of repositories for managing and sharing data resulting from federally funded research.

The NIH Scientific Data Sharing website is also a great resource. We’ve worked to support this area of need at Galter with resources, training, and services to support the Feinberg community. Highlights include the Prism Repository, classes on data management, and Galter Guides on the NIH Public Access Policy and NIH Data Management Plans.

Several benefits of open science have been identified, including:

- **Accelerated Knowledge Dissemination** when investigators share their findings, data, and methodologies openly with the global scientific community. This rapid dissemination of knowledge accelerates innovation and discovery.

- **Enhanced Collaboration and Innovation** fostered across disciplines, institutions, geographies, and roles. By sharing resources and expertise, scientists can address complex challenges more effectively and develop innovative solutions that might not have been possible within isolated research silos.

- **Increased Reproducibility and Transparency** in research methods, data collection and analysis enhance reproducibility and reliability of research, critical for building trust and credibility.

- **Greater Public Engagement and Accessibility** as research products are accessible to a wider audience, including policymakers, educators, journalists and the public, supporting public engagement, accountability, informed decision-making and benefit from scientific advancements.

- **A scaffold for problem-solving** to leverage diverse perspectives and knowledge, inspiring bold strategies to address some of most complicated global challenges including climate change, healthcare disparities and innovation.

Open science holds the potential to drive advancements that benefit individuals and communities alike. As open science continues to bridge the gap between investigators, clinicians and the public, its role in shaping a healthier and more informed society becomes increasingly significant. We are excited about supporting open science at Galter. Please contact us any time for support, training or resource needs, or with questions.

Learn more about open science

- Open Science at UNESCO, including the UNESCO Recommendation on Open Science
- Federal open science programs and initiatives
- NASA’s Open-Source Science Initiative
- FAIR Principles
- GalterGuides on Open Access Health Resources, Open Access Publishing, and Prism


High Impact (continued from previous page)


Featuring Core

Center for Advanced Microscopy and Nikon Imaging Center

The Center for Advanced Microscopy (CAM) offers a variety of light and electron microscopy service, and provides Northwestern investigators access to cutting-edge imaging technologies and research expertise.

The Nikon Imaging Center (NIC) is an integral component of CAM, serving as a learning center for Northwestern staff, scientists and students by introducing cutting-edge imaging technology to Northwestern investigators. The center’s mission is to augment basic research by providing access to state-of-the-art imaging equipment, provide training courses and organize symposia on light microscopy techniques, and serve as an instrument evaluation and testing site for new equipment from Nikon.

CAM is supported by Nikon, the Feinberg School of Medicine, the Department of Cell and Developmental Biology and the Robert H. Lurie Comprehensive Cancer Center of Northwestern University.

Contact: Constandina Arvanitis, PhD, director 312-503-7139 c-arvanitis@northwestern.edu
Location: 310 E. Superior Street, 2nd floor