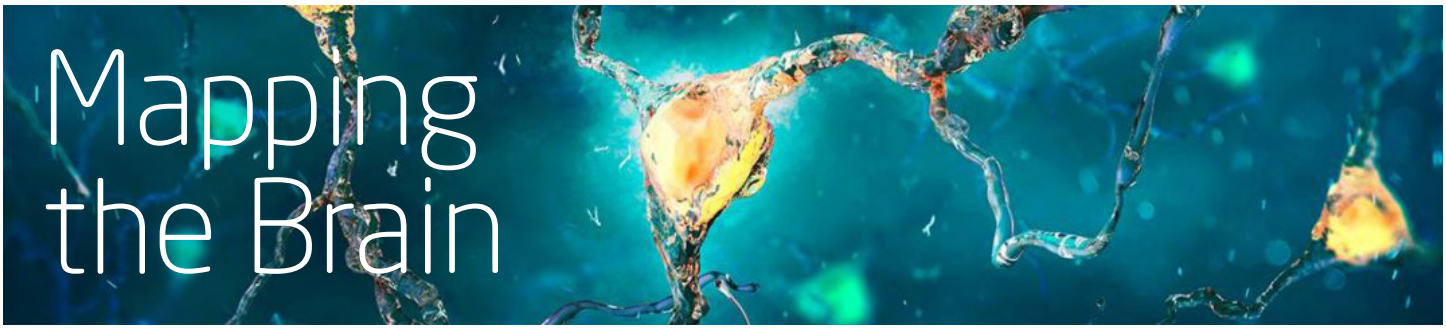
Breakthroughs

Feinberg School of Medicine Research Office

December 2022



Mapping the Brain

By Melissa Rohman

At Feinberg, investigators across the medical school are studying the brain at the molecular, cellular, systems and behavioral levels and using advanced research methodologies and leading-edge technologies to translate scientific discoveries into novel and effective treatments.

Thanks to the constant development of new technologies and research strategies, studying the innerworkings of the brain and how they go awry in different neurological diseases have become less and less of challenge and more so an incredible opportunity for discovery and innovation.

"Our research programs span basic and translational topics in neuroscience and take advantage of cutting-edge tools at the molecular, cellular, systems and behavioral levels," said D. James Surmeier, PhD, the chair and Nathan Smith Davis Professor of Neuroscience.

According to recent data published in *JAMA Neurology*, in the U.S. alone, the number of patients diagnosed with neurological diseases has steadily increased over the last three decades. As this number continues to rise, producing more robust research that informs the development of novel therapeutic strategies must remain a top priority, according to Dimitri Krainc, MD, PhD, chair and the Aaron Montgomery Ward Professor of the Ken and Ruth Davee Department of Neurology.

"While the number of patients diagnosed with serious neurological conditions such as Alzheimer's and Parkinson's is on the rise, treating these disorders has long proven difficult," Krainc said. "Recent technological advancements have improved our understanding and diagnosis of these conditions, while emerging insights into their genetic basis bring exciting possibilities for the creation of more precise targeted therapies."

Using Technology to Analyze Behavior

Ann Kennedy, PhD

In the laboratory of Ann Kennedy, PhD, assistant professor of Neuroscience, investigators are looking at how survival and defensive behaviors such as aggression are regulated in the brain.

Aggression between members of a particular species can be gradual in an attempt to prevent unnecessary fighting or injury, a process Kennedy discussed in an essay recently published in *Science*. In an effort to better understand the mechanisms underlying this process, Kennedy's team used head-mounted miniaturized microendoscopes in freely interacting mice to determine neuronal activity in the ventrolateral portion of the ventromedial hypothalamus region of the brain.

To their surprise, Kennedy's team discovered a subset of neurons that expressed a gradual increase in activity after any fighting between the mice ended. But when the neuronal activity was weak, however, the mice ignored one another, suggesting that constant activity within the ventrolateral portion of the ventromedial hypothalamus directly controls an animal's motivational state.

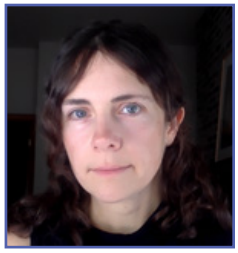
"If you look at activity of these hypothalamic neurons, you can pull out this signal that gradually ramps up over the course of an aggressive counter and is correlated with animals' overall level of aggression. It's not a decision to attack, but it's like this scalable knob of how 'angry' the mouse is that gets cranked up over the course of an interaction," Kennedy said.

Kennedy is also the recent recipient of the 2022 Eppendorf and *Science* Prize for Neurobiology, which is awarded annually to one scientist younger than 35 years old for their outstanding neurobiological research based on methods of molecular and cell biology that was conducted in the past three years.

(continued on page 2)

Mapping the Brain *(continued from cover page)*

Narrowing it Down



Christina Zelano, PhD

Research efforts from other Feinberg investigators pinpointed their focus to study specific regions of the brain. These investigators include Christina Zelano, PhD, assistant professor of Neurology in the Division of Epilepsy and Clinical Neurophysiology, whose research aims understand how the brain processes and decodes odors.

For example, Zelano's laboratory recently discovered the characteristic electrophysiological response to odor in human primary olfactory cortex, showing that a distinct set of brainwaves are generated when we smell, and that high-frequency waves—or neural oscillations—help us accurately identify smells, with their findings published in *PLOS Biology.*

In partnership with the Northwestern Medicine Comprehensive Epilepsy Center's epilepsy monitoring unit, which is directed by Stephen Schuele, MD, MPH, chief of Neurophysiology and Epilepsy in the Department of Neurology and professor of Physical Medicine and Rehabilitation, and Joshua Rosenow, MD, professor of Neurological Surgery and of Physical Medicine and Rehabilitation, Zelano's team worked with patients with epilepsy who volunteered to participate in the research during their pre-surgical brain mapping and had electrodes implanted deep in their brains to help guide the surgery.

For the study, Zelano's team recorded the patients' brain activity measured by the electrodes while the patients smelled different odors and tried to identify them. They found that when processing an odor, the human olfactory cortex generates a characteristic set of low-, medium- and high-frequency oscillations called theta-, beta, and gamma-band, and that gamma-band oscillations were missing when the patients couldn't correctly identify the odor.

Understanding the mechanisms of human olfaction opens up future research directions to address olfactory pathologies, such as the unprecedented level of smell loss caused by COVID-19 infection, according to Zelano.

"The olfactory system is one of the few sites in the human brain where neurogenesis occurs throughout adulthood, and through receptor neurons that touch air in the nasal cavities and project directly into the brain, the inside of the nose is the only place where the central nervous system makes direct contact with the external environment," Zelano said.

This same methodology was used in another recent study from Zelano's team, which found that neurons in the olfactory cortex synchronize low-frequency oscillations to prepare the cortex to quickly identify and respond to odors. This anticipatory response may be key to understanding early olfactory loss, which is a common symptom of Alzheimer's and Parkinson's disease.

"With a number of unique properties compared to other sensory systems, the human olfactory system presents an increasingly attractive and powerful model for studying brain function under normal and pathological conditions," Zelano said.

Other research from Feinberg investigators aims to uncover genetic factors that influence one's risk of developing different neurological disorders.

Steven Lubbe, PhD

In a recent study published in *Brain*, investigators led by Steven Lubbe, PhD, assistant professor in the Ken and Ruth Davee Department of Neurology Division of Movement Disorders, discovered novel short tandem repeat sequences — short sequences of DNA repeated many times next to each other — in four genes that are independent from currently known genetic variants of Parkinson's disease and also influenced the expression of nearby genes.

"Unfortunately, at the cellular level, we do not yet know how these repeats lead to Parkinson's disease, but they represent candidate variants for further functional studies which will hopefully take us one step closer to identifying a novel therapeutic target," Lubbe said.

While there is still much left to uncover about the brain and related diseases, Lubbe's research and other work from Feinberg investigators are a testament to the power of scientific discovery and its ability to inform innovative therapeutic strategies and, most importantly, improve patient outcomes.

CONTENTS

Feinberg Investigators Featured on Global 'Highly Cited' List

Twelve faculty with appointments at Feinberg were named to the 2022 "Highly Cited Researchers" list, published by Clarivate Analytics. The annual list identifies investigators who have demonstrated significant influence in their field through the publication of highly cited publications during the last decade.

The data in the list is pulled from papers published in science and social sciences journals from 2011 through 2021. The list includes those investigators who rank among the top one percent as the most cited for their subject field and year of publication.

"When I arrived on campus in 2014, six investigators from Feinberg were recognized on the Clarivate 'Highly Cited' list. Remarkably, just eight years later, the number of highly cited investigators has doubled," said Kristi Holmes, PhD, director of the Galter Health Sciences Library. "While citation counts are not the only indicator of the impact of a body of work, this recognition clearly demonstrates that these investigators are highly productive, with research that drives discovery and innovation on the global level."

Continued investment in Feinberg research creates an environment that nurtures and sustains this excellence, according to Holmes.

"Our faculty continue to lead in their fields and across fields to publish research that has a major impact on the scientific community and human health," said Rex Chisholm, PhD, vice dean for scientific affairs and graduate education and the Adam and Richard T. Lind Professor of Medical Genetics.

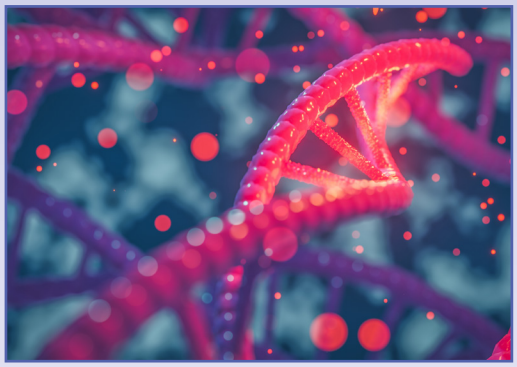
The Feinberg investigators included in the list and recognized for their exceptional impact on their fields are:

- David Cella, PhD, professor of Medical Social Sciences
- Navdeep S. Chandel, PhD, David W. Cugell, MD, Professor of Medicine in the Division of Pulmonary and Critical Care
- Mark Hersam, PhD, professor of Medicine in the Division of Pulmonary and Critical Care
- Shana Kelley, PhD, professor of Biochemistry and Molecular Genetics
- Donald Lloyd-Jones, MD, ScM, chair and Eileen M. Foell Professor of Preventive Medicine
- Chad Mirkin, PhD, professor of Medicine in the Division of Hematology and Oncology
- Brian Mustanski, PhD, professor of Medical Social Sciences
- Amy Paller, MD, chair and Walter J. Hamlin Professor of Dermatology
- John Rogers, PhD, Louis Simpson and Kimberly Querrey Professor of Materials Science and Engineering, Biomedical Engineering and Neurological Surgery
- Sanjiv Shah, MD, Neil J. Stone, MD, Professor of Medicine in the Division of Cardiology
- Richard Wunderink, MD, professor of Medicine in the Division of Pulmonary and Critical Care
- Clyde Yancy, MD, MSc, chief and Magerstadt Professor of Cardiology in the Department of Medicine

Breakthroughs Podcast

Understanding how genes function is a vital part of understanding how to better treat cancer. Research led by Mazhar Adli, PhD, is grounded in the development of a systematic approach to identify the function of each gene in the human body. His team aims to discover novel therapeutic drug combinations to prevent cancer development and chemotherapy resistance.

Listen to the episode.



Graduate Student/Post-Doc Events and Opportunities

Beyond 'Walking While Trans': How Gendered Spatial Stigma and Biased Police Deployment Drive Transgender Discrimination in Sex Work Arrests

January 10, Noon to 1:00 p.m.

The Institute for Sexual and Gender Minority Health and Wellbeing (ISGMH) invites you to the January "Current Issues in LGBTQ Health" lecture featuring Northwestern sociology graduate student Kris Rosentel. Existing research suggests that trans women of color experience discrimination related to the policing of sex work, which can increase vulnerability to victimization and negative mental health outcomes. This will be a hybrid event; guests may attend via Zoom or in person at our office. Lunch will be provided for in-person attendees who register by January 5.

Stonewall Conference Room
625 N. Michigan Avenue, Suite 1400, Chicago
More information

Global Health Experience Information Session

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

The Robert J. Havey, MD Institute for Global Health invites you to join a Global Health Experience Information Session. We will explore opportunities to engage in global health, available funding and our network of global partners. A successful global health experience starts with thoughtful consideration of our partner sites, timelines, policies and funding opportunities. All applicants are strongly encouraged to attend one of these group information sessions.

Hosted via Zoom
More information

Active Inclusion Virtual Workshop

January 25
9:00 to 11:30 a.m.

This diversity, equity and inclusion workshop is open to staff and faculty. Held in a live-virtual format, this two-part interactive workshop builds awareness and provides practical tools for participants to enact change towards fostering inclusive environments. Participants will learn how unconscious bias, intersectionality, power, privilege and oppression overlap and create barriers which support exclusionary practices. Participants will also learn how to create an action plan for utilizing concepts learned to actively foster inclusive environments. Participants should have previously attended an Unconscious Bias workshop.

More information

White Light Therapy

Mondays, Tuesdays, Wednesdays and Fridays in January, 10:30 a.m. to 5:00 p.m.

WELL has partnered with the Women's Center to provide light therapy on the Chicago campus Mondays, Tuesdays, Wednesdays and Fridays in January. All are welcome in this space. This service is also available on the Evanston campus in the Henry Crown Sports Pavilion Wellness Suite. Light therapy, exposure to artificial light, can be a safe and effective way to treat Seasonal Affective Disorder (SAD) and some types of depression and sleep disorders. Benefits that may be experienced include: alleviation of SAD symptoms and other types of depression and improvement in sleep disorders, mood and energy.

Abbot Hall, Women's Center, 14th Floor
710 N. Lake Shore Drive, Chicago

Research in the News

***Chicago Tribune,* November 2**
Northwestern Performs First Heart Transplant in Illinois Using 'Heart-in-a-Box' Device
Benjamin Bryner, MD, was featured.

***Associated Press,* November 9**
Mindfulness Worked as Well for Anxiety as Drugs in Study
Sheehan Fisher, PhD, was featured.

***Crain's Chicago Business,* November 14**
ER Visits by Youth with Suicidal Ideation Spiked in Fall of '19
Audrey Brewer, MD, MPH, and Joseph Feinglass, PhD, were featured.

***USA Today,* November 21**
Black Women Make up the Majority of New HIV Cases among Women. But They Aren't Getting Care.
Maria Nicole Pyra, PhD, was featured.

***US News & World Report,* November 24**
Tips for 'Stomaching' the Holidays If You Have IBS
Tiffany Taft, PsyD, was featured.

***The Washington Post,* November 26**
Parkinson's Patients and Researchers Search for Exercise 'Prescription'
Daniel M. Corcos, PhD, was featured.

Investigating the Dynamics Underlying Memory and Cognitive Control

Elizabeth Johnson, PhD, assistant professor of Medical Social Sciences and Pediatrics

Elizabeth Johnson, PhD, is a faculty member and director of Feinberg's Dynamic Brain Laboratory. Her research aims to uncover the brain dynamics underlying memory and cognitive control with the ultimate goal of advancing basic science and improving people's quality of life.

What are your research interests?
We're interested in the brain dynamics that support memory and cognitive control across the human lifespan. Research in our lab combines cognitive psychology with advanced neuroscientific techniques, including intracranial (invasive) and scalp (noninvasive) EEG, structural neuroimaging, electrical stimulation and eye tracking. Our research is organized into three overlapping areas: neural mechanisms of cognition, cognitive performance enhancement and development and aging. Findings inform models of cognition across the lifespan and translate to better quality of life by revealing how, and in whom, decline may be prevented or remediated.

What is the ultimate goal of your research?
I am a scientist out of sheer curiosity, yet the ultimate goal of our research is translational. If we ever understand how the brain supports cognition, we should be able to fix it when it breaks.

How did you become interested in this area of research?
Most of us have known someone who has lost memory function, say, from head trauma, stroke or dementia. Loss of function makes clear how integral memory is to our daily functioning and sense of self. I have long wondered how this organ in our heads enables impressive feats of thinking such as memory.

How is your research funded?
Our lab is funded by grants from the National Institutes of Health BRAIN Initiative and National Institute of Mental Health, and startup funds from the Department of Medical Social Sciences.

Where have you recently published papers?
We publish in neuroscience, biology, and general journals. This year, we published two papers each in *Current Biology* and *NeuroImage*.

What types of collaborations are you engaged in across campus (and beyond)?
Collaboration is critical to our research. We are privileged to conduct research with neurosurgical patients who let us look directly into their brains, and this is made possible by a network of clinical collaborators. At Northwestern, we work with Stephan Schuele, MD, MPH, and Joshua Rosenow, MD. We also launched an innovative pediatric research program at Lurie Children's Hospital, where we work with Joyce Wu, MD, Sandi Lam, MD, Jeffrey Raskin, FAANS, FAAP, David Bieber, MD, and Priscilla Duong, PhD. Our team science approach extends beyond Northwestern, where we exchange data and expertise with labs and clinicians at Wayne State University (Noa Ofen and Eishi Asano), the University of California (Robert Knight, Jack Lin, Olivia Kim McManus, Shifteh Sattar and Kurtis Auguste), Washington University in St. Louis (Peter Brunner and Jarod Roland) and Ohio State University (Ammar Shaikhouni). This list is not exhaustive!

Outside the hospital, we've been doing exciting work challenging the status quo with researchers at Brown University (David Badre), Ruhr University Bochum (Nikolai Axmacher), the University of Nevada-Reno (Marian Berryhill) and the University of California-San Francisco (Kevin Jones, Theodore Zanto and Adam Gazzaley). Last, I'd be remiss not to mention Joel Voss, PhD and Rodrigo Braga, PhD, each of whom has been very supportive as we continue to establish our new lab at Feinberg.

Investigating the Connection Between Estrogen and Fibrosis

Tanvi Potluri, fourth-year PhD student, Driskill Graduate Program in Life Sciences, Department of Obstetrics and Gynecology

Tanvi Potluri is a fourth-year PhD student in the Driskill Graduate Program in Life Sciences in the Department of Obstetrics and Gynecology. She is investigating the role estrogen plays in the development of fibrosis in the laboratory of Serdar Bulun, MD, the chair and John J. Sciarra Professor of Obstetrics and Gynecology.

Where is your hometown?
I grew up in the South Indian city of Hyderabad. It's famous for pearl jewelry and has a popular rice dish (biryani) named after it.

What sparked your interest in science or medicine?
I've always loved learning about biology. It was my favorite subject in school. Everything from cells to organisms – I wanted to know more and learn more. A career in biological sciences was a clear-cut decision.

What are your research interests?
My primary research interest is studying the role of sex hormones in various tissues and disease systems. During my master's studies, I worked on understanding how sex and sex hormones impact influenza vaccine responses. As a PhD student, I am looking into estrogen in skeletal muscle.

What are you currently working on?
My project started with an accidental discovery! When my lab inserted a human version of the Aromatase gene into mice, all the males spontaneously developed scrotal hernias – a prevalent condition whose etiology has long been a mystery. My PhD involves trying to understand how the muscle weakens in these mice to cause hernias, what estrogen has to do with this, and testing the translatability of the targets for human therapy. We hope to one day be able to treat a hernia non-surgically or maybe even prevent one.

Please tell us about a defining moment in your education at Feinberg thus far.
It's hard to pick one. I firmly believe it's an accumulation of multiple moments. Supportive peer network, mentors, being a part of grad student associations, brainstorming and interacting with experts – all added to my growth in science and as a person.

What do you hope to do with your degree?
As I am wrapping up my PhD, I am amazed at the skills and abilities I've gathered that can be applied anywhere. I am leaning towards pursuing a career in industry and finding a role where I can apply these skills, geek out about data, problem-solve and innovate.

Breakthroughs Podcast

Bariatric surgery is proving to be an effective tool to help teenagers with severe obesity lose weight and reverse the progression of weight-related conditions, according to findings from the Teen Longitudinal Assessment of Bariatric Surgery study (Teen-LABS). Thomas Inge, MD, PhD, principal investigator of Teen-LABS, shares results of the study, which is the only multicenter National Institute of Health sponsored research on adolescent bariatric surgery.

Listen to the episode.

Integrating into the Research Environment

Sameeha Saied, associate research administrator in the Basic Science Administration

At Feinberg, Saied helps to facilitate research proposals, grant applications and funding for a variety of projects within the Department of Pharmacology and the Department of Neuroscience.

Where is your hometown?

I was born and raised in Florida. I was born in Miami but moved to Orlando when I was pretty young, so I consider both to be home. If anyone wants the inside scoop on Disney or humidity, I'm your gal.

What led you to Northwestern?

Northwestern has always been one of my favorite universities. I went to Syracuse University for my bachelor's degree and worked closely with the institution, both as a student and as a staff member. After graduating, I wanted to take some time off before going back to school for clinical/counseling psychology, and I knew I wanted to continue working in the higher education sector during that time. Given that this position is in a city I have always loved and focuses on research, Northwestern ended up being a great fit for me.

What are you currently working on?

I am currently working as an associate research administrator. I work with a set of PIs within the Basic Sciences Administration to maintain the grants, proposals and funding for their various lab projects. Most of my portfolio is currently within the Neuroscience department, but I also have PIs in Pharmacology, Biochemistry, and Cell and Developmental Biology. Overall, any administrative components of those labs fall in my wheelhouse.

How does your work support the research enterprise at Feinberg?

Having majored in a scientific field and worked on research myself, I know how difficult it can be to juggle all the different components that go into it. People often think of research and see only the physical, scientific research, but there are so many steps that need to be taken before, during and after. Research administrators like myself are here to take on the more administrative work so our faculty can focus more acutely on their actual research.

Why do you enjoy working at Northwestern?

It's interesting to see what comes before and after research, especially because I will eventually be going to grad school and have to participate myself. I like to have a full understanding of my situations so I can control as many outcomes as possible, so being able to understand the intricacies of research beyond the science is super helpful for me in the long run. Beyond this, I love the atmosphere our office creates. Our community is full of such kind, fun people. I love that I can be excited to come into the office on the days that I do. That's surprisingly rare nowadays.

New Faculty

Leonard Verhagen Metman, MD, PhD, joined as professor of Neurology and Neurological Surgery in July 2022. He brings decades of experience and knowledge with him to the Parkinson's Disease and Movement Disorders Center. Verhagen is an internationally recognized expert in the medical and surgical management of patients with Parkinson's disease and other movement disorders such as essential tremor and dystonia. Most recently, he was professor of Neurological Sciences at Rush University, and he was the founder and longtime director of the Movement Disorder Surgery Program as well as the Interventional Program at Rush University Medical Center. Verhagen earned his medical and doctorate degrees from the University of Leiden in the Netherlands, completed his residency training in Neurology at Thomas Jefferson University in Philadelphia and his fellowship training at the NIH in Bethesda, MD.

NUCATS Corner
Clinical and Translational Sciences Institute

NUCATS Launches 'Science in Translation' Podcast

The NUCATS Institute has launched ***Science in Translation,*** a new podcast telling the stories of faculty members, staff and trainees who are dedicated to accelerating a transformational finding in the lab into a treatment, cure or solution that will improve human health. Listeners will discover how to use the tools, resources and educational opportunities available through NUCATS serve to catalyze, accelerate and transform translational science.

Each episode will be about 20 minutes in length and feature investigators like Sadiya Khan, MD, MSCI, who has achieved significant early-career successes; Satish Nadig, MD, PhD; director of Northwestern's Comprehensive Transplant Center; and Rod Passman, MD, who was recently was awarded a $37 million grant to study wearables and stroke prevention in patients with atrial fibrillation.

The podcast episodes may be of particular interest to Feinberg faculty and trainees as NUCATS communicates what translation is, how it impacts listeners and what the Institute has to offer through the stories of investigators.

Visit the Science in Translation webpage or listen wherever you get your podcasts.

NIH News

NIH establishes website for self-reporting COVID-19 test results

Reporting a positive or negative test result just became easier through a new website from the National Institutes of Health. MakeMyTestCount.org, developed through NIH's Rapid Acceleration of Diagnostics (RADx®) Tech program, allows users to anonymously report the results of any brand at-home COVID-19 test. COVID-19 testing remains an essential tool as the United States heads into the holiday season and people navigate respiratory issues. While taking rapid COVID-19 tests has become commonplace, test results are often not reported. RADx Tech has been working on a system to standardize test reporting for at-home tests in a secure manner. The MakeMyTestCount.org website is built on this system for logging results.

NIH Names Dr. Joni L. Rutter director of the National Center for Advancing Translational Sciences

Joni L. Rutter, PhD, has been named director of NIH's National Center for Advancing Translational Sciences (NCATS). Rutter will oversee a diverse portfolio of research activities focused on improving the translational process of turning scientific discoveries into health interventions. The portfolio includes the Clinical and Translational Science Awards (CTSA) Program, which is one of NIH's largest supported programs and has played an important role in the agency's COVID-19 response. In addition, she will direct innovative research programs to advance diagnoses and treatments, including gene therapies, for some of the more than 10,000 known rare diseases. She will also lead labs at NIH that drive team science with the private sector to create and test innovative methods for improving the drug development process.

NIH's Climate and Health Initiative tackles global health effects associated with a changing climate

Leaders from the National Institutes of Health discuss the agency's plan to address the risk to human health posed by changing climate in a commentary published in The Lancet. As floods, hurricanes, tornadoes, wildfires and heat waves become more extreme, the risk to human health grows, exacerbating existing health threats and creating new public health challenges around the world. The authors, a coalition of leaders at NIH, outline how the NIH Climate Change and Health Initiative is uniquely poised to lead and engage with communities and agencies globally to address the health effects associated with climate change.

Sponsored Research

PI: Mazhar Adli, PhD**, associate professor of** Obstetrics and Gynecology **in the Division of** Reproductive Science in Medicine

Sponsor: National Human Genome Research Institute

Title: Molecular and cellular characterization of essential human genes

We propose to generate barcoded and conditional null alleles in a cellular system that can model early human development and a broad range of human diseases. We will establish a data production research and development center in response to the RFA-HG-21-029: Molecular Phenotypes of Null Alleles in Cells (MorPhiC) Phase 1, which aims to establish a catalog of molecular and cellular phenotypes of null alleles for ultimately every human gene, using *in vitro* multicellular systems.

Our center will utilize a chemically inducible and reversible system that enables the rapid depletion of target proteins. The approach permits temporal control of protein levels to study the consequences of null alleles. We will utilize a super sensitive degron that rapidly degrades the target protein of interest in response to a low dose of auxin, a cell membrane diffusible small chemical plant hormone. We will combine CRISPR-based targeted locus engineering to homozygous knock-in a mini auxin-inducible degron (mAID) at the end of the target gene to create a chemically controllable switch to create null-alleles in an open-access human induced pluripotent stem (hiPSC) cell, which can be differentiated into various cell lineages and multicellular organoids to model human development and diseases. Notably, each AID-degron will also contain gene-specific barcodes, allowing tracking the fate of hundreds of thousands of null alleles when these engineered null alleles are pooled. The proposed approach is generalizable and can rapidly deplete target proteins codded by various classes of human genes.

Our strategy will be particularly advantageous and critical to study the null phenotypes of essential genes, which cannot be studied by chronic depletion using genetic approaches (such as CRISPR KO) because of the knock-in results in cell death. Therefore, to highlight the utility of our strategy, we prioritize creating null alleles by CRISPR mediated knock-in processes to introduce barcoded AID degron in 250 essential genes. We chose genes implicated in human diseases and subviable phenotypes in the International Mouse Phenotyping Consortium (IMPC). We propose to catalog the cellular phenotypes (survival, proliferation, mitotic function, and differentiation) and molecular phonotypes, including gene expression and chromatin accessibility for select null alleles. This information will provide unique insights into the biological function of these developmentally critical genes. It will highlight the utility of establishing the chemically inducible degron system as a generalizable strategy for the goals of the MorPhiC consortium. The created barcoded and conditional null allele resource will provide a unique opportunity to temporally control the timing of null alleles in pluripotent stem state and various terminally differentiated cell types or multicellular organoid systems that can be generated from the pluripotent stem cells.

Read more about the project.

PI: Jaline Gerardin, PhD**, assistant professor of** Preventive Medicine **in the Division of** Epidemiology

Sponsor: Bill and Melinda Gates Foundation

Title: Modeling to support high-burden countries

There is a critical gap between modeling, which is usually performed in academia, and translation of modeling results, predictions, and knowledge into evidence-based decision-making by policymakers. Our research team is a group of infectious disease modelers with a focus on translation to policy.

Since 2019, in close collaboration with the World Health Organization (WHO), our team has supported national malaria programs in four countries in developing their five-year national malaria strategic plans: Nigeria, which has the highest malaria burden; Burkina Faso, with the highest per-capita burden; Guinea, where malaria is the number one killer of children and malaria control is vital to maintaining vigilance against emerging hemorrhaging fevers; and Togo. We built detailed agent-based models parameterized by, calibrated to, and validated against a diverse array of country data.

Thoughtful scoping and stakeholder engagement is critical to developing capacity-building initiatives that are realistic, inclusive, and truly collaborative. Our team is engaged in a feasibility study and landscape analysis to identify key players, relationships, and considerations for potential pilot countries. This study will also assess the dynamics of key challenges and the feasibility of the recommendations provided by key partners.

Our long-term goal is to train a critical mass of modeling scientists who are 1) retained within Sub-Saharan Africa; 2) training the next generation of modelers; 3) working closely with local malaria control programs to provide operational support; 4) competitive in obtaining grants from international funding agencies; and 5) closely networked with each other across Africa and with international partners.

Scholars with skills in mathematical modeling of infectious diseases, including malaria, do exist in Sub-Saharan African universities. However, most are not engaged in their country's public health programs, although many are keen to apply their skills to pressing public health needs. Modelers in malaria-endemic countries indicate that they are hampered by 1) limited data access and experience with using public health data and 2) lack of facility with the state-of-the-art models needed for operational modeling. To address these gaps, we developed, piloted, and evaluated a 16-week intensive in-person training program in operational malaria modeling in 2022 and will implement a revised second iteration in 2023.

We are partnering with the West Africa mathematical Modeling CApacity Development (WAMCAD): Anglophone-francophone-lusophone partnership, another Gates-funded project, to train West African modelers over the next three years.

More to come on 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.

Arthritis Research Grants

More information

Sponsor: Arthritis National Research Foundation
Submission deadline: January 20
Upper amount: Up to $125,000 (two-year grants at $250,000)

ANRF seeks applications focused on studying arthritis and related autoimmune diseases including, but not limited to osteoarthritis, rheumatoid arthritis, juvenile arthritis, lupus, psoriatic arthritis, gout, scleroderma, fibromyalgia and ankylosing spondylitis.

Research Networks to Promote Multidisciplinary Mechanistic Studies on Music-Based Intervention for Pain or Alzheimer's Disease and Alzheimer's Disease Related Dementias (U24 Clinical Trial Optional)

More information

Sponsor: National Institutes of Health, National Center for Complementary and Integrative Health, National Institute on Aging
Submission deadline: January 10
Upper amount: $300,000 per year up to a five-year project period

Music has the remarkable ability to enhance child development, improve adult function and well-being and optimize quality of life during aging. Some studies have shown that music may also have the potential to ameliorate the symptoms of a broad range of diseases and disorders that occur throughout the lifespan. The purpose of this funding opportunity is to support a collection of research networks that promote multidisciplinary mechanistic studies of music-based interventions for pain or Alzheimer's disease and Alzheimer's disease-related dementias.

HEAL Initiative – Sleep Predictors of Opioid-Use Disorder Treatment: Leadership and Data Co-ordinating Center (U01 Clinical Trial Optional)

More information

Sponsor: National Institutes of Health, National Institute on Drug Abuse, National Institute on Alcohol Abuse and Alcoholism
Submission deadline: February 10
Upper amount: Maximum of $1.5 million in direct costs, over a maximum of four years

Opioid use disorders and disorders of sleep and/or circadian rhythm are intricately interconnected. Opioids have a disruptive effect on sleep and sleep quality, while sleep and circadian rhythm disturbances contribute to initiating and maintaining drug use and can increase risk for relapse. The overall goals of this program are to uncover novel mechanisms underlying the bidirectional interrelationship between sleep/circadian rhythm and to delineate sleep and/or circadian-based predictors of opioid use disorder treatment response and outcomes.

Schizophrenia and Related Disorders During Mid- to Late-Life (R01 Clinical Trial Optional)

More information

Sponsor: National Institutes of Health, National Institute of Mental Health
Submission deadline: February 22
Upper amount: $3 million to fund five to seven awards, maximum project period is five years

The purpose of this funding opportunity announcement is to encourage applications that will advance translational research to better understand the emergence, trajectory and outcomes of schizophrenia and related psychotic disorders in mid- to late-life and to identify targets for future development of prevention and treatment interventions. Research to identify mechanisms for targets with an experimental therapeutics approach leading to intervention development or that identify ways to modify existing healthcare and community-based services to better support individuals with schizophrenia and related psychotic disorders in mid- to late-life is of special interest.

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.

Scholarly Communication and Publishing Developments: A Sampling

By Ramune Kubilius, Collection Development and Special Projects Librarian

Developments within the scholarly communication and publishing ecosystem directly impact phases of the research and information lifecycle. This month we look at a few shifts and innovations that have affected scholarly communications and publishing in 2022, and how those changes will inform research in the upcoming year.

Sharing and Repositories

To encourage the replication of studies and sharing of biomedical research data, the National Institutes of Health's Final Policy for Data Management and Sharing will go into effect January 25, 2023. As researchers are informed about the new policy, resource sharing and repository communities continue to build services and tools to support the transition. This past July the Confederation of Open Access Repositories (COAR), to which Galter belongs, announced a new Community Framework for Good Practices in Repositories, dedicated to consistent evaluation and improvement of repository operations. In collaboration with the Centre pour la Communication Scientifique Directe (CCSD), COAR also announced a directory of open access preprint repositories providing a valuable resource to researchers seeking the best platform for their work.

The NIH launched the Generalist Repository Ecosystem Initiative (GREI), dedicated to enhancing access to biomedical research through establishing a common set of capabilities across generalist repositories and promoting the adoption of FAIR principles. Learn more about the importance of this initiative and how it is impacting the data ecosystem at the National Cancer Institute by breaking down barriers to sharing cancer data. Northwestern and the European Organization for Nuclear Research (CERN) announced a collaboration that enables Zenodo's participation in GREI.

The Galter team has been compiling resources and developing instruction to support the Feinberg community through the transition. Galter staff members wrote ten simple rules for maximizing the recommendations of the NIH data management and sharing plan published in *PLoS Computational Biology* in August.

The National Library of Medicine

In October 2022, the National Library of Medicine's (NLM) National Center for Biotechnology Information released version 14 of NCBI Datasets expanding access and improving interoperability in support of the Data Management and Sharing Policy. NLM also announced efforts to leverage its information resources to improve accessibility and released a statement that it stands ready to support NIH's implementation of updated policy guidance issued by the White House Office of Science and Technology Policy (OSTP).

The life and legacy of Donald A.B. Lindberg, MD, longtime NLM director, was honored this year through a symposium and the publication of Transforming Biomedical Informatics and Health Information Access: Don Lindberg and the U.S. National Library of Medicine (Studies in Health Technology and Informatics, vol.288, 2022). The book is a tribute to his profound impact during his tenure as NLM Director (1984–2015) and guides readers through the significant shifts in biomedical research and health information access over the past three decades.

Societies and Publishing

Societies enjoy a long tradition of providing professional development and publishing opportunities for members. There are several key items of note:

- In January 2023, Radiological Society of North America will publish a final 100th anniversary print edition of *Radiology* before moving its journals to all digital format.
- The American Academy of Pediatrics will launch *Pediatrics Open Science* as its flagship journal, *Pediatrics,* marks 75 years.
- Microbiology Society celebrates *Microbiology's* 75 years and re-launch of *Access Microbiology* as an open research platform.
- New York Academy of Medicine celebrates its 175th anniversary. It began publishing *Bulletin of the New York Academy of Medicine* in the 1860's, was renamed the Journal of Urban Health in 1997, continues today outside of NYAM auspices.
- The Royal Society of London's venerable *Philosophical Transactions* has published works by Charles Darwin, Dorothy Hodgkin and other scientific notables. *A History of Scientific Journals: Publishing at the Royal Society, 1665-2015* explores 350 years of scientific publishing.
- The *Journal of Clinical Investigation (JCI),* published by American Society for Clinical Investigation (ASCI), finds a home at Northwestern with the journal's first female editor in chief, Elizabeth McNally, MD, PhD. Read McNally's inspiring charge, Make it even better (March 2022).

Galter Library provides information and support during various stages of scholarly publishing and data management, including our DataLab, publication support, training on various NIH and NLM resources and more. Request a consultation or contact us for more information.

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High-Impact Factor Research

Ascha M, Sasson DC, Sood R, Cornelius JW, Schauer JM, Runge A, Muldoon AL, Gangopadhyay N, **Simons L, Chen D,** Corcoran JF, **Jordan SW**. Top Surgery and Chest Dysphoria Among Transmasculine and Nonbinary Adolescents and Young Adults. *JAMA Pediatrics*. 2022;176(11):1115-1122.

Cabrera E, Crespo G, VanWagner LB. Diagnosis and Management of Hereditary Hemochromatosis. *JAMA-Journal of the American Medical Association*. 2022;328(18):1862-1863.

Creager MA, Hernandez AF, Bender JR, Foster MH, Heidenreich PA, Houser SR, **Lloyd-Jones DM,** Roach WH, Roger VL. Assessing the Impact of the American Heart Association's Research Portfolio: A Scientific Statement From the American Heart Association. *Circulation*. 2022;146(18):E246-E256.

Dardani I, Emert BL, **Goyal Y,** Jiang CL, Kaur A, Lee J, Rouhanifard SH, Alicea GM, Fane ME, Xiao M, Herlyn M, Weeraratna AT, Raj A. ClampFISH 2.0 enables rapid, scalable amplified RNA detection in situ. *Nature Methods*. 2022;19(11):1403-1410.

de Leval L, Alizadeh AA, Bergsagel PL, Campo E, Davies A, Dogan A, Fitzgibbon J, Horwitz SM, Melnick AM, Morice WG, Morin RD, Nadel B, Pileri SA, Rosenquist R, Rossi D, Salaverria I, Steidl C, Treon SP, Zelenetz AD, Advani RH, Allen CE, Ansell SM, Chan WC, Cook JR, Cook LB, d'Amore F, Dirnhofer S, Dreyling M, Dunleavy K, Feldman AL, Fend F, Gaulard P, Ghia P, Gribben JG, Hermine O, Hodson DJ, Hsi ED, Inghirami G, Jaffe ES, Karube K, Kataoka K, Klapper W, Kim WS, King RL, Ko YH, LaCasce AS, Lenz G, Martin-Subero JI, Piris MA, Pittaluga S, Pasqualucci L, Quintanilla-Martinez L, Rodig SJ, Rosenwald A, Salles GA, San-Miguel J, Savage KJ, Sehn LH, Semenzato G, Staudt LM, Swerdlow SH, Tam CS, Trotman J, Vose JM, Weigert O, Wilson WH, **Winter JN,** Wu CJ, Zinzani PL, Zucca E, Bagg A, Scott DW. Genomic profiling for clinical decision making in lymphoid neoplasms. *Blood*. 2022;140(21):2193-2227.

Elsawy M, Chavez JC, Avivi I, Larouche JF, Wannesson L, Cwynarski K, Osman K, Davison K, Rudzki JD, Dahiya S, Dorritie K, Jaglowski S, Radford J, Morschhauser F, Cunningham D, Martin Garcia-Sancho A, Tzachanis D, Ulrickson ML, **Karmali R**, Kekre N, Thieblemont C, Enblad G, Dreger P, Malladi R, Joshi N, Wang WJ, Solem CT, Snider JT, Cheng P, To C, Kersten MJ. Patient-reported outcomes in ZUMA-7, a phase 3 study of axicabtagene ciloleucel in second-line large B-cell lymphoma. *Blood*. 2022;140(21):2248-2260.

Grange LJ, Reynolds JJ, Ullah F, Isidor B, Shearer RF, Latypova X, Baxley RM, Oliver AW, Ganesh A, Cooke SL, Jhujh SS, McNee GS, Hollingworth R, Higgs MR, Natsume T, Khan T, Martos-Moreno G, Chupp S, Mathew CG, Parry D, Simpson MA, Nahavandi N, Yüksel Z, Drasdo M, Kron A, Vogt P, Jonasson A, Seth SA, Gonzaga-Jauregui C, Brigatti KW, Stegmann APA, Kanemaki M, Josifova D, Uchiyama Y, Oh Y, Morimoto A, Osaka H, Ammous Z, Argente J, Matsumoto N, Stumpel C, Taylor AMR, Jackson AP, Bielinsky AK, Mailand N, Le Caignec C, **Davis EE**, Stewart GS. Pathogenic variants in SLF2 and SMC5 cause segmented chromosomes and mosaic variegated hyperploidy. *Nature Communications*. 2022;13(1):6664.

Halpern JA, Davis AM, Brannigan RE. Diagnosis and Treatment of Infertility in Men. *JAMA-Journal of the American Medical Association*. 2022;328(20):2056-2057.

Iizuka T, Yin P, Zuberi A, Kujawa S, Coon JS, Björvang RD, Damdimopoulou P, Pacyga DC, Strakovsky RS, Flaws JA, **Bulun SE**. Mono-(2-ethyl-5-hydroxyhexyl) phthalate promotes uterine leiomyoma cell survival through tryptophan-kynurenine-AHR pathway activation. *Proceedings of the National Academy of Sciences of the United States of America*. 2022;119(47):e2208886119.

Jacquet S, Culbertson M, Zhang C, El Filali A, De La Myre Mory C, Pons JB, Filippi-Codaccioni O, Lauterbur ME, Ngoubangoye B, Duhayer J, Verez C, **Park C**, Dahoui C, Carey CM, Brennan G, Enard D, Cimarelli A, Rothenburg S, Elde NC, Pontier D, Etienne L. Adaptive duplication and genetic diversification of protein kinase R contribute to the specificity of bat-virus interactions. *Science Advances*. 2022;8(47):eadd7540.

Kim JT, Ouyang W, Hwang H, Jeong H, Kang S, Bose S, Kwak SS, Ni X, Kim H, Park J**, Chen H, Soetikno A,** Kim J, **Xu S**, Chamorro LP, **Rogers JA**. Dynamics of plosive consonants via imaging, computations, and soft electronics. *Proceedings of the National Academy of Sciences of the United States of America*. 2022;119(46):e2214164119.

Levin MG, Tsao NL, Singhal P, Liu C, Vy HT, Paranjpe I, Backman JD, Bellomo TR, Bone WP, Biddinger KJ, Hui Q, Dikilitas O, Satterfield BA, Yang YF, Morley MP, Bradford Y, Burke M, Reza N, Charest B, Judy RL, **Puckelwartz MJ**, Hakonarson H, Khan A, Kottyan LC, Kullo I**, Luo Y, McNally EM, Rasmussen-Torvik LJ,** Day SM, Do R, Phillips LS, Ellinor PT, Nadkarni GN, Ritchie MD, Arany Z, Cappola TP, Margulies KB, Aragam KG, Haggerty CM, Joseph J, Sun YV, Voight BF, Damrauer SM. Genome-wide association and multi-trait analyses characterize the common genetic architecture of heart failure. *Nature Communications*. 2022;13(1)

Liu L, Khan A, Sanchez-Rodriguez E, Zanoni F, Li Y, Steers N, Balderes O, Zhang J, Krithivasan P, LeDesma RA, Fischman C, Hebbring SJ, Harley JB, Moncrieffe H, Kottyan LC, Namjou-Khales B, **Walunas TL**, Knevel R, Raychaudhuri S, Karlson EW, Denny JC, Stanaway IB, Crosslin D, Rauen T, Floege J, Eitner F, Moldoveanu Z, Reily C, Knoppova B, Hall S, Sheff JT, Julian BA, Wyatt RJ, Suzuki H, Xie J, Chen N, Zhou X, Zhang H, Hammarström L, Viktorin A, Magnusson PKE, Shang N, Hripcsak G, Weng C, Rundek T, Elkind MSV, Oelsner EC, Barr RG, Ionita-Laza I, Novak J, Gharavi AG, Kiryluk K. Genetic regulation of serum IgA levels and susceptibility to common immune, infectious, kidney, and cardio-metabolic traits. *Nature Communications*. 2022;13(1):6859.

Luo JK, Pinto L. Genetically tagging cholinergic diversity. *Neuron*. 2022;110(22):3650-3652.

Ma Q, Yang QH, Xu JA, Zhang XY, Kim D, Liu ZP, Da QE, Mao XX, Zhou YQ, Cai YF, Pareek V, Kim H, Wu GY, Dong Z, Song WL, Gan L, Zhang CX, Hong M, Benkovic SJ, Weintraub NL, Fulton D, Asara JM, **Ben-Sahra I**, Huo YQ. ATIC-Associated De Novo Purine Synthesis Is Critically Involved in Proliferative Arterial Disease. *Circulation*. 2022;146(19):1444-1460.

Montauti E, Weinberg SE, Chu P, **Chaudhuri S, Mani NL, Iyer R**, Zhou Y, Zhang Y, Liu C, Xin C, **Gregory S, Wei J, Zhang Y,** Chen W, Sun Z, **Yan M, Fang D**. A deubiquitination module essential for T(reg) fitness in the tumor microenvironment. *Science Advances*. 2022;8(47):eabo4116.

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High-Impact Factor Research

Opie-Martin S, Iacoangeli A, Topp SD, Abel O, Mayl K, Mehta PR, Shatunov A, Fogh I, Bowles H, Limbachiya N, Spargo TP, Al-Khleifat A, Williams KL, Jockel-Balsarotti J, Bali T, Self W, Henden L, Nicholson GA, Ticozzi N, McKenna-Yasek D, Tang L, Shaw PJ, Chio A, Ludolph A, Weishaupt JH, Landers JE, Glass JD, Mora JS, Robberecht W, Van Damme P, McLaughlin R, Hardiman O, van den Berg L, Veldink JH, Corcia P, Stevic Z, **Siddique N**, Silani V, Blair IP, Fan DS, Esselin F, de la Cruz E, Camu W, Basak NA, **Siddique T,** Miller T, Brown RH, Al-Chalabi A, Shaw CE. The SOD1-mediated ALS phenotype shows a decoupling between age of symptom onset and disease duration. *Nature Communications*. 2022;13(1)

Shah NS, Luncheon C, **Kandula NR, Khan SS**, Pan L, Gillespie C, Loustalot F, Fang J. Heterogeneity in Obesity Prevalence Among Asian American Adults. *Annals of Internal Medicine*. 2022;175(11):1493-1500.

Tang Q, Leung J, Peng Y, Sanchez-Fueyo A, Lozano JJ, Lam A, Lee K, Greenland JR, Hellerstein M, Fitch M, Li KW, Esensten JH, Putnam AL, Lares A, Nguyen V, Liu W, Bridges ND, Odim J, Demetris AJ, **Levitsky J,** Taner T, Feng S. Selective decrease of donor-reactive T(regs) after liver transplantation limits T(reg) therapy for promoting allograft tolerance in humans. *Science Translational Medicine*. 2022;14(669):eabo2628.
Walsh PS, Schnadower D, Zhang Y, **Ramgopal S**, Shah SS, Wilson PM. Association of Early Oseltamivir With Improved Outcomes in Hospitalized Children With Influenza, 2007-2020. *JAMA Pediatrics*. 2022;176(11):e223261.

Watari H, Kageyama H, Masubuchi N, Nakajima H, Onodera K, **Focia PJ,** Oshiro T, Matsui T, Kodera Y, Ogawa T, Yokoyama T, Hirayama M, Hori K, Freymann DM, Imai M, Komatsu N, Araki M, Tanaka Y, Sakai R. A marine sponge-derived lectin reveals hidden pathway for thrombopoietin receptor activation. *Nature Communications*. 2022;13(1):7262.

Xu J, Song F, Lyu H, Kobayashi M, Zhang B, Zhao Z, Hou Y, Wang X, Luan Y, Jia B, **Stasiak L, Wong JH, Wang Q, Jin Q, Jin Q, Fu Y, Yang H**, Hardison RC, Dovat S, **Platanias LC**, Diao Y, Yang Y, Yamada T, Viny AD, Levine RL, Claxton D, Broach JR, Zheng H, **Yue F**. Subtype-specific 3D genome alteration in acute myeloid leukaemia. *Nature*. 2022;611(7935):387-398.

Yamada Y, Zhang X, Henderson MET, et al. (including **Kushner RF, Leonard WR**). Variation in human water turnover associated with environmental and lifestyle factors. *Science*. 2022;378(6622):909-915.

Zhao SB, Li J, Zhang HY**, Qi L, Du YC,** Kogiso M, Braun FK, **Xiao S**, Huang YL, Li JF, Teo WY, Lindsay H, Baxter P, Su JMF, Adesina A, Laczik M, Genevini P, Veillard AC, Schvartzman S, Berguet G, **Ding SR, Du LP**, Stephan C, Yang JH, Davies PJA, **Lu XY,** Chintagumpala M, Parsons DW, Perlaky L, **Xia YF**, Man TK, Huang Y, Sun DQ, **Li XN**. Epigenetic Alterations of Repeated Relapses in Patient-matched Childhood Ependymomas. *Nature Communications*. 2022;13(1)

Featured Core

Northwestern Medicine Enterprise Data Warehouse

The Northwestern Medicine Enterprise Data Warehouse (NMEDW) aims to create a single repository of all clinical and research data sources on Northwestern Medicine's campus to facilitate research, clinical quality, healthcare operations and medical education. NMEDW is a joint initiative across the Feinberg School of Medicine and Northwestern Memorial Healthcare Corporation.

NMEDW services include:

NMEDW Data Analysts

The NMEDW employs a team of data analysts dedicated to satisfying requests for data from the NMEDW for research purposes. To make a request of an NMEDW data analyst, please go to the NMEDW website from the NU or NMHC networks and log in with your NU or NMHC credentials. Once logged in, click on "Add New Data Request," and follow the form to add the needed information relative to your research request. A NMEDW research analyst will contact you shortly.

NMEDW Pilot Data Program

This is an initiative to help jump-start research projects led by less established investigators who do not yet have adequate funding. The purpose of this grant is not to internally fund entire research projects. Rather, the goal is to allow young investigators to obtain feasibility or early pilot data to seek sustained funding.

Powerusers

Individuals who have skills using advanced database languages can apply to become a Poweruser. Powerusers are granted direct access to the NMEDW to do their work. They must be named on a valid IRB protocol, pass a skills assessment and take a training course. They are also obligated to comply with all NMEDW policies and procedures.

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