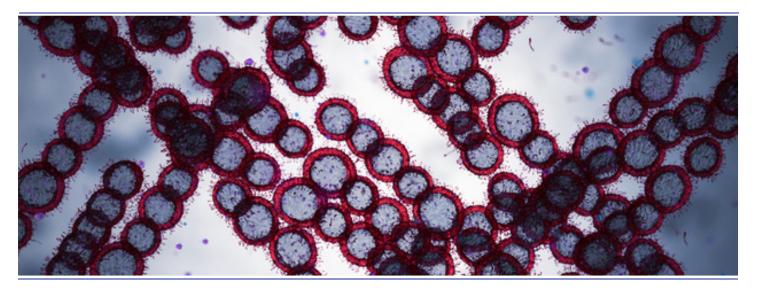
Breakthroughs

Feinberg School of Medicine Research Office

April 2023



Northwestern Investigators Lead Global Research on Antimicrobial Resistance

By Olivia Dimmer

It's sometimes called the 'Silent Pandemic,' and has emerged as the third-leading cause of death globally, according to a <u>2022 study</u> that provided the first comprehensive picture of its lethality.

The issue of antimicrobial resistance – including antibiotic and antifungal resistance – is poised to become one of the greatest threats to global human health, said <u>Mehreen Arshad, MBBS</u>, assistant professor of <u>Pediatrics</u> in the Division of <u>Infectious</u> <u>Diseases</u> and leader of the <u>Buffett Institute for Global Affairs</u> <u>Antibiotic Resistance Working Group</u>.

"We just had the Covid pandemic; But we call this the silent pandemic, because if you look at the number of deaths associated with antimicrobial resistance on a global scale, it's so much more than Covid was and is," said Arshad. "It's spread over years and geographical areas, and it sort of comes in ways people don't recognize as a pandemic, where it really is." As global consumption of prescribed antibiotics has increased — <u>46 percent globally</u> between 2000 and 2018, according to one study — so too have deaths from antibiotic-resistant infections. Antimicrobial resistance was associated with <u>4.95</u> <u>million deaths</u> worldwide in 2019 and roughly 1.7 million were directly attributable to antimicrobial-resistant infections, according to a study published in *The Lancet*.

The Antibiotic Resistance Working Group, established in 2020 with faculty from Feinberg and Weinberg and supported by the Buffett Institute, is an interdisciplinary, global effort to fully understand the issue of antimicrobial resistance and develop strategies to mitigate the impact.

While attending medical school in Pakistan, Arshad noticed a rise in antibiotic-resistant infections. It made sense, Arshad said, that a developing country with lax rules around prescribing antibiotics would see an increase in antibiotic resistance, but when she came to the U.S. for her residency and fellowship in pediatric medicine and saw cases climb, she realized it would take a global effort to address this complex global problem.



Antimicrobial Resistance (continued from cover page)

"We're seeing more and more resistant organisms in our pediatric population and we're finding it more difficult to treat them," Arshad said. "Our patients are dying from resistant infections, whereas that was not ever something that we thought about before. This concept of a post-antibiotic era, where our anti-microbials don't work anymore, is becoming a very real thing for us physicians, even in a country like the U.S."

Currently, the working group has established research relationships at Aga Khan University and a partnership with the National Institutes of Health (NIH) in Pakistan. With these partnerships, the group aims to establish a pathogen surveillance program to understand the relationship between genomic, phenotypic and clinical characteristics associated with disease due to resistant organisms.

In the future, the groups will survey providers on the reasons behind overprescription of antibiotics and expand capacity for antimicrobial resistance surveillance in Pakistan.

In 2021, the group secured a \$2.5 million grant from the Centers for Disease Control and Prevention to study antimicrobial resistance patterns and develop a roadmap for coordinating responses to antimicrobial resistance across academic, political, pharmaceutical and medical institutions.

Arshad and her collaborators are also conducting antimicrobial surveillance in Chicago and have revealed some alarming early findings.

"We've had some notable data we've collected; We've found that 15 percent of healthy pregnant mothers in the community in Chicago are carriers of these multi-drug resistant bacteria, which is pretty high if you think about it, because these are adults that have had no recent antibiotic use or hospital exposures which are typically thought of risk factors for carriage of drug resistant bacteria. About half of those mothers also transmitted these bacteria to their infants at the

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time of delivery, which is concerning because infants have low immunity and can become sick with these highly resistant and difficult to treat bacteria," Arshad said. "I think that what we're capturing is very much the tip of the iceberg. This community prevalence of resistant bacteria is very underappreciated. Resistant bacteria have been reported in developing countries, but we sort of never thought this would happen in the U.S., and in Chicago, too."

In March, the Centers for Disease Control <u>released an alert</u> for a circulating multi-drug resistant fungus, *Candida auris*, as it has spread quickly through hospitals in New York, New Jersey and Chicago.

"Most people don't think they have to worry about resistant infections, because unless you get a severe infection in the hospital, you're not going to get infected with these antimicrobial-resistant bacteria or fungi. But that's changing," said Egon Ozer, MD, PhD, '08 GME, assistant professor of Medicine in the Division of Infectious Diseases and director of the <u>Center for Pathogen Genomics and Microbial Evolution</u> and member of the working group. "We are all very worried about the potential for a post-antibiotic era, where we go back to the way it was before we had even penicillin."

While the issue of antimicrobial resistance is mounting, there's still hope that the issue can be addressed before it spreads any further, said <u>Erica Hartmann, PhD</u>, associate professor of <u>Civil</u> and <u>Environmental Engineering</u> and co-leader of the working group.

"One of the things we're working on right now is understanding how widespread antimicrobial resistance is in the community," Hartmann said. "In hospitals, especially in the developed world, there's a lot of monitoring for antimicrobial resistance, and we're relatively good at tracking and preventing outbreaks within a facility. But many people probably carry antimicrobialresistant organisms without even knowing about it. We want to know where this resistance comes from and whether it can become a medical issue. This feeds into the bigger picture of understanding the full scope of the problem so we can make better decisions about when and how to use the drugs that we have."

Understanding antimicrobial resistance is just the first step to solving this complicated issue, Hartmann said, which will require interdisciplinary cooperation across the globe.

"Antimicrobial resistance is a huge issue that will require coordinated action across many disciplines and across the world. The reassuring thing is that a lot of people are thinking about it from a lot of different perspectives. I think the situation is often framed as an arms race between us and the microbes, but really, it's more like we accidentally created a system with feedback and now we need to rearrange the speakers and mics, and maybe get some noise-canceling headphones."

CRISPR Pioneer Delivers Inaugural Kimberly Prize Lecture

By Melissa Rohman

Jennifer A. Doudna, PhD, the Li Ka Shing Chancellor's Chair in Biomedical and Health Sciences and professor of Biochemistry, Biophysics and Structural Biology at the University of California, Berkeley, delivered the inaugural <u>Kimberly Prize in Biochemistry</u> and <u>Molecular Genetics Lecture</u> to Feinberg faculty, staff, fellows and students in a <u>full Hughes Auditorium</u> on Tuesday, April 4.

Doudna, who is also an investigator of the Howard Hughes Medical Institute, is the inaugural recipient of the Kimberly Prize for her fundamental biochemical research providing molecular insight into the function of CRISPR/Cas9 systems as tools for genome editing and the application of her work to science and medicine.

In 2020, Doudna and Emmanuelle Charpentier, PhD, received the Nobel Prize in Chemistry for co-developing CRISPR-mediated genome editing.

"The Kimberly Prize in Biochemistry and Molecular Genetics is recognizing and honoring Jennifer for her ongoing work and further development of the CRISPR/Cas system, her work and development of the Innovative Genomics Institute that she has created at Berkeley, and her



work from her lab and the work that she's doing with pharma," said <u>Ali Shilatifard</u>, <u>PhD</u>, the Robert Francis Furchgott Professor and chair of <u>Biochemistry and Molecular Genetics</u> and director of the <u>Simpson Querrey Institute for Epigenetics</u>.

During her lecture, Doudna gave an overview of the last decade of CRISPR discoveries and developments, sharing her excitement about how far the technology has come and its widespread adoption in science and medicine.

"It is powerful technology. Over the last decade or so, it's been developed for not only disrupting genes or replacing genes, but also for controlling transcription. That means controlling the output of genes, diagnosing the presence of different kinds of nucleic acids like RNA and DNA, including during the pandemic when CRISPR was developed in a number of groups for detection of the SARS-CoV-2 virus, and for molecular imaging," Doudna said. She also discussed how ensuring both the delivery and precision of editing is essential to the future of *in vivo* genome editing.

"How do we actually make sure these editing molecules get into the cells where we need them to do their job. It's one thing if we're doing that in the laboratory...but it's pretty different if we're thinking about trying to do it in a person's body. CRISPR has tremendous potential to be a one-and-done type of therapy if this challenge can be met," Doudna said.

"The second challenge then, of course, is once they get there, we need the editing to be precise. We need the editing to be accurate and we don't want CRISPR doing something or causing a change in the DNA that might cause problems," Doudna said.

In addition to delivering the inaugural Kimberly Prize lecture, Doudna had the opportunity to speak with current Feinberg students and postdoctoral fellows during a meet-and-greet lunch earlier that afternoon.

> "It was really a great conversation and really gives me hope for the future to know that all of you are so on fire about the work that you're doing and just going after it with such passion," Doudna said.

The <u>Kimberly Prize in</u> <u>Biochemistry and Molecular</u> <u>Genetics</u>, given by Kimberly Querrey in honor of her late husband, Lou Simpson, is awarded every year to a scientist who has made

outstanding research contributions into the molecular basis of life with a direct demonstrated link of their discovery into clinic for the betterment of humankind.

Prize recipients are nominated and reviewed by the dean of Northwestern University Feinberg School of Medicine, the director of Simpson Querrey Institute for Epigenetics and other luminaries. The annual prize of \$250,000 is given by the <u>Simpson Querrey Institute for Epigenetics</u> and administered by the Feinberg School of Medicine.

"We are building a program here at Northwestern University that is 100 percent supportive of doing innovative, cutting-edge science, and we are recognizing nationally and internationally individuals who contribute to that process," Shilatifard said. "Kimberly and Lou have been great friends in supporting this extraordinary and essential mission of the University."

Campus Events and Opportunities

29th Annual Alzheimer Day May 11, 9:00 a.m. to 2:30 p.m.

Join the Mesulam Center for Cognitive Neurology and Alzheimer's Disease for our 29th Annual Alzheimer Day in Feinberg Pavilion Conference Center. Northwestern Alzheimer Day was established to showcase Alzheimer's-related dementia and aging research conducted throughout Northwestern and to bring this information to the community. Attendees will have the opportunity to connect with community members and researchers over lunch and through the presentation of research posters.

Northwestern Memorial Hospital Feinberg Pavilion Feinberg Pavilion Conference Center, Third Floor 251 E. Huron St., Chicago More information

Simpson Querrey Institute for Epigenetics Forum on Biochemistry, Epigenetics and Metabolism (BEaM) May 12, Noon to 1:00 p.m.

The BEaM Forum is a data group where Simpson Querrey Institute for Epigenetics members present ongoing work being conducted. Presenters will give a 20-minute talk with ten minutes for discussion and questions. This presentation will feature Qixuan Wang a PhD candidate in biochemistry and molecular genetics at the Yue Lab and Huijue Lyu a PhD candidate of biochemistry and molecular genetics at the Yue Lab. Pizza and soda are provided.

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

Global Health Education Day May 17, Noon to 4:00 p.m.

Global Health Education Day is an exciting opportunity to draw together global health researchers, educators and students. Led by the Havey Institute for Global Health Center for Global Health Education, the day's events will include a poster session, luncheon, an informative workshop and prominent guest speakers. The keynote address will feature Dr. Andrew Pinto and Dr. Ross Upshur.

Prentice Women's Hospital Conference Center 250 E. Superior St., Chicago More information

EQuaTR Conference June 1, 8:30 a.m. to 3:30 p.m.

The Enhancing Quality in the Translational Research Workforce Conference (EQuaTR) offers the opportunity for clinical research staff to learn from leaders in the field, gaining practical knowledge on current trends and issues in clinical research. This conference is open to professionals in clinical and translational research including clinical research coordinators, research nurses, monitors, project and site managers, investigators, regulatory staff, research assistants and allied health professionals.

Northwestern Memorial Hospital Feinberg Pavilion Feinberg Pavilion Conference Center, Third Floor 251 E. Huron St., Chicago More information

Research in the News

WBEZ Chicago, March 8 Meet the Northwestern Scientist in Charge of New Bioscience Lab Funded by Mark Zuckerberg and Priscilla Chan Shana Kelley, PhD, was featured.

The Washington Post, March 9 Why Daylight Saving Time is Fun but Bad for You Phyllis Zee, MD, PhD, was featured.

Wall Street Journal, March 16 U.S. Maternal Mortality Hits Highest Level Since 1965 Sadiya Khan, MD, MSc, was featured. NBC 5 Chicago, March 28 Strep Is on the Rise in Kids. Parents Should Be Aware of These Less Common Symptoms. Alin Abraham, MD, was featured.

New York Times, March 29 Exercise May Help Counteract the Toll of Poor Sleep Donald Lloyd-Jones, MD, ScM, was featured.

Reuters, March 29 US FDA Approves Over-the-Counter Sale of Overdose Reversal Drug Narcan Maryann Mason, PhD, was featured.

Investigating the Clinical, Anatomic and Pathologic Correlations of Neurodegenerative Disorders and Aging



Tamar Gefen, '15 PhD, is an assistant professor of Psychiatry and Behavioral Sciences in the Division of Psychology. An academic clinical neuropsychologist and associate director of Clinical Neuropsychology in the Department of Psychiatry and Behavioral Sciences, Gefen codirects the clinical core of the Alzheimer's Disease Research Center (ADRC) within the Mesulam Center for Cognitive

Neurology and Alzheimer's Disease.

Her laboratory, the Laboratory for Translational Neuropsychology, studies neurodegenerative disorders and trajectories of aging through the integration of antemortem features during life and postmortem neuropathology at autopsy, and her clinical work is focused on the careful characterization of dementia syndromes and age-related disorders.

What are your research interests?

I am interested in neurodegenerative disorders and trajectories of human aging, both abnormal and successful. My lab and I conduct our research with the active and generous participation of over 500 ADRC research participants, some of whom are cognitively-normal and others who are diagnosed during life with a range of disorders like dementia of the Alzheimer's type, or frontotemporal lobar degeneration. We also recruit SuperAgers, individuals over 80 years old with extraordinary memory ability. We follow these individuals longitudinally throughout their lives, and collect annually a range of cognitive, psychological and biological (blood, MRI imaging, etc.) data. Many of these participants donate their brains postmortem.

My research focuses on the clinical, anatomic and pathologic correlations of cognitive decline, successful aging and neurodegenerative dementias. We are constantly asking questions about the vulnerability of brain regions to disease. Why does Alzheimer's disease target memory regions of the brain leading to memory loss? What are the factors that contribute to exceptional memory capacity in SuperAgers? How does neurodegenerative disease lead to symptoms that can strip away a person's ability to speak, to move, to emote — all necessary elements of personhood and self-identity? By matching antemortem behaviors with changes found at autopsy at the cellular level, we can begin to address these exciting questions.

What is the ultimate goal of your research?

The ultimate goal of my research is to help identify a biomarker, treatment or cure to neurodegenerative dementias.

But before this can happen, function or dysfunction in the brain needs to be linked to its structural counterpart; for example, that the cognitive disorder (progressive memory loss) observed in the clinic is caused by a distinct microscopic pathology (Alzheimer's disease). Establishing these clinicopathologic correlations in dementia is a more immediate goal. Without this critical step, it would not be possible to develop a sensitive or specific biomarker for early detection of disease, let alone a viable treatment. There is a quote that hangs in the lab, "structure without function is a corpse; function without structure is a ghost" (Vogel and Wainwright, 1969); these two components rely on each other for an in-depth study of the anatomic and histologic basis of human behavior.

How did you become interested in this area of research?

I became interested in establishing clinicopathologic correlations in dementia in my first year as a PhD student at the Mesulam Center. On a single floor, there are social workers, anatomists, neurologists, psychologists and molecular biologists, all of whom are working towards the goal of helping those suffering from dementia. I was training to become a clinical neuropsychologist, which entails the administration and interpretation of psychometric tests to characterize human cognition and behavior. But I wanted to understand the human brain multidimensionally, tangibly — through interview and assessment — and by holding the organ itself, dissecting it, examining its architecture and its chemistry. Over the years, and with instrumental support from Center mentors that crossed several scientific and medical disciplines, I established the first lab at Northwestern that bridges clinical neuropsychology with anatomic pathology.

Who inspires you?

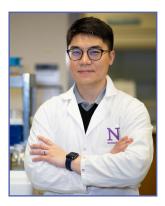
My patients and participants inspire me, and so do their families. Many choose to donate their brain after death, and so I am fortunate to know these individuals intimately in both life and in death.

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

The Northwestern ADRC is one of 33 centers nationwide committed to improving diagnosis and care for people with Alzheimer's disease and related disorders, as well as working to prevent or treat these diseases. The ADRC network is by its nature and design highly collaborative. As co-director of the clinical core, I meet with members of other ADRCs, and other national and global institutions, to discuss how we can pool resources to address common questions. The same is true for internal collaborations across campus; my lab is collaborating with investigators in the Departments of Psychiatry and Behavioral Sciences, <u>Neurology</u>, <u>Pathology</u> and <u>Preventive</u> <u>Medicine</u> to tackle research topics ranging from cognitive dysfunction to glial biology.

Pursuing Further Exploration of the Unknown

Calvin Law, fifth-year PhD student, Driskill Graduate Program



Law graduated from the University of Minnesota, where he studied microbiology. Now working in the laboratory of Jaehyuk Choi, MD, PhD, the Jack W. Graffin Professor, Law aims to identify the transcriptional regulators of T-cells implicated in autoimmune diseases.

Where is your hometown? I've always found this question difficult to answer. I was born in

Rochester, Minnesota, but I was raised in Taiwan. I moved back to the states when I was 15 years old and lived in Minneapolis, Minnesota for the next 10 years before moving to Chicago. I think I would say Kaohsiung city, Taiwan is my hometown.

What sparked your interest in science or medicine?

My father was a surgeon in Taiwan and my inspiration to pursuing a career that can benefit all people. While I initially had planned on going to medical school, my undergraduate research experience opened my eyes to the excitement of discovery. Combined with my natural inclination to solve problems, pursuing a career in research seemed more appealing.

What are your research interests?

I have always been interested in studying immunology. The many ways our immune system protects us from infections

(virus or bacterial) and even ourselves (autoimmunity and cancer) has always fascinated me. I am most interested in understanding the circuitry of our immune system so that we may harness it and finetune to our needs, whether we are combating new forms of infection or diseases originating from within.

What are you currently working on?

I am currently working on identifying major transcriptional regulators of a pathogenic T-cell subset found in autoimmune diseases such as rheumatoid arthritis and systemic lupus erythematosus. My ultimate goal is to identify potential therapeutic targets that allows us to 'calm down' autoreactive T-cells.

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

The fruition of my training at Feinberg became apparent to me when I began mentoring undergraduate student lab assistants and graduate school rotation students. Being able to explain the science behind our lab's research and my project to my mentees and guiding them to perform experiments was a reflection on how much I have learned during my time in the program.

What do you hope to do with your degree?

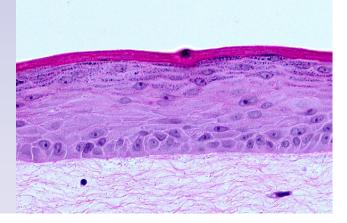
I hope to continue honing my skills in research whether it be in academia or industry. I have learned so much during my time at Feinberg and I would like to continue learning to identify new ways to better the lives of all people.

Breakthroughs Podcast

Advancing Skin Cell Biology with Kathleen Green, PhD

Skin diseases from psoriasis to melanoma affect as many as one in three Americans at any given time. Kathleen Green, PhD, has greatly advanced basic molecular research related to skin diseases. She discusses recent discoveries in her lab that could lead to future therapeutic targets.

Listen to the episode.



Using Neuroimaging to Understand Cognitive Aging Jaiashre Sridhar, research data analyst, Mesulam Center for Cognitive Neurology & Alzheimer's Disease



After attending PSG College of Technology in Coimbatore, India, for her undergraduate studies, Sridhar travelled to Texas to complete her master's at the University of Texas at Dallas.

At the Mesulam Center, she analyzes imaging data to improve the understanding of brain volume and function decline in people living with primary progressive aphasia.

Read a Q&A with Sridhar below.

Where is your hometown? I am from Coimbatore, India.

What led you to Northwestern?

My interest in neuroscience stemmed from my undergrad in India during a guest lecture, and after an internship in computational neuroscience, I applied to do my master's in neuroscience in the United States. During my master's, I worked in an addiction research lab in Dallas where I gained my first-hand experience with neuroimaging. After graduation, I landed at Northwestern University in 2014 for a job as a neuroimaging data analyst and have been here ever since.

What are you currently working on?

I am currently working on using magnetic resonance imaging (MRI) data to understand the decline of brain volume and function in patients with primary progressive aphasia. I am also working on using MRI to study why an exceptional category of elderly population possessing superior memory, called Super Agers, resist typical age-associated changes in the brain.

How does your work support the research enterprise at Feinberg?

I am the lead data analyst and manager of the Imaging Lab at the Mesulam Center. Our center has multiple imaging projects supported by several R01s, U19 and P30. My work involves managing the MRI and PET imaging data acquired through these projects and development of processing and analysis pipelines for the images. The images are then used to study the changes in the brain corresponding to the disease. The images, processed or in their raw form, are also made available to our internal and external collaborators to facilitate research.

Why do you enjoy working at Northwestern?

I am passionate about brain research and the application of novel imaging tools and analytical strategies. I enjoy that my role poses new challenges and learning opportunities every day. The most rewarding and fulfilling part of my role is knowing that my work has direct implications on the community suffering from debilitating diseases.

New Faculty

Philip Gorelick, MD, MPH, joined Feinberg as professor of Neurology in September 2022. Gorelick is a clinical researcher whose main interests are in the areas of stroke prevention and treatment and the exploration of defining, preventing and treating vascular causes of cognitive impairment with the ultimate goal of ensuring maintenance of brain health across life's key epochs. Gorelick has served as a lead author or co-author on national guidance statements on stroke prevention, vascular contributions to cognitive impairment, and brain health. Previously, he was professor of translational science and molecular medicine at Michigan State University and the emeritus medical director of the Hauenstein Neuroscience Center at Saint Mary's Health Care in Grand Rapids, Michigan. He went to medical school at Loyola University and received his Master of Public Health degree from University of Illinois, Chicago.





NUCATS connects scientists to a wide variety of funding opportunities to meet the special needs of each stage of the clinical and translational research continuum. Browse the Institute's updated <u>funding page</u> for information on opportunities or visit the <u>Research Resources</u> page and sort the directory by "funding."

NUCATS also curates and manages the Feinberg Research Pilot Funding <u>directory</u>, which houses a comprehensive list of pilot and seed grant opportunities at the medical school.

If you would like additional information on NUCATSsupported funding mechanisms, please email <u>NUCATS-funding@northwestern.edu</u>.

// Science in Translation//

The NUCATS Institute hosts *Science in Translation*, a podcast featuring Feinberg scientists who are dedicated to accelerating how fast they can move a transformational finding in a lab into a treatment, cure, or solution that will improve human health. Scientists also share how tools and resources available through NUCATS have benefited their careers.

The most recent <u>episode</u> features the story of how NUCATS and Chicago State University are joining forces on a joint mission to foster cross-institution biomedical collaborations in research, training, and education and to accelerate the development of a diverse and inclusive biomedical workforce. In this episode, Matthew Fete, PhD, Dean of Pharmaceutical Studies at Chicago State University College of Pharmacy, and <u>Susanna McColley, MD</u>, director of the NUCATS Institute's TL1, Multidisciplinary Training Program in Child & Adolescent Health program, highlight the initiatives that are driving this mission.

Tamar Gefen

From page 5

How is your research funded?

My research has been funded primarily by the National Institute of Aging, and my students have secured their own funding through the National Science Foundation.

Where have you recently published papers?

We have published recently in high-impact journals that include <u>Brain</u>, <u>Cell</u>, and <u>Journal of Neuroscience</u>. I am so proud of my students and research assistants. Their dedication and creativity have led to significant contributions to scientific knowledge of neurodegenerative disease, aging and the

NIH News

ClinicalTrials.gov is Modernizing to Serve You Better

ClinicalTrials.gov is the world's largest database of privately and publicly funded clinical trials. The National Library of Medicine (NLM) is in the midst of a multiyear effort to modernize ClinicalTrials.gov to deliver an improved user experience on an updated platform that will accommodate future growth and enhance efficiency. In June 2023, the team will reach an important milestone: replacing the current website with the modernized ClinicalTrials.gov website. This modernized site will implement the innovations we have designed on user feedback, including an updated look and feel and improved functionality for searching, viewing and downloading information about clinical trials.

NIH Clinical Trials Reporting Compliance: A Shared Commitment

As the largest public funder of clinical trials in the United States, NIH is committed to the timely dissemination of clinical trial results information so that the benefits of the trial can be realized. In support of this goal, in September 2016, NIH issued the NIH Policy on **Dissemination of NIH-funded Clinical Trial Information** to establish the expectation that summary results of NIH-supported clinical trials to be submitted to ClinicalTrials.gov within 365 days of the actual primary completion date. This policy is complementary to a 2016 updated HHS regulation aimed at further increasing the availability of information about clinical trials. This policy has already proven to be effective as recent analyses have demonstrated increased clinical trial results information reporting. However, NIH has committed to updating their internal controls over the course of the last five years NIH to improve the ability to track and enforce clinical trails information submission.

Request for Information: Re-envisioning U.S. Postdoctoral Research Training and Career Progression within the Biomedical Research Enterprise

The NIH seeks information from extramural research community members regarding the current state of postdoctoral research training and career progression within the biomedical research enterprise. NIH is particularly interested in understanding the perspective and experience of recent and current postdoctoral trainees, postdoctoral office leaders as well as graduate students considering becoming postdoctoral trainees within the academic sector. <u>Click here to submit your</u> <u>thoughts</u>.

Sponsored Research

PI: <u>Lisa Beutler</u>, <u>MD</u>, <u>PhD</u>, assistant professor of Medicine in the Division for Endocrinology

Sponsor: American Diabetes Association

Title: Dissecting sugar-induced modulation of gut-brain circuits



What area of diabetes research does

your project cover? What role will this particular project play in preventing, treating and/or curing diabetes?

Excessive sugar intake is clearly linked with the development of diabetes and obesity, but the mechanisms underlying this association is incompletely understood. This project aims to determine how excessive sugar intake disrupts gut-brain communication and alters neural responses to nutrients in ways that promote the development of these metabolic diseases. It will additionally address whether manipulating the activity of neural populations disrupted by sugar overconsumption can counteract the adverse metabolic effects of a high sugar diet. By dissecting in unprecedented detail how diet composition alters the function of the neural circuits that regulate body weight and blood glucose, this work will reveal novel approaches to treat and prevent diabetes and obesity.

Why is it important for you, personally, to become involved in diabetes research? What role will this award play in your research efforts?

As a clinical endocrinologist, I treat patients with diabetes and obesity every week. It is an exciting time in this field with rapidly improving treatment options finally available to patients. But there is much we still do not understand about the development and progression of these diseases, and unraveling these mechanisms has the potential to transform therapy and even lead to a cure for them. This is what motivates my research program. The ADA Pathway to Stop Diabetes Award will transform my research efforts, enabling my lab to invest in the most cutting-edge neuroscience tools in order to understand how diet promotes metabolic disease by altering neural activity. The goal of this work is to identify and test novel approaches to treat diabetes and obesity.

In what direction do you see the future of diabetes research going?

Advances in technology have enabled the generation of incredibly large and complex neuroscience datasets. This includes the type of single cell resolution neural recording data we will collect as part of this project. A major challenge for the future will be to understand what these data are telling us and how to translate this understanding into treatments for diseases that affect brain function, including diabetes and obesity. This will require collaboration across the fields of neuroscience, endocrinology, computer science, and engineering. As a physician-scientist, it is my goal to lead interdisciplinary groups to pioneer circuit-based therapies for metabolic diseases. PI: Jason Miska, PhD, assistant professor of Neurological Surgery

Sponsor: National Cancer Institute

Title: The hypoxic niche in glioblastoma is maintained by myeloid produced creatine

Glioblastoma (GBM) is the most common brain tumor malignancy in adults that is



characterized by unique niches termed pseudo-palisading necrosis. These hypoxic regions are a defining feature of the disease which promote chemoresistance, radioresistance, and ultimately drive disease progression. Understanding the generation and sustainment of these regions is critical to understanding how effectively treat the disease. Multi-omics analysis of human GBM patients reveals that the creatine transporter, Slc6a8 is specifically expressed by tumor cells in hypoxic and necrotic regions. Surrounding these regions are tumor-associated myeloid cells (TAMCs), which are the most abundant infiltrating immune cell in GBM. Surprisingly, the TAMCs that surround the hypoxic pseudopalisading regions express the enzymes necessary to produce creatine. Therefore, we hypothesize that TAMC-derived creatine promotes the generation of the pseudo-palisading necrotic niche in GBM, and that this metabolic crosstalk promotes both GBM fitness and therapy resistance.

Previous work has identified that the hypoxic pseudo-palisading niche contains glioma stem cells (GSC), which are generated by the hypoxic stress of these regions. Furthermore, Slc6a8 is directly regulated by hypoxia, suggesting creatine uptake exerts a role on GSC phenotypes. Thus, the first aim of this proposal is to examine how creatine transport influences GSC phenotypes in both human and mouse models of GBM. In this aim, we will also utilize inducible models of GBM that recapitulate the genetic and pathologic features of human GBM to determine if Slc6a8 is necessary for the formation of the hypoxic pseudo-palisading niche in tumors. Our preliminary data indicate that TAMCs isolated from both mice and humans with GBM are proficient producers of creatine. Furthermore, we found that this metabolic phenotype is specific to the tumor microenvironment (TME) and is induced by extracellular lactate. Thus, the second aim of this proposal will examine how the ablation of creatine biosynthesis by TAMCs controls tumor growth and progression in mouse models of GBM. This aim will also determine how lactate induces the creatine biosynthetic phenotype of TAMCs in GBM. The third aim of this proposal is to examine if a clinically relevant inhibitor of creatine transport influences GBM growth. We will test how this inhibitor works in the context of chemo and radiotherapy to determine how creatine uptake influences GBM recurrence. To establish translatable value from this work, we will generate tumor samples and patient-derived xenografts from patients, screen them for expression of creatine metabolic genes, then assess sensitivity to creatine metabolic inhibitory therapy. The results of this aim will identify if blocking TAMC-to-tumor metabolic communication is a feasible strategy for GBM therapy.

Read more about this project.

Read more about this project.

Funding

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

Accelerating Drug Discovery for Frontotemporal Degeneration More information

Sponsor: Alzheimer's Drug Discovery Foundation Letter of intent: May 19 Invited full proposal: July 28 Upper amount: \$200,000

The Alzheimer's Drug Discovery Foundation (ADDF) and The Association for Frontotemporal Degeneration (AFTD) seek to accelerate and support innovative small molecule and biologic drug discovery programs for frontotemporal degeneration. The funding priorities include lead optimization of novel disease-modifying compounds, including medicinal chemistry refinement and in vitro ADME; as well as *in vivo* testing of novel lead compounds, biologics or repurposed drug candidates in relevant animal models for pharmacokinetics, dose-range finding, targeting engagement, in vivo efficacy and/or preliminary rodent tolerability studies.

Climate and Health Interdisciplinary Awards More information

Sponsor: Burroughs Wellcome Fund Deadline: August 31 Upper amount: \$375,000

The Burroughs Wellcome Fund Climate and Health Interdisciplinary Award provides support for collaborative exploratory work that opens new ground for comprehensively assessing or mitigating the impacts of climate change on human health. This program will support both individual scientists and multi-investigator teams. Early career faculty and postdoctoral fellows nearing their transition to independence are encouraged to apply. The goal is to prime new discoveries in areas that are difficult to reach through discipline-specific, silo-driven approaches.

Read more about the highlights of our educational programs, innovative research and discoveries, and our outstanding students, faculty, and staff in the <u>Feinberg News Center</u>.

Fundamental Research to Understand the Mechanisms of Neurotropic Virus-mediated Disease More information

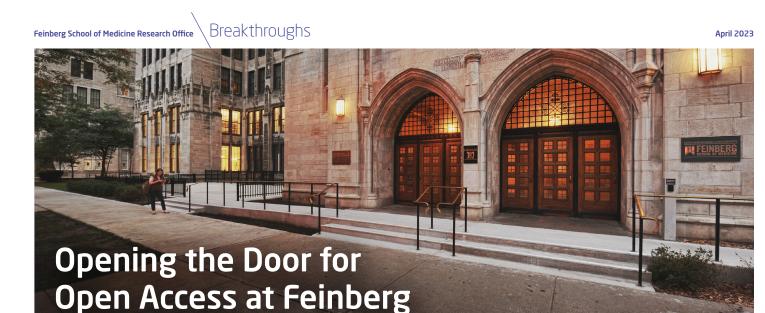
Sponsor: National Institutes of Health (NIH) and National Institute of Allergy and Infectious Diseases (NIAID) Deadline: August 25 Upper amount: NIAID intents to commit \$2.8 million to fund 5–6 awards

The purpose of this funding opportunity is to promote basic research to better understand the mechanisms underlying viral invasion of the central nervous system, virus-and/ or host immune-mediated neuropathogenesis and the associated clinical manifestations for emerging and reemerging neurotropic viruses. This funding opportunity is intended to stimulate interest in this understudied research area with the goal of gaining a better understanding of the fundamental mechanisms that underlie acute viral neuropathogenesis and its associated clinical manifestations. In turn, this would provide a solid foundation for future research to understand the long-term effects of neurotropic viruses and for the development of effective prevention and treatment interventions.

Implementing and Evaluating New Models for Delivering Comprehensive, Coordinated, Person-Centered Care to People with Long COVID (U18) More information

Sponsor: Agency for Healthcare Research and Quality (AHRQ) Deadline: June 12 Upper amount: AHRQ intends to commit \$9 million to fund up to 9 awards

This opportunity will support existing, multidisciplinary Long COVID clinics in the United States in developing and implementing new or improved care delivery models that enhance access to care and quality of care for people with Long COVID, particularly underserved, rural, vulnerable, or minority populations that are disproportionately impacted by the effects of Long COVID. Many minority and at-risk populations for Long COVID face barriers that can worsen the impact of Long COVID on their lives and complicate their recovery. Examples of such barriers include difficulty with healthcare access, communication, and Internet accessibility; lack of health insurance; greater medical and social vulnerabilities; and many more.



By Karen Gutzman, Head, Research Assessment and Communications Librarian

Open access (OA) publishing can present a myriad of options and challenges to authors. Though many funders require research outputs to be made publicly accessible, there are authors who wish to publish OA regardless of any funderrelated mandate. These authors have many decisions to make, including selecting appropriate OA journals and deciding which type of OA publishing suits their needs. Ultimately, the decision to publish OA can be hindered by the cost of article processing fees (APCs).

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Finally, research funders may also support authors who choose to publish open access. NIH-funded investigators may consider including the cost of publishing in their NIH grant applications, according to the <u>NIH Grants Policy Statement</u>. Some funders, like the NIH, allow APCs to be included in the initial grant budget, while others allow grantees to use remaining research funds for APCs, offer a dedicated open access fund, or distributes OA funds via block grant or overheads as part of an individual grant. SpringerNature has <u>compiled a list of research funders</u> and institutions worldwide that fund OA APCs to see if any of these options apply to your grant.

If you have any questions or need assistance with finding OA journals, please contact your Galter <u>liaison librarian</u>.

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Featured Core

Neurodevelopmental Core

The mission of the <u>Neurodevelopmental Core</u>, part of Northwestern's <u>Institute for Innovations in Developmental</u> <u>Sciences</u>, is to ensure that rigorous neurodevelopmental research methods are accessible for all Northwesternaffiliated investigators, faculty and students.

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Core services include:

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