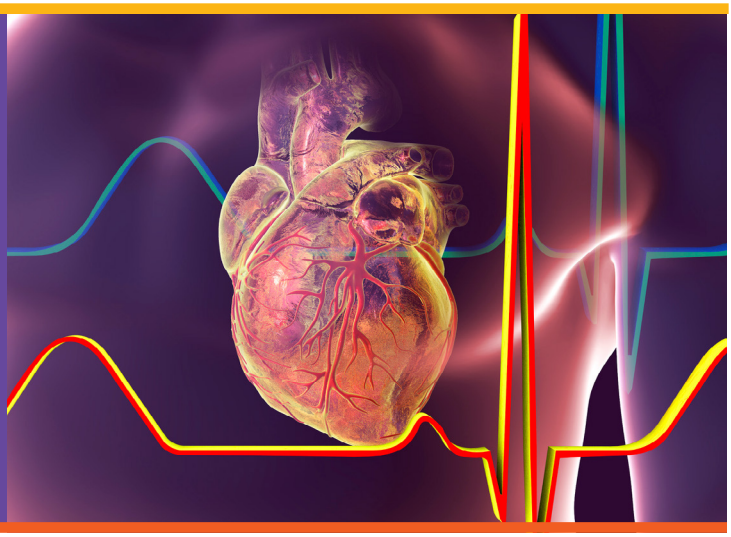
Breakthroughs

Feinberg School of Medicine Research Office

March 2022

Pursuing Deeper Understanding about the Most Common Type of Heart Failure



By Melissa Rohman

Of the estimated five million patients in the U.S. diagnosed with heart failure annually, nearly half will have heart failure with preserved ejection fraction (HFpEF). Also known as diastolic heart failure, HFpEF occurs when the heart's lower left chamber loses its ability to relax and fill up with enough blood in between in each heartbeat.

To compensate, the heart increases pressure inside the ventricle to properly fill with blood. This increased filling can cause fluid buildup in the lungs, leading to shortness of breath, fatigue, irregular heartbeat and ultimately heart failure.

While HFpEF accounts for most heart failure-related hospitalizations in the U.S. for people over 65, there is still limited understanding about the underlying biological mechanisms and how to effectively prevent and treat the disease.

At the forefront of HFpEF research are investigators at the Feinberg School of Medicine, who were recently awarded an $18.1 million grant from the National Institutes of Health (NIH) to study the underlying pathophysiology of HFpEF. The grant is part of the NIH's HeartShare program, a multi-institutional research effort with the goal of characterizing the mechanisms driving HFpEF and identifying new therapies.

Sanjiv Shah, '00 MD, the Neil J. Stone, MD, Professor of Medicine in the Division of Cardiology and director of Northwestern Medicine's Bluhm Cardiovascular Institute - Clinical Trials Unit, will lead HeartShare's Data Translation Center at Northwestern, which will coordinate patient phenotypic data for all six HeartShare program sites.

"The HeartShare grant from the NIH is a phenomenal opportunity to continue our research to improve the classification of the heterogeneous HFpEF syndrome, understand the biological basis of HFpEF phenotypes and set the stage for precision medicine clinical trials for HFpEF," said Shah, who is also director of the Center for Deep Phenotyping and Precision Therapeutics in the Institute for Augemented Intelligence in Medicine.

Northwestern will also be home to one of HeartShare's six clinical centers. Sadiya Khan, '09 MD, '14 MSc, '10, '12 GME, assistant professor of Medicine in the Division of Cardiology and of Preventive Medicine in the Division of Epidemiology will lead the center, along with Laura Rasmussen-Torvik, PhD, chief of Epidemiology in the Department of Preventive Medicine, to recruit and enroll patients with HFpEF.

(continued on page 2)

Northwestern Medicine®

Heart Failure *(continued from cover page)*

"Collectively, the field has come far, but we have not sufficiently addressed HFpEF. Uniquely here at Northwestern, we have the talent and now the resources to allow us to further study the pathophysiology of this particular iteration of heart failure," said Clyde Yancy, MD, MSc, the Magerstadt Professor and vice dean for Diversity and Inclusion, chief of Cardiology in the Department of Medicine and a professor of Medical Social Sciences.

Improving Diagnosis and Treatment

HFpEF is one of the most challenging cardiovascular conditions to diagnose and treat. Unlike heart failure with reduced ejection fraction, there are currently no clear diagnostic tests for HFpEF. Healthcare providers must rely on interpreting patient signs and symptoms or cardiac imaging results, which often leads to a missed diagnoses.

A lack of clear definitions for subtypes of HFpEF has also contributed to confusion and misdiagnosis, therefore not all HFpEF patients receive the same treatment, and while some proven treatments are available and FDA-approved, long-term benefit is limited.

"Major work is still necessary in the areas of increasing recognition and diagnosis of HFpEF, discovering new biological pathways underlying the HFpEF syndrome, and identifying and validating novel phenotypes of HFpEF that can be targeted with specific therapies, which is consistent with our goal of advancing precision medicine for common, heterogeneous disorders like HFpEF," Shah said.

Nevertheless, Shah added that in the past 15 years, investigators have learned more about the underlying biological basis of HFpEF. For example, risk factors such as physical inactivity, obesity, metabolic stress, hypertension and autoimmune diseases contribute to the development of HFpEF.

In 2007, Shah developed the world's first HFpEF-dedicated clinical program at Northwestern to improve HFpEF prevention, diagnosis, treatment and prognosis. In February, his team found that patients with HFpEF could benefit from an atrial shunt, publishing their findings in *The Lancet*. The novel, minimally invasive device which is placed through a catheter could potentially lower pressure in the heart's left atrium and reduce HFpEF symptoms.

Northwestern's recent support from the NIH will expand upon this work, enabling Feinberg investigators to further study HFpEF to improve diagnosis, treatment and patient outcomes. Additionally, Feinberg investigators have already made significant contributions to the advancement of HFpEF treatments and identifying at-risk patient groups.

In a study published in *Nature Medicine,* a team of investigators including Shah and Khan found that dapagliflozin — a drug commonly used to treat type 2 diabetes — improved symptoms and physical limitations in patients with HFpEF.

Utilizing Machine Learning

Feinberg investigators have also employed machine learning to identify patients diagnosed with hypertension who were at risk of HFpEF. Led by Yuan Luo, PhD, associate professor of Preventive Medicine in the Division of Health and Biomedical Informatics and chief AI officer for the Institute for Augmented Intelligence in Medicine, the team used machine learning technologies to identify subgroups of patients with hypertension who expressed abnormal cardiac mechanisms.

"Such subtyping is important for heterogeneous clinical syndromes like hypertension and HFpEF," Luo said. "Our results offer new avenues to systematically and coherently deriving such subtypes, which can lead to earlier identification of targeted interventions and improve patient outcomes."

Expanding Cardiovascular Research and Care

Northwestern will soon have the opportunity to increase its cardiac care capacity with the creation of Northwestern Medicine's new Bluhm Heart Hospital at Northwestern Memorial Hospital. Made possible by Chicago philanthropist Neil G. Bluhm and the Bluhm Family Charitable Foundation, the hospital will expand cardiovascular research and modernize cardiovascular care services at Northwestern and help Feinberg investigators recruit more patients in clinical trials with greater speed and diversity.

"With the new Bluhm Heart Hospital we hope to expand the multidisciplinary nature of our program, see more patients, and offer even more clinical trials," Shah said. "In addition, we are one of the leading centers for developing interventional HFpEF therapies, and our vision is to house a center for interventional heart failure therapies in the Bluhm Heart Hospital where we can develop and test novel interventional treatments for our HFpEF patients."

CONTENTS

Feinberg Hosts 2022 Research Retreat

By Haleigh Ehmsen

Nearly 200 principal investigators from Northwestern University Feinberg School of Medicine gathered at the Fairmont Hotel for discussion and brainstorming to generate the research priorities that will help guide the Feinberg research enterprise for the next five years.

"We gather to reflect on where we have been and where we are going," said Eric G. Neilson, MD, vice president for Medical Affairs and Lewis Landsberg Dean of the Feinberg School of Medicine.

Rex L. Chisholm, PhD, vice dean for Scientific Affairs at Feinberg, presented data that showed an increase in research funding and research activity has contributed to improved rankings by the National Institutes of Health and U.S. News and World Report, as well as more support for the growing faculty and student populations.

In 2021, Feinberg received $610.4 million in funding, which is a nearly 30 percent increase since FY17 when the last retreat was hosted.

To continue to grow and stand out in a competitive biomedical research landscape, Chisholm noted that Feinberg must outline strategic priorities to improve human health and contribute to novel research discoveries.

In three rounds of discussion, the scientists discussed and shared impactful and strategic research ideas for Feinberg leadership to consider. During each round of table discussion, participants had the opportunity to share comments and ideas through an online application called Slido that was accessible via phone or computer. The ideas were projected onto screens around the room.

Hundreds of thoughts and suggestions generated during the retreat were recorded for future use and review. The event was managed by the University Office of Administration and Planning, with support from Northwestern Information Technology and Special Events.

Attendees were able to share their feedback and responses via an app called Slido on their computers or by smartphone.

Faculty discussed the research priorities of Feinberg and enjoyed seeing colleagues in-person at the retreat in February.

The sponsor group for the retreat will meet post-retreat to review the data gathered and form a proposal for strategic research areas.

The retreat was hosted by Dean Neilson and Chisholm.

Breakthroughs Podcast

David Gate, PhD, assistant professor in the Ken and Ruth Davee Department of Neurology discusses his study on the detrimental role the immune system plays in Lewy body dementias. Gate's new research published in *Science* suggests pathways toward unprecedented treatment for this devastating disease.

The Gate Laboratory is focused on the intersection of the immune system and neurodegenerative disease. Interested especially in genomics, Gate and his team use human samples to identify potential disease targets as well as therapeutic modalities for neurodegenerative disorders.

Graduate Student/Post-Doc Events and Opportunities

Breaking Open the Word
Friday, March 18 and 25
12:10 to 1:00 p.m.

Gospel reading, reflection and interpretation each Friday during the academic year. Join other students, staff, and faculty during the academic year to reflect on the upcoming Sunday gospel reading. Bring your lunch and enjoy an inspiring lunch hour! Located at the Religious Life Center, Level M.

Religious Life Center, Level M
Abbot Hall
710 N. DuSable Lake Shore Drive, Chicago
More information

CDB Seminar: Regulating Heart Regeneration: Kenneth Poss, PhD
Thursday, March 24
9 to 10:00 a.m.

The Department of Cell and Developmental Biology presents "Regulating heart regeneration" with Kenneth Poss, PhD. Tissue regeneration involves the rewiring of expression of hundreds to thousands of genes, shifting focus of an organ or appendage from function to morphogenesis. Understanding how these changes in gene expression are orchestrated and interpreted is a great challenge in the field of regenerative biology. Poss will describe findings from his lab that relate to new concepts and applications in gene regulation during regeneration.

Robert H Lurie Medical Research Center
Lurie 1-123
303 E. Superior St., Chicago
More information

PCCM Grand Rounds: Pulmonary Disease and Critical Care Medicine Division
Wednesday, March 30
12 to 1:00 p.m.

All conferences will have a joint videoconference session. Fellow research talks, morbidity, MICU outcomes, challenges, journal club or a dual faculty/fellow presentation.

Prentice Women's Hospital
Conference Room M
3rd Floor
250 E Superior St
More information

Simpson Querrey Institute for Epigenetics Distinguished Lectureship
Tuesday, April 5
10 to 11 a.m.

The Simpson Querrey Institute for Epigenetics presents Bing Ren, PhD, professor of Cellular and Molecular Medicine at Luwdig Institute for Cancer Research at University of California San Diego.

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

Research in the News

***US News & World Report*, February 10**
Coronavirus can destroy the placenta and lead to stillbirths
Jeffrey Goldstein, MD, PhD, was featured.

***The Washington Post*, February 11**
Bob Saget died of head injury after falling, autopsy says. Here's what to know about head trauma.
Borna Bonakdarpour, MD, FAAN, was featured.

***Chicago Tribune*, February 17**
Vaccination during pregnancy helps protect babies from COVID-19, according to CDC study
Emily Miller, MD, MPH, was featured.

***The Washington Post*, February 17**
Is it safe? In the movie theater business, the question is how much to promise older audiences.
Mercedes Carnethon, PhD, was featured.

***WGN*, February 22**
Facing fibroids as a Black woman: What you need to know
Magdy Milad, MD, MS, was featured.

***Yahoo! News*, February 24**
Over 65? Here's What to Quit Doing Now
Dorothy Dunlop, PhD, was featured.

More media coverage

Employing Bioinformatics and Single-Cell Sequencing to Identify Underlying Mechanisms of Human Disease

Ruli Gao, PhD, assistant professor of Biochemistry and Molecular Genetics

Ruli Gao, PhD, is an assistant professor of Biochemistry and Molecular Genetics and a member of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University. Gao's laboratory utilizes single-cell sequencing technologies and computational methodologies to identify the molecular and cellular mechanisms of human disease, with the ultimate goal of advancing the field of cancer genomics through novel bioinformatics and sequencing approaches.

Q&A

What are your research interests?

As a computational biologist, my research interest is centered around discovering unknown molecular and cellular mechanisms of human diseases using bioinformatics and sequencing approaches. I have played key roles in developing new methods for analyzing high-throughput single cell genome and transcriptome data. My research in cancer genomics has led to the development of paradigm-shifting models for tumor evolution and chemoresistance evolution. My current research laboratory at Northwestern harbors both a wet lab and dry lab under one roof. We are currently developing new single-cell sequencing methods and computational tools to analyze both genotypes and phenotypes from the same cells. With these approaches and tools, we will dissect the functional outcomes of somatic mutations in human cancer and aging diseases.

What is the ultimate goal of your research?

My ultimate goal is to translate our research findings into clinical applications. We are aiming to develop combinatorial therapeutics to treat patients based on the spatial and temporal dynamics of cellular populations within individual patients. We also hope to develop new preventative therapeutics for diverse aging diseases by targeting mosaic mutations in human organs.

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

I have been very fortunate to collaborate with many excellent investigators, including both clinicians and basic research scientists at the Feinberg School of Medicine, the Lurie Cancer Center, Lurie Children's Hospital, Houston Methodist Hospital and MD Anderson Cancer Center. We are working with surgeons and pathologists to perform single cell multi-omics analysis of human tissues, and we also collaborate with local translational scientists to transform our research findings.

How is your research funded?

We are funded by grants from National Institute of General Medical Sciences, the National Heart, Lung, and Blood Institute, as well as funding from Northwestern University and the Lurie Cancer Center.

Where have you recently published papers?

My recent research findings have been published in *Nature Biotechnology*, *Cell*, *Nature Communications*, *Nature Genetics* and more.

Who inspires you? Who are your mentors?

I am very grateful for having multiple great mentors throughout my training stages. My PhD mentor, Dr. Frederic Kaye from the University of Florida, provided me lots of freedom in exploring different research topics including cancer genomics, population genetics, statistics, as well as bioinformatics. My postdoc advisor, Dr. Nicholas Navin at MD Anderson Cancer Center, played key roles in my career advancement, with whom I gained fundamental knowledge and skillsets to develop a career in single-cell computational biology. I was also inspired by several invited speakers during my postdoc training, who encouraged me to be persistent in science. Additionally, I want to thank multiple established investigators who generously shared their experience in how to develop a successful research program.

Macrophage Metabolism and Heart Failure

Mallory Fillip, Driskill Graduate Program in Life Sciences

Mallory Filipp, student in the Driskill Graduate Program in Life Sciences (DGP), studies sterile inflammation, a type of chronic inflammation that occurs in the absence of infection, in the laboratory of Edward Thorp, PhD, associate professor of Pathology in the Division of Experimental Pathology.

Q&A

Where is your hometown?
I grew up in Fitchburg, WI, a small town just outside of Madison.

What are your research interests?
My research interests center around the functioning of the innate immune system, particularly in the setting of sterile inflammation (a type of inflammation in the absence of infection). Medical science is beginning to understand how many diseases are associated with chronic aseptic inflammation, and further understanding and characterizing the derangements causing chronic inflammation is a scientific passion of mine.

More recently I've come to appreciate the impact of chronic inflammation on cardiac function. Another cardinal aspect of my research interest is my desire to apply basic science to clinical problems in medicine. To better prepare myself for this kind of work, I concurrently enrolled in a Master of Science in Biostatistics here at Feinberg, to complement my doctoral degree.

What exciting projects are you working on?
My thesis project in the Thorp lab is at the intersection of immunology and cardiology, where I am studying how macrophage metabolism is associated with heart failure with preserved ejection fraction (HFpEF). Little is known about the role of innate immunity during HFpEF, so my thesis began with characterizing cardiac immune cells in a new animal model. I found that macrophages had significant changes in lipid metabolism during HFpEF and that modulating macrophage lipid uptake could reduce monocyte recruitment to the myocardium and improve cardiac function. I've linked this reduction in recruitment to macrophage regulation of splenic hematopoiesis and am currently teasing out the mechanism behind how splenic macrophage lipid metabolism may be fueling the development and progression of HFpEF. My preliminary data and scholarly accomplishments have resulted in an National Institutes of Health Ruth L. Kirschstein Predoctoral Individual National Research Service Award.

In collaboration with Dr. Sanjiv Shah, I am also looking at clinical metabolomics data to try and identify novel metabolic biomarkers of HFpEF outcomes, including how metabolites might be associated with specific inflammatory pathways.

What attracted you to your program?
It was clear from the beginning that the DGP was a highly collaborative interdisciplinary program. Having the opportunity to rotate through several labs was tremendously helpful in finding the best fit for me in many respects: mentorship, scientific area of study and lab environment. I also found the campus to be very lively and the students welcoming and friendly.

What has been your best experience at Feinberg?
DGP's integration within an academic medical center has allowed me to really understand the clinical perspective of my research. On top of regularly discussing with expert clinicians, I had the opportunity to gain first-hand experience in the clinic through the Kids-Inspired Innovation in Careers and Science (KIICS) Program at Lurie Children's Hospital. These experiences have allowed me to improve the clinical relevance of my studies and really exemplified the impact my research will have.

How would you describe the faculty at Feinberg?
Faculty are always willing to talk science or give advice and often treat you as a peer rather than a trainee. This culture was evident even when I was interviewing with the DGP and has remained consistent throughout my time here. I've enjoyed the many joint lab meetings and impromptu collaborative discussions with members across many departments in Feinberg. I've also really appreciated how supportive my mentors have been of me concurrently pursuing an MS in Biostatistics, even when it takes time away from the lab.

What do you do in your free time?
My family holidays growing up were always centered on my Italian grandmother's cooking, from fresh pasta to intricate desserts. I've grown to appreciate the art of cooking and love to recreate her recipes! I also used to play competitive soccer and keep that hobby going by playing in a recreational league in Chicago. In the past few years, I have taken full advantage of Lake Michigan during the summers by biking on the lakefront path and sailing on the weekends!

What are your plans for after graduation?
First and foremost, spend some time traveling! Afterwards, I plan to be involved in clinical trial design and implementation, where I can use my expertise to help better our understanding of the immune response in human disease. My interests remain broad regarding opportunities in various sectors, such as government, industry and academic hospitals.

Grant Support for Microbiology and Neuroscience

Kayla Palmer, MS, research administrator in the Basic Science administration

Kayla Palmer, MS, research administrator in the Basic Science administration, supports investigators in the Departments of Microbiology-Immunology and Neuroscience, along with those at the Department of Cell and Developmental Biology

Q&A

Where are you originally from?
I grew up in the city of Bloomington-Normal, Illinois, about two and a half hours south of Chicago.

What is your educational background?
After graduating high school, I attended DePaul University in Lincoln Park where I received my Bachelor of Science in biological sciences in 2017. I then relocated to Baltimore, Maryland to pursue a Master of Science in biotechnology with concentrations in regenerative medicine and stem cell technologies at Johns Hopkins University.

Please tell us about your professional background.
Prior to joining the staff and faculty here at Feinberg, I coupled my graduate studies and research with my work at the American Physiological Society (APS). While at APS, my primary focus was working with early-stage investigators, postdoctoral fellows, graduate students and undergraduates to promote opportunities and exploration through physiological research, with a specific focus on reaching underrepresented racial and ethnic groups not typically recognized in science, technology, engineering and medical fields.

While I completed my graduate program at Johns Hopkins, I worked with a philanthropic and science-minded group called eNABLE, combining the need for prosthetic appendages like mechanical forearms and hands with functioning fingers to individuals across the globe with congenital deformities and veterans who lost their limbs in battle.

In total, I was able to assist with grant-writing and administering and coordinating projects, awards and programs for close to 800 students, researchers and educators.

Why do you enjoy working at Northwestern?
I enjoy working at Northwestern for a variety of different reasons, and in my short time at Feinberg, there is always another new thing to add to the list. My work environment and day-to-day operations really allow me to explore all aspects of research projects, from inception to close, which makes me appreciate the process and the innovation it takes to be a scientist even more. I also appreciate the many opportunities to learn more about other departments, participate in forums throughout the university and sit in on discussions about the research being conducted throughout the organization.

How do you help scientists at the medical school?
My primary responsibilities as a research administrator is to support eight principal investigators and their lab members in the proposal development, submission, management and closeout of their projects. Each phase of support requires a different set of skills, including assisting with communication with grant officials, managing finances and assisting with program requirements so that research continues to perform well and with few hassles.

What is your favorite part of the job?
Working remotely since my hiring has limited my exploration into the job, but working with and learning more about each project my PIs are working on is extremely fascinating. I enjoy reading about the work that is being proposed during development, as well as seeing how external factors can cause fluctuation in the research being conducted, like how COVID-19 has affected some of the research two or three years in versus the research that only just began in the last six months.

What exciting projects are you working on?
Drs. Chisholm, Rasmussen-Torvik and McNally in the Center of Genetic Medicine are working on a project that involves clinical trials related to the COVID-19 pandemic. Though the recruitment has been slightly delayed, the project is beginning to pick up momentum and I can't wait to see what results come out of the project as a whole.

What do you like to do in your spare time?
When I'm not completing my duties as a research administrator, I am finding a new course to take on Coursera or working on business proposals for dream ventures to pursue with my two sisters. For fun, I love to cook and often challenge myself to find new and inventive ways to create tasteful meals from the remnants in the pantry or refrigerator right before "grocery shopping day." I've most recently taken a liking to baking after binge-watching "The Great British Bake Off" and attempting some of Paul Hollywood's most famous recipes. I am also a card and board game connoisseur of sorts; I'm always challenging someone to play against me in one the games within my 32-game collection.

Anything else we should know about you?
I'm a volunteer-aholic! Though the pandemic has proven many limitations to the places and people I can serve, you can find me participating in two or three service projects every month. Whether that is helping my church's food pantry organize the grocery baskets for our community, being a "day buddy" at a nursing home or being a virtual math tutor, I find that serving is the warmest gift you can give someone.

NUCATS Corner
Clinical and Translational Sciences Institute

Increase the Competitiveness of Your Grant Submission with NUCATS

Northwestern University Clinical and Translational Sciences Institute (NUCATS) continues to offer expert guidance to increase the competitiveness of grant submissions. If you are in the planning stages of an R, U, T or P-type award with significant scope of work and infrastructure needs, you may be eligible for a NUCATS Studio session. These one-hour consultations bring together investigators and leadership from NUCATS and our affiliates to identify relevant resources available to support and enhance the competitiveness of grant submissions. If you'd like to request a NUCATS Studio consultation, please contact our Research Navigator team.

The Institute's First-Submission Studios for early career or new Northwestern University researchers are designed to help investigators who are in the planning stages of a first time K or R grant, or a first re-submission of an R grant.

These efficient consultations include an abbreviated review of how our centers and programs may provide support, maximize efficiency and enhance your grant proposal. The NUCATS team can also provide a letter of support for your grant submission that highlights existing infrastructure and collaboration. To learn more, or to schedule a 30-minute First Submission Studio, contact Senior NUCATS Research Navigator Toddie Hays (312-503-2308), or complete a NUCATS Studio Request Form.

Our Facilities and Other Resources document is a compendium of resources and services available to and provided by NUCATS, our clinical affiliates and university research cores and units. This document is updated biannually ahead of major National Institutes of Health (NIH) deadlines. The NIH requires research proposals to identify the facilities to be used and other resources that are directly applicable to the proposed work unless otherwise noted in a funding opportunity announcement. This document has been created to fulfill that requirement. Request FOR document.

NIH News

New NIH Administrative Supplements Available to Support Diversity Mentorship

NIH is pleased to share the availability of a new administrative supplement that recognizes the important role mentors play in developing future medical researchers. Research has shown mentorship has vast benefits including career progression. Supplements are available for various grant types, including career development, training and Research Project Grants (R01). These grants will provide up to $250,000 in direct costs. Investigators may use these funds to develop curricula or training activities to strengthen mentor training or help foster research career development of students, post-doctorates or other trainees. Proposals are due by April 7. More information is available here.

The Center for Scientific Review (CSR) is Open for Public Comment

The Center for Scientific Review (CSR) draft strategic plan is now open for public comment. This five-year plan will serve as guidance to ensure NIH grant applications receive fair, independent, expert and timely scientific reviews, so NIH can fund the most promising research. CSR hopes to ensure these goals align with NIH's core values – ensuring a high-quality and fair peer-review process. Comments on the strategic plan will be accepted through March 23. View the full plan here.

K99/R00 Candidates Can Continue to Take Advantage of COVID-Related Eligibility Extensions

Under normal circumstances individuals must have no more than four years of postdoctoral research experience to apply for a K99/R00 Pathway to Independence Award. However, due to the COVID-19 pandemic, NIH will continue to allow up to a two-receipt cycle eligibility extension for candidates on K99/R00 applications. Candidates must meet all other eligibility criteria.

Research on the Disparities in Breast Cancer

Recent findings published in *JAMA Oncology* found that individual insurance status and residential zip codes were correlated with overall survival among women with early hormone receptor-positive breast cancer. Additionally, the study found that Black women experienced shorter spans of time free of relapse, as well as overall survival compared with white women.

"This study shows that where you live and what type of health insurance you have can matter," said Betina Yanez, PhD, associate professor of Medical Social Sciences and a co-author of the study. "The findings also suggest that the disparities we see with mortality rates in Black and white women are not just one factor that's predicting these outcomes, it's social determinants of health. It's a mix of structural, individual and environmental factors that are predicting breast cancer outcomes." Read the full story here

Sponsored Research

PI: Hidayatullah Munshi, MD, the Robert and Lora Lurie Professor of Medicine in the Division of Hematology and Oncology

Sponsor: National Cancer Institute

Title: Co-targeting BET Bromodomain Proteins and MNK Kinases in Pancreatic Cancer

A growing body of research has demonstrated that inhibitors targeting bromodomain and extra-terminal domain (BET) proteins, which mediate mRNA transcription, have anti-tumor effects against pancreatic ductal adenocarcinoma (PDAC). BET inhibitors can also normalize the PDAC stroma by suppressing the activation of cancer-associated fibroblasts (CAFs). However, BET inhibitors induce Rac1-mediated activation of MNK kinases, which mediate mRNA translation. Importantly, targeting MNK kinases and the MNK effector hnRNPA1 enhances the efficacy of BET inhibitors. Significantly, MNK inhibitors induce CD8+ T cell infiltration, but their effector function is suppressed by the tumor-associated macrophages (TAMs). Notably, BET inhibitors can decrease the infiltration of TAMs. The objective of this application is to elucidate the mechanisms by which the combination of BET and MNK inhibitors demonstrates anti-tumor responses against PDAC.

The central hypothesis is that the combination effectively targets the cancer cells, modulates the tumor immune microenvironment, and normalizes the pancreatic stroma to suppress PDAC growth. Three specific aims are proposed: 1) Define and target negative feedback loops to enhance the anti-tumor effects of BET inhibitors in vivo; 2) Evaluate the effects of the combination of BET and MNK inhibitors on CD8+ T cell infiltration and activation; and 3) Determine the effects of the combination of BET and MNK inhibitors on the pancreatic stroma.

There are several innovative elements in this proposal, including the novel therapeutic approach to enhance anti-tumor responses in PDAC patients; novel concepts on how the combination therapy of BET and MNK inhibitors modulates the tumor immune microenvironment and the stromal reaction for synergistic anti-tumor responses; and the unique combination of complex models of PDAC, including in vivo orthotopic, organoid, and transgenic mouse models. This proposed research is significant because it will have important clinical-translational implications and should result in the development of novel combination therapies for PDAC patients.

Read more here

PI: Han-Xiang Deng, MD, PhD, research professor in the Division of Neuromuscular Disease in the Ken & Ruth Davee Department of Neurology

Sponsor: National Institute of Neurological Disorders and Stroke

Title: Mouse Model Studies of TMEM230-Linked Parkinson's Disease

Through our previous work funded by the American Parkinson Disease Association and the National Institute of Neurological Disorders and Stroke, we have discovered a new Parkinson's disease (PD) genetic locus on the short arm of chromosome 20, and identified a new PD gene, TMEM230.

TMEM230 encodes a transmembrane protein of secretory and recycling vesicles, including synaptic vesicles in neurons. TMEM230 is the first transmembrane protein of synaptic vesicles identified in PD to date. Our findings, therefore, directly point to the dysfunction of synaptic vesicles in the pathogenesis of PD. The precise physiological functions of TMEM230 and pathogenic mechanism of the TMEM230-mediated PD remain unclear.

Based on the molecular features of TMEM230, and its relationship with synaptic vesicle and endosomal markers tested in our study, we hypothesize that TMEM230 is a trafficking protein of synaptic vesicles, and it may function in synaptic vesicle biogenesis, exocytosis, endocytosis and recycling, and synaptic transmission in neurons. But it remains to be determined where in the subcellular compartments and what functions that TMEM230 plays.

We propose to develop and characterize a total of six TMEM230 mouse models. Successful completion of the proposed studies will provide essential information to understand the physiological function of TMEM230 and the pathogenic mechanism underlying TMEM230-linked PD.

Moreover, since TMEM230-linked PD shows clinical and pathological features compatible with those in classical PD, the outcomes from this study may also have important implications in understanding the pathogenic mechanisms in other forms of PD, including sporadic PD.

Read more here

Funding

Simons Collaboration on Plasticity and the Aging Brain – Transition to Independence Award

More information

Sponsors: Simons Foundation
Submission deadline: April 11
Upper Amount: $495,000

Synopsis: The Simons Collaboration on Plasticity and the Aging Brain (SCPAB) Transition to Independence Award seeks scientists from historically underrepresented groups to research independence in the field of cognitive aging. This includes, but is not limited to, any identifying as Hispanic/Latinx, Black/African American, Native Hawaiian/ Pacific Islander or American Indian/Alaska Native. A previous background in aging research is not required to be considered for this award.

Polsky Urologic Cancer Institute Research Award

More information

Sponsor: Polsky Urologic Cancer Institute of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University
Submission deadline: May 1
Terms of Award: Up to $200,000 annually for a two-year award period

The objective of the Polsky Urologic Cancer Institute Research Award is to increase understanding of urologic cancers and enable novel approaches to the prevention, detection and treatment of these cancers. Research supported through this mechanism should directly address questions in basic, clinical or translational urologic cancer research and result in meaningful data that could lead to subsequent extramural funding.

Pediatric Research Grants

More information

Sponsors: The Gerber Foundation
Submission deadline: May 15
Upper Amount: $350,000

Synopsis: The Gerber Foundation's mission focuses on infants and young children, specifically, prioritizing projects that improve the nutrition, care and development of infants and young children from the first year before birth until three years of age. Major target areas for research include: new diagnostic tools that may be more specific or less invasive, preventative measures and assessment of deficiencies or excesses. This grant specifically is looking for projects that will result in new information, treatments or tools that will result in a change of practice.

Program to Accelerate Clinical Trials (PACT)

More information

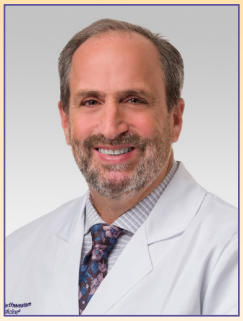
Sponsors: Alzheimer's Drug Discovery Foundation
Letter of intent: May 20
Full proposal: July 22

Upper Amount: $3 million

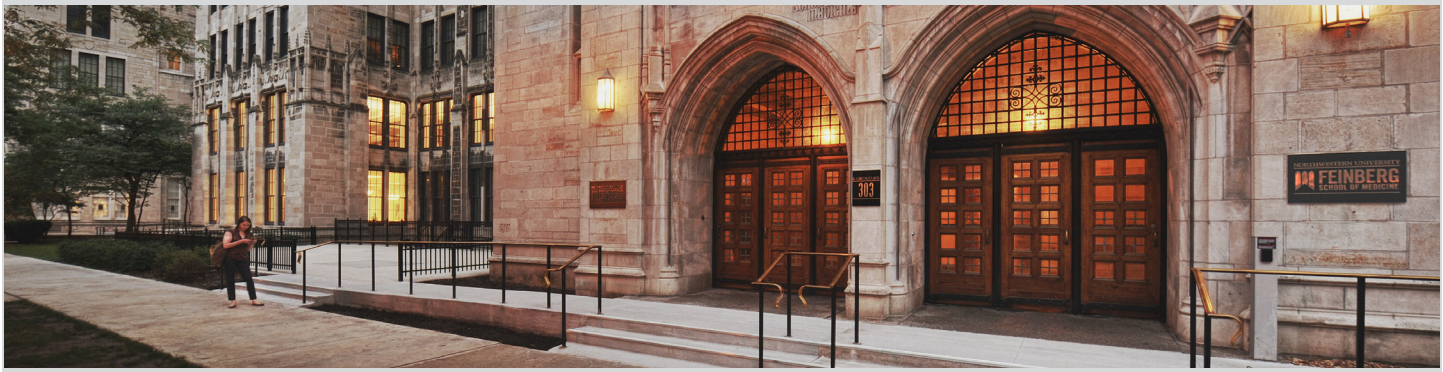
Synopsis: This funding opportunity enables studies and early-phase clinical trials that test promising pharmacological interventions and devices for Alzheimer's disease and related dementias. This opportunity prioritizes diverse drug mechanisms and other modes of action related to the biology of aging and other emerging therapeutic areas for dementia. Novel, repurposed and repositioned drugs, as well as natural products and devices will be considered as types of therapy.

New Faculty

Rudolph J. Castellani, MD, joined as professor in the Department of Pathology in September 2021. Castellani's research interests in neuropathology vary from neurodegenerative diseases to adult and pediatric traumatic brain injury. He is currently a member of the International Consensus Committee for Concussion in Sport. Prior to coming to Northwestern, he was a tenured professor at the University of Maryland, Baltimore School of Medicine, and has directed neuropathology divisions at the University of Maryland Medical Center, Western Michigan University Homer Stryker MD School of Medicine, and West Virginia University.



Reporting Systematic Reviews: Transitioning from PRISMA 2009 to PRISMA 2020



By Q. Eileen Wafford, MSt, MLIS, Research Librarian

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement is an evidence-based reporting guideline for systematic reviews. The original PRISMA statement, published in 2009, presented 27 checklist items under the following sections: title; abstract; introduction; methods; results; discussion; and funding. The corresponding Explanation and Elaboration (E&E) document by Liberati et al. offered descriptions, rationales and examples of each checklist item. At first glance, some checklist items such as Title (Item 1) may appear unnecessary or self-evident to investigators. However, the E&E document provided guidance on how to report the title to communicate research/document type and improve the discoverability of systematic reviews.

PRISMA 2009 highlighted the importance of the PICOS (Participants, Intervention, Comparisons, Outcomes) framework in the systematic review process. For example, it encouraged authors to incorporate the PICOS components in the objective statement (Item 4), eligibility criteria (Item 6) and list of data items (Item 11). PRISMA 2009 emphasized the assessment of risk of bias (Items 12, 15, 19, 22) preferrable with a validated risk of bias tool. Item 24 addressed assessing the quality of evidence, or "summary of evidence," for each outcome in the discussion section of the report. PRISMA 2009 also featured an item (Item 5) for protocol registration. This was an important addition since developing and registering a protocol promoted transparency, reduced bias and helped teams identify areas of potential challenge in the process.

The 2009 guidelines encouraged authors to employ the PRISMA flow diagram (Items 9, 17) to report the flow of records found during the database searches and selection phases.

Changes in methodology and an increase in systematic reviews addressing non-interventional questions led to researchers and stakeholders updating the PRISMA Statement in 2020. Although PRISMA 2020 kept many key elements, there are noticeable differences between the two versions. Like the 2009 document, PRISMA 2020 has 27 checklist items, however, there are now more subitems to report. Other key changes include the following:

- There is a new "Other" section, which now includes the protocol and protocol registration information (Items 24a-24c). This section introduces Item 26, "Competing interest" and Item 27 "Availability of data, code and other materials."
- Subitem 10a and 10b added to "Data items", promotes additional analysis of data items and the data extraction process.
- "Synthesis of Results" expanded from a single item in 2009 to six subitems in 2020 (Items 13a-13f).
- "Study Selection" (Items 16a-16b) in the Methods section places new emphasis on describing the selection processes and tools in more detail.

The PRISMA 2020 Statement introduced four versions of the updated PRISMA flow diagram. The updated flow diagrams offer space for authors to report each searched information source. The new diagrams also present opportunity to document evidence from sources such as websites.

Many journals have established PRISMA 2020 as the standard by which submitting authors should report systematic reviews. The E&E document will help teams that are working on existing reviews to make necessary adjustments. Teams starting a review should familiarize themselves with the PRISMA 2020 recommendations at the start of the process. This will help with developing the protocol and completing a review that makes it to publication.

Take Galter's Conducting a Systematic Review: Part 1 - Planning the Process or Conducting a Systematic Review: Part 2 - Tools & Resources to learn more about the process. Your liaison librarian will also be happy to discuss your review and the Systematic Review service at Galter.

High-Impact Factor Research

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Featured Core

Program Evaluation Core

The Northwestern University Program Evaluation Core supports university investigators of all levels and in areas of study in evaluating their outcomes and success of their grant-funded educational programs and activities. Core staff and faculty work with investigators to design evaluation plans for grant proposals, collect and analyze data, interpret data and results, write reports and co-develop strategies for program improvement. The core provides a range of pre- and post-award services, and offers in-person and online workshops and training programs for university investigators.

The Program Evaluation Core was founded in September 2021 with support from Northwestern University's Office of Research, Feinberg School of Medicine, McCormick School of Engineering and Weinberg College of the Arts and Sciences.

Core services include:

Initial consultations

Proposal writing in pre-award:
- Logic model development
- Evaluation plan
- Text for evaluation section

Post-award services:
- Survey design and administration
- Focus group design and administration
- Interviewing
- Quantitative and qualitative data analysis
- Evaluation report writing
- Development of data-driven program improvement plans

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