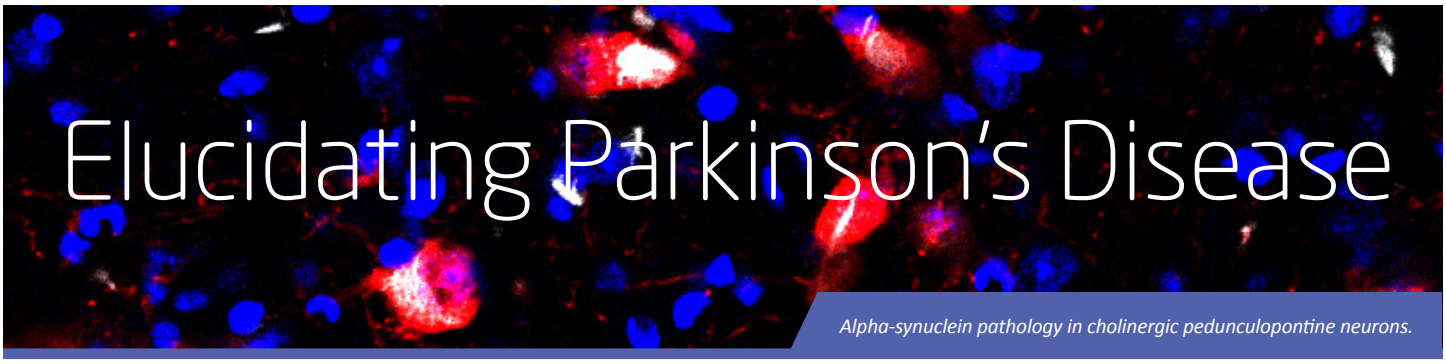
Breakthroughs

Feinberg School of Medicine Research Office

February 2022

Elucidating Parkinson's Disease



Alpha-synuclein pathology in cholinergic pedunculopontine neurons.

By Will Doss

Parkinson's disease is a complex illness. Even with an abundance of basic science discoveries, a curative treatment is still out of reach. However, recent advances have powered a new, deeper understanding of the disease that could reveal the last pieces of this decades-long puzzle and pave the way to a disease-modifying treatment.

Outlining the Stages of Disease

The death of dopamine-producing neurons that innervate the basal ganglia is responsible for the core motor symptoms of Parkinson's disease (PD), which include slowness of movement and rigidity. In a study published in *Nature,* D. James Surmeier, PhD, chair and the Nathan Smith Davis Professor of Neuroscience, found that damage to mitochondria — cellular power plants — in mouse dopaminergic neurons produced a progressive "Parkinsonism" closely resembling that seen in humans with PD.

Investigators found that damage to mitochondria first affected the axons of dopaminergic neurons, causing an inability to communicate with distant parts of the brain, particularly a region called the striatum. It had previously been thought that this communication failure was responsible for the movement difficulty experienced by patients with PD. However, Surmeier's group found that this failure was not enough and resulted in only modest deficits in learning and fine movements. The key impairment in movement only appeared later, when dopaminergic neurons stopped communicating with their closest neighbors in the substantia nigra.

"This suggests that there are at least two major stages in the disease: an early stage where the striatum stops doing its job but where other parts of the brain compensate and a late stage when the basal ganglia begins to disrupt the function of the rest of the brain — this is when symptoms become debilitating," Surmeier said.

The study also demonstrated the feasibility of a new therapy for patients with late-stage PD that uses a gene therapy to boost effectiveness of current therapies, whose efficacy wanes as the disease progresses.

"Our study demonstrates that if you can keep dopamine levels up in the substantia nigra, it may be enough to keep many of the motor symptoms at bay," Surmeier said.

Understanding Cell Waste Management

Another major feature of PD is the neuronal protein alpha-synuclein. In healthy cells, the protein helps vesicles travel from neuron to neuron, but in neurons affected by PD the protein is misfolded, aggregating in large clumps. These clumps in the brain are linked to a variety of harmful effects, including oxidative stress, inflammation and mitochondrial dysfunction.

"Why alpha-synuclein aggregates and why can't the neurons eliminate it — those are the big questions we need to answer," said Joseph Mazzulli, PhD, associate professor in the Ken and Ruth Davee Department of Neurology in the Division of Movement Disorders.

Mazzulli studies how the lysosome, the organelle responsible for waste disposal in the cell, is impeded by alpha-synuclein. In a recent paper published in *Neuron,* Mazzulli found that alpha-synuclein-induced lysosomal dysfunction leads to a buildup

(continued on page 2)

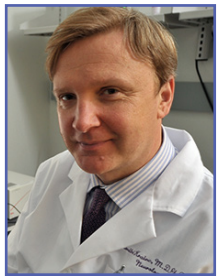
Northwestern Medicine®

Parkinson's *(continued from cover page)*

of malformed proteins that are unable to exit the endoplasmic reticulum and proceed to the lysosome, as would occur in healthy cells. This begets a vicious cycle, where additional proteins aggregate and further impede disposal.

Using patient-derived midbrain neurons modeling the disease, Mazzulli and his collaborators found that an FDA-approved drug — diltiazem — can restore proper folding and prevent clumping of enzymes, representing a possible therapeutic pathway.

"Combining diltiazem with protein trafficking enhancers known as farnesyltransferase inhibitors has shown to be the best strategy for reducing protein aggregates in patient cultures, since they synergistically target two key dysfunctional pathways in PD," Mazzulli said.



Dimitri Krainc, MD, PhD, the Aaron Montgomery Ward Professor and chairman of the Ken and Ruth Davee Department of Neurology, studies lysosomal and mitochondrial function in PD. According to findings published in *Science,* dysfunction of these organelles leads to an accumulation of toxic oxidized dopamine that contributes to preferential degeneration of dopaminergic neurons in PD.

A study from the Krainc laboratory published in *Nature* showed that mitochondria and lysosomes form direct contacts, and recent work published in *Nature Communications* showed that these contacts are disrupted in PD. Based on these findings, the Krainc laboratory used patient-derived neurons to develop and test a new strategy to treat PD by mitigating the effects of dysfunctional lysosomes and mitochondria, as detailed in a study published in *Science Translational Medicine.*

"These key pathological features of PD were only seen in human neurons and not in mouse models, further emphasizing the value of patient-derived neurons for drug development in Parkinson's disease," said Krainc, who is also director of the Simpson Querrey Center for Neurogenetics.

Searching for Biomarkers

As the basic mechanisms underlying PD pathogenesis are progressively uncovered, those discoveries are whisked into a therapeutic pipeline of which Feinberg is an important part. Tanya Simuni, MD, the Arthur C. Nielsen, Jr., Research Professor of Parkinson's Disease and Movement Disorders and director of the Parkinson's Disease and Movement Disorders Center, is the principal investigator on several ongoing clinical trials, including some testing novel therapeutics. However, the trial that could produce the largest benefit is one that's not testing drugs at all.

"While a number of diseases routinely use biomarkers in research and clinical practice, Parkinson's disease still does not have such objective measures," said Simuni, who is also chief of Movement Disorders in The Ken and Ruth Davee Department of Neurology.

This is one reason why Northwestern is one of 50 institutions participating in the Parkinson's Progression Markers Initiative (PPMI), a longitudinal clinical and biomarker dataset involving more than 1,400 participants with idiopathic Parkinson's, individuals with genetic forms of PD, participants with early symptoms of the disease, as well as healthy controls. Simuni serves on the study steering committee and has published extensively using PPMI data, including a recent publication in *Lancet Neurology* detailing 'soft' symptoms that appear before the disease affects daily life.

"PPMI data are essential to developing better tools to advance and accelerate novel therapies for this increasingly common disease of aging," Simuni said.

However, the question of pathways remains: with the variety of pathogenic mechanisms that have been uncovered, devising a single treatment that works for all patients would be exceedingly difficult. Instead, subtyping PD based on genetic mutations and devising specific therapies is the most promising route to a cure, according to Simuni.

"We need to identify the biological signature of individuals' disease and use that to target the relevant pathways," Simuni said.

Better biomarkers — genetic or otherwise — would also aid in the ultimate effort: prevention. PD is often progressing silently for years before a patient comes into the clinic with symptoms, Simuni said, so developing methods to identify PD early is critical to preventing the illness.

"We need to intervene before someone develops the full clinical picture of disease," Simuni said. "To do that, we need biologically-based measures of disease — and that's what we hope to find with PPMI."

CONTENTS

New Potocsnak Longevity Institute Hopes to Lengthen Human 'Healthspan'

By Marla Paul

We want to make it possible to live healthily for a longer period of time.

In the not-too-distant future, you'll be able to check into the Human Longevity Laboratory to find out how old you really are, physiologically speaking.

If the news is less than optimal, clinicians will determine why and check a litany of body systems as well as your neurological and orthopaedic health. Then, you'll be prescribed an intervention to stave off further decline or — better yet — restore your vitality.

Sounds sci-fi, but it's actually the mission of the new Potocsnak Longevity Institute, which launched in January at Feinberg School of Medicine.

The Human Longevity Laboratory is just one part of the ambitious multi-center institute, whose goal is to foster new discoveries and build on Northwestern's ongoing research in the rapidly advancing science of aging.

"The biological processes that drive aging may be malleable," said Douglas Vaughan, MD, director of the new institute and chair of medicine at Northwestern. "We think we can slow that process down, delay it, even theoretically reverse it. The curtain is being pulled back on what drives aging. We want to contribute to that larger discovery process."

The goal of the institute, funded by a very generous gift from Chicago industrialist John Potocsnak and family, is to extend what Vaughan terms the human "healthspan." Scientists and clinicians will address the period of life when people are at the greatest risk for aging-related comorbidities — arthritis, dementia, heart disease, diabetes, aging-related cancer and hypertension and frailty.

"We want to make it possible to live healthily for a longer period of time, not just live longer," said Vaughan, who is the Irving S. Cutter Professor of Medicine. "Aging is the most important risk factor for every disease we care for in adult medicine. If we can push that process back, we can push back the onset of disease."

The new institute builds on the decades of work by Vaughan and scientists across Northwestern, unifying programs studying populations that seem resistant to some of the negative consequences of aging. These include certain members of an Amish community in Berne, Indiana or a group of cognitively young octogenarians called "SuperAgers." Other projects will continue to seek biological levers that drive aging and investigate approaches — including new drugs — to minimize the impact of aging and extend the healthy lifespan of older adults.

"We are grateful for the opportunity to support the vision put forth by Northwestern's leaders, scientists and physicians to help people live their longest, healthiest lives possible," said Potocsnak. "The promise of the amazing work being done by Doug, Frank and many others holds the potential to profoundly impact quality of life for millions. My wife Laura, myself and my family are proud to support this important work as we strive to make the world a better place than when we got here."

"The Potocsnak Longevity Institute is a momentous step forward for the science of aging and lifespan," said Eric G. Neilson, MD, vice president for medical affairs and Lewis Landsberg Dean. "The potential impact of this institute's advancements can't be overstated; the time is now right to push the field forward."

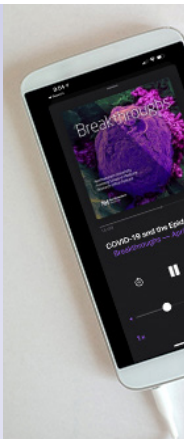
Read more about the Institute

Top 5 Breakthroughs Podcasts of 2021

By Amanda Dee

Of the more than 20 episodes of the medical school's ***Breakthroughs*** podcast produced in 2021, the most popular ranged across specialties from gastroenterology to nanotechnology. Listen to the top five episodes of the year, and earn Continuing Medical Education credit.

5. Esophageal Diseases and Symptom Anxiety and Hypervigilance with John Pandolfino, MD
4. A Promising Obesity Drug with Robert Kushner, MD
3. Neurological Complications of COVID-19 with Igor Koralnik, MD
2. Northwestern Drug Kills Glioblastoma Tumor Cells with Priya Kumthekar, MD
1. Reversing Severe Spinal Cord Injuries with Samuel Stupp, PhD



McNally named Editor-in-Chief of the Journal of Clinical Investigation

In December, Elizabeth McNally, MD, PhD, the Elizabeth J. Ward Professor of Genetic Medicine and director of the Center for Genetic Medicine, was announced as the next editor-in-chief of the *Journal of Clinical Investigation* (*JCI*). She is the first woman to be the editor of the publication in its nearly 100-year history.

Read a Q&A with McNally as she discusses what it means for Feinberg School of Medicine to host *JCI*.

You noted that "we will be drawing on our outstanding scientists to guide the *Journal of Clinical Investigation (JCI)* over these next 5 years." Can you expand on what hosting the journal means for Feinberg investigators?

Yes, the Deputy Editors and Associate Editors are mostly from Feinberg. These editors will be handling manuscripts and, ultimately, deciding what is published in the journal. In addition, this is also an opportunity for assistant professors and even some advanced trainees to gain experience in reviewing, and potentially contributing to commentaries in the *JCI*. It will be a good deal of work for our faculty, but we're up to the task, and it is an honor to have this role. We are also excited about hosting the *JCI* through its 100th anniversary year in 2024.

How does hosting *JCI* at Feinberg benefit the FSM scientific community?

The prior institutions that have held this role are all exceptional institutions, and so it really identifies Feinberg as being at the highest level. The recognition is really significant. With this recognition comes the responsibility and opportunity to steer the *JCI* for the next five years. We do not envision substantially altering the *JCI*, since it has been working well for the last century. But, at the same time, there have been many changes in publishing and this presents the opportunity to make the *JCI* even better than it has been.

What do you feel is the significance of being the first woman editor of *JCI*?

It is remarkable that there has not been a woman as editor up until this point. Women have been well represented in medical schools for decades, but women are not yet represented in a balanced manner in leadership positions. So, I do acknowledge the importance of being in this position, and I look forward to being the best editor I can. There is a lot of attention being paid to fairness and equity in publishing — as authors and reviewers — and we very much want to ensure that every author has a fair chance at publishing in the *JCI* without bias.

Anything else you want Feinberg investigators to know?

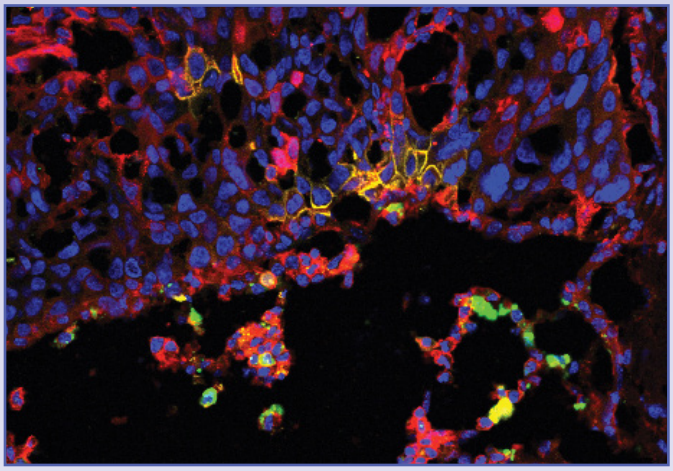
Hopefully, we'll be able to rely on so many of our great investigators here at Feinberg for help in the reviewing process. I am hopeful we can use this as a learning opportunity for our many scientists in training since publishing is such an important part of what we do as scientists.

Neural Stem Cell Therapy May Improve Metastatic Cancer Survival

By Melissa Rohman

Neural stem cells (NSCs) engineered by Northwestern Medicine investigators used in combination with the HER2 inhibitor drug tucatinib improved survival in mice with HER2-positive breast cancer brain metastases, according to findings published in *Proceedings of the National Academy of Sciences.*

Read the full story



Representative immunostainings of brain sections harvested from mice treated with LM008 anti-HER2 neural stem cells (NSCs). The amount of anti-HER2 antibodies released by NSCs (green) was measured with antihuman IgGs (yellow). Presence of HER2 antibodies binding to the membrane of HER2-positive BT474-Br cells (red). Nuclear staining (DAPI) is shown in blue.

Graduate Student/Post-Doc Events and Opportunities

"What We Do, What We Know: NU Environmental Impact Survey" Exhibit
February 14 — March 4

In this exhibit you will see the results of One Book One Northwestern's university-wide survey on how we have interacted with the environment and get some ideas for how we can be better stewards of our planet!

University Library
One South study area
1970 Campus Drive, Evanston

More information

"You've Got Somewhere Else to Be" Art Exhibit by Ambrin Ling
February 17 — March 18

"You've Got Somewhere Else to Be" locates art and drawing as sites of erasure, reinvention, and engagement that have acquired renewed significance amidst global pandemic and a complex network of related social upheavals that reveal how individual selfhood is shaped by and itself shapes larger perceptions of power, value, labor and being human in complex, interdependent, not-just-human environments.

Norris University Center, Dittmar Gallery
1999 Campus Drive, Evanston

More information

Key Ingredients for Successful Biopharma Partnering Discussions
Friday, February 18
10 a.m., online

Niels Emmerich, will share his insight into having a successful partnering/licensing discussion with large biopharma companies.

More information

Translational Research in Solid Tumors (TRIST) Seminar: Developing DISE into pan-cancer therapy
Tuesday, March 1
11:00 a.m. to Noon

Marcus Ernst Peter, PhD, to give lecture on a novel way to kill cancer cells based on targeting critical survival genes by RNAi.

Baldwin Auditorium, Robert H. Lurie Medical Center, Northwestern University
303 E. Superior St., Chicago

More information

Research in the News

***Washington Post*, January 15**
Not a morning person? A sunrise alarm clock could be the answer, experts say.
Phyllis Zee, MD, PhD, was featured.

WGN
Painting a new path to Covid recovery: Doctor uses art to process pandemic experience
Justin Fiala, MD, was featured.

***Chicago Tribune*, January 21**
Illinois schools could see fewer student quarantines from COVID-19 close contacts
Robert Murphy, MD, was featured.

***MSN online*, January 24**
5 Secrets of Seniors Who Keep Their Minds 'Young'
Emily Rogalski, PhD, was featured.

***The New York Times*, January 25**
Why Does Alcohol Mess With My Sleep
Sabra Abbott, MD, was featured.

***CNN*, January 28**
BA.2, the newly detected version of Omicron, is not cause for alarm, scientists say
Ramon Lorenzo-Redondo, PhD, was featured.

More media coverage

Uncovering How Stress Affects Brain Structure and Function to Optimally Treat Mental Illness

Sachin Patel, MD, PhD, chair and the Lizzie Gilman Professor of Psychiatry and Behavioral Sciences

Sachin Patel, MD, PhD, is chair and the Lizzie Gilman Professor of Psychiatry and Behavioral Sciences. Joining Feinberg in January, Patel is also psychiatrist-in-chief at Northwestern Memorial Hospital's Norman and Ida Stone Institute of Psychiatry. An internationally recognized physician-scientist in the field of psychiatric neuroscience, Patel's work combines cellular, molecular and behavioral neuroscience research with clinical expertise in psychiatry and addiction medicine.

Q&A

What are your research interests?
We are interested in understanding how environmental and social stress affects brain structure and function that ultimately leads to the development and exacerbation of mental illnesses. We are particularly interested in how the brain's "endogenous cannabinoid" signaling system, which is the target of cannabis constituents like THC, regulates stress adaptation and how understanding the role of this system in stress response physiology could reveal new cannabinoid-based approaches to the treatment of mental illnesses such as PTSD and depression.

What is the ultimate goal of your research?
The ultimate goal of our research is to define novel signaling systems and molecules that mitigate the adverse effects of stress on brain function and promote resiliency. Identification of such novel targets could lead to the development of mechanistically innovative drug treatments for a broad range of major mental illnesses affected by stress.

How did you become interested in this area of research?
My interest in stress neurobiology arose early in my academic career when I recognized that almost all forms of mental illness and many physical illnesses are strongly affected by stress. Disorders such as depression, schizophrenia and substance use disorders are all worsened by stress exposure. People under stress are also more susceptible to cardiovascular disease and infection. Therefore, understanding the biological mechanisms by which stress is translated into increased susceptibility to mental and physical illnesses could have broad impact on human health.

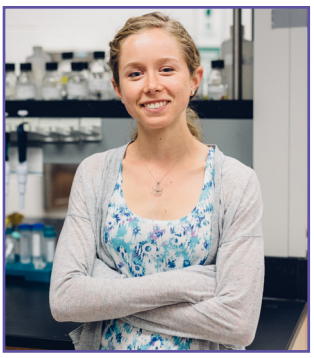
How is your research funded?
Our research is primarily supported by the National Institutes of Health, but has been funded by industrial and non-profit partners as well.

Where have you recently published papers?
Our most recent publications have appeared in *The Journal of Clinical Investigation*, *Nature Neuroscience*, *Neuron*, *eLife*, and the *Proceedings of the National Academy of Sciences*.

What inspires you?
Inspiration for our work comes from those developing novel technologies for investigating brain and behavior relationships in model systems. Incorporating novel technological approaches enables creativity and innovation in the way we ask questions and can answer them.

Untangling Disease Mechanisms of PACS1 Syndrome

Lauren Rylaarsdam, student in the Northwestern University Interdepartmental Neuroscience (NUIN) program



Lauren Rylaarsdam, a student in the Northwestern University Interdepartmental Neuroscience (NUIN) program, studies rare genetic neurodevelopmental disorders in the laboratory of Alicia Guemez Gamboa, PhD, assistant professor of Neuroscience. Read a Q&A with Rylaarsdam below.

Q&A

Where is your hometown?
I grew up in Stillwater, Minnesota, which is about 30 minutes from the Twin Cities.

What are your research interests?
I am fascinated by human genetics and am interested in studying the genetic etiologies of neurodevelopmental disorders. Determining what causes patient symptoms is a very critical step in therapy development.

What exciting projects are you working on?
My thesis research is focused on determining the disease mechanisms of PACS1 syndrome, a neurodevelopmental disorder caused by a single recurrent variant in a gene called PACS1. The goal is to figure out how this variant is causing neurological conditions, such as intellectual disability and epilepsy, and to identify therapeutic targets. To do this, I culture cells from patients and differentiate them to neurons. Then I use various techniques like single-cell RNA sequencing to figure out what goes wrong in PACS1 syndrome cells as the neural tissue develops.

What attracted you to your program?
I was drawn to the depth and variety of research at NUIN. With roughly 140 research faculty across 20 departments, the opportunities for graduate students are quite diverse. I was impressed by the common resources, such as the Center for Advanced Microscopy, which make state-of-the-art equipment available to smaller labs. Chicago also seemed like an exciting change from the town I grew up in. It has been a great place to live these last five years — there are tons of activities, but at the same time it doesn't feel overwhelming.

What has been your best experience at Feinberg?
My best experience here has been learning R and Unix programming, which really expanded the types of questions I was able to ask in my research. My background is primarily molecular, but when I submitted my first sample for single-cell RNA sequencing to the NUSeq core, I felt like I might be missing out if I couldn't analyze the data myself. I slowly acquired the necessary foundational computational skills through Research Computing Services, online resources and a class at Cold Spring Harbor Laboratory. It was very much worth it and my bioinformatics analysis has yielded key insights into my research I would not have had otherwise. Throughout this process, I became fascinated with the power of computational approaches and this has been formative in determining the next steps of my career.

How would you describe the faculty at Feinberg?
I have had very positive interactions with the faculty at Northwestern. My mentor, Alicia Guemez Gamboa, is a huge reason for my constructive experience. I feel very fortunate to be in her lab. She always thinks of others and is very invested in my development both as a person and as a scientist. She is highly collaborative and this has allowed me to learn new techniques and perform experiments I would not have been able to do otherwise. I have especially appreciated partnerships with the labs of Gemma Carvill, Evangelos Kiskinis, and Peter Penzes.

What do you do in your free time?
I am an avid runner. I ran competitively in college and am now part of the Fleet Feet racing team here in Chicago. I like outdoor activities in general. I also love to draw and have a little art business on the side. The artist in me is very attracted to the beauty and complexity of neurons in the brain.

What are your plans for after graduation?
I plan to pursue a postdoctoral position to study the genetic etiology of neurodevelopmental disorders. I particularly want to strengthen my computational skills and complement resulting findings with molecular approaches.

New Executive Director for Research Facilities

Andrea Hall, PhD, started as executive director February 1

Andrea Hall, PhD, started as executive director for research facilities effective February 1. Previously, she served as director of research safety on the Chicago campus and biosafety officer. Hall is a specialist microbiologist in the National Registry of Certified Microbiologists and a certified biosafety professional.

Passionate about research safety, Hall is excited to begin her new role. Read a Q&A with Hall about her career path and why she has been with Northwestern for 15 years.

Q&A

Tell me a little bit about your career background.

I earned my PhD in microbiology and immunology. I started my work at the University of Illinois Chicago and then my investigator moved to Northwestern, so I followed him here and finished my last year at Northwestern. Since then, I have been focused on biosafety. When I started in 2006 I was the only person in the biological safety program. Now I manage a team of three others and oversee the institutional biosafety committee, which approves research with biological materials.

What inspired you to become involved in research safety?

Originally, I got into safety because I didn't want to open up my own lab. I was looking for positions and found a role in research safety as the assistant director of Biological Safety, which seemed like a perfect fit. I enjoy the day-to-day changes, working with others and collaborating on various types of research. I have a hand in lots of different research and I really enjoy that.

What are you most looking forward to in this new role?

I'm looking forward to working in such a rapidly changing environment. I've spent the last few years learning about laboratory design and construction. My husband is in the construction field too, so it's fun to discuss the challenges we both face. I find it rewarding to see these construction projects come to fruition and support the PIs with the tools they need to perform their research. I enjoy the challenge of balancing everything — the costs, needs and timing. I love project management and using creativity to accomplish our goal. I was involved in the design of the Simpson Querrey Biomedical Research Center and it's so rewarding to see the project completed. Walking into that building now I feel like I contributed to the process, and it's amazing to see.

You have been at Northwestern for 15 years — why Northwestern?

Northwestern is a really great place to work. The benefits are great, and with three children I'm really looking forward to the tuition benefit. I also feel very proud to work at Northwestern. When you look at the research that comes from Northwestern, it's impactful. To see that I had a hand in that, I like the part I play in the research process. It just feels like home.

Welcome New Faculty

Amy Heimberger, MD, joins as the Jean Malnati Miller Professor of Brain Tumor Research in the Department of Neurological Surgery. Heimberger's scientific interests focus on elucidating the mechanisms of tumor-mediated immune suppression and identifying actionable targets for immune therapeutics. Her laboratory was pivotal in the development of a peptide (PEP-3-KLH/CDX-110) vaccine strategy that targets the epidermal growth factor receptor. In addition, she has clarified that the signal transducer and activator of the transcription 3 (STAT3) pathway is a key molecular hub of gliomagenesis and tumor-mediated immune suppression. She also conducted the pre-clinical development of a novel small molecule inhibitor of STAT3, WP1066, which was introduced into clinical trials in 2018 for melanoma patients with CNS metastasis and primary glioma patients. She was previously a professor in the Department of Neurosurgery at the University of Texas MD Anderson Cancer Center.

NIH News

NIH Data Management and Sharing Policy Update

Over the past two years NIH has been working to make the research they fund available to the public. In 2020 NIH issued its Data Management and Sharing (DMS) Policy. Their goal is to lead a cultural shift that makes data sharing the norm.

Over the course of 2022 you can expect to hear more information on principles for protecting research participant privacy, plans for further merging NIH's data management and sharing expectations, and helpful tips for developing budgets in plans describing data management and sharing. NIH has also published a new set of FAQs that respond to frequently asked questions since the release of the DMS policy.

Clarification and Guidance for Applicants for Spring 2022 During the COVID-19 Pandemic

Due to the COVID-19 pandemic, lab occupancy restrictions, declines in patient accrual and other constraints will be resolved during the project period. Reviewers are instructed to assume these constraints and therefore should not affect their scores.

As a result, NIH applications should NOT include emergency incident plans for problems resulting from the COVID-19 pandemic. Applicants may include effects of COVID-19 on productivity or other Issues in their personal statement. If needed, NIH staff will request and assess plans to resolve specific problems arising from the COVID-19 pandemic prior to funding.

Applicant Forms Information Reminder

This is a reminder that applicants must use FORMS-G application packages for due dates on or after January 25. FORMS-G Grant Application Instructions are posted on the How to Apply - Application Guide. Applicants are encouraged to submit early to allow time to work through any discrepancies.

NUCATS Corner
Clinical and Translational Sciences Institute

NUCATS Launches On Demand Resources

The NUCATS Institute recently launched a new tool that allows 24/7 access to resources addressing your needs on your time. NUCATS On Demand is home to a robust set of training videos, learning modules, reference guides, regulatory templates and clinical research glossaries for faculty, trainees and staff.

Elements of the site are also grouped into categories that include:

Data Management & REDCap

Data management is a crucial part of clinical research, which is why we have curated resources designed to help you better understand its ins and outs. From the logistics of setting up your REDCap account and understanding the terminology this system uses to the theories behind designing an effective survey, we aim to support clinical research coordinators and investigators as they manage their study data.

Research Studies During COVID-19

The pandemic highlights the importance of clinical research more and more each day. But it has also shown us how our work needs to evolve. We have compiled COVID-19 resources to share the most up-to-date information, recordings of relevant seminars from across contexts and downloadable materials that can be referenced when considering the effects of COVID on clinical research.

Mentorship

Our resources will help both mentors and mentees grow into their professional roles by establishing goals through individual development plans and networking maps. Those especially devoted to mentoring may be eligible to join our monthly mentoring workshop series or pursue the mentor training certificate program.

Good Clinical Practice

Good Clinical Practice (GCP) is an international, ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects. Learn more about the different components of GCP by exploring resources following the stages of a research study from recruitment to closeout.

Sponsored Research

PI: Linda Van Horn, PhD, RD, chief of Nutrition in the Department of Preventive Medicine and professor of Preventive Medicine, one of the senior principal investigators

Title: Nutrition Precision Health for All of Us

Sponsor: National Institute of Child Health and Human Development

Northwestern, the University of Chicago, Illinois Institute of Technology, University of Illinois, Chicago and Rush University are part of a $170 million National Institutes of Health (NIH) program that is the first comprehensive study to investigate precision nutrition. The goal of "Nutrition for Precision Health" (NPH), powered by the All of Us Research Program, will be to develop algorithms to predict individual responses to food and dietary routines.

"We will learn more precisely how to match dietary recommendations to the needs of an individual," Van Horn said.

Northwestern and its partners will comprise the Illinois Precision Nutrition Research consortium, one of six centers around the country. Their grant will be $13,321,184 awarded over five years, pending availability of funds.

The NPH clinical studies are empowered by the All of Us Research Program already underway at Northwestern and led by principal investigator Philip Greenland, MD, the Harry W. Dingman Professor of Cardiology. In addition to Van Horn, All of Us is implemented locally by Joyce Ho, PhD, research associate professor of Preventive Medicine in the Divisions of Behavioral Medicine and Epidemiology, who is a multiple principal investigator with this newly funded Illinois Precision Nutrition Research consortium along with Marilyn Cornelis, PhD, associate professor of Preventive Medicine in the Division of Nutrition.

Read more

PI: Amisha Wallia, MD MS, assistant professor of Medicine in the Division of Endocrinology and of Preventive Medicine in the Division of Epidemiology, member of the Center for Health Services and Outcomes Research in the Institute of Public Health and Medicine

Title: Adaption, Implementation and Testing of a Telehealth Diabetes Discharge Intervention to Improve Transitions of Care

Sponsor: National Institute of Diabetes, Digestive and Kidney Diseases

High-risk medication use is essential for certain disease states, such as diabetes mellitus (DM), and transitions of care can be an especially hazardous time for those new to diabetes medications. Novel delivery methods, especially for telehealth are needed in for the peri- and post-COVID era. The sickest population of patients — those with diabetes in the hospital — often require in-depth knowledge and education transfer, as they transition from the inpatient to outpatient setting, but currently are getting in person and/or telemedicine training.

The goal of this research project is to adapt a diabetes discharge toolkit for use in a telehealth setting, utilizing novel learning science methods. The system will combine integrated software (website, app and print) and hardware (a 3D printed kit). We will work closely with the Segal Design Institute and the McCormick School of Engineering to utilize novel methods from across disciplines, (including human-computer-interaction, computer-supported collaborative learning and learning sciences) to adapt the toolkit for telemedicine care delivery.

We then propose to integrate and implement an intervention testing the newly adapted Telehealth Diabetes Discharge Toolkit for those requiring new or additional DM medications and additional diabetes education at discharge.

The goal will be to evaluate the implementation of the DM Toolkit at discharge and then assess the feasibility of a pilot clinical trial of the intervention on glycemic control and glycemic excursions as well as other self-care and psychosocial measures.

This intervention has the potential to be generalized to DM care in other settings, such as an emergency department or outpatient clinic, and has the potential to reach patients worldwide at scale.

Read more

Funding

Clinical Relevance of the Linkage between Environmental Toxicant Exposures and Alzheimer's Disease and Related Dementias (R01 Clinical Trial Not Allowed) More Information

Sponsors: National Institutes of Health
Submission deadline: March 11, 2022
Award ceiling: $500,000

Synopsis: There is consensus that environmental toxicants are a risk factor for AD/ADRD, but causality has been largely elusive. While human studies demonstrating an association of AD/ADRD with toxicant exposures are relatively abundant, there is a clear unmet need for more mechanistic research to support or refute the clinical relevance and the biological plausibility of an impact on disease initiation, progression or modification. This is especially important for understanding the potentially modifiable causes of racial and socioeconomic inequities. The RFA will encourage neuroscientists to conduct mechanistic AD/ADRD research on the actions of neurotoxicants on the nervous system.

Distinguished Scientist Award – Brain Cancer

More information
Sponsors: Sontag Foundation
Submission deadline: March 16, 2022
Upper Amount: $600,000 over four years

Synopsis: The Distinguished Scientist Award (DSA) seeks to provide career and research support to early career scientists who demonstrate outstanding promise for making scientific and medical breakthroughs in the field of brain cancer research. The applicant's career track and proposed research should demonstrate potential to generate new knowledge relating to causes, cure or treatment of primary brain tumors/brain cancer.

Fellowship Awards – Cancer Research

More information
Sponsors: Damon Runyon Cancer Research Foundation
Submission deadline: March 15, 2022
Upper Amount: $231,000 over four years

Synopsis: Fellowships are available for theoretical and experimental research relevant to the study of cancer and the search for cancer causes, mechanisms, therapies and prevention. Candidates must apply for the fellowship under the guidance of a Sponsor – a scientist capable of providing mentorship to the Fellow.

COVID-19 Mental Health Research (R01 Clinical Trial Optional)

More information
Sponsors: National Institute of Mental Health
Submission deadline: April 25, August 25 or December 23
Letter of intent due: 30 days before application due date(s)
Upper amount: $750,000

Synopsis: This funding aims to address timely mental health research questions related to COVID-19. Proposed studies should focus on the understanding of virus impact and function on the brain, populations at risk and mechanisms of illness profoundly impacted by the pandemic. This funding also covers global mental health research examining the impact of pandemic-related changes in social determinants of health: loss of employment, food insecurity, housing, insecurity and how these affect mental health and functioning in low and middle income countries.

Industry Sponsored Research

PI: Satish Nadig, MD, PhD, the Edward G. Elcock Professor of Surgical Research and chief of Organ Transplantation in the Department of Surgery

Sponsor: Pandorum International Inc.

Title: Cell Farming: A Scalable & Translational Tissue Regeneration Platform Technology

The objective of Pandorum-Northwestern University collaboration is to translate Pandorum's bioengineered human tissue — namely, the liquid cornea formulation for human application through various stages of de-risking to address unmet medical needs. These studies will be used as a platform for further assessing the viability of cellular infrastructures to serve as hepatic bioreactors, for example. Research scientists working on the collaboration will utilize the findings at Northwestern University to translate the processes of liquid cornea and bioartificial liver for potential clinical trials.

The project supports cell therapy and close coordination with the Center for Cellular Therapy for Good Manufacturing Practice (GMP) based liquid cornea development to use in clinical trials. In addition, hepatocyte cultures will be maintained as a base for future hepatic bioreactor development.

Clarivate Analytics Announces 2021 Highly Cited Researchers

By Annette R. Mendoza, Research Impact Librarian

Each year, Clarivate Analytics releases a list of highly cited researchers, who have "demonstrated significant and broad influence, reflected in the publication of multiple papers frequently cited by their peers during the last decade." Below is a list of the Feinberg researchers who made the list in 2021, their appointment at the medical school and the category they were identified in. Congratulations! (Please note that faculty may have more than one appointment.)

Brian Mustanski, PhD, Medical Social Sciences in Social Sciences

Chad A. Mirkin, PhD, Medicine (Hematology and Oncology) in Cross-Field

Clyde W. Yancy, MD, MSc, Medicine (Cardiology) in Cross-Field

David Cella, PhD, Medical Social Sciences in Social Sciences

Donald M. Lloyd-Jones, MD, ScM, Preventive Medicine (Epidemiology) in Clinical Medicine

Navdeep S. Chandel, PhD, Medicine (Pulmonary and Critical Care) in Molecular Biology and Genetics and Biology and Biochemistry

Philip Greenland, MD, Preventive Medicine (Epidemiology) in Cross-Field

Samuel Weinberg, MD, PhD, Pathology in Cross-Field

Sanjiv J. Shah, MD, Medicine (Cardiology) in Clinical Medicine

Clarivate evaluates papers that were published and cited from 2010 to 2020 and ranked in the top 1 percent by citations for the field and year. A total of 6,602 highly cited researchers were identified in 2021, with 3,744 in specific fields and 2,828 for cross-field performance.

Twenty-seven Northwestern researchers are included on this 2021 list and represent departments across the university. This year, Northwestern is one of six universities to increase more than 10 places in the top 50 list of institutions from which the highly cited researchers hail (currently at 39th).

The specific fields that Clarivate Analytics utilizes for classification are the 21 fields that are delineated in the Essential Science Indicators (ESI), a database focused on emerging science trends that is updated every two months and contains a 10-year rolling file. They determine the number of researchers to be selected in each field by taking the square root of the authors that are listed in that field's highly cited papers. The thresholds for fields related to Feinberg are noted in the table below:

ESI Field	Number of Highly Cited Researchers
Biology and Biochemistry	206
Clinical Medicine	453
Cross-Field	2,828
Molecular Biology and Genetics	177
Social Sciences, General	263

Clarivate began identifying researchers with cross-field impact in 2018 in an effort to recognize individuals who demonstrate "exceptional performance across several fields." Their calculation methods for this distinction involves normalizing the highly cited paper and citation counts through fractional counting according to the thresholds required for each field. There is detailed information on their methodology available on their website. While a researcher can be a highly cited researcher in more than one ESI field, a cross-field notation indicates the researcher has met the criteria based on the normalization methodology indicated above.

The full report on Highly Cited Researchers for 2021 can be found here.

High-Impact Factor Research

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High-Impact Factor Research

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Featured Core

Analytical bioNanoTechnology Equipment Core (ANTEC)

The Analytical bioNanoTechnology Equipment Core (ANTEC), located within the Simpson Querrey Institute (SQI), offers Northwestern University investigators and local industry and visiting scientists research equipment for the evaluation of materials and biological preparations in the core's bionanotechnology laboratory. Very recently, the core added 3D scientific illustrations to its offerings, becoming the first core facility at the university to provide this service. Core staff members provide equipment training and technical assistance on open-access instrumentation.

Equipment in the core is self-service and training is required. To start using ANTEC, the core invites investigators to open a NUCore account.

Core services include:

- Equipment training, user assistance
- 3D scientific illustration
- Staff service

Available equipment includes:

- Azure300 Chemiluminescent Gel Imager (Azure Biosystems)
- Centrifuge Sorvall Legend X1R (Thermo Fisher)
- CFX Connect Real-Time PCR System (Bio-Rad)
- Cytation3 Cell Imager and Plate Reader (BioTek)
- Freezer/Mill (Spex SamplePrep)
- IncuCyte Live Cell Analysis System (Sartorius)
- Lyophilizers FreeZone 6 and 6+ (Labconco)
- Nanosight300 (Malvern Panalytical)
- Plasma Cleaner (Harrick Plasma)
- Piuma Nanoindenter (Optics11)
- Rheometer MCR302 (Anton Paar)
- Zetasizer Nano ZSP (Malvern Panalytical)

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