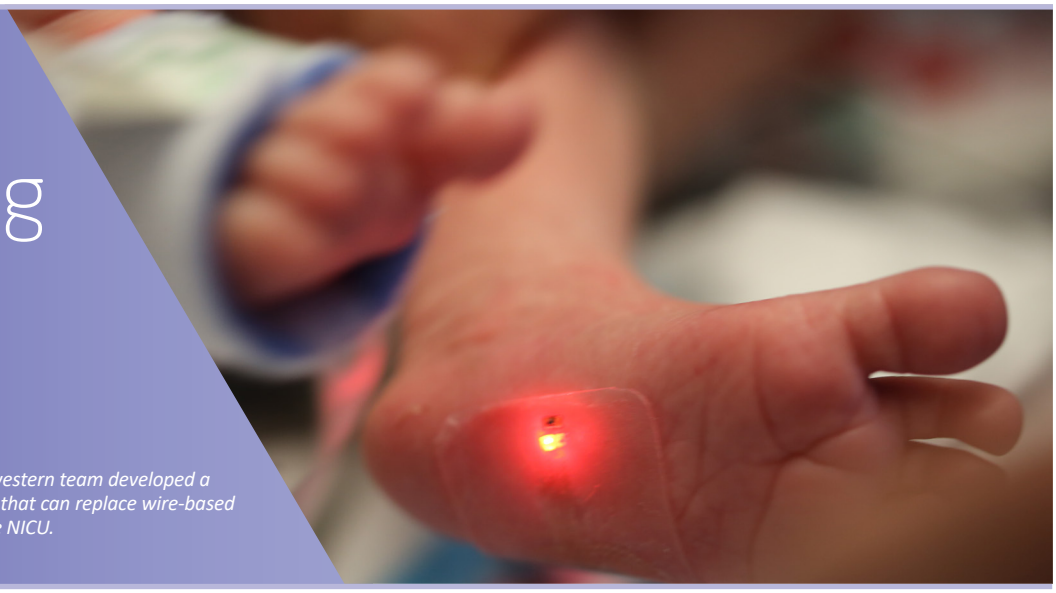
Breakthroughs

Feinberg School of Medicine Research Office

December 2019

Discovering New Frontiers



This past year, an interdisciplinary Northwestern team developed a pair of soft, flexible wireless baby sensors that can replace wire-based sensors currently monitoring babies in the NICU.

Feinberg has had an exceptional year of scientific inquiry, ranging from examining the most basic systems that make our bodies tick to developing breakthrough therapies and treatment strategies. With the opening of the new Louis A. Simpson and Kimberly K. Querrey Biomedical Research Center, the pace of discovery will only quicken.

Feinberg principal investigators secured a record-breaking $534 million in sponsored research funding and awards during the 2018-2019 fiscal year, a 10.2 percent increase in funding over 2018. Over 4,000 clinical trials and research studies were conducted at Feinberg, led by 652 principal investigators. A total of 66 patents and five new start-up companies were established within the last fiscal year alone.

"The high-impact discoveries made by Feinberg investigators this year reflect the continued growth of our extraordinary research enterprise. The publications we are highlighting here represent just a small sampling of the substantial contributions our faculty members led across a range of scientific disciplines in 2019," said Rex Chisholm, PhD, vice dean for Scientific Affairs and Graduate Education and the Adam and Richard T. Lind Professor of Medical Genetics.

In the final issue of *Breakthroughs* for 2019, we're taking a look back at a few of the exciting research stories that marked the past year at Feinberg. The following are summaries; please click through each headline to read our full coverage.

Newly Discovered Protein Explains Leukemia's Treatment Resistance

A previously-unknown protein called cTORC may explain why many therapies are ineffective in treating leukemia, according to a study published in *Blood* and led by Leonidas Platanias, MD, PhD, the Jesse, Sara, Andrew, Abigail, Benjamin and Elizabeth Lurie Professor of Oncology, director of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University. A protein complex, called mTORC, drives cancer proliferation in leukemia but was previously believed to be the only complex of its kind exhibiting this behavior — until the current study, when Northwestern scientists discovered a never-before-seen counterpart that was being missed by current therapies.

Radiation Plus Chemotherapy Doesn't Improve Endometrial Cancer Recurrence-Free Survival

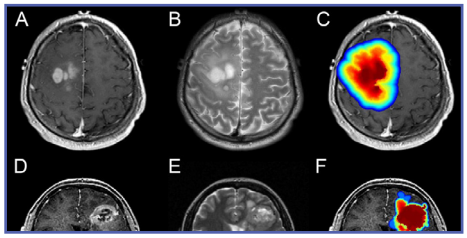
The standard of care for women with late-stage endometrial cancer following surgery has been chemotherapy to prevent recurrence, but a study published in *The New England Journal of Medicine* found that this combination did not increase recurrence-free survival in these women. The findings merit further investigation, according to Daniela Matei, MD, the Diana, Princess of Wales Professor of Cancer Research, a professor of Medicine in the Division of Hematology and Oncology and first author of the study.

Northwestern Medicine®

(continued on page 2)

New Frontiers *(continued from cover page)*

Tumor Mutations Predict Response to Immunotherapy



An MRI showing tumor cell density in patients with glioblastoma.

A study published in *Nature Medicine* found that patients with glioblastoma responded better or worse to immunotherapy depending on the presence of certain mutations in their tumors. Incorporating these findings — including how tumors with mutations in the MAPK pathway respond better to immunotherapy — into clinical guidelines could improve management of patients with glioblastoma, according to Adam Sonabend Worthalter, MD, assistant professor of Neurological Surgery and co-senior author of the study.

Total Heart Disease Deaths on the Rise

Total deaths from heart disease, stroke, diabetes and hypertension — known collectively as cardiometabolic disease — have been increasing since 2011, according to a study published in *JAMA.* While the overall rate of heart disease deaths decreased over time, the rate of decline slowed after 2010. Deaths from stroke and diabetes declined from 1999 to 2010 but leveled off after that. Deaths from high blood pressure increased between 1999 and 2017, according to the study led by Sadiya Khan, MD, MSc, assistant professor of Medicine in the Division of Cardiology.

Groundbreaking Sensors Wirelessly Monitor Babies in the NICU

An interdisciplinary team of Northwestern faculty developed a pair of soft, flexible wireless sensors that can replace wire-based sensors currently monitoring babies in the hospital's neonatal intensive care units and ultimately increase parent-baby bonding through allowing easier skin-to-skin contact between parent and child. The study was published in the journal *Science* and led by John Rogers, PhD, a professor at the McCormick School of Engineering and of Neurological Surgery.

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Women Scientists Get Less Federal Funding Than Men

A study co-led by Teresa Woodruff, PhD, the Thomas J. Watkins Memorial Professor of Obstetrics and Gynecology, dean of The Graduate School and associate provost for graduate education, found that first-time women principal investigator scientists received an average $41,000 less in funding from the National Institute of Health than first-time male principal investigators from both bottom- and top-tier institutions. The Northwestern Medicine and the Kellogg School of Management study, published in *JAMA*, is the first of its kind to show women scientists receive less money when they submit grants to the federal government.

Scientists Identify Therapeutic Target in Diabetic Kidney Disease

An international team of collaborators led by Susan Quaggin, MD, chief of Nephrology and Hypertension in the Department of Medicine and director of the Feinberg Cardiovascular and Renal Research Institute, demonstrated that inhibiting a protein called VE-PTP preserves microvascular and kidney function in diabetic mice. The findings, published in the *Journal of Experimental Medicine*, identify a new therapeutic target that may help protect kidney function in patients with diabetic kidney disease in addition to other diseases where the kidneys are targeted.

Genetically Modified Protein Improves Repair of Muscle Injuries

By using microscopy, Northwestern Medicine investigators identified that annexin A6 — a protein previously identified as a genetic modifier for muscle injury and disease — can enhance the repair of acute injuries by more than 50 percent. The study, published in the *Journal of Clinical Investigation*, was led by Alexis Demonbreun, PhD, a research assistant professor of Pharmacology, and senior author Elizabeth McNally, MD, PhD, the Elizabeth J. Ward Professor of Genetic Medicine and a professor of Medicine in the Division of Cardiology.

Experimental Drug May Reduce Cancer Growth and Progression

A team led by Sui Huang, MD, PhD, associate professor of Cell Developmental Biology, found that an experimental drug called metarrestin suppressed metastatic tumors and extended tumor bearing animal survival without prompting any adverse side effects. The study, published in *Science Translational Medicine,* could be used with existing drug therapies to help extend patient survival and ultimately improve a patient's quality of life.

Personalized Approach to Parkinson's Treatment

Instead of trying to fix broken enzymes that contribute to Parkinson's disease, Feinberg scientists amplified healthy ones — an approach that successfully alleviated symptoms in human brain cells and in mouse models. The study, published in *Science Translational Medicine* and led by Dimitri Krainc, MD, PhD, chair and Aaron Montgomery Ward Professor of Neurology, points to the potential of tailoring treatments to the unique genetic conditions of patients.

New Center for Translational Pain Research Launched

Northwestern has established the Center for Translational Pain Research, which aims to advance basic and clinical science relating to chronic pain and analgesic therapies, as well as develop novel treatments to treat chronic pain conditions.

"Our center is a new, exciting phase for pain research at Northwestern," said A. Vania Apkarian, PhD, director of the center and a professor of Physiology, Anesthesiology and Physical Medicine and Rehabilitation. "We are the only such program in the U.S. and as such, we hope to spearhead the science necessary to combat chronic pain; identify underlying mechanisms and relationships with opiate misuse and opiate analgesia; and uncover new drug targets in this domain."

Treating chronic pain continues to be a difficult undertaking. The wide range of mechanisms underlying the condition are not very well understood, Apkarian said, and there are currently no treatments that address the underlying cause of most chronic pain. Instead, current pain-relief drugs merely treat symptoms, and many of these drugs can leave a patient susceptible to addiction.

Building on decades of pain science performed at Northwestern, Apkarian said he envisions a translational approach. Northwestern scientists have developed neuro-imaging methods for studying pain in the human brain and models to identify circuits and receptors that reorganize due to chronic pain. Working to improve these tools, along with new investigations, will feed into drug discovery and eventually clinical trials to develop novel, non-addictive drugs to treat different types of pain.

"We hope to rapidly expand to generate subgroups who would pursue these goals in specific types of chronic pain, such as chemotherapy pain, osteoarthritis pain and chronic pain in children, for example," Apkarian said.

Apkarian notes that the Center for Translational Pain Research won't just be a forward-looking enterprise; a major priority of the center will be to identify clinical biomarkers than can flag patients who might be susceptible to opioid addiction, an innovation that could be put into practice sooner than later.

"These could be implemented in the clinic to identify patients who could be treated with opioids without developing dependence, and also to identify those who should not be treated with opioids as they would be at risk for dependence," Apkarian said. "We want to establish an experimental pain clinic and conduct trials with direct impact on pain management."

The interdisciplinary nature of the center is seen in its core faculty, including D. James Surmeier, PhD, chair and the Nathan Smith Davis Professor of Physiology; Jelena Radulovic, MD, PhD, the Dunbar Professor in Bipolar Disease and a professor of Psychiatry and Behavioral Sciences, Pharmacology and Physiology; Rajeshwar Awatramani, PhD, associate professor

A. Vania Apkarian, PhD, director of the Center for Translational Pain Research and a professor of Physiology, Anesthesiology and Physical Medicine and Rehabilitation, speaks at the Center for Translational Pain Research launch event.

in the Ken and Ruth Davee Department of Neurology Division of Movement Disorders; Marco Martina, MD, MSc, PhD, associate professor of Physiology and Marwan Baliki, '09 PhD, assistant professor of Physical Medicine and Rehabilitation.

"These faculty have been collaborating for many years and are directly responsible for making this program happen," Apkarian said.

The center, sponsored by a National Institutes of Health P50 grant, joins other recent Northwestern P50 initiatives including the Brain Tumor Specialized Program of Research Excellence (SPORE), a program investigating bench-to-bedside discoveries for glioblastoma.

Awatramani is a member of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University.

Listen to Apkarian on the Breakthroughs podcast

In this episode, Apkarian explains his recent discoveries related to chronic pain and how placebos may be a very effective option for some. Listen here.

Understanding and Combating Virulent Viruses

Gregory Smith, PhD, professor of Microbiology-Immunology

Gregory Smith, PhD, is a professor of Microbiology-Immunology. He studies the neuroinvasive herpesviruses with a focus on the molecular mechanisms by which these pathogens propagate and disseminate within the nervous system.

Q&A

What are your research interests?

An ancient group of viruses that has co-evolved with the animal kingdom: the herpesviruses. These agents are more related to viruses of bacteria (bacteriophage) than they are to other animal viruses, and they are remarkably successful. Individual viruses from this group infect mammals ranging from mice to elephants to seals, as well as ourselves. We study one such virus that is carried by the majority of people on earth: herpes simplex virus (HSV), and a related but particularly virulent veterinary virus that infects many farm and companion animals called pseudorabies virus (PRV). Of particular interest for me is the propensity of both of these viruses to invade the nervous system.

What is the ultimate goal of your research?

We are striving to obtain a working understanding of these viruses, which I like to think of as nano-machines, and to translate this knowledge into tools to develop vaccines and advanced viral vectors for a range of applications, including oncolytics to treat cancer and neural tracers to map brain circuitry. In parallel to this, we are studying why in rare circumstances these viruses cause severe encephalitic infections.

How did you become interested in this area of research?

Since my graduate thesis research, I have been interested in what pathogens can teach us about ourselves. I am particularly fascinated by the molecular mechanisms employed by bacteria and viruses to manipulate the biology of our cells and how they manifest in disease. In graduate school, I was researching a food-borne bacterial pathogen, Listeria monocytogenes, which manipulates the actin cytoskeleton to rocket between cells while hiding from the immune system. As amazing as Listeria is, it causes only sporadic outbreaks that generally involve people with compromised immune systems. By contrast, HSV has spread to the majority of the human population: essentially the biggest outbreak possible. And it infects us for life by hiding in our nervous system. How could I not become interested?

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

The people in my lab are engaged in highly interdisciplinary research. Our bread and butter is molecular virology with healthy doses of cell and neuronal biology. We've pioneered genetic methods to manipulate the virus and live-cell imaging techniques to watch individual viruses "running" down axons to establish infections in sensory ganglia. All of this is augmented by our collaborations. On the cell biology side, Volodya Gelfand, PhD, the Leslie B. Arey Professor of Cell, Molecular, and Anatomical Sciences in the Department of Cell & Developmental Biology, is an exceptional scientist and colleague who has made some of our recent discoveries possible. Drs. Gary Pickard and Patricia Sollars (University of Nebraska at Lincoln) are long-term neuroscientist collaborators who are core to our research program. In fact, together with Dr. Pickard and Dr. Katya Heldwein of Tufts Medical School, we have founded a company, Thyreos LLC, to advance some of the vaccine technology that has resulted from our research. My lab also participates in a scientific consortium with Drs. Jean-Laurent Casanova and Shen-Ying Zhang (Rockefeller University), Dr. Luigi Notarangelo (National Institutes of Health) and Dr. Lorenz Studer (Memorial Sloan Kettering Cancer Center) to unravel the genetic predispositions that result in lethal HSV encephalitis.

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Using Molecular Approaches to Solving Clinical Problems

Andrew Chiu, PhD, Medical Scientist Training Program

Andrew Chiu, PhD, an eighth-year student in the Medical Scientist Training Program (MSTP) is interested in molecular solutions to clinical problems. His doctoral research in the laboratory of Antonio Sanz Clemente, PhD, assistant professor of Pharmacology, led to a publication in *Cell Reports,* where Chiu and Sanz-Clemente reported a new mechanism to transport neuroreceptors.

Q&A

Where is your hometown?
I grew up in Los Angeles and went to University of California-Los Angeles, where I majored in biochemistry.

What are your research interests?
While I'm not entirely sure what I would like to medically specialize in yet, I'm really motivated by the concept of using molecular approaches to solving clinical problems. Going forward, I think I'd like to continue studying molecular neuroscience and to have a more active role in trying to translate findings from the lab to useful solutions for the clinic.

What exciting projects are you working on?
For my graduate work, I worked in the lab of Dr. Antonio Sanz-Clemente. My work focused on understanding how NMDA receptors, a type of neurotransmitter receptor, are localized in neurons. These receptors are crucial for normal brain function, but when they are activated in the wrong areas, it can lead to cellular dysfunction. It's now thought that this process might be involved in a number of diseases, such as Alzheimer's. My work identified the enzyme protein phosphatase 1 as a key player in controlling now neurons control NMDA receptors localization.

What attracted you to the Medical Scientist Training Program?
There were a few things I kept in mind during my medical school decision process. I knew I wanted to be at an institution that was strong both clinically and in research. At the time that I was starting medical school, Feinberg was in the process of overhauling its curriculum to make clinical education more integrated with traditional science-based education. This concept was pretty progressive at the time and really intrigued me.

I also appreciated how important research was to the medical school. I knew that even though my peers might not be pursuing a research degree, because everyone would be participating in their own Area of Scholarly Concentration research projects, I would be able to share the experience of doing research with other students. Importantly, I also knew that I wanted to perform neuroscience research, which is something that Northwestern excels at.

Finally, I knew that I wanted to experience living in a big city, so living in Chicago was an appealing opportunity.

What has been your best experience at Feinberg?
Without a doubt, my most rewarding experience at Feinberg has been earning my doctoral degree. It was the culmination of five years of work and I think is a testament of how perseverance pays off.

How would you describe the faculty at Feinberg?
I've found all of the faculty at Feinberg to be thoroughly collaborative and to be genuinely invested in the development and wellbeing of students. I've had no trouble reaching out to both clinical and research faculty and have always felt that, despite being a trainee, my thoughts and opinions were valued and respected.

What do you do in your free time?
I love exploring Chicago, trying new restaurants, and enjoying movies and concerts.

What are your plans for after graduation?
Following graduation, I'm planning to continue my medical education through a residency program.

Jeremiah Stamler, MD, Turns 100

Jeremiah Stamler, MD, celebrated his 100th birthday Oct. 27. The founding chair of the preventive medicine department at Northwestern in 1972, Stamler has had tremendous influence on the understanding of diet and cardiovascular health. He's considered the founding father of preventive cardiology.

Read more about his legacy and the celebration of his milestone birthday.

Recruiting Feinberg's Future Talent

Jessica Voth, assistant director for Admissions and Recruitment in the Department of Medical Education

Q&A

Where are you originally from?
While I was born in Charleston, South Carolina and spent a few formative years there, I'm a Midwesterner at heart and spent most of my childhood in northern Indiana (near South Bend, about a mile away from Michigan).

What is your educational background?
I received my Bachelor's of Art degree from Lake Forest College — majored in psychology and double minored in sociology and religion. These are all different approaches to understanding human behavior, which remains perpetually fascinating to me.

I received my Master's of Science degree in higher education administration and policy from Northwestern University's School of Education and Social Policy. This was accomplished while working full time as a curriculum coordinator in the Augusta Webster Office of Medical Education (AWOME) —four very long years of hard work and commuting to Evanston. Brutal, but worth it!

Please tell us about your professional background.
I had a fortuitous entry into the world of medical education. Upon graduation from Lake Forest, I furiously applied to hundreds of jobs like any nervous newly-minted "adult." One of the positions was through a temporary staffing agency, which led to a surgery clerkship coordinator position at Feinberg. I loved working with the faculty, residents and students and felt like a valued team member despite my lack of medical background. I found my people and never looked back.

A couple years later, I was promoted to the curriculum coordinator role in AWOME, where I was fortunate to participate in the curriculum renewal process.

After I finished my Master's degree in Higher Education Administration and Policy, I wanted to stay in Medical Education at Feinberg in some way. In June 2018 I began my tenure in the Office of MD Admissions as the program administrator and in May 2019 I was promoted to my current role of assistant director for the office. I feel like I won the lottery. I have a fantastic team and have the honor of working closely with the ever-inspiring Dr. Roopal Kundu, the Associate Dean for Admissions. Plus I get to share with excited applicants the many wonderful things about the institution I have come to adore. Feinberg is the easiest "sell" ever.

Why do you enjoy working at Northwestern?
Easy — the people here make Feinberg the wonderful place it is! Faculty, fellows, residents, students and staff! I feel that I have found a supportive work family at Feinberg. I also appreciate having great confidence in Feinberg's ability to accomplish its mission to educate the future leaders in medicine. I feel good about the work we are doing to recruit and train the future medical workforce. I know that we are producing excellent physicians and am so pleased to know that I am able to contribute to this in some small way.

What exciting projects are you working on?
This year we created and implemented a new Early Decision Program (EDP) for the MD program. Helping to figure out how to build and establish a new program in keeping with the regulations set out by both the Association of American Medical Colleges (AAMC) and Feinberg was a very engaging challenge! And I'm happy to report that this endeavor was successful and we will be matriculating our first EDP student next year!

Another project we're working on this year is to build a social media presence for the Office of MD Admissions. We have just begun work on this endeavor, but I am very excited to see how it all comes together and develops over the next year. In my personal life I'm a social media neophyte, so please send me your social media tips and tricks!

And finally, we are working on the 2020 Second Look event in which we invite all accepted applicants back to campus in April for a…second look…before they have to make the difficult decision of where they will be matriculating. This is our biggest event of the year and are always looking for ways to enhance the applicant experience. We have a few ideas about some new things we're going to try this year…very exciting!

What do you like to do in your spare time?
Not very exciting, but I'm an audiobook fanatic — I read (okay, listen to) at least 2-3 each week. I find that having something engaging to listen to makes the not-so-savored tasks (commuting, cleaning, exercising) more palatable! I'm also a stand-up comedy nerd and have had the great fortune to see some of my comedy heroes in person here in Chicago — Jerry Seinfeld, John Mulaney, Jim Gaffigan, Alli Wong, Pete Holmes, to name a few. I try to see as many shows as possible. Luckily Chicago tends to attract many of the best!

Research in the News

Chicago Tribune, November 6

A new strain of HIV has been found for the first time in almost 20 years — by a team of scientists based in the Chicago suburbs

Thomas Hope, PhD, was quoted.

Crain's Chicago Business, November 11

Northwestern discovery sheds light on ALS origins

Pembe Hande Ozdinler, PhD, was quoted.

WTTW News, November 14

At Age 100, Heart Health Pioneer Still Doing Research

Jeremiah Stamler, MD, was featured.

Health Day, November 17

Cheap, Older Gout Drug Could Be a Lifesaver After Heart Attack

Donald Lloyd-Jones, MD, Sc-M, chair, Department of Preventive Medicine, was quoted.

CNN, November 20

New 'smart skin' may let you reach out and virtually touch — anyone

John Rogers, PhD, was featured.

More media coverage available online.

Northwestern University NUCATS Clinical and Translational Sciences Institute

NUCATS Corner

The Biostatistics Collaboration Center's annual seminar series, Statistically Speaking, provides staff, faculty and trainees with broadly accessible and useful information on timely biostatistics topics. The lunchtime sessions, which are supported in part by NUCATS, are held in Baldwin Auditorium from noon to 1 p.m. and are accessible via BlueJeans livestream. Video recordings and presentation slides from past sessions (such as sessions focused on REDCap, reproducible research, statistical graphics, power and sample size calculations) are available on the Biostatistics Collaboration Center's website.

Upcoming 2019–2020 Statistically Speaking series sessions:

Wednesday, January 15, noon to 1 p.m.

To p or not to p: reflections on recent p-value statements
Mary Kwasny, ScD, Professor, Division of Biostatistics, Department of Preventive Medicine

Wednesday, March 18, noon to 1 p.m.

Biostat Basics: Some Practical Things to Know
Nina Srdanovic, MS, Statistical Analyst, Division of Biostatistics, Department of Preventive Medicine

Monday, May 11, noon to 1 p.m.

Logistic Regression: Odds & Ends
Lauren Balmert, PhD, Assistant Professor, Division of Biostatistics, Department of Preventive Medicine

Registration is available online.

Smith *Continued from page 4*

How is your research funded?
We are currently funded entirely by the National Institutes of Health (NIH) with prior support coming from the Burroughs Wellcome Fund, Schweppe Foundation, Cold Sore Research Foundation and Life Sciences Research Foundation. The NIH funds projects to study the neuroinvasive properties of these viruses as well as the genetic in-borne errors that predispose to encephalitic infections.

Who inspires you?
My number one inspiration is my postdoctoral mentor, Dr. Lynn Enquist (Princeton University). His love of research and discovery combined with his supportive and well-meaning nature is a rare combination among the most successful in this field. Dr. Julie Theriot (Stanford University) was an early role model both because of her brilliance and passion for science.

Featured Core

Northwestern Proteomics Core

A research center and service-oriented core, the Northwestern Proteomics Core develops advanced, cost-effective proteomics technologies designed to be applied to basic, translational and clinical research of proteomes — a set of proteins produced or modified in a living organism or system. Northwestern Proteomics offers various types of experiments made possible by mass spectrometers available through the core facility. The core operates on both Chicago and Evanston campuses and provides a full array of services for study design, sample preparation, data generation, data analysis, interpretation of results and manuscript assistance.

Northwestern Proteomics works closely with investigators to ensure that efficient access and technological expertise is available to all research teams. The goal is to accomplish research objectives in a timely and cost-effective manner. Through initial consultation and study design, the Proteomics Core provides following services:

- Protein identification from complex, Co-IP and BioID samples
- Quantitative proteomics (labeled and label-free)
- Top-down proteomics (qualitative and quantitative)
- PTM analysis – phosphorylation, acetylation, methylation, glycosylation, palmitoylation and ubiquitination
- Cross-link mass spectrometry
- Targeted proteomics (SRM, MRM, PRM)
- Epiproteomics histone modification panels
- Advanced proteomics sample preparation from body fluids (blood, urine, CSF), tissue, secretome, exosome and mitochondria
- Pre- and post-project consultation, support for publication in primary literature and grant-writing support

In addition, the Proteomics Core generates new assay platforms as needed. The Northwestern Proteomics core facility is directed by Young Ah Goo, PhD, research assistant professor of Proteomics Center of Excellence and Biochemistry and Molecular Genetics.

Contact
Director, Young Ah Goo
young.goo@northwestern.edu
312-503-4427

Location
710 N. Fairbanks Ct.
Olson 8-305

Learn more here.

Sponsored Research

Co-PI: Mark Huffman, MD, MPH, director of the Center for Global Cardiovascular Health, Quentin D. Young Professor of Health Policy and associate professor of Epidemiology in the Department of Preventive Medicine and of Cardiology in the Department of Medicine

Co-PI: Jody Ciolino, PhD, associate professor of Biostatistics in the Department of Preventive Medicine and of General Internal Medicine and Geriatric in the Department of Medicine

Sponsor: National Heart, Lung, and Blood Institute

Title: A Double-Blind Randomized Controlled Trial to Assess the Efficacy and Safety of a Quadruple Ultra-Low-Dose Treatment for Hypertension (QUARTET USA)

This trial will investigate whether initiating treatment with ultra-low-dose quadruple-combination therapy (LDQT; including candesartan 2 mg, amlodipine 1.25 mg, indapamide 0.625 mg, and bisoprolol 2.5 mg) will lower automated office blood pressure and 24-hour ambulatory blood pressure at 12 weeks more effectively, and with no increase in side effects, compared with initiating standard dose monotherapy (candesartan 8 mg) in adults with raised blood pressure (SBP>140 mmHg or DBP>90 mmHg) and without cardiovascular disease.

Our team's preliminary data from a short-term four-week crossover trial of 18 participants suggest that LDQT lowers office blood pressure by 22/13 mmHg on average compared with placebo with no difference in serious adverse events. Effects on 24-hour ambulatory blood pressure were similar. We has begun to perform this phase II, single-site, randomized controlled trial in the Access Community Health Network of federally qualified health centers in the Chicagoland area because this population bears a disproportionate burden of blood pressure-related diseases, and our team has previously successfully conducted clinical studies in this population. This trial also complements the ongoing QUARTET trial of a similar combination in Australia, led by Drs. Clara Chow at the University of Sydney and Anthony Rodgers from The George Institute for Global Health

This new and simpler treatment paradigm has potential to eliminate blood pressure disparities in this population, which provides the motivation for this proposal. While we hypothesize this intervention will be easily implemented and efficacious for all patients and clinicians, we will explore variation in treatment effect by potential moderating variables, including age, sex, race/ethnicity, and health literacy level. Beyond examining efficacy, we also plan to assess feasibility of implementing this intervention in a clinical setting by simultaneously evaluating implementation outcomes of acceptability, preferences, and lessons of LDQT among patients and clinicians.

Read more here.

Funding

Natural Experiments of the Impact of Population-targeted Policies to Prevent Type 2 Diabetes and Diabetes Complications

More information

Sponsor: Department of Health and Human Services Centers for Disease Control and Prevention – ERA
Application Deadline: February 4, 2020

Estimated Total Program Funding: $12,500,000
Award Ceiling: $450,000

Synopsis: This NOFO has two components, A and B. Component A (Natural Experiment Research Centers): To support a five-year multi-center network of independent research centers to evaluate innovative, health system and non-health system-based natural experimental approaches to alter the diabetogenic characteristics of U.S. communities.

Applicants will select one of the following two tracks: Track 1 Evaluation of population-level programs or policies that affect population-level risk factors for type 2 diabetes (such as diet or physical activity, as well as other health behaviors; glucose; prediabetes), or Track 2 Evaluation of programs or policies aimed at improving care and management of diabetes, and the risk for diabetes complications.

Component B (Coordinating Center): To fund a Coordinating Center (CC) to provide organizational, logistic and communication support to enhance the efficiency, productivity and public health impact of the Natural Experiments research centers that are funded as part of Component A.

New Investigator Projects on 4DN Organization and Function in Human Health and Disease (U01 Clinical Trial Not Allowed)

More information

Sponsors: National Institutes of Health
Application Deadline: March 2, 2020
Estimated Total Program Funding: $2,500,000
Award Ceiling: $400,000

Synopsis: This funding intends to support projects from NIH-defined New Investigators that apply new or existing tools to monitor and/or manipulate the 4D nucleome (4DN) in the context of human health and disease. Any human disease or biological process relevant to NIHs mission may be proposed, including environmental exposures (e.g., addictive substances, toxins, psychosocial stress), or studies across development or lifespan. Other relevant time frames may include but are not limited to: circadian rhythms, fasting and feeding cycles, reproductive cycles and sleep/wake cycles.

Stem Cell Investigator Awards

More information

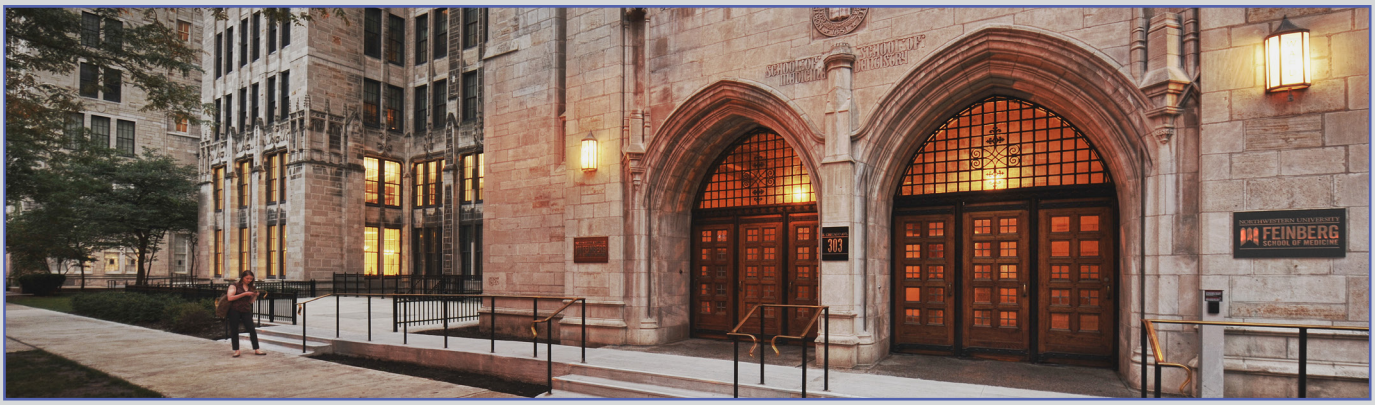
Sponsors: The New York Stem Cell Foundation (NYSCF)
Application Deadline: February 19, 2020
Estimated Total Program Funding: $1.5M over 5 years

Synopsis: NYSCF is soliciting applications from early career investigators for Innovator Awards to be used for exploring the basic biology and translational potential of stem cells. The goal of this initiative is to foster bold and innovative scientists with the potential to transform the field of stem cell research, and advance understanding and use of stem cells in the development of treatments for human disease. In addition to providing funding, NYSCF partners with investigators to advance and translate their research.

Welcome New Faculty

Erica Davis, PhD, joins as associate professor of Pediatrics and Cell and Developmental Biology. She obtained her doctorate degree in molecular genetics from University of Liège (Belgium) in 2005. She was a postdoctoral fellow in the Institute of Genetic Medicine at Johns Hopkins University and completed her postdoctoral work in the Department of Cell Biology at Duke University. An aspiring veterinarian as a child and young woman, she ultimately merged her large animal livestock background with another topic that always fascinated her: genetics. This took her to Belgium to study sheep genetics. Today, her human genetics research focuses on understanding the architecture of rare pediatric disorders impacting development of the brain, face, kidney and heart using zebrafish, mouse and cell-based assays.

Exploring Review Types



By Annie Wescott, Research Librarian

The systematic review sits atop the evidence-based medicine pyramid and is held in high regard in the research community. While a systematic review aims to reduce bias and synthesize evidence, it may not always the best choice for every research question. Whether you are struggling to focus your review question or you are concerned about the time commitment necessary for a systematic review, you may wish to consider other review types that better suit your needs.

Scoping Review

A scoping review can be a standalone review that employs systematic methods or an examination of the literature in preparation for a systematic review. The goal of a scoping review is to assess the scope of a research topic. While a systematic review may ask a specific question, a scoping review can be used to examine a broader research topic. Consider stepping back and looking at the full scope of the literature on your topic if you find yourself struggling to focus your research to a specific question. Note: A scoping review may take as long or longer than a systematc review.

Mapping Review

A mapping review is an excellent option for categorizing the landscape of a research topic and identifying any possible gaps in the literature on a given area. A mapping review may be a good place to start if you find yourself asking a number of questions about a single topic. Similar to a scoping review, a mapping review takes in the scope of the literature and organizes it in order to make sense of the broader conversation.

Literature/Narrative Review

The literature or narrative review is often the first type of review that comes to mind. This review has the most relaxed structure, allowing the author freedom to decide their level of comprehension and synthesis. A literature review is typically narrative in structure and may summarize a topic or cover a range of subjects as it relates to a research question.

Umbrella Review

Are there already a number of reviews on your topic of interest? An umbrella review is a good option when you would like to take a high-level view of the review literature on a research topic and synthesize the information from other reviews. The methods remain similar to the systematic review process, but you are no longer looking for primary research. Instead, you are focusing on identifying what is known and unknown across the review literature on your topic.

Systematized Review

A systematized review allows authors to truncate the systematic review process. This is a great option for those who want to get the feel and structure of a systematic review, but who may not have the time to commit to the process, the necessary team members, or encounter other limitations to the typical systematic review methodology. A systematized review may be a better option for student assignments when the goal is to get a feel for the process without the full commitment to a protracted review process.

Critical Review

A critical review takes a step back from the full scope of the literature on a given topic to focus on the most significant contributions to the research discussion. An author may take a more narrative approach when synthesizing the literature on the topic but would still seek to gather an in-depth understanding of the research question.

Review Type	Typical Use	Important Notes
Systematic Review	• Ask a specific research question • Use pre-specified inclusion criteria • Appraise and synthesize the evidence	• Extended time commitment • Should follow a prepared research protocol
Scoping Review	• Ask a broader question • Identify gaps • Understand the size/reach of a topic	• Extended time commitment • Could involve multiple searches
Mapping Review	• Categorize existing knowledge • Identify gaps in literature • Seeks to understand connections/links	• Does not synthesize results/findings (categorizes)
Literature/Narrative Review	• Summarize or comment on the literature	• Varying levels of comprehensiveness
Umbrella Review	• Review multiple high-level reviews • Focus on competing interventions	• Must include data synthesis • Follows systematic review methods (only includes SRs & meta analyses)
Systematized Review	• Uses elements of the systematic review process • When resources are limited • Used as a graduate assignment	• May be limited in comprehensiveness • Limited consideration of methodology
Critical Review	• Extensive research and critical evaluation of a topic • Looks for significant contributions	• Typically has a narrative output • Subjective output • Launching point for further investigation

Chart adapted from: Grant MJ, Booth A. A typology of reviews: an analysis of 14 review types and associated methodologies. Health Info Libr J. 2009 Jun;26(2):91-108. doi: 10.1111/j.1471-1842.2009.00848.x.

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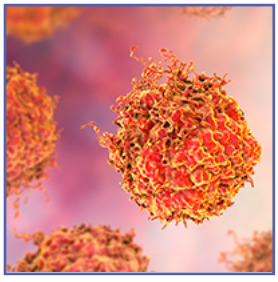

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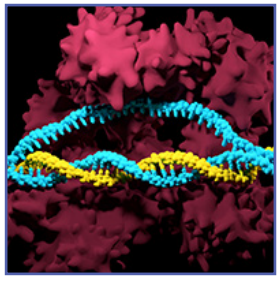

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NIH News

NIH Expands Its Definition of 'Socio-Economic Disadvantaged'

Recognizing the need to encourage and enable careers of biomedical scientists with disadvantaged backgrounds, in 2018 the NIH issued a Guide Notice, encouraging individuals from disadvantaged backgrounds to submit applications. Yet, despite this move, "less than one percent of investigators on diversity supplement applications in FY2018 came in under the disadvantaged background category," wrote Michael Lauer, NIH's deputy director for Extramural Research in a recent post on his "Open Mike" blog.

Lauer goes on to explain that, in order to change these figures, the NIH determined that its definition of "a disadvantaged background" needed improvement. Last month, NIH published a set of new criteria. Read Lauer's full post here.

Extension Policy for K99/R00 Eligibility

Recognizing that childbirth can dramatically interrupt the four-year K99 eligibility window (it is one of the most popular reasons for extension requests), NIH will approve an extension of one year for childbirth, consistent with the New Extention Policy for Early Stage Investigator Status, effective immediately. Men, individuals adopting children and same-sex partners of individuals giving birth can also apply for an extension. For more information, see the full Guide Notice.

Registration Open for the NIH 2020 Regional Seminar

The 2020 NIH Regional Seminar is coming to Baltimore, Maryland, April 20-22. The NIH Regional Seminar offers a comprehensive program for the extramural community about the NIH grants process. Topics include intellectual property, inventions and patents, budget basics, grant writing for success, pre-award and post-award issues for administrators and investigators, animal and human subject research and more. Registration is now open.