Breakthroughs

Feinberg School of Medicine Research Office

November 2022



By Haleigh Ehmsen

Synthetic biology is a robust interdisciplinary field that uses tools and concepts from engineering, physics and computer science to build new biological systems. At Feinberg, scientists are pursuing synthetic biology research to address the health challenges and diseases that humans face. It has been described as using biology's mechanisms of creating molecules to make new molecules biology never knew about. While some may think it's science fiction, new technology makes synthetic biology a reality.

While the field is relatively young, synthetic biology is thriving at Northwestern and driving innovation. Establishing synthetic biology as a research priority at Feinberg has bolstered the university's ability to harness the research and translate it to real-world scenarios.

The <u>Center for Synthetic Biology</u> was established in 2016 to enable scientists from Feinberg, the McCormick School of Engineering and the Weinberg College of Arts and Sciences to engage in collaborative research involving the emerging field. When the <u>Simpson Querrey Biomedical Research Center</u> opened in 2019, the university dedicated space on the 11th floor to allow for collaboration on the Chicago campus.

"Synthetic biology is an exciting field showing enormous promise for scientific impact across many areas—from medicine to national security," said <u>Milan Mrksich, PhD</u>,

professor of Cell and Developmental Biology, vice president for research and founding director of the Center for Synthetic Biology. "Northwestern's leadership in synthetic biology also helps fuel our translational impact, by bringing our innovations from the lab into the marketplace where our research can directly benefit people."

Expanding funding and impact

As the center continues to grow and bring in new faculty to Feinberg, funding is expanding as well. <u>Arthur</u> <u>Prindle, PhD</u>, assistant professor of Biochemistry and Molecular Genetics, received the Early Career Award for Scientists and Engineers (ECASE-Army) from the U.S Army Research Office in 2021. This award allowed his lab to pursue research on bacterial communities known as biofilms. His lab

studies endogenous neurotransmitter production by biofilms, or densely packed communities of bacteria, which could be engineered for strategic advances in in-field biosynthesis and sensing, including within the human gut microbiome.

In his research, Prindle thinks about synthetic biology as programming the cell.



Milan Mrksich, PhD



Arthur Prindle, PhD



Synthetic Biology (continued from cover page)

"If we understand the cell as a machine, we can seek to rearrange the parts of the cell to do a new function," Prindle said.

His research into biofilms continues as Prindle received a <u>R35 Award</u> funded in August 2022. The goal of this work is to uncover how emergent metabolic coordination and cell-to-cell signaling give rise to these collective behaviors in biofilms. This is important because it will reveal new ways to target the unique properties that make biofilms resilient and could impact human health through addressing antibiotic resistance and finding new ways to treat infection.

"With bacterial infections, we want to study biofilms to understand what allows them to thrive and then target that," Prindle said. "Mechanisms inside biofilms keep the bacteria growing slowly, which allows it to dodge antibiotics which target rapidly growing bacteria. We could also use synthetic biology to engineer such bacterial communities to monitor and treat disease within the human gut microbiome."

Often scientists encounter scientific problems for which the technology has yet to be developed to address them. When this happens, investigators can develop the technology they need to address the problem.

Yogesh Goyal, PhD, assistant professor of <u>Cell and Developmental Biology</u>, is doing just that. He joined Feinberg in February 2022 and his lab is studying cancer drug resistance and what is different about cells that develop and become resistant to cancer drugs. He developed a tool called <u>FateMap</u>, which is a framework that combines DNA barcoding with single-cell RNA



Yogesh Goyal, PhD

sequencing to reveal the fates of hundreds of thousands of cells exposed to anti-cancer therapies. Goyal is growing

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into the role and building his lab. "I'm very grateful for the mentorship I've received at Northwestern and opportunity to do this work," Goyal said. "I've been building my lab in a way that our questions — inspired by synthetic biology have no disciplinary boundaries, and we're intentional in the building the team to include members with math, biology and engineering backgrounds so we can approach questions from unique perspectives."

Identifying Protein Structures

High-throughput approaches are designed to increase efficiency and translation to the real world. Recent research_<u>published</u> in Proceedings of the National Academy of Sciences (PNAS) identified a challenging protein design puzzle using a unique high-throughput approach.



Gabriel Rocklin, PhD

Gabriel Rocklin, PhD, assistant professor of Pharmacology

and senior author of the study, noted that the approach could enhance the development of new therapeutics and biotechnology tools.

Protein folding is an essential cellular process that enables proteins to function properly and avoid contributing to disease. As the scientists tried to apply synthetic biology to this problem, one major challenge they ran into when trying to computationally design new protein structures in the laboratory is that most designed proteins are unable to fold into their designed structures when tested.

In the PNAS study, the investigators designed over 10,000 new $\alpha\beta\beta\alpha$ proteins and by using specialized high-throughput experiments, they discovered that more than one-third of them folded into stable structures. The investigators were also able to identify the biophysical properties that stabilize $\alpha\beta\beta\alpha$ proteins as well as compare different protein design methods, according to Rocklin.

"By making changes to our design protocol, we increased our design success rate from two percent to above 30 percent. This clarified better ways to design $\alpha\beta\beta\alpha$ proteins and also helped us understand what makes them stable or unstable," Rocklin said.

The current approach is applicable for any computational protein design effort. Additionally, $\alpha\beta\beta\alpha$ proteins also have the potential to be developed into therapeutics by modifying their surfaces so they can bind to therapeutic targets, according to Rocklin.

The possibilities are endless with synthetic biology, and research on both the Chicago and Evanston campuses, has led to start-up companies established by Northwestern faculty members to provide new technology. In 2021, five of the 19 faculty startups came from synthetic biology.

Melissa Rohman contributed to this article.

Medical School Receives Largest Research Funding in 2022

By Haleigh Ehmsen

Feinberg principal investigators secured <u>\$650 million</u> in research funding and awards during the 2021-22 fiscal year, which is a 6.5 percent increase over the previous year, and the largest amount in the school's history. The medical school receives 70 percent of the university's total funding dollars.

Many research findings were published in the last year. Some key developments included the creation of a <u>pioneering</u> <u>injectable therapy</u> aimed at repairing severe spinal injuries. Scientists also gained additional support to <u>map proteins</u> in the human body, and to understand how the <u>herpes virus</u> invades the nervous system, which can be used to create a vaccine.

"Our growth in research funding demonstrates our faculty's commitment to improving human health through research and continued discovery," said <u>Rex Chisholm, PhD</u>, vice dean for scientific affairs and graduate education and the Adam and Richard T. Lind Professor of Medical Genetics.

"We are continuing to pursue new research areas, while

deepening our understanding of complex mechanisms and the disease that results," Chisholm said. "Going forward, we are also prioritizing implementation science and how to better implement our discoveries in the clinic."

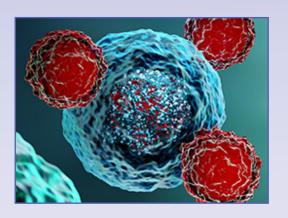
Roughly 29 percent of awarded funds were allocated towards basic science department funding and 71 percent towards clinical department funding. Of the total, \$448 million was awarded from the National Institutes of Health (NIH), a nearly seven percent increase in funding from the NIH over the previous fiscal year. Individual grant awards included 106 individual research fellowships (F awards), 70 career development awards (K awards) and 32 training grants (T awards).

Approximately 6,093 clinical trials and research studies were conducted at Feinberg in the 2021-2022 academic year, led by 686 principal investigators. Additionally, a total of 50 patents and nine new start-up companies were established within the last fiscal year alone.

Breakthroughs Podcast

Uniting scientists and harnessing the power of the immune system to fight disease is at the heart of the new Center for Human Immunobiology. <u>Stephanie Eisenbarth, MD, PhD</u> is leading the new center, she is also the new chief of Allergy and Immunology in the <u>Department of Medicine</u>.

She discusses the variety of immunology research taking place within the new center and its goal of bringing a community of immunologists together to discover and translate innovative science into cures for immune-related diseases. Listen to the episode.



Graduate Student/Post-Doc Events and Opportunities

Global Health Day December 2

Global Health Day, hosted by the Robert J. Havey, MD Institute for Global Health, is an exciting opportunity to draw together global health researchers, educators and students to celebrate and discover more about global health research, education and outreach efforts. This year's event will be held in-person, and will include a poster session, plenary speaker and more. Students, faculty, community members and partners from all disciplines, both at Northwestern and unaffiliated, are welcome to participate and apply to present posters on projects relevant to global health.

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

White Privilege December 7 1:00 to 3:00 p.m.

A lecture/performance featuring Thomas F. DeFrantz with sonicscape by Quran Karriem. Is everyone always automatically expected to share the concerns of people of color? Do we all really have to pay attention to race, religion, sexuality, ethnicity? What constitutes "white privilege"? If I'm not interested in being part of some solution, am I really part of the problem? What if I'm a maker/audience/presenter who happens to be interested in love, or formal structure, or myth, or universal qualities of empathy? What am I to do now? (Approximate run time: 80 minutes)

Abbot Hall 203 (Black Box) 710 N. Lakeshore Dr., Chicago More information

Alzheimer's Disease Seminar Series December 8 Noon to 1:00 p.m.

Join the Mesulam Center for Cognitive Neurology and Alzheimer's Disease for a lecture featuring P. Hande Ozdinler, PhD. Lunch is available for the first 50 attendees on a first-come first-serve basis.

McGaw Pavilion Kellerman Classroom (McGaw 2-322) 240 E. Huron St., Chicago More information

Emily Cooper: Cognitive Science Program Speaker Series, Improving Augmented Reality Through Perceptual Science December 13 4:00 to 5:00 p.m.

Augmented reality (AR) systems aim to enhance our view of the world and make us see things that are not actually there. But building an AR system that effectively integrates with our natural visual experience is hard. AR systems often suffer from technical and visual limitations, such as small eyeboxes and narrow visual-field coverage. An integral part of AR system development, therefore, is perceptual research that improves our understanding of when and why these limitations matter. Cooper will describe the results of perceptual studies to provide guidance on how to optimize the limited visual field coverage supported by many AR systems.

Swift Hall, Room 107 2029 Sheridan Rd., Evanston

Research in the News

U.S News & World Report, October 3 Brain Secrets of the Super-Sharp 'Super-Agers' Tamar Gefen, PhD, was featured.

Reuters, October 11 U.S. Experts Urge Anxiety Screening for Children 8 and Older John Walkup, MD, was featured. The Washington Post, October 17 Ask a Doctor: What Treatments Work for Women with Thinning Hair? Jennifer N. Choi, MD, was featured.

WBEZ Chicago, October 18 Study: South Asian Women See Higher Rates of Diabetes Namratha Kandula, MD, MPH, was featured.

The New York Times, October 25 <u>Uterine Cancer Cases Are Rising. Here's What to Know.</u> Emily Hinchcliff, MD, MPH, was featured.

Understanding and Addressing Cardiovascular Disease Disparities

Nilay Shah, '14 MD, '14 MPH, '20 GME, assistant professor of Medicine in the Division of Cardiology and of Preventive Medicine in the Division of Epidemiology



Nilay Shah, '14 MD, '14 MPH,

20 GME, is a physician-scientist who provides care for adult patients experiencing a range of cardiovascular diseases (CVD). His research aims to understand the development of CVD across the life course, with the goal of identifying an implementing effective CVD prevention strategies. Most notably, he seeks to adapt interventions to

address CVD disparities experienced by populations that are disproportionately affected, specifically South Asian Americans.

What are your research interests?

My research focuses on understanding the factors that underlie the decline in cardiovascular and metabolic health that occurs across the lifespan, with a particular focus on younger adults. The most effective strategies to prevent cardiovascular and cardiometabolic diseases must focus on individuals earlier in life — in childhood, adolescence and young adulthood. I am interested in working toward evidence-based cardiovascular disease (CVD) primordial prevention, which is the prevention of cardiovascular risk factors (like obesity, diabetes, hypertension) from occurring in the first place, which are particularly important at these younger ages.

Currently, I use tools from cohort and surveillance epidemiology, clinical and behavioral intervention trials, implementation science and community engagement to understand the social determinants of suboptimal cardiovascular health in young adults, and I seek to address disparities in cardiovascular disease experienced by populations that are disproportionately affected. Much of my work focuses on the Asian American population which is considerably underrepresented in clinical and population health research, and specifically South Asian Americans because as a group they experience a disproportionately higher burden of cardiovascular diseases at younger ages.

What is the ultimate goal of your research?

I aim for my research to contribute toward equitably preventing CVD for all. There is much to be learned from evidence-based strategies for CVD prevention, but such strategies cannot be uniformly applied in every community and population. I am working to understand how evidence-based prevention can be adapted to communities and populations experiencing disparities and focusing on how to support maintenance of good health starting from younger ages.

How did you become interested in this area of research? My interest in CVD prevention and focus on the Asian American population started at home. I grew up in Chicago's South Asian community. The stories of people in this community and in my own family experiencing diabetes, high blood pressure and heart attacks at younger ages were so common, often as young as their 30s, 40s and 50s. When I decided to train in medicine, public health and research, these narratives echoed, so I applied my training toward clinical care and research focused on this high-risk population. As I worked more in this field, I recognized that the Asian American population more broadly was minimally represented in health research. Now, I focus on cardiovascular disease, cardiovascular health and prevention among the diverse population of Asian Americans.

How is your research funded?

I am primarily funded by a K23 mentored patient-oriented career development award through the National Heart, Lung, and Blood Institute, for which I am the PI of the MASALA-2G Study, which is a second-generation South Asian American offspring cohort to understand cardiometabolic health in young adult South Asians in the Chicago area. I have also received pilot funding from the Northwestern University Clinical and Translational Sciences (NUCATS) Institute and the Eleanor Wood-Prince Grants Initiative.

Where have you recently published papers?

With an interest in cardiovascular health, prevention, health disparities, social determinants and community engagement, my work has recently been published across a range of journals. Some recent work has been published in <u>Annals of Internal</u> <u>Medicine, JAMA Internal Medicine, JAMA, Circulation, Ethnicity</u> <u>& Disease</u> and <u>JAMA Cardiology</u>.

Who are your mentors?

I have sought to build a mentoring community because I value the diverse expertise and perspectives of each of my mentors. I am incredibly fortunate to work with mentors who have invested considerable effort toward my career development, who generously share their expertise, who encourage me to forge my own path, and who I genuinely enjoy working with. My primary mentor is Namratha Kandula, MD, MPH. From our collaboration, I have learned the importance of community engagement and partnering with communities to support health. I also work closely with Mark Huffman, MD, MPH, who is now an adjunct professor of Preventive Medicine and currently a professor at Washington University. He encourages me to be bold and take risks. My first mentor at Northwestern was Donald Lloyd-Jones, MD, ScM, who helped launch my path working in cardiovascular prevention 12 years ago when I was a Feinberg medical student. We have collaborated for several research studies, worked together to implement community health prevention programs and he was my primary mentor for clinical patient care during my cardiology training. I also collaborate closely with Sadiya Khan, MD, MSc, who is an important near-peer mentor who often helps me navigate the early career faculty path.

Identifying How the Innate Immune System Regulates Cardiac Regeneration

Connor Lantz, sixth-year student, Driskill Graduate Program in Life Sciences



Where is your hometown? My hometown is Zionsville, Indiana, a small town about 30 minutes northwest of Indianapolis.

What sparked your interest in science or medicine?

I do not think there was a specific event or circumstance that sparked my interest in

science. I have always been driven to figure out how things work, especially throughout my childhood. For instance, I remember staying up far past my bedtime to build a catapult out of scrap materials in our garage for a science class. After many iterations I was able to optimize the catapult's performance enough to launch a marble across the school, leading to a first-place victory. My inner drive to learn and improve things eventually led me to do an internship at Eli Lilly and Company. There I discovered that I could tap into my motivation to make things work to develop potential treatments and improve human health.

What are your research interests?

During an undergraduate course on immunology, I became deeply fascinated by the immune system's capacity to coordinate the wound healing response after tissue injury. This response is very different than its classical role in protecting the body from foreign organisms such as bacteria and viruses. The wound healing response is crucial in the context of a heart attack, where the adult human heart can permanently lose a billion cardiomyocytes (the heart's muscle cells) and eventually fail to deliver blood to the rest of the body. While adults permanently lose their cardiomyocytes after injury, newborn mammals can remarkably replenish these cells and completely regenerate their heart. The ability of newborns to regenerate their heart is dependent on the presence of innate immune cells. Identifying how the innate immune system regulates cardiac regeneration remains an exciting question yet to be answered and this is my research focus.

What are you currently working on?

As a PhD candidate in the laboratory of <u>Edward Thorp, PhD</u>, I am investigating how the macrophage, a cellular component

of the innate immune system, promotes regeneration within the neonatal heart or maladaptive repair in the adult heart. Little is known about the roles of macrophages during cardiac regeneration; thus, I began characterizing macrophages from neonatal and adult murine hearts. After cardiac injury neonatal macrophages increase distinct phagocytic machinery that may enhance their recognition and engulfment of dying cells. I have linked expression of this phagocytic machinery to increased production of bioactive lipids. Currently, I am teasing out the mechanism behind how recognition and engulfment of dying cells programs macrophages to produce bioactive lipids to coordinate regeneration in the neonatal mammalian heart. My data and scholarly accomplishments resulted in a NIH Ruth L. Kirschstein Predoctoral National Research Service Award.

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

One of the strongest attributes of Feinberg has been the availability of opportunities to develop both in and outside the laboratory. One such opportunity I recently participated in was the Sustained Dialogue series to promote interprofessionalism, which was sponsored by the Office of Diversity and Inclusion. This program brings together students from the graduate, medical, physician assistant, genetic counseling and other programs, to foster relationships and develop strategies to improve interprofessionalism across the Feinberg community. My conversations with my colleagues throughout all these sectors of healthcare helped me realize the importance of my own research outside of the laboratory. Personally, this experience brought to light the necessity for the patient care and research communities to continue to build strong relationships with one another for the overall well-being patients.

What do you hope to do with your degree?

Currently, I am beginning the process of interviewing for postdoctoral fellowships focused on the functions of the innate immune system during development and disease. My dream is to one day be the principal investigator of my own independent laboratory where I would be able to continue to pursue my research interests and more importantly, train the next generation of great scientists.

Building a Career at Northwestern

Den Gonzalez, manager of research administration, Basic Sciences Administration



Where is your hometown?

I was born and raised in Chicago. I spent most of my life here apart from a year I lived in Hawaii. Though my time there was short, I consider it my second hometown which I've missed every day for the past seven years.

What led you to Northwestern?

My family and I have been visiting Northwestern's Evanston campus and its surrounding parks since I was a kid. Such a large campus filled with old buildings, winding pathways, a multitude of trees, with a beach and lake. It was such a beautiful place to explore. I'd never imagine that I'd work here one day but, in 2003, I saw an opening for a program assistant and decided to apply. It's been 19 years since that day and one of the best decisions I ever made. Though I work in Chicago, I do make time to explore the campus and, on special occasions, drive over to Evanston and relive my childhood a little.

What are you currently working on?

As a Manager in BSA, grant administration is just half of what my work entails. The one constant I have is supporting my staff, providing them with all the resources that they need to do their jobs to the best of their abilities. Another part of my role is focusing on onboarding of new hires and continuing education for current staff. We're currently hard at work on revamping our training curriculum for the research administrators as well as updating guidelines, resources and tools for better research administration. When I do find the time, I try to get involved in various campus-wide workgroups regarding research administration processes and tools.

How does your work support the research enterprise at Feinberg?

I would say the work that the research administration team does every day for the Basic Science Administration directly supports the research enterprise at Feinberg. We work closely with our faculty to oversee and manage pre and post-award administration. This would include approvals of procurement and expense reports, proposal development, award setup and management, budget preparation, compliance, effort reporting, financial management and financial reporting and projections. Thus our team has a wealth of shared knowledge to navigate requirements, provide solutions and ensuring compliance to facilitate scientific breakthroughs at Feinberg.

Why do you enjoy working at Northwestern?

In my almost 17 years at Northwestern, I've had the opportunity to work in various positions at central offices such as the Office for Sponsored Research and the Feinberg School of Medicine's Dean's office as well as in the Departments of Physiology, Chemistry, and the Basic Science Administration. At every stop, I've had the pleasure of learning new skills, increasing my knowledge base and being trained and mentored by some of the best managers I've ever worked for. However, the one thing I can single out as being the most enjoyable part of Northwestern are all my colleagues who I've had the privilege of working with. I credit all of them in helping me reach one of my goals to become a Manager of Research Administration, reinforce my dedication and respect for this University, and my growth as the person I am today.

New Faculty

Irene Blanco, MD, MS, joined as professor of Medicine in the Division of Rheumatology in September 2022. She also serves as co-director of Clinical Research Ethics and Equity Consultative Service within Northwestern University Clinical and Translational Sciences (NUCATS) Institute. A rheumatologist by training, she has a particular interest in connective tissue diseases, most notably systemic lupus erythematosus and how it affects underserved populations. Her research focuses on the health disparities in rheumatic diseases and the role of medical education in addressing such disparities to improve patient care and outcomes. Previously she was professor of Medicine and associate dean of diversity enhancement at the Albert Einstein College of Medicine-Montefiore Medical Center. She also serves as co-chair of the diversity, equity and inclusion sub-committee of the American College of Rheumatology.







The NUCATS Institute's Center for Clinical Research (CCR) offers the infrastructure necessary to help you address your study needs, large or small. CCR works closely with local Institutional Review Boards (IRB) at Northwestern University and Ann & Robert H. Lurie Children's Hospital of Chicago as well as external IRB offices to reduce investigator burden, share best practices, maximize quality and efficiency of all programs, and quickly resolve issues when they arise.

If you know which CCR services you would like to use, please complete the <u>CCR intake form</u>. If you are not sure where to start, request a virtual <u>Studio Consultation</u> for an opportunity to learn how CCR services can help with your research project or browse the links below. To learn more about how we can help you, email <u>ccr@northwestern.edu</u>.

Among its many services, CCR offers participant recruitment resources to assist with research study advertisement that you can find by <u>visiting our Research Resources page</u> and sort the Toolkit Directory by "Recruitment." If you'd like to learn more about what participating in a clinical trial involves or to sign up to participate, <u>visit the Feinberg Research site</u>.

Other mechanisms at CCR, include support for:

Multicenter Clinical Trials

The Trial Innovation Network offers support to help investigators execute multi-center clinical trials and studies better, faster and more cost-efficiently.

Clinical Research Coordinator Resources

We offer a number of resources for clinical research staff, intended to support and complement departmental efforts to standardize onboarding and training initiatives.

Clinical Research Units

We offer research-specific nursing and laboratory services for the implementation of clinical research at Northwestern Memorial Hospital and Ann & Robert H. Lurie Children's Hospital of Chicago.

CCR Regulatory Unit

This unit assists investigators with meeting essential regulatory activities and provides training, mentoring and general support to their research staff.

CCR Finance Unit

The Finance Unit assists investigators and study teams with finance-related activities by negotiating budgets and helping to finalize contracts.

NIH News

Feedback Sought on Strengthening Capacity for Emergency Clinical Trials

The White House Office of Science and Technology Policy (OSTP) and National Security Council recently released a request for information seeking ideas on strengthening the national capacity of clinical trial infrastructure and emergency clinical trials. Some areas OSTP is interested in include:

- What do institutions and scientists need to keep the research base warm and ready for action?
- How can we get the enterprise rowing in the same direction from day one, asking the right scientific questions and efficiently coordinating resources?
- How can we ensure that all Americans and all communities have the opportunity to participate in high-quality, impactful clinical research studies?
- How can we make sure this is organized and governed appropriately, across public and private sectors?

Individuals are requested to send ideas in response via email to <u>emergencyclinicaltrials@ostp.eop.gov</u> (including "Emergency Clinical Trials RFI" in the subject line).

Announcing the Inaugural UNITE Progress Report

Covering fiscal years 2021-2022, the UNITE progress report describes NIH's actions to identify and address structural racism that may exist within the NIH and in the biomedical and behavioral research enterprise. It discusses UNITE's initial efforts across four focus areas that aim to elevate health disparities and minority health research across institutes and centers, promote equity in the NIH-supported biomedical and behavioral research ecosystem, promote equity in the internal NIH workforce and improve accuracy and transparency of racial and ethnic equity data related to these efforts. A few achievements since UNITE was launched include facilitating support for funding opportunities on the impact of structural racism on minority health and transformative research to address health disparities, launching the Faculty Institutional Recruitment for Sustainable Transformation (FIRST) program through the NIH Common Fund to enhance and maintain scientific environments that cultivate and benefit from a full range of talent, and harnessing the power of inclusive imagery with the power of an inclusive workspace recognition project so that more NIH staff see themselves reflected on the walls and web pages of NIH.

Feinberg School of Medicine Research Office Breakthroughs

Sponsored Research

PI: <u>Stacy Bailey, PhD, MPH</u>, associate professor of Medicine in the divisions of <u>General Internal</u> Medicine and <u>Geriatrics</u>

Sponsor: National Heart, Lung and Blood Institute



Title: Supporting Transitions to Primary care among Under-resourced, Postpartum women: The STEP-UP

We will test the effectiveness and fidelity of a

technology-enabled, 'stepped care' strategy to connect high-risk, postpartum patients to primary care within under-resourced community healthcare settings. Gestational diabetes mellitus (GDM) and hypertensive disorders of pregnancy (HDP) affect eight to 14 percent of pregnancies annually in the U.S. While GDM and HDP often resolve post-pregnancy, women with these disorders remain at increased, long-term risk of adverse cardiometabolic outcomes. Clinical guidelines therefore recommend that postpartum individuals with prior GDM and/or HDP transition from obstetric care to primary care for ongoing evaluation and/or treatment. Yet studies show only one third of women with GDM and about half of women with HDP see a primary care provider within six months postpartum.

Of those with GDM, only one in five complete recommended dysglycemia testing. Limited patient understanding of cardiometabolic risks, poor coordination between OB and primary care and logistical challenges have been identified as barriers. Women who are Black, Hispanic and/or low-income, with less education and/or low health literacy, are less likely to receive follow-up care. As early detection and treatment of hypertension and dysglycemia reduces disease progression, complications, and mortality, poor transitions in care is an issue of maternal health equity.

In response, we will implement and test our Supporting Transitions to Primary care among Under-resourced, Postpartum women (STEP-UP) strategy. STEP-UP leverages available technologies to support transitions within health centers, from postpartum obstetric to primary care. Specifically, clinical decision support (CDS) in the EHR will prompt provider counseling on the primary care transition; it will also enable providers to order referrals and recommended glycemic tests with a single click. Patients will receive language-concordant materials that reinforce counseling, along with text messages to motivate and remind them to schedule and attend a primary care visit.

STEP-UP was designed to be a low cost and 'low touch' intervention, yet while a technology-based strategy may work for most patients, it will not work for all. A 'stepped care' approach that provides additional, individualized outreach for only those who need it may be necessary. Thus, a centralized outreach coordinator will provide additional, phone-based support for any patient who has not scheduled a primary care visit by four months postpartum. We will test STEP-UP vs. usual care in a steppedwedge trial at four large safety-net health centers. Our aims are to: 1) test the effectiveness of STEP-UP, compared to usual care, to improve: a) primary care visit completion among women with prior GDM and/or HDP, b) testing for dysglycemia among women with prior GDM, and c) detection of dysglycemia and hypertension cases among women with prior GDM and/or HDP. We will also: 2) investigate the heterogeneity of STEP-UP intervention effects by patients' race, ethnicity and language; and 3) assess the reach, adoption, implementation, maintenance and costs of STEP-UP components. If successful, STEP-UP can be readily disseminated to community health centers nationwide.

PI: <u>Rui Yi, PhD</u>, Paul E. Steiner Research Professor of Pathology and professor of <u>Dermatology</u>

Sponsor: Eunice Kennedy Shriver National Institute of Child Health and Human Development



Title: Modeling p63-associated Human Birth Defects with Systems Developmental Biology Approaches

The overarching goal of the proposed research is to understand how point mutations in the DNA binding domain (DBD) of p63 cause different phenotypes in Ectrodactyly, Ectodermal Dysplasia, and Cleft lip/palate (EEC) syndrome. The transcription factor p63 is the most critical regulator governing epithelial fate specification and the maintenance of stemness in adult epithelial tissues. Loss of p63 expression during mouse embryonic development leads to widespread failure of epithelial and limb development. In humans, heterozygous p63 mutations causes birth defects that include ectodermal dysplasia, orofacial clefting and hand/foot malformation. Interestingly, p63 mutations in the DBD often cause different phenotypes in the skin of human patients. This suggests the existence of p63 DBD mutationsensitive enhancers and their regulated genes.

Our preliminary studies have revealed that: 1) p63 profoundly changes transcriptome, chromatin accessibility and signaling competence of epithelial cells during skin development; 2) signaling pathways that are directly relevant to hair morphogenesis, including Wnt and EDAR signaling, are direct targets of p63. This establishes a molecular basis to examine the mechanism of hair defects observed in EEC; 3) our novel R279C and R280C heterozygous and homozygous mutant mice show different defects than p63 KO, revealing distinct biological functions of each mutation; 4) R279C and R280C het mutations differentially affect critical genes involved in epidermal fate specification and induction of hair follicles; 5) R279C het mutation affects the H3K27Ac levels of a subset of p63 bound enhancers.

Our hypothesis is that a subset of p63 enhancers is sensitive to p63 DBD mutations, and their dysregulated genes underlie the defects in the skin of p63 mutants. To investigate this hypothesis, we propose to use systems developmental biology tools including scRNA-seq, scATAC-seq and their associated computational tools, combining with a high-fidelity CRISPR-mediated knockin approach, to examine p63-controlled enhancers and gene regulatory networks (GRNs) in murine skin. We propose to 1) investigate the role of EEC-associated p63 mutations in epidermal fate specification; 2) investigate the role of EEC-associated p63 mutations in hair morphogenesis; 3) elucidate the impact of p63 DBD mutations on open chromatin accessibility, enhancer activity and genome organization. Success of these aims will provide genetic, genomic and molecular insights into the etiology of birth defects caused by p63 mutations.

Read more about the project.

Funding

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

AHEAD (Advancing Head and Neck Cancer Early Detection Research) (U01 Clinical Trial Not Allowed)

More information

Sponsor: National Institutes of Health (NIH) Letter of intent due: December 11 Submission deadline: March 15 Upper amount: \$500,000 per year for up to five years

The purpose of this funding opportunity is to accelerate translation of research to improve early detection of head and neck cancers (HNC). This opportunity seeks applications that focus on early detection of HNC by applying molecular, cellular and multi-omic signatures to clinical studies for differentiating benign from premalignant lesions and identifying prognostic signatures on the transformation from premalignant to malignant lesions.

BRAIN Initiative: Theories, Models and Methods for Analysis of Complex Data from the Brain (R01 Clinical Trial Not Allowed)

More information

Sponsor: National Institutes of Health (NIH) Letter of intent due: 30 days prior to application due date Submission deadline: December 15 Upper amount: Up to \$200,000 per year for three years

This funding opportunity announcement seeks the development of theories, computational models and analytical tools to derive understanding of brain function from complex neuroscience data. Proposed projects could develop tools to integrate existing theories or formulate new theories; conceptual frameworks to organize or fuse data to infer general principles of brain function; multiscale/multiphysics models to generate new testable hypotheses to design/drive future experiments; new analytical methods to substantiate falsifiable hypotheses about brain function.

Autism Research Initiative – Pilot Award

More information

Sponsor: Simons Foundation Submission deadline: January 12 Upper amount: \$300,000 over two years

The mission of the Simons Foundation Autism Research Initiative (SFARI) is to improve the understanding, diagnosis and treatment of autism spectrum disorders (ASD) by funding innovative research of the highest quality of relevance. In particular, we encourage applications that propose research to link genetic or other ASD risk factors to molecular, cellular, circuit or basic mechanisms and set the stage for development of novel interventions.

Immunity in Older Adults (U01 Clinical Trial Not Allowed)

More information

Sponsor: National Institutes of Health (NIH) Letter of intent due: 30 days prior to application due date Submission deadline: February 15 Upper amount: \$400,000 per year for up to five years

The purpose of this funding opportunity is to support studies that provide mechanistic insights into innate and adaptive immune changes that occur during the aging process. The main objective of the program is to define the contribution of age-related altercations in different components of the immune system and the functional consequences in relation to infections, vaccine responses and chronic inflammatory conditions.

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

The Copyright Claims Board: What Everyone Needs to Know

In early 2022, the newly created U.S. Copyright Claims Board (CCB) was established as part of the CASE Act passed by Congress in 2020. The CCB enables people to bring a case against anyone they feel has infringed on their copyright (usually through something the other person has uploaded, reproduced, published, created, distributed, performed or displayed) with judgements capped at \$30,000. The U.S. Copyright Office is still creating the rules that implement this new law, so the information will evolve.

Liz Hamilton, the copyright librarian at Northwestern University Libraries has created a helpful guide, <u>The Copyright Claims Board:</u> <u>Small Claims</u>, with guidance from the Northwestern University Office of General Counsel. Below is a Q&A to help answer some of your questions.

How does the Copyright Claims Board impact me?

The CASE Act was passed by Congress in 2020 to provide creators with an alternative process to the highly expensive and time-consuming process involved with federal litigation of a copyright infringement case. Now a three-member tribunal called the Copyright Claims Board (CCB) within the U.S. Copyright Office will handle small copyright claims. This less-formal, streamlined process may mean an increase in copyright infringement challenges and highlights the importance of remaining vigilant about our own practices of re-using materials (source).

What should I do if I receive a notice?

The general advice is that if you receive notice that a claim is filed against you, and you are a Northwestern student, staff or faculty member, and the claim is related to what you do at Northwestern, promptly contact Northwestern's <u>Office of General Counsel</u>.

If you ignore it and do nothing, the case will proceed in the CCB, and a default judgment can be entered against you. This means that the CCB can enter a judgment holding you responsible for all the damages claimed in the notice (up to \$30,000), regardless of whether the assertions are true or whether you could have claimed any defenses.

What is copyright?

As summarized by the <u>U.S. Copyright Office</u>, "copyright is a type of intellectual property that protects original works of authorship as soon as an author fixes the work in a tangible form of expression."

Faculty, staff and students are copyright owners because they create and fix many different types of works* that are protected by copyright law, including presentations, educational materials, handouts, blog posts, books, research articles, sound recordings, illustration, photographs and so much more.

What rights belong to a copyright owner?

U.S. copyright law provides copyright owners with the following exclusive rights:

- Prepare derivative works based upon the work.
- Distribute copies of the work to the public by sale, rental, lease or lending.
- Perform the work publicly.
- Display the work publicly.

Do I own the copyright?

Copyright can be transferred away from the creator to another entity. U.S. copyright law allows employers to claim the copyright of works created by an employee within the scope of their employment. However, the Northwestern University <u>copyright</u> <u>policy</u> does not claim the copyright of work created by faculty members or students, and instead recognizes the freedom of the university academic community to create and disseminate their works.

Another way that copyright can be transferred is in the publishing process. Publishers of books, journal articles and other items created by Northwestern affiliates may require the creator to transfer their copyright to the publisher by signing a copyright transfer agreement. These agreements can vary: some transferring all rights to the publisher while others allow the author to retain specific rights.

Can I share my works or re-use works that are under copyright?

You can re-use copyrighted works if you have the permission of the copyright owner or if your use falls under an exception in the law, like fair use. Many publishers use a company, such as the <u>Copyright</u> <u>Clearance Center</u>, to handle copyright requests, licenses for re-use and payments for re-use.

Copyright owners can apply a <u>Creative Commons License</u> (or other license) to their work that gives general permission for the display, public performance, reproduction and distribution of a work while also providing copyright owners with four optional restrictions: attribution, non-commercial use, no derivative works or permitting derivative works.

What does it mean to infringe copyright?

According to the <u>U.S. Copyright Office</u>, copyright infringement "occurs when a copyrighted work is reproduced, distributed, performed, publicly displayed or made into a derivative work without the permission of the copyright owner."

Where can I get more information?

Liz Hamilton, the copyright librarian at Northwestern University Libraries has created a helpful guide, <u>The Copyright Claims Board:</u> <u>Small Claims</u>, with guidance from the Northwestern University Office of General Counsel.

• Reproduce the work in copies.

*published materials may be impacted by a copyright transfer agreement

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Featured Core

Biological Imaging Facility

The Biological Imaging Facility (BIF) serves the imaging needs of over 500 scientists representing 144 different labs from 23 different departments across Northwestern University. The facility is organized for users to prepare samples, capture and analyze images and create final presentations and publications in one facility. Training for instruments is also available on a request basis. BIF staff are available to assist users with all aspects of their imaging needs, from experimental design to image analysis and data presentations. BIF is continually looking for new ways to enhance existing equipment, acquire new tools and keep pace with current imaging technologies.

BIF core services include:

- Imaging methods
- Super-resolution microscopy
- Confocal laser scanning microscopy
- Spinning-disk confocal microscopy
- Fluorescence correlation spectroscopy
- Fluorescence recovery after photobleaching
- Fluorescence loss in photobleaching
- Fluorescence/Forster resonance energy transfer
- Widefield fluorescence microscopy
- Live-cell imaging
- Differential interference contrast microscopy
- Phase contrast microscopy
- Image processing and analysis
- Specimen preparation
- Poster printing

BIF recently installed a new Nikon Super-resolution by Optical Re-assignment (SoRa) Spinning-disk Confocal System, which can be used for any regular sample preparation methods for both fixed and live-cell imaging. The facility also won the 2022 Nikon Small World Photomicrography Competition's Image of Distinction award.

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