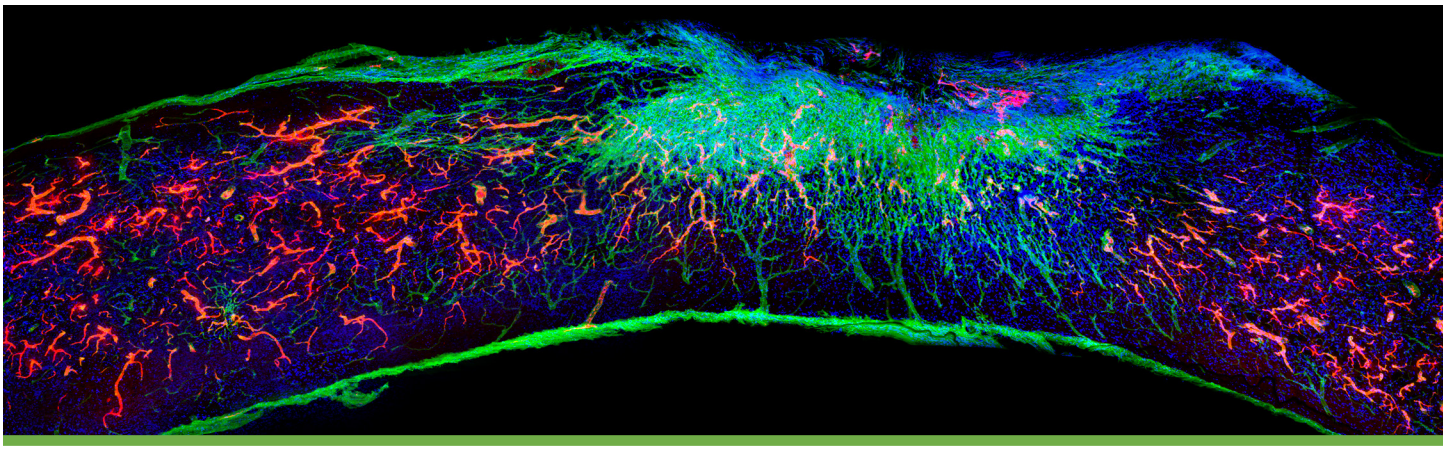
Breakthroughs

Feinberg School of Medicine Research Office

December 2021



Revolutionizing Regenerative Medicine

By Melissa Rohman

In just the last few decades, the field of regenerative medicine has become increasingly interdisciplinary, integrating medicine with areas of science such as chemistry, materials science and biology to further boost the body's own repair mechanisms.

Twenty-two years ago, Samuel Stupp, PhD, joined Northwestern as Board of Trustees Professor of Materials Science and Engineering, Chemistry, Medicine and Biomedical Engineering, with the goal of revolutionizing regenerative medicine using supramolecular chemistry. This emerging branch of chemistry studies how molecules interact with each other to create complex structures such as those observed in living organisms, as opposed to more traditional chemistry which focuses on the synthesis of molecules.

The complex structures that organic molecules can form involve non-covalent interactions, also called "secondary bonds," and the basic science behind this phenomenon is essential for understanding biological processes that rely on these forces to form dynamic structures with remarkable function.

"They are tunable bonds, meaning that we can vary the strength and directionality of those bonds and therefore modify the nature of the structures that form when molecules interact," Stupp said. He is also the founding director of Northwestern's Simpson Querrey Institute for BioNanotechnology (SQI) and its affiliated research center, the Center for Regenerative Nanomedicine.

Innovation with Supramolecular Chemistry

Stupp's research employs supramolecular chemistry to develop functional, self-assembling materials and nanostructures for a range of applications, including tissue regeneration.

In a new study published last month in *Science*, Stupp reported on a strategy to control the collective motion of molecules in supramolecular nanostructures — which contain hundreds of thousands of molecules — and demonstrated how intense motion is a game changer for improving the ability of molecules to activate cellular receptors.

To prove this point, the Stupp laboratory showed that a single injection of nanofibers, in which molecules had intensified supramolecular motion, reversed paralysis within four weeks in a mouse model of severe spinal cord injury. Conversely, diminishing the motion through changes in chemical structure led to only marginal improvement after injury despite using the same biological signals.

Aptly named by Stupp as "dancing molecules," the constantly moving molecules contain two different biological signals and are organized into nanoscale filaments that mimic natural fibrils of extracellular matrices. In addition to restoring walking ability in mice, filaments with "dancing molecules" were linked

(continued on page 2)

Northwestern Medicine®

Regenerative Medicine *(continued from cover page)*

to five signs of repair in the spinal cord. They regenerated axons, reduced glial scarring, rebuilt functional blood vessels, enhanced axonal myelination and saved a high percentage of motor neurons after a severe injury. When motions were slowed through mutations in amino acid sequences of the therapeutic molecules, the efficacy waned significantly.

The recent breakthrough suggests that across many biomedical therapies, the control of supramolecular motion of molecules could help to optimally signal cells for regeneration or to cure diseases. Given the results in the spinal cord injury model, the approach could be particularly useful in treating other conditions in the central nervous system such as stroke, brain injuries and neurodegenerative diseases.

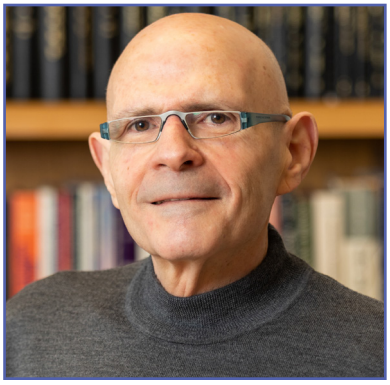
Meeting a Need with 'Dancing Molecules'

There are currently no therapies that trigger spinal cord regeneration after spinal cord injury. According to the National Spinal Cord Injury Statistical Center, nearly 300,000 people in the U.S. are currently living with a spinal cord injury. Less than three percent of people with complete injury will recover basic physical function and many will undergo multiple hospitalizations throughout their lifetimes. Life expectancy for people with spinal cord injuries has not improved for more than 40 years.

"The central nervous system, which is effectively the brain and the spinal cord, has very limited capacity to regenerate," Stupp said.

According to Stupp, the next step is to approach the FDA and begin conversations about what additional tests will be required prior to clinical trials. He also said his team wants to determine whether the therapy can benefit patients who already have spinal cord injury.

"In the initial stages, we envision that this therapy could be used after trauma has occurred, first as a preventive therapy to avoid paralysis or to at least restore more functions," Stupp said.



"Moving forward, we will focus on the chronic injury to see if we can impact patients that already have spinal cord injury. Most importantly, we want to give a better life and a longer health span to those who unfortunately have experienced traumatic injury."

Stupp said the recent publication marks the most important study of his career because it integrated many parts of science and showed how fundamental research could have direct translational impact. The researchers performed molecular synthesis as well as *in vitro* and *in vivo* biological experiments, probed the internal structure and supramolecular motion within the nanostructures using advanced nuclear magnetic resonance techniques and the synchrotron at Argonne National Laboratory, and used computational methods to predict the intensity of the motion.

"Our ability to undertake this huge integration of STEM fields was enabled by the generous support of Lou Simpson and Kimberly Querrey, who established an endowment at SQI to support the field of regenerative nanomedicine," Stupp said. "I think it's a very important message of how basic science is so critical in all of our medical advances."

In 2022, Stupp will receive the American Chemical Society's Ralph F. Hirschmann Award in Peptide Chemistry for his work on the supramolecular chemistry of peptide amphiphiles and their functionality in biological regeneration. The award recognizes and encourages outstanding achievements in the chemistry, biochemistry and biophysics of peptides.

CONTENTS

Reversing Severe Spinal Cord Injuries with Samuel Stupp, PhD

A pioneer in the field of regenerative nanomedicine, Stupp was interviewed on the *Breakthroughs* podcast.

"The way we envision it now, at least in the initial stages, is that it could be used as a therapy after trauma has occurred," Stupp said. "First, as a preventive therapy to avoid paralysis if possible, or at least to restore more functions after trauma has occurred. Moving forward, we will focus on the chronic injury, to see if we can impact patients that already have spinal cord injury."

Listen to the episode here.

Northwestern Receives Grant to Support Equity in Biomedicine

Northwestern University Feinberg School of Medicine has been awarded a grant from the Walder Foundation via the COVID-19 Fund to Retain Clinical Scientists (FRCS) competition, designed to support policies and practices at U.S. medical schools to advance research productivity and retain early-career clinician investigators experiencing family caregiving challenges due to the COVID-19 pandemic.

"COVID-19 had an unprecedented impact on our research enterprise, resulting in a near-complete shutdown of on-campus research operations and shift of our clinical focus, and will affect the careers of our medical school faculty, especially early-career faculty seeking to establish a research program, for years to come. This funding opportunity, supported by the Walder Foundation, will provide a unique opportunity to assist early career clinician investigators negatively impacted by the pandemic due to family caregiving responsibilities by providing resources to help revitalize their research programs," said William Lowe, Jr., MD, vice dean for academic affairs and the Thomas D. Spies Professor of Genetic Metabolism.

The $550,000 grant, part of an overall $12.1 million given to 22 medical schools in 17 states, was made possible by the Doris Duke Charitable Foundation, in concert with the American Heart Association, the Burroughs Wellcome Fund, the John Templeton Foundation, the Rita Allen Foundation and the Walder Foundation. At Feinberg, the funding will award a one-time supplement grant of $30,000 to $50,000 to 12 to 17 early-career clinician investigators experiencing research delays due to family caregiving during the pandemic, while a larger group of faculty will receive further outreach related to support skills and mentoring to help ensure early-career success.

The FRCS is the nation's largest funding collaborative advancing equity in the biomedical sciences. Nationwide, the grants will benefit at least 250 biomedical faculty, supporting faculty experiencing periods of caregiving crisis, such as hiring research personnel, statisticians and technicians, among other uses.

As documented in a recent report by the National Academies of Science, Engineering and Medicine, the COVID-19 pandemic has exacerbated family caregiving demands often borne disproportionately by women and people of color. Faculty in sciences have been especially affected, which may impact representation of women in these fields.

According to the Doris Duke Charitable Foundation, the 22 medical schools including Feinberg chosen for FRCS support all feature a strong body of research, aggressive efforts to provide a more equitable and inclusive environment for faculty and students, and a commitment to further advancing such efforts.

"COVID-19 brought us face-to-face, or Zoom-to-Zoom, with the caregiving demands so many face. This is a crisis for biomedical science — but it can be an opportunity. These medical schools are leading the way in seizing the urgency of the moment to challenge business as usual and to commit to innovative approaches that will assure a more inclusive, equitable future across the biomedical sciences," said Sam Gill, CEO and president of the Doris Duke Charitable Foundation.

NUCATS Corner
Clinical and Translational Sciences Institute

A Year of Resilience, Perseverance and Excellence

By Richard D'Aquila, MD, NUCATS Director

Throughout a global pandemic that has brought unprecedented challenges and altered our workflows and lives in dramatic ways, the NUCATS Institute continues to advance research from bench to bedside to population impact for all.

Following a dynamic and fast-paced reaction to the spread of COVID-19, the NUCATS Institute funded or supported numerous studies that highlight the breadth and scope of research at Northwestern and its affiliates.

Our 11 programs and centers support each step along the translational spectrum: from pre-clinical discovery and entrepreneurship; through clinical trials to assess efficacy; to implementation into widespread practice that improves public health. As one of 61 NIH National Center for Advancing Translational Science (NCATS) Clinical and Translational Science Award-funded hubs — with strong and generous institutional support from Northwestern University — we continue to strengthen resources and opportunities for our members.

Our 2021 Impact Report details some of our accomplishments over the past year.

Additionally, several new initiatives were started this year that I expect to have impact in the coming months. These include more research support for our regional clinical affiliates; community engagement as well as diversity, equity and inclusion; stronger emphasis on the "science" of translational research (for example, how to improve processes applicable to all diseases/disciplines, including implementation science); and new hub and national Clinical and Translational Science Awards (CTSA) consortium collaborations. If you have an idea how we can better accelerate YOUR impact on better health for all, please let us know. Read more.

Graduate Student/Post-Doc Events and Opportunities

Christmas Eve Mass

Friday, December 24, 2021
4 p.m. 7:30 p.m. and 9:15 p.m.
Sheil Catholic Center
Newman Center, 2110 Sheridan Road, Evanston, IL 60208
More Information

Join the Sheil Catholic community for mass on Christmas Eve at Sheil Catholic Center's Evanston campus. Carols begin 15 minutes prior to the scheduled service time and a reception will follow mass. No mass will be held Christmas Day.

Ariel Quartet with Orion Weiss

Friday, January 14, 2022
7:30 p.m. to 9:30 p.m.
Pick-Staiger Concert Hall
50 Arts Circle Drive, Evanston, IL 60208
More information

Recipient of the Cleveland Quartet Award and the Grand Prize at the 2006 Fischoff National Chamber Music Competition, the Ariel Quartet has garnered critical praise worldwide over the course of more than two decades. The quartet regularly collaborates with such eminent and rising musicians and ensembles as violist Roger Tapping, cellist Paul Katz, and the American, Pacifica, and Jerusalem String Quartets, as well as cellist Alisa Weilerstein and pianists Jeremy Denk and Menahem Pressler.

Northwestern University Postdoctoral Association (NUPA) Book Club

Wednesday, January 26, 2022
9 p.m. to 10 p.m.
Online
More information

The NUPA Book Club meets on the fourth Wednesday of each month to discuss the Book Club Read for that month. While hosted by NUPA, you do not have to be a postdoc to join — all Northwestern bibliophiles are welcome.

January Book: "The Black Swan: The Impact of the Highly Improbable" by Nassim Nicholas Taleb

Upcoming Book Club Reads:
February: "Girls Burn Brighter" by Shobha Rao
March: "On Earth We're Briefly Gorgeous" by Ocean Vuong

Mendi + Keith Obadike – Numbers Station 2 [Red Record]

Saturday, January 29, 2022
Wirtz Center for the Performing Arts, Josephine Louis Theater
1949 Campus Drive; 10-30 Arts Circle Drive, Evanston, IL 60208
1 p.m. to 1:45 p.m.
More information

How has art been used to protest, process, mourn and memorialize anti-Black violence within the United States?

Originating at Northwestern University's Block Museum of Art, "A Site of Struggle" explores how artists have engaged with the reality of anti-Black violence and its accompanying challenges of representation in the United States over a 100-year period.

In this piece, artists Mendi + Keith Obadike sonify data from Ida B. Wells' 1895 publication, "The Red Record: Tabulated Statistics and Alleged Causes of Lynching in the United States," with chants and sounds generated from the dates of lynching contained in Wells' text.

Research in the News

***U.S. News & World Report*, November 12**
Mouse Study Points to Possible Breakthrough Against Spinal Cord Injury
Samuel Stupp, PhD, was featured.
This research was also featured in *HealthDay* and *WGN News 9*.

***HealthDay*, November 17**
Too Often, Fatal Heart Attack or Stroke Is First Sign of Heart Trouble in Smokers
Sadiya Khan, MD, MSc, was featured.
This research was also featured in *U.S. News & World Report*.

***Crain's Chicago Business*, November 18**
Northwestern Medicine launches lung center

***WGN 9*, November 20**
The Latest Research on the COVID-19 Vaccine and Pregnancy
Elisheva Shanes, MD, was featured.

***U.S. News & World Report*, November 22**
Booster Shots Prompt Stronger, Longer Protection Than Original Shots: Study
Alexis Demonbreun, PhD, and Thomas McDade, PhD, were featured.

***HealthDay*, November 23**
AHA News: Pulmonary Embolism is Common and Can Be Deadly, But Few Know the Signs
Karlyn Martin, MD, was featured.

More media coverage

Improving Organ Transplantation through Patient-centric Innovation

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

Satish N. Nadig, MD, PhD, is the Edward G. Elcock Professor of Surgical Research and chief of Organ Transplantation in the Department of Surgery. He also leads the Comprehensive Transplant Center and the Northwestern Memorial Hospital Solid Organ Abdominal Transplant Program. He is an internationally recognized transplant surgeon and his research focuses on using nanotherapeutic-based targeted drug delivery and immunoregulation to induce organ transplant tolerance and improve solid organ transplantation and patient outcomes.

Q&A

What are your research interests?
I am interested in novel innovation to induce transplant tolerance. Tolerance is when people don't have to take harmful immunosuppressive medications to keep their organs from rejecting. I am investigating ways of doing that by using a nanoparticle patented from our lab that houses these antirejection medications in much lower doses and targets the organ of need.

What is the ultimate goal of your research?
The ultimate goal of my research is to get organs to last longer after transplant and for people to be free of the shackles of immunosuppressive medications.

How did you become interested in this area of research?
I have always been interested in the idea of transferring tissues and organs from one person to another and the immunology behind this miracle. I was lucky to have been encouraged by pioneers in the field. Since it is such a young field, these pioneers were also the forefathers of the field.

What types of collaborations are you engaged in across campus and beyond?
I am engaged with collaborations across different institutions, most notably with bioengineers and other clinicians.

How is your research funded?
My research is funded both by the National Institutes of Health and by industry funding. This combination is, in my opinion, the most efficient way to get these technologies where they are needed most: to the patient.

Where have you recently published papers?
I have recently published in the *American Journal of Transplantation*, our field's top journal, and the *Journal of the American Medical Association (JAMA)* and *Nature Medicine*.

Who inspires you? Who are your mentors?
I am inspired every day by my patients. My career was inspired most notably by Dr. Kathryn Wood, whom I did my PhD under at Oxford University, and Dr. Anthony Monaco, who was a pioneer in the field and one of the forefathers whom I trained under at Beth Israel Deaconess Medical Center at Harvard University.

Studying Immune Response to Viral Vaccines

Nicole Palacio, fifth-year student in the Driskill Graduate Program in Life Sciences (DGP)

Nicole Palacio, a fifth-year student in the Driskill Graduate Program in Life Sciences (DGP), studies immune response to viral vaccines in the laboratory of Pablo Penaloza-MacMaster, PhD, assistant professor of Microbiology-Immunology.

Q&A

Where did you grow up?
I was born and raised in the west area of Puerto Rico, in a town called Mayagüez. My parents are from Medellín, Colombia, so I grew up influenced by these two amazing cultures.

What are your research interests?
I'm very interested in understanding the immune system in different scenarios, but especially during infection and vaccination. Even though we have made tremendous progress with anti-infective agents, new or improved therapies against pathogens are still needed.

Similarly, in the vaccinology area, improving some of the existing vaccines to induce even more optimal immune responses would have a great impact on public health. Most importantly, we still lack approved vaccines for life-threatening infections such as human immunodeficiency virus (HIV). Understanding how the immune system mounts a response in both scenarios (infection and vaccination) is critical to help us combat infections with powerful anti-infectives and to develop highly protective vaccines to prevent infections.

What exciting projects are you working on?
My thesis work in the Penaloza laboratory aims to develop a novel strategy to substantially improve the immune response and protection induced by viral vaccines. Using preclinical models, we have focused on modulating molecules called interferons during viral immunization. Interferons are immune system molecules that are critical for viral control and immunity to pathogens.

Publishing our findings in the *Journal of Experimental Medicine*, we found that although necessary for the development of a robust immune response following immunization, production of these molecules immediately following vaccine delivery can impair the magnitude and breadth of the immune response.

Interestingly, we have shown with different models of viral immunization that transiently blocking interferons results in higher immune responses and increased protection against infection.

Given the SARS-CoV-2 pandemic, the lab shifted to conduct research to better understand the immune response in COVID-19, immune mechanisms following vaccination, and vaccine development for this virus. I have been lucky to be in a position where I had the immunology expertise to quickly contribute to this new avenue of research in the Penaloza laboratory as well as to participate in our current COVID-19-related collaborations within and outside Northwester.

What attracted you to your program?
The DGP offered flexibility for our laboratory rotations during our first year and this, coupled with the diversity and quality of scientific research at Northwestern, was very appealing to me. Additionally, the friendliness of students, staff and the location of Feinberg convinced me that this was the right place for me to conduct research, receive high quality training and become a successful scientist.

What has been your best experience at Feinberg?
Northwestern has many exceptional and prestigious schools, and both the university and my program enabled me to use those to gain more knowledge and experience in areas outside of science. For example, I took the Management for Scientists and Engineers Certificate offered by Kellogg and the Clinical Research Coordinator course offered by the NUCATS center at Feinberg. This has allowed me to use my time in graduate school to not only develop as a scientist but also to be better equipped for my future career.

How would you describe the faculty at Feinberg?
From the moment I interviewed at Northwestern, I noticed how friendly and approachable the faculty at Feinberg were. In the past four years, I have experienced firsthand how talented, highly collaborative and willing to help faculty members are across departments.

What do you do in your free time?
When I'm not in the lab, I love to cook, travel, try out new restaurants, spend time with friends and family, read, listen to podcasts (I'm an avid podcast listener!) and exercise.

What are your plans after graduation?
Following my PhD completion, I plan to transition into the pharmaceutical industry with the goal of using my scientific expertise to improve patient outcomes in the clinic.

Getting the Word Out: Communications at IPHAM

Adela Mizrachi, communications specialist at the Institute for Public Health and Medicine (IPHAM)

Adela Mizrachi, communications specialist at the Institute for Public Health and Medicine (IPHAM), disseminates research findings by Feinberg investigators and lends her editing skills to grants and manuscripts.

Q&A

Where are you originally from?
I grew up in Des Plaines, a near northwest suburb of Chicago.

What is your educational background?
I have a bachelor's degree in finance with a minor in math from University of Illinois Urbana-Champaign. I also have a master's degree in international education from George Washington University in Washington, D.C..

Please tell us about your professional background.
I started at Northwestern in 2010 as the communications manager for the Center for Global Health (which is now the Robert J. Havey, MD Institute for Global Health). Prior to that, I spent six years at the American Institutes for Research (AIR) in D.C., where I worked in project management and communications. AIR is a non-profit organization that implemented large international development projects primarily funded by the United States Agency for International Development (USAID), so I worked on projects all over the world, including Cambodia, Egypt, Malawi and Ethiopia. I lived in Ethiopia for a year as the head of a project that trained 20,000 sixth, seventh and eighth grade English teachers in a new teaching methodology.

How do you help scientists or research students at the medical school?
I help our researchers get the word out about their research. I do this by using various internal and external communications channels, including the weekly IPHAM Bulletin that goes out to over 4,000 subscribers, the weekly IPHAM public health seminar series, our website, social media channels and a variety of additional Feinberg publications. I also help edit grants and manuscripts for our investigators.

What is your favorite part of the job?
My favorite part of the job is learning about the complex science performed by our investigators and translating the findings so they can be understood by the general public. I enjoy science communications and finding creative ways to communicate complicated topics in a simple way.

What exciting projects are you working on?
I'm currently delving into data visualization as the next skill I'd like to develop to help our researchers communicate about their research.

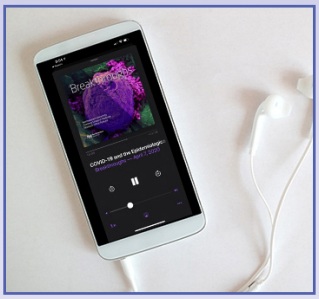
What do you like to do in your spare time?
I am a big fan of podcasts, so I created a side project called Podcast Brunch Club, which is like book club, but for podcasts. I initially set it up for friends in Chicago as a way to gather and chat about podcasts, but since it started in 2015 it has really taken root.

We now have 50+ chapters across five continents, each run by a different local volunteer. I find that it's a great way to learn new things, meet new people and have interesting conversations — and brunch, of course! I also play guitar and love learning languages.

Anything else we should know about you?
I'm a first-generation American. My father is Israeli, my mother is British. I was fortunate enough to grow up traveling around the world to visit family. That really sparked the travel bug for me. Since then, I've traveled to about 25 countries — so many that I had to add pages to my passport.

Tune in to the Latest *Breakthroughs* Podcast Episodes

Listen to candid interviews with the Northwestern physicians and scientists behind the latest high-impact medical discoveries on the *Breakthroughs* podcast. Stay up-to-date on COVID-19 research and other scientific advances, claim continuing medical education credit and subscribe to the show, so you never miss an episode.



Human Genome Project for Proteins with Neil Kelleher, PhD

Earliest Signs of Parkinson's Disease with D. James Surmeier, PhD

More *Breakthroughs* podcast episodes here.

NIH News

NIH UNITE's Listening Sessions: NIH wants to listen and learn from you! Join a session and make your voice heard.

The UNITE initiative was established to identify and address structural racism within the NIH-supported community and the greater scientific community. UNITE initiative will be holding a series of listening sessions from December 2021 through February 2022 to learn about the full range of issues and challenges in achieving racial equity in biomedical research. To learn more or sign up for a session, click here.

ICYMI: Resources and Recording Available From the 2021 NIH Virtual Grants Seminar

Over 15,000 individuals from across the globe joined the 2021 NIH Virtual Seminar on Program Funding and Grants Administration on November 1-4. Whether you attended the event or not, you are still able to view the session recordings and access seminar resources.

Session recordings and staff contacts:

- Session recordings, transcripts and slides: Bookmark the online 2021 NIH Virtual Seminar Presentation Materials webpage.
- Visit the Help page for guidance.
- Looking for a specific presenter? On the Presenters page, click on their names for contact information.

Reference Letter Resource Roundup

Some NIH programs, such as fellowship and mentored career development awards, require the submission of reference letters. Principal investigators designate 3-5 referees to submit letters directly through eRA Commons which are then linked to their submitted applications.

The eRA Commons screens for submitting reference letters were recently updated to enhance user experience, security and stability (see New Look and Feel for Submit Reference Letter Screen in eRA Commons). Since many resources were updated to reflect the new link used for submitting a reference letter, NIH had created a resource roundup to help navigate through these updates.

- How to Apply – Application Guide: Reference Letters – general guidance including tips for selecting referees, instruction documents to provide to referees (fellowship, career development) and an overview of the submission processes
- Reference Letter FAQs
- Video tutorial for submitting reference letters – This short (less than five minutes) video guides referees through the process of submitting reference letters through the eRA Commons.
- Have a referee submit a reference letter – includes step-by-step instructions for using eRA Commons to submit reference letters, screenshots of the information requested through the system and links to online system documentation
- Reference Letters vs. Letters of Support: What's the Difference

Reference letters are only required and only accepted when specifically requested in a funding opportunity announcement. When requested, refer to these resources for a smooth submission process.

Welcome New Faculty

Christopher Crutchfield, PhD, joins as associate professor of Pathology in the discipline of clinical chemistry. He also serves as associate medical director for the Northwestern Memorial Hospital Clinical Chemistry Laboratory. A board-certified clinical chemist, Crutchfield earned his PhD at Princeton University, then completed a research fellowship at the National Institutes of Health and a fellowship in clinical chemistry at Johns Hopkins Hospital. Previously, he was the technical director for clinical chemistry, toxicology and point-of-care in the Department of Pathology and Laboratory Medicine at the University of Cincinnati as well as medical director of the UCMC Ridgeway Tower Clinical Laboratory.

Sponsored Research

PI: Laimonis Laimins, PhD, **chair, Department of** Microbiology-Immunology **and the Guy and Anne Youmans Professor of Microbiology-Immunology**

Sponsor: National Institute of Allergy and Infectious Diseases

Title: Regulation of HPV Replication

Human papillomaviruses (HPV) infect stratified squamous epithelia and link their productive life cycles to the differentiation of the host cell. HPVs infect cells in the basal layer of stratified epithelia and establish genomes as low copy nuclear episomes. When HPV infected cells migrate from the basal layer, they re-enter S/G2 phases in the most differentiated layers to allow for vegetative viral DNA replication in a process referred to as amplification. HPV replication is regulated by viral proteins as well as cellular factors that control cell cycle progression, differentiation and DNA damage repair pathways.

Our recent studies have shown that activation of both the ataxia telangiectasia (ATM) pathway as well as the ataxia telangiectasia and Rad3-related (ATR) pathway is necessary for differentiation-dependent amplification of viral genomes and we have identified many members of these pathways that provide important functions. Our studies further indicate that enhanced levels of DNA breaks in HPV positive cells are responsible for activation of these pathways but the mechanism behind this increase has not been identified.

DNA breaks can be induced by exposure to exogenous DNA damaging agents or through endogenous pathways such as through the action of topoisomerases. We have recently demonstrated that the type II topoisomerase TOP2b is responsible for generating over 50% of DNA breaks in HPV positive cells. Topoisomerases regulate higher order chromatin structures through the transient breaking and re-ligation of one or both strands of the phosphodiester backbone of duplex DNA. Our studies have shown that the levels of TOP2b are increased by a 3 to 5-fold in cells with high-risk HPV genomes. Importantly, knockdown of TOP2b blocks HPV genome replication and moderately reduces viral transcription but has no effect on cell proliferation. Furthermore, knockdown of TOP2b reduced the amount of DNA breaks in HPV positive cells which results in decreased DDR nuclear repair foci.

While our assays demonstrated that over half of total DNA breaks in HPV positive cells were induced by TOP2b, other factors must be responsible for the remaining breaks. Strong candidates for this activity are two other topoisomerases, TOP2a and TOP1, and investigation of this possibility as well as an examination of the role of these enzymes in viral replication are the focus of future work. These studies will provide important insights into how the differentiation-dependent HPV life cycle is regulated.

Read more

PI: Karen Ridge, PhD, **professor of** Medicine **in the Division of** Pulmonary and Critical Care **and of** Cell and Developmental Biology

Sponsor: National Heart, Lung, and Blood Institute

Title: Investigating the Mechanisms that Promote Lung Tissue Repair in Patients with Severe Viral Pneumonia

The multi-collaborative P01 research program is divided into four sub-projects and three research cores led by several Feinberg investigators including Ridge; Navdeep Chandel, PhD, the David W. Cugell, MD, Professor of Medicine in the Division of Pulmonary and Critical Care and professor of Biochemistry and Molecular Genetics; Scott Budinger, MD, the Ernest S. Bazley Professor of Airway Diseases and chief of Pulmonary and Critical Care in the Department of Medicine; Benjamin Singer, '07 MD, 10 GME, the Lawrence Hicks Professor of Pulmonary Medicine; Jacob Sznajder, MD, the Ernest S. Bazley Professor of Asthma and Related Disorders; Richard Wunderink, MD, professor of Medicine in the Division of Pulmonary and Critical Care; and Alexander Misharin, MD, PhD, assistant professor of Medicine in the Division of Pulmonary and Critical Care.

In patients with severe viral pneumonia caused by the influenza A virus or SARS-CoV-2 (the virus that causes COVID-19), dysregulated immune responses drive persistent inflammation and development of the early phases of acute respiratory distress syndrome (ARDS), which occurs when the lower respiratory tract becomes damaged due to fluid buildup in the lungs' air sacs, depriving organs of oxygen.

Despite advances in supportive care, no specific therapies currently exist for patients with ARDS. Unfortunately, most patients will succumb to persistent respiratory failure and multi-organ dysfunction soon after initial infection.

For their project, Ridge and fellow Feinberg investigators plan to identify the immunologic and cellular mechanisms that regulate these immune processes to resolve inflammation and ultimately promote lung tissue repair.

Co-investigators include Deborah Winter, PhD, assistant professor of Medicine in the Division of Rheumatology; Bria Coates, MD, '08, '11 GME, assistant professor of Pediatrics in the Division of Critical Care; Curt Horvath, '92 PhD, professor of Medicine in the Division of Hematology and Oncology and of Microbiology-Immunology; Laura Dada, PhD, research associate professor of Medicine in the Division of Pulmonary and Critical Care; Susanne Herold, MD, PhD, adjunct associate professor of Medicine in the Division of Pulmonary and Critical Care; SeungHye Han, MD, MPH, assistant professor of Medicine in the Division of Pulmonary and Critical Care; and Hiam Abdala-Valencia, PhD, associate professor of Medicine in the Division of Pulmonary and Critical Care.

Read more

Funding

Age-related Macular Degeneration (AMD) Integrative Biology Initiative: Discovery of AMD Pathobiology using Patient-Derived Induced Pluripotent Stem Cell (iPSC)-derived Retinal Pigment Epithelium (RPE) (U01 Clinical Trial Not Allowed) More information

Sponsor: National Institutes of Health and National Eye Institute (NEI)
Letter of Intent Due: January 22, 2022
Application Deadline: February 17, 2022
Upper Amount: $250K

Synopsis: This award aims to support collaborative studies of a unique resource of patient-derived induced pluripotent stem cell (iPSC) lines generated by the NEI age-related macular degeneration (AMD) Integrative Biology Initiative. This resource also includes clinical, genomic and imaging data from the patients from which these cells were derived, and a set of isogenic control cell lines in which the risk allele(s) have been corrected. These cell lines and clinical data are from patients with AMD carrying high prevalence risk alleles selected from the Age-Related Eye Disease Study 2 (AREDS2). The goal of this funding is to determine if these iPSC-derived cell lines can be used to discover the underlying pathophysiology of AMD. Collaborative effort is highly encouraged with investigators bringing in the needed areas of expertise for successful projects.

Understanding Place-Based Health Inequalities in Mid-Life (R01 Clinical Trial Not Allowed)

More information

Sponsors: National Institutes of Health and National Institute on Aging
Letter of Intent Due: February 3, 2022
Application Deadline: March 3, 2022
Upper Amount: $400K

Synopsis: This award intends to support research that uncovers potential modifiable explanations about how 'places' (e.g., countries, U.S. Census regions, states, counties, neighborhoods and locations across the urban-rural continuum) are related to morbidity and mortality among middle-aged adults in order to inform policy responses to address poor mid-life health and health disparities. Specifically, this funding will support studies that: 1) clarify social, economic, behavioral and institutional explanations for place-based health disparities (levels and trends), 2) examine intersections between place and sociodemographic characteristics (e.g., gender, race, ethnicity) to better understand and address processes driving other health disparities and/or 3) include data collection and data enhancements to support the latter.

Research Professor Grants

More information

Sponsor: American Cancer Society
Letter of Intent Due: February 1, 2022
Application Deadline: April 1, 2022
Award Information: Up to two awards are made annually for a five-year term that can be renewed once. The award of up to $80,000 per year (direct costs only) may be used for salary or research project support.

Synopsis: The American Cancer Society offers grants to mid-career investigators who have made seminal contributions that have changed the direction of basic cancer research. It is expected that these investigators will continue to provide leadership in their research area. Applicants will have attained the rank of full professor.

Global Health Day Celebrates Research, Education and Impact

Feinberg's Robert J. Havey, MD Institute for Global Health hosted the 10th annual Global Health Day symposium on December 3, featuring keynote speakers, online poster presentations and question-and-answer sessions.

Held virtually this year, the symposium brought together global health investigators, educators and students to celebrate and learn about global health research, education and outreach efforts being done at Northwestern and beyond.

This year's symposium also coincided with the recent renaming of the institute in honor of Robert Havey '80 MD, '83 '84 GME, deputy director of the institute and clinical professor of Medicine in the Division of General Internal Medicine and Geriatrics. This year also marked the establishment of the Ryan Family Center for Global Primary Care, which was made possible by a historic gift from Northwestern trustees and alumni Patrick G. Ryan and Shirley W. Ryan.

Attendees were able to attend 49 online poster presentations and breakout rooms for Feinberg students and faculty, community members and partners to share global health research and outreach efforts.

To see a full list of poster presentation winners, view the story here.

DataLab at Galter Library

Do you have questions about data use, management and analysis? Not sure where to start with cleaning, organizing or preserving your data? Galter Health Sciences Library and Learning Center's DataLab can help. The DataLab is focused on collaborative innovation, training and development and connecting faculty, staff and students in the Feinberg School of Medicine to data-related resources here at Northwestern. Through our free DataClinic service, we provide consultation and training for all stages of the research data life cycle and link researchers with experts who can help to resolve issues. We engage the research community by teaching, hosting and sponsoring training events and workshops that promote best practices related to data management, reproducibility, compliance with data sharing policies and open science, as well as a range of associated technical topics. Our services and projects reflect our commitment to good data practices and a collaborative culture at Feinberg and beyond.

What can the DataLab do for you?

DataClinic

Galter Library's DataClinic employs a primary care model for data management and analysis. In addition to providing training and best practices support, we offer free consultations for researchers with data issues involving:

- Collection and Management
- Cleaning and Organization
- Analysis
- Visualization
- Preservation

For long-term or specialized support, we refer researchers to our partners here at Northwestern. To request a Data Clinic consultation, please complete our contact form.

Data Education and Community Engagement

Galter Library actively promotes reproducibility and open science best practices by organizing and hosting special events featuring cutting-edge organizations and software tools in the field. For a list of upcoming workshops and events, please visit the Galter Library classes page or our partners at NUIT Research Computing. We also develop resources to serve as a reference for "just-in-time" information support for investigators looking for guidance on Data and Data Management and Biosciences and Bioinformatics.

Innovations

Galter Library is dedicated to building a collaborative clinical and translational research data infrastructure. Projects include:

InvenioRDM: a born-interoperable research data management repository and data catalog to enable best practices in research data management, sharing and reuse. InvenioRDM makes it easy to collect, preserve and disseminate a wide range of research products to enhance individual and institutional visibility, promote people and their expertise, support discovery and accessibility by the international scientific community, and promote open and FAIR science. We're developing InvenioRDM in collaboration with CERN, other national and international partners, and NUCATS.

CTS Personas: a portfolio of role-based profiles representing the translational workforce. Personas can help guide development of resources and services for the translational workforce, such as software, trainings, communication and more.

Credit and Attribution: We are involved in variety of efforts including the Contributor Attribution Model, which provides a data model for representing information about contributions made to research products and the FORCE11 Attribution Working Group, an international collaboration to address issues related to contributor roles and better understanding of research processes and credit.

Clinical Research Data Management Training: To bolster clinical data research support and resources for Feinberg and the Northwestern Medicine Enterprise Data Warehouse, the DataLab is developing an end-to-end training program that introduces clinical researchers to clinical database architecture and clinical coding standards, teaches them how to translate their research questions into queries that will allow them to extract data properly, and how to do so in a way that supports transparency and reproducibility while still respecting guidelines for proper data sharing. This work has been funded in part by the Network of the National Library of Medicine Greater Midwestern Region (NNLM-GMR).

Read more about how Galter's DataLab can help you or reach out for a DataClinic consult.

High-Impact Factor Research

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Featured Core

Neurodevelopmental Core

The Neurodevelopmental Core, housed within Northwestern's Institute for Innovations in Developmental Sciences, provides support to Northwestern investigators, clinicians and students with research, education and assessment technology related to neurodevelopmental research methods. The core offers instrumentation, research space and support, and expertise and training in a variety of developmentally sensitive methods. The core welcomes investigators at all stages of their careers who would like to use cognitive or neurophysiological measures to identify critical neurobiological developmental mechanisms.

Core services include:

- Scientific consultation, workshops and training
- EEG/ERP services
- Eye-tracking services
- Clinical and behavioral measures

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