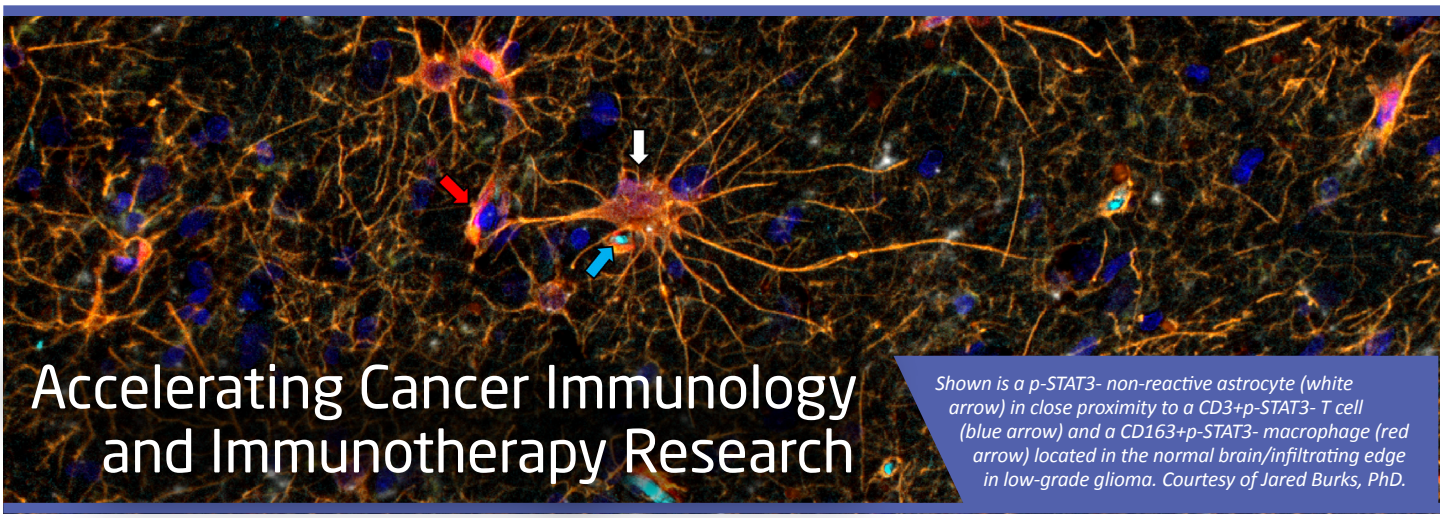
Breakthroughs

Feinberg School of Medicine Research Office

May 2022

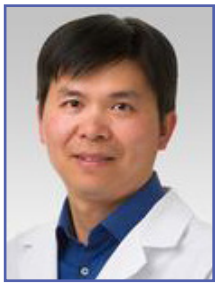


# Accelerating Cancer Immunology and Immunotherapy Research

*Shown is a p-STAT3- non-reactive astrocyte (white arrow) in close proximity to a CD3+p-STAT3- T cell (blue arrow) and a CD163+p-STAT3- macrophage (red arrow) located in the normal brain/infiltrating edge in low-grade glioma. Courtesy of Jared Burks, PhD.*

**By Melissa Rohman**

The accelerated advancement of cancer immunology and immunotherapy, a type of biological therapy that boosts the immune system's ability to recognize and kill cancer cells, has significantly improved the effectiveness of cancer treatment and patient outcomes. One initiative is bringing together investigators who study immunotherapy to increase collaboration and accelerate high-impact immunotherapy research: the Cancer Immunology and Immunotherapy Initiative (CII) at the Robert H. Lurie Comprehensive Cancer Center of Northwestern University.



*Sosman, above and Zhang below.*

Together, Jeffrey Sosman, MD, professor of Medicine in the Division of Hematology and Oncology, and Bin Zhang, MD, PhD, professor of Medicine in the Division of Hematology and Oncology and of Microbiology-Immunology, lead the CII. The initiative, established in June 2020, aims to improve the understanding of the underlying mechanisms of cancer immunology and immunotherapy response, resistance and toxicity.

Since the discovery of immune checkpoint inhibitors in the 1990s, the field of cancer immunology has been advancing rapidly and improving the treatment of solid tumors entirely. Immune checkpoints keep the body's immune system "in check", ultimately preventing it from becoming too strong and accidentally destroying healthy cells.

These immune checkpoints are recruited into immune activation when immune checkpoint proteins, which are located on the surface of T-cells, engage with similar proteins on other cells such as cancer cells. When these proteins bind, they signal T-cells to turn off completely, preventing the immune system from destroying the cancer cell. Immune checkpoint inhibitors, however, prevent these proteins from binding together and allow T-cells to destroy cancer cells.

Over the last 15 years, immune checkpoint inhibitors and other types of immunotherapies have become the main line of defense against more than 10 different types of solid tumor cancers, including breast cancer, skin cancer, bladder cancer and hematologic malignancies.

"I think immunologic approaches have become even more important than chemotherapy for many cancers. It's been a complete transformation of oncology care," Sosman said.

## The Cancer Immunology and Immunotherapy Initiative

The CII provides resources and programs that foster collaboration among basic scientists and clinical investigators across the Lurie Cancer Center and Feinberg who are studying and treating the immune regulation of cancer.

"The overarching goal of the initiative is to integrate the resources and facilities across the center in cancer immunotherapy and help translate benchwork science findings into clinical applications," Zhang said.

Currently, the CII supports investigators pursuing the following research topics: targeting immune suppression in the tumor microenvironment, nanotechnology and biomolecular engineering immunotherapy for cancer treatment, immune-related adverse

(continued on page 2)

## Accelerating Cancer Research *(continued from cover page)*

events in cancer immunotherapy and immune profiling. They are also supporting new strategies that combine epigenetic modulation and immune checkpoint blockade in brain tumors, prostate tumors, skin cancers, renal carcinomas, bladder cancers, pancreatic cancers and ovarian cancers.

According to Sosman and Zhang, the overarching goal of the CII is to increase collaboration, excel high-impact immunotherapy research at the cancer center and help increase visibility and extramural funding for ongoing and future research projects.

"It's great to have everybody interested in studying cancer immunology together pursuing a common goal. It's also important for people who come at this research from different directions to be able to communicate their skills and try to drive more collaboration," Sosman said.

Currently, the CII hosts monthly presentations and meetings for investigators to learn about and discuss research interests and seek collaborative opportunities, as well as workshops and roundtables, research progress meetings and a cancer immunology journal club.

The CII's Immunotherapy Assessment Core also supports investigators by providing cutting-edge, high-throughput technologies and expertise for clinical and translational studies that aim to identify the mechanisms of immunopathogenesis at the single-cell level. The core is also equipped to support investigators who are exploring novel disease-specific biomarkers that may improve personalized immunotherapy approaches.

"That's going to really guide us in how we stratify which patient populations will respond to more intensive therapy, different combinations of therapy or even less intensive therapy," said Zhang, who co-directs the core with Isabelle C Le Poole, PhD, professor of Dermatology and Microbiology-Immunology.

As for the CII, Sosman and Zhang said their hope is for the initiative to eventually become a home for cancer immunotherapy investigators at the Lurie Cancer Center and across Northwestern.

"We'd like to see cancer immunology become a strong enough effort that it can become a major program within the cancer center and provide us a high profile in that area," Sosman said.

### Feinberg Investigates Cancer Immunology

Recently, Feinberg investigators have made the following discoveries that have significantly reshaped the understanding of cancer immunology and immunotherapy:

- A team led by Amy Heimberger, MD, the Jean Malnati Miller Professor of Brain Tumor Research, recently discovered differences in the distribution and interaction of T-cells within the microenvironment of different regions of both brain tumors and brain metastases, according to findings published in the journal *JCI Insight*. The findings demonstrate how the immune cell interactome is distinct between cancer lineages.
- Northwestern Medicine scientists led by Adam Sonabend, MD, associate professor of Neurological Surgery, discovered a new biomarker to identify which patients with glioblastomas, the most common and malignant of primary brain tumors, might benefit from immunotherapy, with their findings published in *Nature Cancer*.
- Research led by Daniela Matei, MD, the Diana, Princess of Wales Professor of Cancer Research, chief of Reproductive Science in Medicine in the Department of Obstetrics and Gynecology, was senior author of the study published the *Journal of Clinical Investigation,* which found the protein FOXK2 promotes survival of cancer stem cells in ovarian cancer and that blocking this protein could reduce cancer recurrence after initial treatment.
- Investigators led by Dong-Hyun Kim, PhD, associate professor of Radiology in the Division of Basic and Translational Radiology Research, found that boosting function of natural killer cells with magnetic nanoparticles could make cancer immunotherapy more efficient, according to a Northwestern Medicine study published in *ACS Nano*. This method could unlock the potential to use natural killer cells on a variety of solid tumors.
- Maha Hussain, MBChB, the Genevieve E. Teuton Professor of Medicine in the Division of Hematology and Oncology, was co-author of the clinical trial published in *Nature* which used circulating tumor DNA to identify patients at risk of urothelial cancer relapse after surgical resection. The findings could help improve post-surgery treatment and demonstrate the power of personalized medicine in cancer therapy.
- Research led by Chyung-Ru Wang, PhD, professor of Microbiology-Immunology, found that boosting mitochondrial function in a subpopulation of T-cells could make cancer immunotherapy more effective, according to findings published in the *Proceedings of the National Academy of the Sciences*. Specifically, Wang's team found that CD1d-restricted natural killer T-cells are much more reliant on mitochondrial metabolism during development when compared with conventional $CD4^+$ T cells, making them an attractive target for boosting immune function in cancer immunotherapy.
- Jaehyuk Choi, MD, PhD, the Jack W. Graffin Professor, discovered that an especially deadly subtype of T-cell lymphoma is distinguished by unique mutations in a specific protein signaling pathway, according to findings published in the journal *Blood*. Correcting the downstream effect of these mutations with a pharmacological inhibitor could be a promising precision medicine treatment.

## CONTENTS

# Women in Medicine Conference Celebrates Gender Equity

**By Melissa Rohman**

Enthusiastic attendees gathered in the Feinberg Conference Center at Northwestern Memorial Hospital for the fourth annual Women in Medicine conference on Friday, April 22, which was held in-person for the first time in three years.

The theme of this year's all-day conference, which was also live-streamed, was "Celebrating Our Voices," and featured presentations and discussion panels that shed light on the gender disparities that exist within medicine and offered opportunities for attendees to network and share experiences and tools to overcome these barriers.

"I do want to acknowledge that it's been a very tough two years for many of us in healthcare, especially women in healthcare, for a variety of reasons. This has caused a huge emotional toll on our communities and ourselves. I look around the room and see many people that are part of my community, so thank you for being here and for being a part of this community today," said Cybele Ghossein, MD, vice chair for Academic and Faculty Affairs in the Department of Medicine and a co-organizer of the conference.

Sarah Friedewald, MD, chief of Breast Imaging in the Department of Radiology, and Angira Patel, MD, MPH, '10, '11 GME, associate professor of Pediatrics in the Division of Cardiology and of Medical Education, were also co-organizers.

Kathleen Hagerty, MBA, provost of Northwestern University, delivered opening remarks on the topic of her own professional journey as a woman in business and higher education, the importance of mentorship for women and what society must do to help more women fill leadership roles.

"These kinds of cultural shifts require commitment and true investment in equity. Gender equity in medicine, or in any field for that matter, is not a woman's issue; it's a societal issue. To create women leaders, you need the buy in from everyone who wants to understand the bariers that women face," Hagerty said.

Presentations and Q&A discussions centered on overcoming barriers to leadership, recognizing and mitigating gender bias in medicine, and promoting one's voice and scientific research in the media.

Ruchi Gupta, MD, MPH, professor of Pediatrics, of Medicine and of Preventive Medicine, and director of the Center for Food Allergy and Asthma, spoke about how scientific research can be used a tool for advocacy and creating policy change and how conducting scientific research is an attainable and fulfilling career path.

"Figuring out what brings you joy, what your skillsets are, and where can you have the most impact and where can you make the biggest change happen, let them percolate in your mind and you'll find your direction," Gupta said.


A panel discussion was moderated by Friedewald, in which panelists talked about recruiting, developing and retaining strong and engaged faculty. Panelists included Howard Chrisman, MD, MBA, professor of Radiology in the Division of Vascular Interventional Radiology and of Surgery; Peggy Kirk, RN, president and chief executive officer of the Shirley Ryan AbilityLab; and Thomas Shanley, MD, president and chief executive officer of Ann and Robert H. Lurie Children's Hospital.

In one presentation, Sandi Lam, '98 MD, PhD, vice chair for Pediatric Neurological Surgery in the Department of Neurological Surgery, discussed the barriers and biases she faced as a woman in neurosurgery, the lessons she learned and why it's important that healthcare professionals and institutions work to achieve gender equity in leadership.

"It's not just because it's the right thing to do, it's because it's the right thing to do for our patients and it's the right thing to do for society," Lam said.

Another panel discussion was about navigating and leading in medicine, and was moderated by Manjot Gill, MD, professor of Ophthalmology and Medical Education.

Panelists included Lam, Amy Krambeck, MD, professor of Urology; Erin Rowell, MD, associate professor of Surgery in the Division of Pediatric General Surgery; and Linda Suleiman, MD, assistant professor of Orthopaedic Surgery and Medical Education, assistant dean of Medical Education, and director of Diversity and Inclusion at the McGaw Medical Center of Northwestern University.

Marianne Green, MD, the Raymond H. Curry, MD, Professor of Medical Education and vice dean for Education, delivered closing remarks to this year's attendees. Green discussed the importance of meaning and growth for women in medicine and how community is essential to achieve both.

"This conference highlights the power of women supporting each other, and I challenge us to take the lessons we've learned from this conference and the community that is here and all around us and insist on systems that ensure equal opportunity for all women. We must promote not only mentorship, but more importantly sponsorship for each other. We must build a culture that recognizes not one definition of success, but many, and provides the path that allows for individual priorities and growth to be supported," Green said.

# Graduate Student/Post-Doc Events and Opportunities

## Telling Time: The Fifth Annual Northwestern Bioethics and Medical Humanities Conference

**Thursday, May 19, 9 a.m. to 5 p.m.**

The Center for Bioethics and Medical Humanities and the Medical Humanities and Bioethics Graduate Program will host a one-day conference dedicated to engaging the Northwestern and Chicagoland communities in the rich, multidisciplinary research and scholarship of our field. Historian and physician Jeremy Greene will deliver the keynote presentation "The Ends of Epidemics: Temporality, Disease and the Uses of History." Additionally, an exciting lineup of panel discussions, centered around this year's theme: time, will showcase diverse work by a mix of Northwestern Medicine clinicians and researchers, colleagues from other Chicagoland institutions and alumni of the Medical Humanities and Bioethics graduate programs.

Baldwin Auditorium, Robert H. Lurie Medical Research Center
303 E. Superior Street, Chicago More information

## TEAM/SBDRC Seminar: Cytosine Modifications and Alternative DNA Structures in Cellular Differentiation and Transformation

**Friday, May 20, Noon to 1 p.m.**

Hear from Vipul Shukla, PhD, assistant professor of Cell and Developmental Biology at Northwestern University Feinberg School of Medicine. The Shukla lab is interested in understanding how cytosine modifications and alternative structural conformations in DNA regulate function genomic states. Shukla will also discuss recent work on how the alternative structural conformations in DNA can impact many established paradigms in genome biology and could serve as unique code for regulating genomic states.

Ward Building, Ward 3-015 conference room
303 E. Chicago Avenue, Chicago
More information

## Global Health Education Day

**Thursday, May 26, 2 to 6 p.m.**

Global Health Day is an exciting opportunity to draw together global health researchers, educators and students to highlight the ongoing work and research in the global health space. Guest speakers include Lise Saffran, MPH, MFA, and Juliet Sorenson, JD.

Simpson Querrey Biomedical Research Center
Potocsnak Atrium, 303 East Superior Street, Chicago
More information

## 29th Annual Cancer Survivors' Celebration Walk and 5K

**Sunday, June 5, 8:30 to 11:30 a.m.**

After two years of celebrating virtually, Lurie Cancer Center and Northwestern Medicine will welcome cancer survivors and supporters back to Grant Park for the 29th Annual Cancer Survivors' Celebration Walk and 5K. The celebration is open to everyone whose life has been touched by cancer, regardless of where they were treated. Highlights include a non-competitive walk or chip-timed 5K race along Chicago's lakefront, t-shirts, music and entertainment, inspiring speakers, activities for the family and an opportunity to share a message on the dedication wall.

Arvey Field
Grant Park, Chicago
More information

# Research in the News

***ABC News, April 1***
COVID booster and pregnancy: Doctors working to combat vaccine hesitancy among expecting mothers
Melissa Simon, MD, MPH, was featured.

***US News & World Report, April 7***
Could Viagra, Cialis Raise Men's Odds for Eye Trouble?
Nicholas Volpe, MD, was featured.

***The Washington Post, April 16***
A tale of many pandemics: In year three, a matter of status and access Mercedes Carnethon, PhD, was featured.

***WTTW, April 16***
Hispanic Transplant Program Encourages Latinos to Become Donors Juan Caicedo-Ramirez, MD, was featured.

***Crain's Chicago Business, April 22***
Heartbeat-tracking tech raises patients' and doctors' worries
Rodd Passman, MD, was featured.

***The New York Times, April 26***
Can Virtual Reality Help Ease Chronic Pain?
Apkar V Apkarian, PhD, was featured.

# Studying the Cancer Cell Transcriptome and Epigenome to Improve Cancer Therapy Response

## Shannon Lauberth, PhD, associate professor of Biochemistry and Molecular Genetics

Shannon Lauberth, PhD, is an associate professor of Biochemistry and Molecular Genetics. Her laboratory is focused on the discovery of clinically distinct alterations in the cancer cell transcriptome and epigenome and how these changes impact patient response to cancer therapies.

**What are your research interests?**
Our research efforts are focused on the discovery of clinically distinct alterations in the cancer cell transcriptome and epigenome, and how these changes impact patient response and resistance to cancer therapies.

With advances in DNA and RNA sequencing technologies, we are uncovering new secrets into the stretches of DNA sequence located between protein coding genes that support production of non-coding RNAs (ncRNAs) that make up the majority of RNAs in our genome. A major focus of our lab is to unravel the biological significance of emerging classes of noncoding RNAs. Excitingly, we have recently found a subset of ncRNAs that are robustly produced in colon and breast cancer and are linked to poor patient survival, lymph node spread and increased tumor grade. Our research efforts are focused on addressing remaining questions that include how these ncRNAs produced in cancer and if they are functional molecules that contribute to tumorigenesis.

**What is the ultimate goal of your research?**
To identify mechanisms underlying tumorigenesis and to uncover novel biomarkers and potential therapeutic targets that will advance the current treatment options for cancer patients.

**How did you become interested in this area of research?**
When I was an undergraduate student at the University of Illinois at Urbana-Champaign, I became interested in gene regulation, or the process of turning genes on and off in different patterns to control cellular functions during development. As a graduate student, I further pursued this interest by studying how a family of developmental transcription factors turned genes off to regulate kidney morphogenesis. During my postdoctoral studies at Rockefeller University, I purified more than 97 polypeptides from the human cell to reconstitute the factors that are sufficient to turn a gene on in a test tube.

The power of this system is that you can examine the direct (causal) roles that individual factors play in regulating a gene and how manipulations in one factor versus another can impact whether a gene is turned on or off. Now in my lab, we study gene control in a variety of human cancers and focus our efforts on discerning how the normal switches of turning particular genes on and off are hijacked in the disease state to mediate very different patterns of gene expression.

**What types of collaborations are you engaged in across campus (and beyond)?**
Northwestern is a very collaborative research environment which has allowed my group to propel our research forward in exciting new directions. For example, we have collaborations with clinical research scientists in the Department of Pathology that provide us with access to patient tissues that are instrumental in confirming our findings performed in human cancer cell lines.

We also have several exciting collaborations with faculty in the Department of Molecular Biosciences in Evanston. Through these collaborations, we are exploring the molecular mechanisms underlying how large protein complexes engage with DNA using state of the art cryo-electron microscopy (cryo-EM) and single molecule tweezers that trap strands of DNA to examine how various proteins manipulate and control the forces and movements of DNA with unprecedented resolution. We have numerous other exciting collaborations both in the local Chicagoland area, across the US and internationally.

**How is your research funded?**
Our research is primarily supported by the National Institutes of Health.

**Where have you recently published papers?**
This week, we published a review article in *Molecular Cell* that is focused on raising awareness of an emerging class of noncoding RNAs that my lab is currently investigating. We have also published in other journals including *Nature Communications*, *Nature Structural and Molecular Biology* and *Blood Cancer Discovery*.

# Epilepsy-associated Gene Mutations

## Rummi Ganguly, Northwestern University Interdepartmental Neuroscience (NUIN) program

Rummi Ganguly, student in the Northwestern University Interdepartmental Neuroscience (NUIN) program, studies epilepsy-associated mutant sodium channel dysfunction in the laboratory of Alfred George, Jr., MD, chair and the Alfred Newton Richards Professor of Pharmacology.

**Where is your hometown?**
I grew up in Portland, OR. Keep it weird!

**What sparked your interest in science or medicine?**
My interest in science and medicine is rooted in my curiosity about the world and a desire to help people. I find it endlessly fascinating that every observation I have and will ever make is the complex product of measurable mechanisms of action at the smallest of scales. My natural tendency to question "why," "what" and "how" is well-exercised in this field, and the idea of identifying and quantifying these mechanisms in pursuit of the diagnosis and treatment of human disease is most fulfilling.

**What are your research interests?**
I wish to connect molecular and cellular processes to systems level phenomenon and clinical phenotypes. I am specifically interested in utilizing computational methods in the diagnosis, analysis and treatment of neurological disease. In my current work, I use electrophysiological and computational techniques in the characterization of epilepsy-associated mutant sodium channel dysfunction to examine its influence on neuronal excitability and epilepsy phenotype.

**What are you currently working on?**
There exists a gap in knowledge in connecting the consequences of epilepsy-associated SCN2A (gene encoding for sodium ion channel Nav1.2) mutations, mutant channel dysfunction and epilepsy phenotype. This makes it challenging to discriminate between benign variants and pathogenic mutations from genetic screenings, which results in imprecise diagnosis and treatment of such individuals. My thesis project narrows this knowledge gap by examining the effects of Nav1.2 mutations on ion channel function and neuronal excitability using electrophysiological, pharmacological and computational tools.

I've examined the functional and pharmacological properties of a recurrent SCN2A mutation and revealed that developmentally-regulated alternative splicing of SCN2A impacts the severity of mutant channel dysfunction. I've also demonstrated that the previously unrecognized enhancement of slow inactivation appears to be a major driver of the mutant channel's loss-of-function phenotype. Through integrating a computational model of Nav1.2 into an induced pluripotent stem cell-derived neuron via dynamic-clamp electrophysiology, I've also demonstrated the ability of Nav1.2 to modulate neuronal firing with respect to its expression and voltage-dependent property perturbations. My hope is that these studies will contribute to drawing the line from genetic screenings, to channel dysfunction, to neuronal excitability and ultimately to clinical phenotype, which in turn will hopefully – eventually – inform the precise and effective diagnosis and treatment of SCN2A-epilepsy patients.

**Please tell us about a defining moment in your education at Feinberg thus far.**
In my third year as a graduate student, I attended a presentation by Dr. Timothy Errington titled 'Increasing Rigor and Reproducibility: Lessons Learned from the Reproducibility Project: Cancer Biology.' This talk coincided with a particularly challenging period of my research when results I observed were inconsistent with published studies and with preliminary studies conducted in my own thesis lab. It was challenging to identify and control for every variable — especially for the minute differences between individuals' research techniques — that contributed to an observation, and the lack of detail in published experimental and analysis protocols made me skeptical of the validity of any studies I read. In his presentation, Dr. Errington acknowledged that there is essentially no such thing as exact replication and suggested complete transparency to qualify any reported experimental results. This concept should be intuitive and common practice in research, but it is not. This presentation significantly shaped my own emphasis on transparency in reporting experimental design and methods just as thoroughly as sharing results and conclusions of my studies.

**What do you hope to do with your degree / what are your plans for post-graduation?**
After completing my PhD, I plan to pursue a career in computational neuroscience or data science in industry. I wish to apply my interdisciplinary neuroscience training towards the treatment of neurological disease, ideally in the field of neural prosthetics or brain-computer interface technology.

# Providing Tools and Data through I.AIM

## Ngan MacDonald, chief of Data Operations at the Institute for Augmented Intelligence in Medicine

Ngan MacDonald, chief of Data Operations at the Institute for Augmented Intelligence in Medicine (I.AIM), helps match investigators with an idea to the data and resources they need to realize research and other projects.

**Where are you originally from?**
I'm originally from Vietnam. My family lived in Saigon, and I was born in the midst of the Vietnam War. We were one of the "boat people" and made our way across the South China Sea to the Philippines. We eventually got accepted into the US in 1980 after nine months at the refugee camp. My aunt lived in Elgin, a suburb of Chicago, so we came here.

**What is your educational background?**
I am a Northwestern alum! I got my bachelor's from Northwestern in 1996. Back then, it was a BS from the School of Speech. I didn't really know what I wanted to do so I accepted a job in human resources. I worked for a few years and realized that I really liked the technology field, so I went back to school at DePaul for my master's in information systems.

**Please tell us about your professional background.**
After graduate school, I spent five years in consulting helping clients build out their business intelligence solutions. This was everything from installing databases and integrating data to creating reports to answer business questions. When I had my first child, the travel was too much, so I went to Health Care Service Corporation (HCSC), a member of the Blue Cross Blue Shield System. At HCSC, I helped to create the Information Governance Program and was responsible for a team of information analysts.

The consulting world lured me back, and I spent four years doing management consulting for payers, providers and software vendors before I was recruited back to the Blue Cross Blue Shield System to be the vice president for Enterprise Data Solutions.

**Why do you enjoy working at Northwestern?**
Working at Northwestern is an entirely different experience than anywhere else I've been. I.AIM was launched right before all the COVID lockdowns and I was the first full-time employee. It is a unique blend of a startup, but inside the confines of a historic institution. Additionally, I really love working on my passion project. This isn't just a paycheck, it's really a lifelong goal I have had of liberating data for healthcare.

**How do you help scientists at the medical school?**
We are the matchmakers and connectors of people, data and tools. We know that when a researcher has an idea, rarely do they also have access to talent and data and tools to be able to execute on that idea. We help to bridge across the university, the medical school and the hospital to find matches between what people need and what others know how to do.

We are building out a health data "gymnasium" that responsibly connects data sets, people and tools. The thing about work in this area is that rarely is there easy access to data and when you do get access, you lack the knowledge for how that data should and can be used. The health data gymnasium makes the data available, connects to tools and also has what I call "data sherpas" to help make sense of the data.

**What is your favorite part of the job?**
I love talking to people and so being an ambassador to what we are doing comes naturally. While my prior jobs have definitely had impact, I feel like my role here at Northwestern, it is more direct. It's much more gratifying to see how we help researchers and students right now, compared to seeing how my data strategy helped a company recoup $1B three years down the road.

**What exciting projects are you working on?**
In addition to the health data gymnasium that I talked about above, we are also working on the second year of the AI Bowl. This year, we are broadening participation and rebranding it the Third Coast Augmented Intelligence for Health Bowl. There are five schools currently on the steering committee and two additional schools who have committed to fielding a team. We will be opening up the applications in May and they will be due August 1. I'm excited to see what the teams come up with!

**What do you like to do in your spare time?**
I like to bake and sew, which I had a lot of time to do during the pandemic. I also have three kids who are 17, 15 and 10. We do a lot of camping and hiking with them. Someday they will be gone and my husband and I plan to trade the house in for a trailer and travel across the US.

NUCATS Corner
Clinical and Translational Sciences Institute

## Do You Have an Upcoming NIH Deadline?

If you are preparing to submit an NIH funding proposal, the NUCATS Institute offers services and resources to support and enhance your grant submission. The NUCATS Navigator Portal provides access to a/an:

- Editable Facilities and Other Resources document
- Request form for a letter of support from NUCATS Director Rich D'Aquila
- Request form for a NUCATS Grant Development and Implementation Studio
- Request form for a consultation or a First-Submission Studio
- NUCATS Navigator who is available to answer your questions about opportunities to leverage NUCATS' services and resources

The NUCATS Institute maintains a suite of services and resources to support and enhance your grant submission. Regardless of what NIH award you are applying for, we have services and resources that can help you and your team through the process.

## Grants Repository Continues to Grow

The NUCATS Grants Repository has expanded to include more grants to aid your grant writing process. A new table of contents has been created and can be searched by:

- Federal non-NIH awards
- F-Series and K-Series
- R-Series, T-Series, and U-Series
- Grant resources
- Industry/Foundation awards
- Budget justification
- Resubmission
- Response to review committee comments
- Human research
- Progress report

All grants in the NUCATS Grants repository are generally younger than five years old, and award start dates are included in each listing. To access the NUCATS Grants Repository, please fill out this access request form. If you are willing to share your funded grants in the repository, please submit your grant here. If you have any questions, email jaime.ziegler@northwestern.edu.

# NIH News

### Insights on the Federal Budget Process and What it Means for NIH Research

Since the release of President Biden's Fiscal Year 2023 budget proposal, many stakeholders questioned where NIH stands in the budget process. President Biden's budget proposes an increase over the FY2022 Continuing Resolution for all of NIH's 27 Institutes and Centers. Major funding initiatives include cancer research, pandemic preparedness, nutrition science, combatting overdose and addiction, and health disparities and inequities research.

### Reducing Administrative Burden in Laboratory Animal Research: What Have We Done Recently and What's Coming…

NIH has been working diligently to reduce administrative burdens associated with laboratory animal research programs, while maintaining high standards of animal welfare as well as the integrity and credibility of the research. NIH's Office of Laboratory Animal Welfare (OLAW) offers virtual trainings to assist institutions to optimize animal welfare, enhance communication with investigators and recognize pitfalls that increase unnecessary administrative burden.

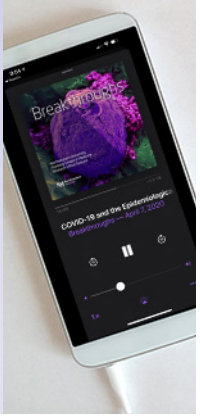
### FY 2021 Data on Age at Enrollment in Clinical Research Now Available

NIH is pleased to announce that for the first time, data are now available on the age of participants in NIH-supported clinical research. The newly available information on age adds to already reported data on participant sex or gender, race and ethnicity. NIH hopes these age-related data, and the updates to them going forward, will be helpful to get a better understanding of who is participating in NIH-supported clinical research. The NIH Inclusion Across the Lifespan (IAL) policy requires individuals of all ages be included in supported research absent compelling scientific or ethical reasons.

## Breakthroughs Podcast

A novel gene therapy promoted transfusion independence in more than 90 percent of adult and pediatric patients with transfusion-dependent beta-thalassemia. Study co-author Jennifer Schneiderman, MD, discusses results, published in the *New England Journal of Medicine*.

Listen to the episode here.



# Sponsored Research

**PI: Rishi Arora, MD, Professor of Medicine in the** Division of Cardiology

**Sponsor: National Heart, Lung, and Blood Institute**

**Title: "New and Disruptive Therapeutic Approaches to Target Fundamental Molecular Mechanisms Underlying Atrial Fibrillation"**

Atrial fibrillation (AF) is the most common heart rhythm disorder that affects more than six million Americans and is a major cause of stroke. Since AF is primarily an age-related disease, it is fast becoming an epidemic in a rapidly aging population. Unfortunately, current therapeutic approaches to AF, both pharmacological and ablation-based, are sub-optimal in patients with persistent AF. This is thought to be because current treatments do not target the fundamental, molecular mechanisms that cause AF.

Over the last several years, the Arora lab at Northwestern University has worked hard to better understand the molecular mechanisms underlying AF, with the long-term goal of developing a mechanism-guided therapeutic approach to AF. Work done in the Arora lab over the last several years in large animal models of AF has demonstrated that autonomic nervous system signaling, oxidative injury and CAMKII signaling are important mechanisms leading to electrical remodeling of key ion channels and excitation contraction coupling proteins in the atrium, thereby leading to the establishment of substrate for paroxysmal AF.

The goal of the Arora lab over the next several years is to obtain a better understanding of the molecular mechanisms that underlie the progression of paroxysmal AF to persistent AF. We postulate that structural changes in the atrium such as new parasympathetic nerve sprouting, NLRP3 inflammasome mediated fibrosis and HDAC6 mediated breakdown of microtubules (derailed proteastasis) are key mechanisms underlying this progression of AF. We will study these mechanisms in chronically tachypaced large animal models of AF by using novel gene therapy approaches developed in our lab over the last several years. Success of these gene therapy approaches in arresting progression of paroxysmal AF to persistent AF will also demonstrate their therapeutic potential.

Read more about this project.

**PI: Kathryn Macapagal, PhD, Research Associate Professor of** Medical Social Sciences and Psychiatry and Behavioral Sciences

**Sponsor: National Institute of Mental Health**

**Title: "Effectiveness and implementation of text messaging to improve HIV testing in sexual and gender minority adolescents"**

Adolescent sexual minority males, transgender girls, and gender diverse teens (ASMM/TGD) are disproportionately affected by HIV, accounting for 79 percent of new infections among 13–18-year-olds. Although the Centers for Disease Control and United States Preventive Services Taskforce recommend HIV screening among teens, testing rates among this group are very low (1 in 4 ASMM; <1 in 10 TGD). Increasing HIV testing in these adolescents is critical to mitigating transmission rates and in linkage to care for those who test positive. Despite being disproportionately affected by HIV, few developmentally tailored HIV prevention interventions exist for these adolescents, and to date, no CDC best-evidence interventions for this group are focused on increasing HIV testing as a primary outcome. Moreover, widespread adoption of digital HIV prevention programs has lagged due to lack of attention to implementation throughout software development, intervention design, and testing.

G2G was a six-week text message-based HIV risk behavior reduction program originally designed for cisgender, gay, bisexual and queer teen boys. The G2G pilot showed adolescents in the active treatment arm were over three times more likely to report being tested for HIV at follow-up versus those in the control arm, even though only a minority of messages focused on testing.

A team led by Macapagal will conduct a Hybrid Type 1 effectiveness-implementation trial that will establish G2G's effectiveness and identify best practices for implementing digital HIV prevention/testing for teens via three specific aims. 1) They will collaborate with youth to add content reflecting our increased emphasis on HIV testing and update gender inclusivity and cultural relevance of existing content. 2) They will test G2G's effectiveness on the primary outcome of HIV testing in a nationwide randomized controlled trial with 360 ASMM/TGD aged 13-18. 3) They will convene a group of experts in sexual and gender minority youth research and service provision to identify and achieve consensus in processes of, requirements for, and barriers/facilitators to reaching and engaging adolescents for HIV testing/prevention.

Read more about this project.

# Funding

The Feinberg School of Medicine has increased seed funding 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 here.

## Michelson Prizes (Immunology and Vaccines)

More information

**Sponsors: Human Vaccines Project/Gary Michelson Medical Research Foundation**

**Submission deadline: June 26**

**Upper amount: $150,000**

**The Michelson Prizes:** Next Generation Grants are research grants given annually to support promising researchers who are applying disruptive concepts and inventive processes to advance human immunology, vaccine discovery and immunotherapy research for major global diseases. The committee will be looking for research aimed at tackling the current roadblocks that exist in human vaccine development and expanding our limited understanding of key immune processes that are fundamental to successful vaccine and immunotherapy development.

## Rising Star Awards (Neuropsychiatric disorders)

More information

**Sponsor: One Mind Institute**

**Submission deadline: June 6**

**Upper amount: $300,000 over three years**

The One Mind Rising Star Awards fund pivotal, innovative research on the causes of and cures for brain disorders. Proposals on any of a wide range of neuropsychiatric conditions are in scope, with studies focusing on bipolar disorder of special interest, including applications that would advance therapies for bipolar disorder. The award winners will be awarded a $300,000 research grant over the course of three years to catalyze a deep mechanistic understanding of psychiatric disorders and therapeutic action, with the end goal of identifying or developing biomarkers and therapeutic interventions to better diagnose, treat and prevent such disorders.

## Research Grants and Fellowships for SCI/D

More information

**Sponsor: Paralyzed Veterans of America Foundation**

**Submission deadline: July 1**

**Upper amount: $150,000**

The Paralyzed Veterans of America Research Foundation is focused on funding projects grounded in basic laboratory science and the education of scientists working towards breakthroughs directed toward a cure for paralysis or the secondary medical conditions and technologies associated with spinal cord injury or disease (SCI/D). These projects should be designed to find better treatments and cures for paralysis and support efforts to improve the quality of life of individuals with SCI/D until improved clinical treatments, technologies or cures are discovered.

## Cancer Prevention, Detection, Diagnosis and Treatment Technologies for Global Health (U01 Clinical Trial Optional)

More information

**Sponsors: National Institutes of Health and National Cancer Institute**

**Submission deadline: June 18**

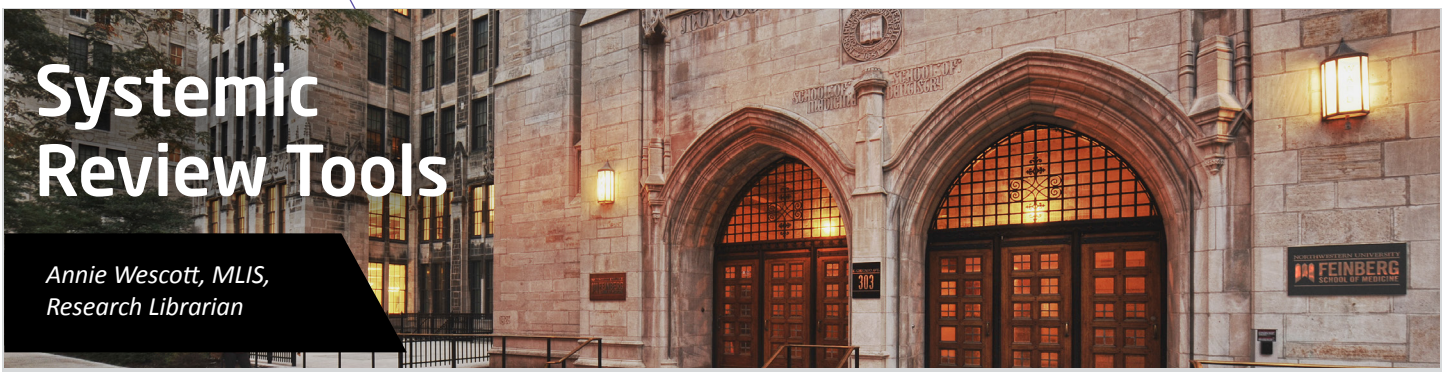
**Upper amount: $475,000 per year, up to 5 years**

The funding opportunity supports the development of cancer-relevant technologies suitable for use in low/middle-income countries. Specifically, this opportunity solicits applications for projects to adapt, apply and validate existing or emerging technologies in a new generation of user-friendly, low-cost technologies for preventing, detecting, diagnosing and/or treating cancers in people living in low/middle-income countries.

# New Faculty

Jochen Lorch, MD, joined as professor in the Department of Medicine (Hematology and Oncology) in November 2021 and is leading the Head and Neck and Thyroid Medical Oncology Programs. Lorch specialized in cancer of the head and neck including squamous cell, salivary gland and thyroid cancer. Prior to coming to Northwestern, he was a medical oncologist at Dana Farber Cancer Institute where he was the director of the Thyroid Center as well as associate professor of Medicine at Harvard Medical School.

# Systemic Review Tools




*Annie Wescott, MLIS, Research Librarian*

A systematic review aims to capture and appraise the full scope of literature on a specific research question. Systematic reviews follow a multistep, fully transparent process. Various resources exist to reduce bias, aim for transparency and make the process easier to navigate.

### Guidelines and checklists

The PRISMA 2020 and PRISMA-P checklists are the most well-known guidelines for systematic reviews and their associated protocols. These checklists can be used as a guide to complete a high-quality review. You can learn more about PRISMA 2020 and PRISMA-P in the Protocol Development GalterGuide.

### Registration

It is important for a systematic review to have an established protocol to ensure transparency with the systematic review process. The protocol should be registered and available to others prior to the screening process. PROSPERO is one of the best-known sites to register a systematic review. It is also useful to search PROSPERO to check whether a review protocol has previously been registered on your topic of interest to avoid duplicating the effort of another team. There are other options for registration available, including publishing a protocol with Systematic Reviews Journal.

### Information sources

One of the main objectives of a systematic review is to capture the complete picture of a specific research question. To do so, it is best to search across several databases. The search syntax and controlled vocabulary (database indexing language used to identify literature by topic) vary by database. Database rules are always available in the "help" or "training" sections of the platform. Check out our Systematic and Scoping Review GalterGuides to learn about partnering with a Galter librarian on your next systematic review.

### Data management

Searching multiple databases results in a large set of references. Duplicate references are common because of the overlap of journals indexed across various databases. Citation management software can be used to organize, deduplicate and manage references. EndNote is the supported citation management software at Galter Library and the library offers monthly classes to support your research and work.

### Selection process

Systematic reviews require at least two screeners who are blinded to each other's inclusion and exclusion decisions. Covidence and Rayyan are two reputable screening tools available to systematic review teams. Covidence is a subscription-based software that can be purchased by review teams. Rayyan has a free platform (at the time of this article) that allows for blinded screening and easy comparison for conflict resolution. Check out the Rayyan GalterGuide for more tips.

### Risk of bias

When evaluating studies, it is important to discuss the risk of bias within each study as it can be present at any stage of the research process. Bias happens, and the risk of bias assessment is not necessarily a discussion of study quality. It is meant to communicate instances of bias that may have been introduced in each study's research process. No standard for risk of bias assessment exists, so it is up to each review team to select a risk of bias checklist that best suits the study design being evaluated or the publishing journal's recommendations or preferences. The Tools for Reviewers GalterGuide includes links to various Risk of Bias checklists.

### Data collection

Data collection processes are unique to each systematic review since there is not a set standard of practice for data collection. The Cochrane Collection has created guidance and templates that can be adapted to the needs of an individual review. Systematic review teams should determine how to effectively communicate supporting data with transparency and consistency and acknowledge when data is unclear or missing.

### Confidence in cumulative estimate

It is important to articulate the strength of evidence collected when synthesizing the included literature in a systematic review. The Confidence in Cumulative Estimate can be determined using tools such as GRADE, which stands for Grading of Recommendations Assessment, Development and Evaluation. Discussing the quality of evidence in a systematic review helps to determine certainty of evidence based on factors like inconsistency, publication bias or imprecision in the study.

Galter Library provides a wide range of services to support the systematic review process. For questions or support please contact your Liaison Librarian.

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# Featured Core

## Lurie Cancer Center Clinical Trials Office

The Lurie Cancer Center Clinical Trials Office facilitates the development, conduct, quality assurance monitoring, compliance with regulatory agency requirements and evaluation of clinical research trials at the cancer center. The office coordinates all aspects of clinical research conducted in medical oncology, malignant hematology, gynecologic-oncology, neuro-oncology, radiation oncology, surgical oncology and chemoprevention.

The office provides robust oversight on all aspects of clinical research through several committees, which work together to provide comprehensive review and monitoring oversight for investigators. The office provides support for pharma-sponsored studies and investigator-initiated studies, including filing investigational new drug (IND) applications. The office also offers a variety of clinical office tools and supports the cancer center's partnership with their National Cancer Trial (NCTN) affiliate network to further advance oncology research.

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