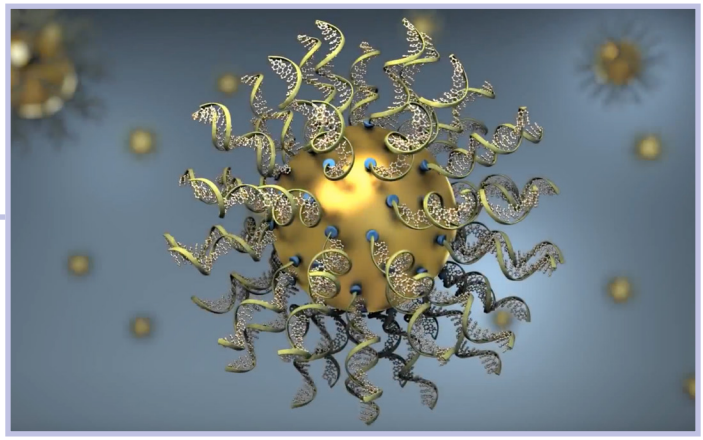
Breakthroughs

Feinberg School of Medicine Research Office

September 2021

Translational Science: Glioblastoma



By Will Doss

Glioblastoma is one of the deadliest known cancers. While the advent of immunotherapy and other cutting-edge treatments have prolonged life for people afflicted with other types of cancer, the prognosis for glioblastoma has remained relatively constant: just 18 months.

That year and a half can be brutal as the brain is bombarded with radiation in an attempt to force the cancer into submission, often with little success. Glioblastoma is notoriously resistant to therapy, quickly adapting and roaring back with deadly results.

"It's not an exaggeration to say that nearly every glioblastoma patient will, unfortunately, succumb to the cancer. It is, in nearly all cases, incurable," said C. David James, PhD, professor emeritus of Neurological Surgery.

The SPORE is led by Maciej Lesniak, MD (left), and C. David James, PhD (right).

The lethality of glioblastoma and the paucity of effective treatments is what spurred Maciej Lesniak, MD, chair and Michael J. Marchese Professor of Neurosurgery, along with James, to apply for a Specialized Program of Research Excellence (SPORE) grant from the National Cancer Institute. They didn't do this alone: The 2017 arrival of renowned neuro-oncologist Roger Stupp, MD, the Paul C. Bucy Professor of Neurological Surgery and chief of Neuro-Oncology in the Department of Neurology, bolstered the glioblastoma expertise at Northwestern, and his continued leadership has been a tremendous boon to the program, Lesniak said.

Northwestern's Brain Tumor SPORE — part of the Robert H. Lurie Comprehensive Cancer of Northwestern University — is now 3 years old, and the bench-to-bedside process is producing results. Under Lesniak's leadership, the SPORE has made advances in understanding the genetic basis of the disease and developed potential therapies that reduce treatment resistance and clinical trials using immunotherapies, all while upholding the SPORE philosophy of collaboration and team science under one roof.

Genetics of glioblastoma

Since The Cancer Genome Atlas (TCGA) published its landmark 2008 analysis of the genetics of glioblastoma, scientists such as Alexander Stegh, PhD, associate professor in the Ken and Ruth Davee Department of Neurology Division of Neuro-Oncology, have used that roadmap to guide their research.

"The TCGA gave us this 'periodic table' of genes that are deregulated in glioblastoma," said Stegh, who is also an associate professor of Medicine in the Division of Hematology and Oncology.

While some cancers have oncogene activations that are relatively simple to single out, there's an emerging understanding that glioblastoma is caused by variants of many genes. This is why previous attempts at therapies targeting single genes failed, such as those targeting alterations of the *EGFR* gene, and why Stegh focuses on genetic deregulation that contributes to therapy resistance.

"Rather than going in there with the very ambitious goal of identifying multiple genes and dialing down their expression levels, we take a slightly different approach," Stegh said. "How can we specifically downregulate genes that cause therapy resistance, as an adjuvant therapeutic approach."

Stegh has published several papers identifying important genes implicated in glioblastoma therapy resistance, but one gene, called *Bcl2L12*, was found to be especially amenable to therapeutic delivery.

Combining his genetic expertise with the nanotechnology expertise of Chad Mirkin, PhD, professor of Medicine in the Division of Hematology and Oncology; and the clinical trial expertise of Priya Kumthekar, MD, '08, '11, '12 GME, associate professor of Neurology in the Division of Neuro-Oncology, the investigators designed a spherical nucleic acid (SNA) drug that crossed the blood-brain barrier and primed tumor cells for death.

(continued on page 2)

Glioblastoma *(continued from cover page)*

The trial, published in *Science Translational Medicine*, was the first of its kind to show that a nano-therapeutic crossed the blood-brain barrier and into brain tumor cells in patients.

"This unique 3D design has the ability to infiltrate tumor cells to correct the genes inside and make them susceptible for therapy-induced killing," Stegh said.

Bcl2L12 was initially identified as a treatment target by Stegh in 2007. "To go from identifying this gene during my postdoctoral work, to get to the point of actually targeting it and establishing proof-of-concept in patients, it's very gratifying," Stegh said. "We are looking forward to building on this success."

Breaking through

A recurrent obstacle in glioblastoma treatment is the blood-brain barrier. Efforts to develop treatments beyond simple chemotherapy are often stymied by the selective permeability of the barrier, but projects in the SPORE are using emerging technologies to break through. Beyond the project using SNA's, a group of investigators led by Lesniak used stem cell "shuttles" to deliver immunotherapy directly to the tumor site.

Neural stem cells have an affinity for the brain, often traveling to areas of injury. Taking advantage of this travel pattern, investigators modified neural stem cells to produce an oncolytic virus, which targets cancer cells and jump-starts the body's immune response.

The phase I clinical trial, published in *The Lancet Oncology*, found that this approach was safe and tolerable for patients, and even showed signs that the treatment may improve progression-free and overall survival.

"This is the first in-human clinical trial to test the neural stem cell delivery of an engineered oncolytic adenovirus," Lesniak said.

Planning for the future

This emphasis on results — or clinical trials testing therapies — is what unites all members of the Brain Tumor SPORE. Kumthekar, who has a hand in nearly all clinical trials coming out of the SPORE, chalks up their success to two things: planning and people.

"When we are testing drugs in the pre-clinical phase, we are planning the early clinical phase I. When we are in phase I, we are planning phases II and III," Kumthekar said. "We are always planning the next phase with the goal to get drugs that work to patients as fast as possible."

Left to right: Roger Stupp, MD, and Priya Kumthekar, MD, '11 '12 GME, were co-authors of the study published in Brain. *Atique Ahmed, PhD, was senior author.*

Further, the wealth of bright minds around Northwestern have made collaboration seamless and stimulating for participating faculty. From her work with Stegh and Mirkin to pre-clinical work with Atique Ahmed, PhD, associate professor of Neurological Surgery, the greatest resource of the Brain Tumor SPORE has been its people, Kumthekar said.

One collaborative project between Kumthekar, Ahmed and Stupp found that a drug currently used to prevent organ rejection in transplant patients could also reduce chemotherapy resistance in glioblastoma. Published in *Brain*, investigators found this drug blocks one molecular synthesis pathway used by cancer cells being treated with radiation therapy; when unable to create molecules essential for DNA synthesis, the cancerous cells are more likely to succumb to the therapy and die.

Back-and-forth collaboration between Kumthekar and Ahmed — bringing clinical trial and laboratory expertise together — is part of why this drug was selected by the Alliance for Clinical Trials in Oncology, part of the National Clinical Trials Network (NCTN). Planning for the phase I trial at Northwestern is already in full swing, and a potential phase III trial could be at several alliance network locations across the U.S.

"The field is very interested in drug repurposing right now, and this helps us speed availability of drugs to patients," Kumthekar said.

The end goal of patient care is what unites all members of the SPORE and as these therapies march forward through the lengthy process of clinical trial evaluation, some scientists are hopeful that better treatments are just around the corner.

"Over the last 10 to 15 years, our body of knowledge about the molecular characteristics of glioblastoma has increased tremendously," James said. "As we take the information generated by dozens, if not hundreds, of labs and analyze individual patient tumors to determine characteristics that can be targeted with specific therapies, I think we will begin to see more rapid progress in effective treatment of this cancer."

Lesniak, James, Stegh, Mirkin, Kumthekar and Ahmed are members of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University and part of the Lou and Jean Malnati Brain Tumor Institute of the Lurie Cancer Center. Lesniak is director of neuro-oncology at the Lurie Cancer Center.

CONTENTS

Welcome New PhD Students

PhD students from around the world have arrived on the Chicago campus to join the Driskill Graduate Program in Life Sciences (DGP), Northwestern University Interdepartmental Neuroscience (NUIN) program, Medical Scientist Training Program (MSTP), Clinical Psychology PhD Program and Health Sciences Integrated PhD Program (HSIP).

CLINICAL PSYCHOLOGY

Peter Cummings, Tulane University

Saadia Elahi, Northwestern University

Sarah Ethridge, Davidson College

Sabrina Gebreselassie, University of Pittsburgh

Ashley Murphy, Northwestern University

Afiya Sajwani, DePaul University

HSIP

Saki Amagai, Carleton College

Benjamin Barrett, Johns Hopkins University

Peter Graffy, Northwestern University

Noah Forrest, University of Portland

Tobias Holden, Yale University

Arielle Eagan, Boston College

William Liem, Washington Univ., St. Louis

Tubanji Walubita, University of Massachusetts

Lauren Leviton, University of Chicago

Roberto Lopez-Rosado, The Sage Colleges

MSTP welcomes 16 new students hailing from institutions from coast-to-coast, including UCLA, Yale University and Northwestern. This year the Clinical Psychology program had a record 878 applicants for six spots. HSIP enrolled 10 students into the 2021 cohort, including two MD/PhD candidates. DGP welcomes 43 new PhD students — the second largest and most diverse class the program has seen yet.

MSTP

Nicholas Bodkin, Duke University

Teresa Chou, University of California-Los Angeles

Jane Donnelly, Georgetown University

Brian Druciak, Johns Hopkins University

Christopher Eyo, University of Maryland

Siyuan Feng, Johns Hopkins University

Justin Geier, Northwestern University

Meital Gewirtz, Yale University

Gretchen Greene, Macalester College

Vijeeth Guggilla, Grinnell College

Jonathan Gurkan, University of Michigan

Danielle Jacobsen, Haverford College

Brian Lee, Cornell University

Ryan Lu, Johns Hopkins University

Katherine Simpson, Washington University

NUIN

Justin Anair, University of Michigan

Alex Benedetto, Pennsylvania State University

Donnisa Edmonds, University of Pennsylvania

Reem Ibrahim, Smith College

Tainhao Lei, Northwestern University

Fangze Li, Macalester College

Sebastian Malagon Perez, University of Navarra

Joseph Mastroni, University of Notre Dame

Niyati Mehta, Hamilton College

Jacob Nadel, Oberlin College

Zuoheng Qin, Northwestern University

Isabelle Rieth, Carleton College

Kevin Shen, Amherst College

Ziyad Sultan, University of Wisconsin-Madison

Linqing Sun, Carnegie Mellon University

Sophia Vann-Adibe, University of Chicago

Syed Wafa, University of Cambridge

Xunhui Wu, Northwestern University

Erika Yamakazi, Binghamton University

Qiaohan Yang, Northwestern University

Ruize Yang, Georgia Institute of Technology

Xin Zhang, Northwestern University

DGP

Hannah Ball, University of Arizona

Matt Barraza, University of California-Berkeley

Mia Broad, University of California-Los Angeles

Adrian Carcamo, University of Chicago

Claire Chaikin, Loyola University of Chicago

Jessie Chen, Loyola University of Chicago

Harun Cingoz, Orta Doğu Teknik Üniversitesi

Se Ferrell, Mount Holyoke College

Emmie Grody, University of Michigan-Ann Arbor

Karla Guerra, St. Mary's University-San Antonio

Irena Gushterova, Pratt Institute

Nana Haruna, Rutgers University-New Brunswick

Prianka Hashim, Muhlenberg College

Giha Kim, Yonsei University

Sun Kim, University of Wisconsin-La Crosse

Austin Klein, University of Arizona

Szu-Yu Kuan, Pennsylvania State University

Michelle Lee, Grinnell College

Iris Liu, Bryn Mawr College

Lucy Liu, University of California-San Diego

Nick Markov, Moscow State University

Hannah McDowell, University of Miami

Nicole McGrath, University of Maine

Brian Miller, Northeastern University

Jori Mills, University of California-San Diego

Toni-Ann Nelson, Alcorn State University

Ian Olson, University of Minnesota-Twin Cities

Claudia Oropeza, University of California-San Diego

Chloe Parker, Loyola University of Chicago

Grace Peters-Schulze, Florida Institute of Technology

Tanu Priya, University of Washington

Brooke Simonton, Northeastern University

Giangela Stokes, University of Wisconsin-Madison

Abbey Tierney, University of Illinois at Urbana

Gabriel Torres-Mejias, University of Puerto Rico

Aliki Valdes, Western Washington University

Madeleine Vessely, Grinnell College

Kameron Walker, Howard University

Qixuan Wang, Nanjing Agricultural University

Josiah Hiu-yuen Wong, The Chinese University of Hong Kong

Julia Yescas, New Mexico State University

Charles Zhang, University of California-San Diego

Chenlin Zhao, Northwestern University

Graduate Student/Post-Doc Events and Opportunities

Fall 2021 Mindfulness-Based Stress Reduction Course

Tuesdays, October 5 – November 23
9:00 a.m. – 11:30 a.m. CST
All-day retreat on Saturday, November 13
9:30 a.m. – 4:00 p.m.
Parkes Hall (Evanston campus)
1870 Sheridan Road, Evanston, IL 60208
More information

Mindfulness-Based Stress Reduction (MBSR) is considered the gold standard in curricula designed to guide participants into cultivating a practice of mindfulness through techniques of body awareness, sitting and walking meditation and mindful movement. MBSR fosters comprehensive personal wellness including an increase in emotional resilience and management of stress, anxiety and pain. The eight-week course is open to all students, employees, alumni and community members. Register here for the next MBSR course by September 28 or to learn about future sessions.

American Sign Language Mini Course

Mondays, October 11 - November 29
Time: 6:00 p.m. – 7:30 p.m. CST
Online via Zoom - Register here
More information

This eight-session course introduces the basics of American Sign Language. American Sign Language (ASL) is quickly becoming one of the most widely used languages in the United States. This class will explore basic sign vocabulary and basic grammatical structures such as English to ASL and ASL to English. This class will also cover basic Sign Language and a basic introduction to the world of Deaf Cultures.

More at the Museum: Online Collection Talk

Thursday, October 14
12:30 p.m. – 1:00 p.m. CST
Online via Zoom – Register here
More information

Join the Block Museum for a look at artworks from the collection that explore ideas of excess, consumption and the environment, and offer an interdisciplinary perspective on the climate crisis. This online talk is led by Block staff and inspired by "The Story of More: How We Got to Climate Change and Where to Go from Here" by Hope Jahren, Northwestern University's 2021-22 One Book One Northwestern selection.

Presented by the Block Museum in partnership with the Northwestern alumnae.

Confidential Providers

Northwestern Student Affairs offers confidential services that you can utilize during these challenging times courtesy of Counseling and Psychological Services (CAPS), Religious and Spiritual Life (RSL), and Center for Awareness, Response and Education (CARE).

Please visit the **Confidential Providers** webpage for these resources.

Research in the News

***Fox 32*, August 6**
Study finds almost half of Chicago parents with guns at home store them loaded
Karen Sheehan, MD, MPH, was featured.
This research was also featured in *Chicago Tribune*.

***HealthDay*, August 11**
One Key Question Can Help Spot Skin Cancer
Murad Alam, MD, was featured.

***U.S. News & World Report*, August 18**
Dangerous Diabetes Tied to Pregnancy Is on the Rise
Sadiya Khan, MD, MSc, was featured.

***Crain's Chicago Business*, August 19**
NU launching accelerator for faculty-led startups
John A. Rogers, PhD, was featured.

***WGN 9*, August 30**
How dogs are helping advance important cancer research
Amy Heimberger, MD, was featured.

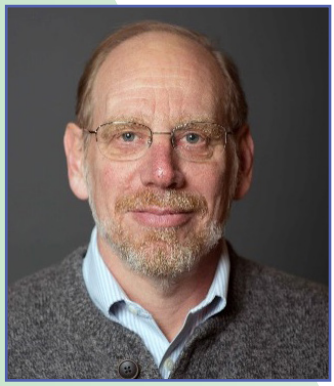
***Fox 32*, August 30**
Northwestern study sheds light on long-term effectiveness of vaccines
Thomas McDade, PhD, was featured.
This research was also featured in *U.S. News & World Report*, *Yahoo! News*, *WTTW* and *HealthDay*.

***National Public Radio*, September 2**
Crowded U.S. Jails Drove Millions of COVID-19 Cases, A New Study Says
Eric Reinhart, MD, was featured.

More media coverage >>

Studying the Evolution and Pathogenicity of Novel Bacteria in Humans

Hank Seifert, PhD, the John Edward Porter Professor of Biomedical Research and professor of Microbiology-Immunology



Hank Seifert, PhD, is the John Edward Porter Professor of Biomedical Research and a professor of Microbiology-Immunology. His laboratory studies how various species of bacteria cause disease in humans and how the process of gene conversion occurs in a bacterial chromosome. He is also a member of the Center for Genetic Medicine, Northwestern University Clinical and Translational Sciences (NUCATS) Institute and the Simpson Querrey Institute for Epigenetics.

Q&A

What are your research interests?

My laboratory group studies the human-restricted *Neisseria* species, with a concentration on the pathogenic species *Neisseria gonorrhoeae* (the gonococcus or Gc) and *Neisseria meningitidis* (the meningococcus or Mc). While there are 10 *Neisseria* species that only live within humans, only Gc and Mc can cause pathology resulting in sexually transmitted infection: gonorrhea (Gc), bacterial meningitis (Mc) or bacteremia (both Mc and Gc). Most of our work revolves around the Type IV pilus, which is a proteinaceous organelle that is essential for colonization and pathogenicity. We study the mechanisms and biology behind the pilus antigenic variation system of Gc and Mc, which is a complex diversity-generation system that uses DNA recombination to alter the amino acid sequence of the major subunit of the pilus, pilin. We are determining how the pilus protects against host-derived, oxidative and nonoxidative antimicrobial mechanisms. We are also determining how the pilus fiber is expressed on the bacterial cell surface and what regulates the pilus extension and retraction cycle. Finally, we have begun a project to mutate every non-essential gene in the Gc chromosome to provide a resource for the broader research community.

What is the ultimate goal of your research?

We are trying to understand how these bacteria cause disease in otherwise healthy people, how high-frequency gene conversion can occur in a bacterial chromosome and what evolutionary paths allowed the pathogenic *Neisseria* to derive from a commensal progenitor.

How did you become interested in this area of research?

As a graduate student at Penn State, I heard my postdoctoral advisor Magdalene So give a talk on the early description of the pilus antigenic variation system. Immediately after her talk, I asked if she had any open postdoctoral positions, and after checking my referees and an interview in La Jolla, California, I started my studies on the pilus antigenic variation system.

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

We do a lot of different techniques within the laboratory, but we collaborate in areas where we do not have the expertise. We have an ongoing collaboration with James Garnett and Joseph Atherton of King's College London who are structural biology experts to study a new pilus associate protein we discovered. We have a collaboration with biophysicist Berenike Maier at the University of Cologne to measure pilus dynamics. We have collaborations with several Northwestern faculty including Chi-Hao Luan and Gary Schlitz to conduct a small molecule screen and to make derivatives of lead compounds as potential antivirulence antimicrobial agents.

Where have you recently published papers?

In the past five years our papers were published in *mBio*, *Biochemistry*, *mSphere*, *Molecular Microbiology*, *Journal of Bacteriology*, *mSystems*, *PLoS Genetics*, *Journal of Biological Chemistry* and the *Journal of Proteome Research*.

Who inspires you? Who are your mentors?

I've had many mentors over my career. My PhD advisor, Ron Porter, at Penn State accepted a raw student with little research experience into this lab and let me explore and learn without pressuring me for immediate results. My postdoctoral mentor, Maggie So, at the Scripps Research Institute provided a rich intellectual environment and resources to develop a research portfolio that allowed me to obtain a faculty position at Northwestern. Pat Spear hired me and always had sage advice. Over the past 33 years, I have leaned on many senior and junior faculty, both at Northwestern and beyond, for mentoring and am always learning from my laboratory group.

Unmet Needs: Mental Health Services in the Youth Justice System

María José Luna, Clinical Psychology PhD Program

María José Luna, a student in the Clinical Psychology PhD Program, studies the mental health needs and outcomes of youth in the justice system. Read a Q&A with Maria José below.

Q&A

Where is your hometown?
I was born in Quito, Ecuador. When I was 6 years old, my family and I moved to Boston, Massachusetts. Because I was raised in these two cities, I'm always missing the mountains and the ocean now that I live in Chicago. Even though Chicago's geography is a bit different, I am starting to call this city my home, too!

What are your research interests?
I am interested in health inequities in mental health and mental health service use. I'm passionate about investigating questions such as: What individual, social and systemic factors contribute to inequities? What factors contribute to resilience and facilitate mental health service use? How can we leverage this information to improve our service systems and public health policies?

What exciting projects are you working on?
My current project uses data from the Northwestern Juvenile Project, a longitudinal study of the mental health needs and outcomes of 1,829 youth who were arrested and detained in the juvenile justice system in Chicago. We re-interview participants up to 13 times over the next 16 years after detention. At each follow-up, we conducted diagnostic clinical interviews and obtained detailed information on mental health service use. Our prior studies demonstrated that mental health disorders are prevalent and persistent among those involved in the justice system. But, do those who need services receive them?

I am examining the patterns of mental health service use among participants with mental health disorders as they aged, up to 16 years after detention (median age: 32). Results are astonishing — fewer than 20 percent of participants with a disorder received services as they aged. Black participants, especially Black males, were the least likely to receive services compared to Hispanic/Latinx and white participants. The type of disorder impacted service use: participants with substance use or disruptive behavior disorders — the most common disorders in criminal justice populations — were less likely to receive services than those with mood and anxiety disorders.

Our next step is to use a mixed-methods approach to integrate our quantitative data with new qualitative data to examine the individual, social and systemic factors that contribute to these inequities.

What attracted you to your program?
For my graduate education, I was looking for a program that could provide rigorous scientific and clinical training to gain the necessary skills to fulfill my professional goal of becoming a clinical psychologist. My experiences in the clinical psychology program, particularly those with the Northwestern Juvenile Project and clinical externships, have exceeded my expectations!

What has been your best experience at Feinberg?
The best experience, so far, has been growing professional and social networks throughout Feinberg. I enjoy learning from colleagues and mentors across Feinberg's multidisciplinary communities. Shoutout to my PhD cohort and to members of the Health Disparities and Public Policy Program, whose support has been critical to my progress.

How would you describe the faculty at Feinberg?
In my experience, Feinberg faculty are welcoming, highly driven and collaborative. I admire the adaptability and flexibility they demonstrate during stressful situations, including the COVID-19 pandemic.

What do you do in your free time?
I love jigsaw puzzles! My parents told me that I've been doing jigsaw puzzles since I was 2 years old. I also enjoy taking long walks with my dog to explore the parks throughout Chicago. I took up boxing when I started graduate school, and I'm looking forward to starting again after the pandemic.

What are your plans for after graduation?
The very first thing I will do is to go home to visit my family in Ecuador (and have some fresh *choclo con queso y ají*). After? I plan to start a postdoctoral fellowship at an academic medical center. Ultimately, I hope to facilitate more collaborations between community mental health and academic settings.

Untangling Red Tape

Sharnia Lashley, MS, senior regulatory coordinator, Northwestern University Clinical and Translational Sciences (NUCATS) Institute

Sharnia Lashley, MS, senior regulatory coordinator at the Northwestern University Clinical and Translational Sciences (NUCATS) Institute, helps scientists and study teams navigate regulatory aspects of research.

Q&A

Where are you originally from?
I am from Phoenix, Illinois.

What is your educational background?
I have a bachelor's degree in biology and a master's degree in clinical research administration.

Please tell us about your professional background.
I have spent several years working in data collection, data quality and data preparation in social science research. I managed multiple studies, most of them government-funded.

The primary study I managed was an annual U.S. research doctorate educational census study. As manager, I oversaw data collection and data preparation, teams, and activities for medium and large-scale studies. I also contributed to study questionnaire design revisions and major revisions to the survey instrument as well as authored sections of the annual report. I also worked on two studies people may be familiar with: Florida Ballots after the 2000 presidential election and the National Tragedy Study after the 9/11 attacks.

Why do you enjoy working at Northwestern?
I enjoy social and clinical research tremendously and Northwestern is an ideal place to contribute to research in numerous specialty areas. My work at Northwestern has allowed me to collaborate with a great group of individuals within and across departments.

How do you help scientists and research students at the medical school?
I help scientists and study teams navigate regulatory aspects of research, handling various FDA submissions and generating documents and submissions for local and external institutional review boards.

What is your favorite part of the job?
I am a magnet for "first-time" encounters — one of my favorite parts of the job is encountering new study formats or scenarios and navigating the related new regulatory processes, in addition to assisting and guiding others.

What exciting projects are you working on?
I currently provide regulatory and FDA support for two COVID-19 studies, in addition to various other exciting studies.

What do you like to do in your spare time?
I like to read and try new plant-based recipes.

NUCATS Corner
Clinical and Translational Sciences Institute

Three Named KL2 Scholars, RFA to be Released in October

The 2021 cohort of KL2 scholars are united by their dual backgrounds in clinical and research settings. Over the next two years, their experiences working with patients and in the lab will help them conduct novel translational, multidisciplinary, clinical research.

The Northwestern University Clinical and Translational Sciences (NUCATS) Institute KL2 program will provide mentorship, education and career development opportunities to Kyle MacQuarrie, MD, PhD, '17, '20 GME, who is conducting research on the pediatric cancer rhabdomyosarcoma; Colleen Peyton, DPT, who is studying infant motor disorders; and Anna Pfenniger, MD, PhD, who is investigating atrial fibrillation.

Programs such as the KL2 are critical during a time when MacQuarrie says there are often high barriers to entry, keeping many people from breaking into research.

"I was so excited when I got notice that I had been awarded the KL2 because I think that there is a bottleneck in developing physician-scientists. We certainly see that in pediatrics, which is my specialty," MacQuarrie says, whose KL2 project centers around the pediatric cancer rhabdomyosarcoma and its nuclear organization.

"Programs like this — that help support people as they begin their journey to fully independent researcher— it cannot be overemphasized how important they are to people like myself, who are in that junior or early phase of their careers."

The KL2 program serves to resolve a major hurdle that often exists at the beginning of research careers: Receiving grants to conduct research requires research experience and mentorship. The next KL2 Request for Applications is scheduled to be released in early October.

NIH News

NIH Loan Repayment Program Application Cycle is Open

NIH Loan Repayment Programs (LRPs) are a set of programs established by Congress, designed to recruit and retain highly qualified health professionals into biomedical or biobehavioral research careers by countering the financial pressures of an advanced education and training in medicine and clinical specialties. This year, awards are now up to $100,000 over a two-year period and the new Research in Emerging Areas Critical to Human Health (REACH) LRP is available for extramural applicants. Submit your application **by November 18**. For more details and to apply, visit the NIH LRP website.

Clarified Guidance for Applicants Preparing Applications During the COVID-19 Pandemic

In response to questions related to lost productivity and other pandemic-related issues, the NIH issued guidance indicating that while grant applications should not include contingency or recovery plans for problems resulting from the COVID-19 pandemic, investigators may address effects due to the pandemic on productivity or other scoreable issues in the personal statement of the biosketch. Reviewers will be instructed to take these pandemic-related circumstances into account when assessing applicants' productivity and other score-driving factors. If needed, NIH staff will request and assess plans to resolve specific problems arising from the COVID-19 pandemic prior to funding.

NIH will allow the submission of a one-page update with preliminary data as post-submission materials for applications submitted for the May 2022 council (applications submitted beginning with September 25, 2021 due dates for spring 2022 review meetings), provided that the funding opportunity announcement allows preliminary data. As with other types of post submission materials, information must be submitted no later than 30 days before the study section meeting unless specified otherwise in the funding opportunity announcement. One page of preliminary data will be accepted for single component applications or for each component of a multi-component application. Because applications for emergency competitive revisions and urgent competitive revisions undergo expedited review, post-submission materials will not be accepted for those applications. (See details in NOT-OD-21-179.)

UEI to Replace DUNS

For many years, the NIH and other federal agencies have required organizations to obtain a Dun & Bradstreet DUNS number issued as part of the registration process to apply for and receive federal funding. By April 2022, the federal government will phase out the use of DUNS numbers and move to a 12-character unique entity identifier (UEI) created in SAM.gov. This transition, led by the General Services Administration, streamlines SAM.gov registration for new entities and eliminates the need to work through Dun & Bradstreet for ongoing entity management.

What does this mean for NIH applicants and recipients?

- If already registered in SAM.gov, a UEI was automatically generated for your entity and is visible in both SAM.gov and Grants.gov.
- Beginning October 2021, entities registered in eRA Commons will begin to see their UEI populated in the institutional profile file. No entity action is required.
- Entities registering in SAM.gov prior to April 2022 must still obtain a DUNS number before registering in SAM and a UEI will be assigned during registration.
- Beginning October 2021, recipients' UEI will be populated on Page One of the Notice of Award. The recipient UEI will also be transmitted in award data reported to the HHS Tracking Accountability in Government Grants System and USASpending.gov.
- For applications due on or after January 25, 2022, applicants must have a UEI at the time of application submission. Grant application forms and instructions will be updated to reflect and require UEI instead of DUNS.

Welcome New Faculty

Brenda Bohnsack, MD, PhD, joins as chief of Pediatric Ophthalmology in the Department of Ophthalmology, the Lillian Sherman Cowen Reiger and Harold L.S. Cowen Research Professor of Pediatric Ophthalmology and associate professor of Ophthalmology in the Division of Pediatric Ophthalmology and of Pediatrics. Her clinical research includes studying the outcomes of medical and surgical management of complex pediatric glaucomas and congenital eye diseases, as well as the genetics behind these diseases. Her basic science research is focused on molecular regulation of neural crest migration and differentiation in the anterior segment of the eye. She earned both her medical and doctoral degrees at Baylor College of Medicine. She completed her postdoctoral training at the University of Michigan and a fellowship at Duke University. Before coming to Northwestern, Bohnsack was associate professor at the Kellogg Eye Center at University of Michigan.

Sponsored Research

PI: Juned Siddique, DrPH, associate professor of Preventive Medicine in the Division of Biostatistics and of Psychiatry and Behavioral Sciences

Sponsor: National Heart, Lung, and Blood Institute

Title: Combining Longitudinal Cohort Studies to Examine Cardiovascular Risk Factor Trajectories Across the Adult Lifespan and Their Association With Disease

The development of clinical cardiovascular disease (CVD) is a process that occurs across the lifespan, beginning early in life and spanning late into life as clinical event rates increase. Much of our understanding of the impact of cardiovascular risk factors comes from studies examining the association between risk factor levels measured at a single point in time, often in middle age, with incident disease over the short- to intermediate-term. However, risk factor levels in young adulthood are significantly associated with the development of CVD later in life and our recent work has demonstrated that not only the levels at specific ages, but also cumulative exposures and long-term trajectories in cardiovascular health, are significantly related to the risk for subsequent CVD. Therefore, a life course approach is critical in order to understand how cardiovascular risk factors develop and impact an individual's risk for CVD events later in life. Yet, there is no single study that has collected detailed phenotypic data spanning young adulthood through old age on a broadly representative sample of the U.S. population

We propose to develop a statistical framework for combining longitudinal risk factors and clinical outcomes data from multiple cohort studies to create a "synthetic cohort" enabling the study of long-term cardiovascular health starting in early adulthood. The investigative team of this proposal has pooled the data from 20 community-based CVD cohorts through the Lifetime Risk Pooling Project (LRPP), which now has greater than 11 million person-years of follow-up data on repeated measures of CVD risk factors, detailed information about medication use (including blood pressure- and cholesterol-lowering therapy), nearly 100 percent follow-up for vital status and detailed CVD event adjudication. Few cohorts in the LRPP cover the entire adult lifespan; therefore, we propose to view risk factors and outcomes at ages not included in each cohort study as missing data, and to use multiple imputation to fill in these unobserved measurements to facilitate analysis.

Read more

PI: Stacy Cooper Bailey, PhD, MPH, associate professor of Medicine in the Division of General Internal Medicine and Geriatrics

Sponsor: National Institute of Diabetes, Digestive and Kidney Diseases

Title: Promoting Preconception Care and Diabetes Self-Management Among Reproductive-Aged Women With Diabetes: The PREPARED Trial

Our randomized trial will assess the effectiveness and fidelity of a technology-based strategy to promote preconception care and diabetes self-management among women with type 2 diabetes in primary care. More than 30 million people in the U.S. have diabetes and 1 in 3 adults are projected to have the disease by 2050. While diabetes has historically affected older individuals, its incidence is increasing rapidly among younger adults, including women of reproductive age (18-44 years). Women with early-onset type 2 diabetes (T2DM) are at higher risk of cardiovascular-related morbidity and mortality and adverse reproductive outcomes, including congenital anomalies and perinatal mortality.

Achieving glycemic control is essential to reducing these risks. As half of all pregnancies are unintended, clinical guidelines recommend providers routinely engage all women of reproductive age in preconception care. For women with T2DM, this includes: 1) achieving glycemic control through diabetes self-care, 2) using effective contraception until glycemic control is achieved and pregnancy is desired, 3) discontinuing use of teratogenic medications if pregnancy could occur, 4) taking folic acid daily to reduce increased risk of neural tube defects and 5) managing cardiovascular and other T2DM-related risks.

Despite these recommendations, up to 80 percent of women with T2DM do not receive preconception counseling. Provider time limitations are often cited as a barrier, as is a lack of available resources. Our Promoting REproductive Planning And REadiness in Diabetes (PREPARED) strategy will utilize health information and consumer technologies to "hardwire" preconception care and promote diabetes self- management among reproductive-aged, adult women with T2DM in primary care.

Read more

Funding

Translational and Basic Science Research in Early Lesions (TBEL) (U54 Clinical Trial Not Allowed)

More information

Sponsor: National Cancer Institute (NCI)
Letter of Intent Due: October 3
Application Deadline: November 2
Award Information: NCI intends to commit $8.2M in fiscal year (FY) 2022 to fund up to five awards. Application budgets must reflect the actual needs of the proposed center but must not exceed $1M in direct costs.

Synopsis: The purpose of the funding opportunity is to solicit applications for the establishment of Research Centers, one of the two units of the Translational and Basic Science Research in Early Lesions (TBEL) program. The aim of the Research Centers is to integrate basic and translational cancer research studies to iteratively examine the direct causal relationships and interactions of an early lesion, its microenvironment and host-systemic factors as "co-organizers" of tumor initiation (or suppression) and malignant progression in conjunction with the clinical characteristics of the lesions. The ultimate goals of the TBEL program are to further understand the biological and pathophysiological mechanisms driving or restraining precancers and early cancers and facilitate biology-backed precision prevention approaches. The other unit of TBEL is the Coordinating and Data Management Center.

HEAL Initiative: Interdisciplinary Teams to Elucidate the Mechanisms of Device-Based Pain Relief (RM1 Clinical Trial Optional)

More information

Sponsors:
National Institute of Neurological Disorders and Stroke
National Institute of Dental and Craniofacial Research
National Center for Complementary and Integrative Health
National Center for Advancing Translational Sciences
Letter of Intent Due: October 4
Application Deadline: November 3
Award Information: Award amount undisclosed; NIH intends to fund three awards in FY 2022.

Synopsis: The HEAL Initiative is designed to support interdisciplinary research teams of multiple PD/PIs to investigate the mechanism of action of device-based pain relief with the overall goal of optimizing therapeutic outcomes for FDA-approved or -cleared technologies. Teams must leverage appropriate multidisciplinary expertise to develop new principles and methods for experimentation, analysis and interpretation. Teams are encouraged to consider objectives that will produce major advances in the understanding of device-based pain relief.

Pediatric Centers of Excellence in Nephrology (P50 Clinical Trial Optional)

More information

Sponsor: National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)
Letter of Intent Due: October 18
Application Deadline: November 18
Award Information: NIDDK intends to commit $2.63M in FY 2022 to fund three awards

Synopsis: This funding will award Pediatric Centers of Excellence in Nephrology (PCEN) to support basic, translational and clinical research in pediatric kidney disease. The goals of this program are to: 1) attract new scientific expertise to the study of human pediatric renal physiology, kidney development and pediatric kidney disorders; 2) encourage multidisciplinary research in these areas; and 3) develop the pediatric nephrology research community through a national research symposium, broad sharing of research resources and a national Pilot and Feasibility grant program. These efforts are expected to lead to innovative approaches to study kidney disease in children and the eventual submission of substantial, competitive, investigator-initiated research applications. The PCEN will complement the O'Brien Kidney and Urological Research Centers and are expected to leverage existing institutional resources which may include Clinical Translational Science Awards, Institutional Network Awards for Promoting Kidney, Urologic and Hematologic Research Training (U2C/TL1), and other NIDDK-Division of Kidney, Urologic and Hematologic Diseases (KUH)-funded consortia.

Health Disparities Resources and Research Tools

By Annie Wescott, Research Librarian, and Eileen Wafford, Research Librarian

Background: Health Disparities

There has been a steady rise in requests for studies related to health disparities in recent years. Defined by Healthy People 2020 as "a particular type of health difference that is closely linked with social, economic and/or environmental disadvantage," the topic health disparities has seen an increase from approximately 11,000 articles published on the topic in 2010 to approximately 16,500 articles in 2020 when utilizing the PubMed health disparities search filter. The importance of this topic makes quality searches a necessity, and the frequency of search requests can often result in a duplication of effort.

Background: Search Filters

Librarians can save researchers time by developing reusable and trusted search strategies. Best practices recommend using validated search filters, which are tested for sensitivity, precision, specificity and accuracy. Search filters play an important role in comprehensive and systematic searches. They are especially useful with complex, multifaceted topics like health disparities as they ensure the most relevant and inclusive terminology is being used to capture difficult-to-locate studies.

MEDLINE®/PubMed® Health Disparities and Minority Health Search Strategy

Librarians at the National Library of Medicine developed the MEDLINE®/PubMed® Health Disparities and Minority Health Search Strategy, which identifies a subset of citations on the topic of Health Disparities. This search filter utilizes controlled vocabulary and title/abstract searching related to various topics under the health disparity umbrella.

Librarians and informationists at Galter Health Sciences Library & Learning Center worked to validate a portion of this search filter with a focus on health disparities related to race and ethnicity. Their validation process concluded that the existing filter is an effective search strategy in relation to race and ethnicity; however, they recommend more keywords and broader use of truncation to improve its sensitivity.

Health Disparities Resources at Galter

The Galter Library is constantly striving to update our electronic resources and bring current tools to our patrons' desktops. The library added to its electronic collections and now provides online access to these information resources addressing health disparities.

- Community Health Equity: A Chicago Reader
- Urban Health: Participatory Action-Research Models Contrasting Socioeconomic Inequealities in the Urban Context
- Caring for Patients from Different Cultures (Fifth Edition)
- Just Medicine: A Cure for Racial Inequality in American Health Care
- Medicating Race: Heart Disease and Durable Preoccupations With Difference

Are you engaged in health disparities research? Work with your Galter liaison librarian to ensure you have access to the best tools for the job.

High-Impact Factor Research

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Featured Core

Developmental Therapeutics Core

The Developmental Therapeutics Core (DTC) is an institutional core facility that operates under Northwestern University's Chemistry of Life Processes Institute. Located on the Evanston campus, the core is the key component in preclinical drug development at the university. The core has facilitated the rapid growth of both basic and clinical cancer research with a focus on the development of new therapeutics and diagnostics by providing translational models.

The core provides translational services to both clinical and basic cancer investigators who are interested in moving novel anticancer agents into the clinic but lack the *in vitro* or *in vivo* expertise or the laboratory facilities to accommodate such research. Additionally, the core investigates novel therapeutic targets and approaches and novel animal tumor models by providing additional translational research such as exploratory pharmacokinetics and toxicology assays.

The core offers a full suite of fee-for-service tumor biology tools and translational support services, including:

- *In vitro* and *in vivo* assessment of drug activity and mechanism of action
- Exploratory drug development activities such as pharmacokinetics, biodistribution and toxicology
- Pre-IND clinical trial support
- Proliferation and apoptosis assays. The core has more than 150 cell lines for cytotoxicity testing and drug IC50 value determination.
- Therapy-response experiment. DTC personnel provide expert guidance in determining the most appropriate models for evaluating the efficacy of compounds and biologicals of interest.
- Patient-derived xenograft models (heterotopic and orthotopic). These models offer the closest approximation to the clinical setting for testing cancer therapies, other than immunotherapies.

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