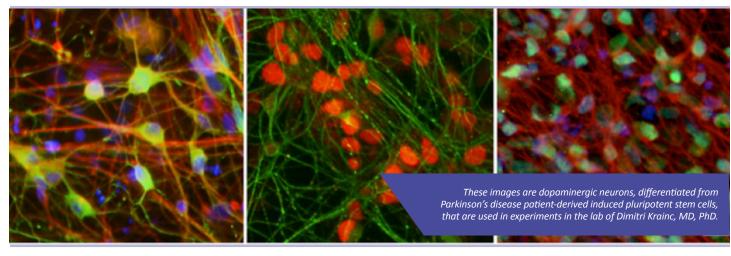
Breakthroughs

Feinberg School of Medicine Research Office

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Breaking Ground in the Field of Personalized Neurology

By Will Doss

The DNA of someone with a chronic neurological disease has the potential to reveal a lot about their diagnosis and how it can be treated. A team from the academic and clinical arms of Northwestern Medicine has been assembled with the purpose of studying the DNA of certain patients with these diseases and pinpointing specific genetic mutations or phenotypes that may be present. Everything from genetic canvassing to generating disease models to creating therapeutic compounds is happening in-house at Northwestern, a unique model in the rapidly expanding field of personalized neurology.

"You need a lot of people to execute this cycle: clinicians, geneticists, stem cell experts, medicinal chemists and clinical trial experts," said <u>Dimitri Krainc, MD, PhD</u>, chair of the <u>Ken</u> <u>& Ruth Davee Department of Neurology</u> and director of the <u>Center for Neurogenetics</u>. "But it's all based on genetics, so we start with patient samples and genetic screening."

Currently, Northwestern experts are focused on subpopulations of patients with Parkinson's disease, amyotrophic lateral sclerosis (ALS) and epilepsy. Creating targeted genetic therapies for these neurological diseases begins with geneticists who analyze patient genomes, looking for mutations that could cause or modify disease. Next, scientists generate induced pluripotent stem cells that differentiate into neurons, mimicking the diseased neurons in the brain of a patient with Parkinson's disease, for example.

The scientists use these models to identify therapeutic pathways, handing those pathways over to medicinal chemists who develop compounds to treat the disease. Once therapies are created they are tested in clinical trials, often in partnership with private companies.

Krainc is on the front lines of personalized neurology, and his lab has a number of high-profile projects, including a recent study published in the journal <u>Science</u>.

"Every patient is different, so treating neurological disease isn't one size fits all," said Krainc, also the Aaron Montgomery Ward Professor of Neurology in the <u>Division of Movement Disorders</u> and of <u>Neurological Surgery</u> and of <u>Physiology</u>. "There are different reasons why people develop disease, so we try to address that in a targeted manner."

Bedside to Bench, Parkinson's and Epilepsy

Obtaining genetic data for Parkinson's disease requires tight integration with the <u>Northwestern University Parkinson's</u>
<u>Disease and Movement Disorders Center</u>, (NUPDMDC) led by <u>Tanya Simuni, MD</u>, the Arthur C. Nielsen, Jr., Research Professor of Neurology in the Division of Movement Disorders.

At the newly established neurogenetics clinic, and its associated collaboration between clinicians and scientists,



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Personalized Neurology

(continued from cover page)

cases that may have a genetic component are brought to the attention of geneticists such as <u>Steven Lubbe</u>, <u>PhD</u>, assistant professor of Neurology and Genetic Medicine in the Division of Movement Disorders and a member of the <u>Center for Genetic Medicine</u>.

"If we find a candidate variant in a patient, through the NUPDMDC biorepository, we then look for that variant in family members," Lubbe said. "If that variant is only seen in individuals with the disease, and not in family members without it, it represents the start of an exciting journey where we try to understand the underlying molecular biology of disease using neurons derived from patient skin cells. The hope here is that if we know what damage the change does in the patient's own neurons, we may be able to develop a novel target that can be returned to the patient for a more personalized approach to disease intervention and management."

Lubbe is also using the same approach to identify modifiers of Parkinson's disease.

"When it comes to certain mutations, not everyone who has them gets Parkinson's, so we're using genetic information from affected and unaffected family members with the same change to help find these modifiers and study them in their own neurons," Lubbe said.

A therapeutic compound for Parkinson's disease developed at Feinberg is currently undergoing clinical trials and the Neurology department will be expanding its focus to include Alzheimer's disease in the near future, demonstrating the productivity of this approach even in early stages.

Genetic data collection of epilepsy patients, similar to Parkinson's, is driven by the relationship between the research enterprise and a <u>patient clinic</u> at Northwestern Medicine.

A desire to integrate genetics into clinical care has led clinicians

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A desire to integrate genetics into clinical care has led clinicians to be more active in sharing interesting cases and genetic data, according to Gemma Carvill, PhD, assistant professor of Neurology and of Pharmacology.

"Neurologists who treat adults weren't thinking as much about genetics seven or eight years ago," Carvill said. "Now, we have clinical epileptologists who are very interested in genetics and asking patients about family history, which is not something that had necessarily happened in adult neurology before."

This heightened awareness has led to a surge in identifying genes connected to epilepsy, ballooning from about five genes to more than 80 genes during the last decade.

"Most of the science revolves around ion channels and neurotransmitters; in the past we thought these were the main pathways affected in epilepsy, but that's not everything," Carvill said. "It turns out there is this whole other class of genes that influence how the brain is made and functions that we can study for connections to epilepsy. We're interested in the proteins that instruct the development of the brain and use stem cells to model epilepsy in the dish."

While identifying genes is beneficial, it only has real impact when it's integrated into therapies or clinical care, which is an important consideration, Carvill said.

"We want to take that next step and find out how we can capitalize on these discoveries and new biological pathways to understand epilepsy and find new treatments," she said. "The genetics and and epilepsy communities have spent a lot of time thinking about how to approach these questions."

Some recent clinical efforts that stem out of genetic studies on epilespy have been led by <u>Elizabeth Gerard</u>, <u>MD</u>, associate professor of Neurology in the Division of <u>Neurophysiology/Epilepsy</u>.

A Team in Place

New faculty with expertise in translational neurogenetics have been recruited to the Department of Neurology over the past four years to help execute the translational program in neurogenetics, under the umbrella of the Center for Neurogenetics. This includes Lubbe and Carvill as well as Niccolo Mencacci, MD, PhD; Evangelos Kiskinis, PhD; Joseph Mazzulli, PhD; Jeffrey Savas, PhD; Robert Kalb, MD; Gabriela Caraveo Piso, PhD and Jianbin Zheng, PhD

The new faculty are essential to providing the scientific framework needed to turn genetic discoveries into patient treatments.

"This is pretty unique, not too many places are doing it like this," Krainc said. "This is extremely important for the future of neurology."

Enabling Discovery Through State-of-the-Art Imaging

Joshua Rappoport, PhD, director of the Center for Advanced Microscopy and Nikon Imaging Center



Joshua Rappoport, PhD, serves as director of the Center for Advanced Microscopy and Nikon Imaging Center at Feinberg. The center supports research across the University through expertise, training and access to state-of-the-art imaging instruments. The facility's services include electron microscopy, as well as light microscopy, and both fluorescent and bioluminescent animal imaging.

Rappoport, also a research professor of <u>Cell and Molecular Biology</u>, is a member of the <u>Robert H. Lurie</u> <u>Comprehensive Cancer Center of Northwestern University</u>.

Q&A

What are your research interests?

My training as an undergraduate at Brown University was in classical comparative respiratory physiology, including an extended research project studying turtles that remain underwater for months each winter without breathing. I earned my PhD in the Division of Nephrology at Mount Sinai Medical School in New York, studying cellular urate transport. This is where I made the transition to molecular cell biology. I completed a postdoctoral fellowship in the Laboratory of Cellular Biophysics at The Rockefeller University, where we developed microscopy-based approaches to study vesicle trafficking and cell migration. This was really the key transitional phase in my scientific training that developed my lifelong love of microscopes, in particular, using fluorescence microscopy to watch life unfold in living cells in realtime. When I ran my own research lab at the University of Birmingham in England, we focused on developing and applying live-cell imaging to study endocytosis, in particular, activated growth factor receptors and manufactured nanomaterials.

Now that I am a full-time core facility scientist, my main focus is supporting the microscopy needs of our user base.

What is the ultimate goal of the Center for Advanced Microscopy and Nikon Imaging Center?

We offer expertise, instruction and support to our user base in the areas of light and electron microscopy. In particular, we try to balance the need for adequate capacity for routine microscopy approaches with providing access to cutting-edge instrumentation and applications.

How is the center funded?

Our facility is funded through a mixed model. We rely primarily on revenue via recharge, which means direct payment for the services we provide and support. However, we also receive extremely generous support from both Feinberg and the Lurie Cancer Center, for uses ranging from staff salaries to supporting new initiatives and investing in new equipment for the facility. Furthermore, as a Nikon Imaging Center, we receive significant direct and indirect support from Nikon Instruments, Inc.

Who makes up your team and what role does each individual play?

We have a total of seven staff members working in the facility, apart from myself. As the director, I handle much of the administrative responsibilities and strategic leadership, along with support from our Faculty Advisory Committee, in particular the chair, <u>Volodya Gelfand</u>, <u>PhD</u>.

Constadina (Dina) Arvanitis, PhD, is the manager of the Nikon Imaging Center and is responsible for all things Nikon in the facility. Peter Dluhy is the primary point of contact for our confocal laser scanning microscopes. Wensheng (Wilson) Liu, MD, handles many of our other light microscopes. David Kirchenbuechler, PhD, is our image analysis specialist. Lennell Reynolds, Jr., is primarily focused on transmission electron microscopy (TEM), including TEM sample preparation. Farida Korobova, PhD, mainly works on advanced TEM techniques, such as immuno-gold TEM as well as scanning electron microscopy (SEM). The newest member of our team is Yashema Hunter, who is helping out with TEM sample preparation.

\$10 Million Gift Creates Simpson Querrey Center for Epigenetics

A new \$10 million gift from University trustees and supporters Louis A. Simpson '58 and Kimberly K. Querrey will create a center at Northwestern University Feinberg School of Medicine to study the effects of environment on the activation and expression of genes.

The new Simpson Querrey Center for Epigenetics will investigate how environmental factors such as emotional experiences, chemical exposure, obesity, exercise, diet and drug therapies can modify genes packaged in human chromatin, causing them to become more or less receptive to new biochemical signals. Epigenetic modifications of chromatin can have a direct effect on the regulation of gene expression. Some of this regulation is good, and some of it causes disease.

"Through their exceptional support of the sciences at Northwestern, Kimberly and Lou are transforming our ability to understand, diagnose and treat disease," said University President Morton Schapiro. "We are truly grateful for their continued partnership."

The center brings together experts in biochemistry, molecular genetics, computational biology, fundamental biology, epidemiology and clinical medicine to develop foundational insights about how environmental conditions impact the human genome using sophisticated molecular, biochemical and computational methods. The Simpson and Querrey gift will support the center's operations, seminar and symposium programs, pilot studies by Northwestern faculty and the new Feinberg Fellows in Epigenetics program. It will also provide funding for the recruitment of outstanding investigators in the area of epigenetics.

"Epigenetic-driven insights are proving fundamental to a myriad of diseases including cancer, heart, immunologic and neurological conditions," said Eric G. Neilson, MD, vice president for medical affairs and Lewis Landsberg Dean. "Understanding the details of how individual genes, groups of genes and environmental factors work together to determine the human condition is at the forefront of medicine today."

The center will be led by <u>Ali Shilatifard</u>, <u>PhD</u>, the Robert Francis Furchgott Professor of Biochemistry and <u>Pediatrics</u> and chair of the Department of <u>Biochemistry and Molecular Genetics</u>. Shilatifard's work focuses on understanding the intricate chromatin mechanisms that regulate gene expression. This year, Shilatifard's laboratory and his collaborators published several groundbreaking discoveries reporting the development of epigenetic targeted therapeutics for childhood leukemia, childhood brain cancer and adult triple negative breast cancer. One study on childhood brain tumors led to a Phase I clinical trial planned for next year at the Ann & Robert H. Lurie Children's Hospital of Chicago.



Caption goes here

"Words cannot describe my gratitude to Kimberly and Lou for their generous support of fundamental research from the epigenetic perspective of gene expression, and how perturbations of this process result in the pathogenesis of diverse human diseases," said Shilatifard. "We will work very hard at the Simpson Querrey Center for Epigenetics, in collaboration with our colleagues across the medical center and on the north campus, to better understand the molecular basis of epigenetic regulation with an eye to developing targeted therapeutics for the treatment of diseases due to epigenetic abnormalities. These efforts, we expect, will lead to more personalized medicine and a better quality of life."

"Solving the world's biggest problems requires creativity and collaboration," Querrey said. "At Northwestern, leading scientists are coming together to study not just the body but also the way the environment and our decisions affect our health. Lou and I are thrilled to be a part of this groundbreaking work."

For more than a decade, Simpson and Querrey have consistently supported Northwestern. Through We Will. The Campaign for Northwestern, many new strategic initiatives have been made possible by their generosity, including the forthcoming Louis A. Simpson and Kimberly K. Querrey Biomedical Research Center, a 14-story, 600,000-square-foot building that will significantly expand Feinberg's biomedical research enterprise. The current gift brings their total giving to \$164 million.

Investigating the Role of Calcium Signaling on Brain Cell Function

Anna Toth, Medical Scientist Training Program



Anna Toth, a seventh-year student in the Medical Scientist Training Program (MSTP), studies calcium signaling in the laboratory of Murali Prakriya, PhD, professor of Pharmacology.

Q&A

Where is your hometown?

I have called many places home! I was born in Budapest, Hungary, and my family moved to the U.S. when my parents won a green card in the lottery. We've lived on Long Island and New Jersey and finally settled in Midland, Michigan, where I spent much of my childhood.

What are your research interests?

Since high school, I have been fascinated with the brain and how it works. I first got involved in research during college, where I was very interested in brain development and the signals that are exchanged between neurons to direct proper synapse formation. In graduate school, I got really interested in the molecular mechanisms by which cells in the brain are able to transform cues from their environment into changes in their functioning, which led me to study calcium signaling in Murali Prakriya's lab. Calcium is a ubiquitous intracellular signaling messenger regulating an enormous range of functions in cells including gene expression and the secretion of important molecules. Specifically, we study calcium signals arising from a type of calcium channel called the CRAC channel. We hope to gain a mechanistic understanding of the basic, essential signaling pathways that neural cells use to properly function and communicate, with the long-term goal of illuminating various diseases in which aberrant calcium signaling is involved.

What exciting projects are you working on?

My main project in the Prakriya lab focuses on astrocytes, a type of support cell in the brain that is also an essential active contributor to brain development, physiology and disease. The goal of my work is to understand how calcium signaling through CRAC channels regulates important astrocyte functions and allows astrocytes to communicate with their neuron

partners. Because dysregulated calcium signaling in astrocytes has been implicated in a number of neurological disorders, including epilepsy, schizophrenia and ALS, this research could help provide new insight into the etiology of these diseases and delineate possible targets for future therapeutic intervention.

What attracted you to the PhD program?

As an MD/PhD candidate, I was drawn to Northwestern both for its exceptional medical environment and topnotch research. Both the MSTP and the Northwestern University Interdepartmental Neuroscience NUIN programs are supportive and committed to training the next generation of leaders in medicine and research. When I visited, I saw that Northwestern had an outstanding, interdisciplinary neuroscience research community with an environment that I knew I could excel in scientifically and professionally. I also love the wonderful, vibrant city that is Chicago!

What has been your best experience at Feinberg?

While at Feinberg, I've had the opportunity to attend several conferences, both in the U.S. and abroad. Last year, I attended the FASEB Science Research Conference on Calcium and Cell Function in Lisbon, Portugal, with Dr. Prakriya and another lab member. It was a phenomenal experience to present my research, talk with and learn from leading scientists in the field from around the globe. And it didn't hurt that the meeting was in one of the most beautiful cities I've ever seen!

How would you describe the faculty at Feinberg?

Very collaborative. I have worked with multiple other labs on various projects and have always found that faculty members are willing to give advice, teach techniques, share materials and join forces to answer interesting questions. We have had very fruitful collaborations and the expertise from other faculty and laboratories has really helped push my research forward.

What do you do in your free time?

I love to travel and see the world! While I am at home in Chicago, I enjoy doing yoga, trying new recipes and performing and teaching magic to children at the Ann and Robert H. Lurie Children's Hospital through an amazing volunteer organization.

What are your plans for after graduation?

After I complete my PhD thesis work, I will return to medical school to finish my clinical studies. After graduation, I plan to complete residency training. I'm not sure yet which medical specialty I'd like to pursue, but since I love the brain, I'm naturally gravitating towards neurology or neurosurgery. My ultimate goal is to become a physician-scientist and use my training to help transform discoveries from the basic science laboratory to clinical practice.

Helping Scientists Engage Community Stakeholders

Grisel Marie Robles-Schrader, MPA



Grisel Marie Robles-Schrader, MPA, research portfolio manager for community and stakeholder engagement at the Northwestern University Clinical and Translational Sciences (NUCATS) Institute, partners with scientists to inform research design, implementation and dissemination. She also helps scientists think about different strategies to engage stakeholders in ways that are meaningful and mutually beneficial.

Q&A

Where are you originally from?

Born and raised in Chicago, however, my family is from Puerto Rico. Every summer my parents would send my sister and I there to stay with our grandparents. These experiences shaped my identity and connection to the island.

What is your educational background?

My bachelor's degree is in communications. In 2010, I received a master's degree in public administration concentrated in metropolitan planning and urban affairs. I obtained both degrees at DePaul University.

Tell us about your professional background.

In college, I became very interested in HIV/AIDS and sexual reproductive health issues. I pursued a position with the policy department at the AIDS Foundation of Chicago, where I had the opportunity to learn about the intersection of public health, community mobilization and public policy. In 2004, I began working on my first research study, with my mentor, Dr. Gary Harper. Connect to Protect®, a multi-site community mobilization study, focused on identifying and achieving structural changes aimed at reducing HIV among adolescents and young adults. Funded by the NIH through the Adolescent Trials Network for HIV/AIDS Interventions (ATN), the project involved 15 sites across the United States and Puerto Rico. Six years later, I transitioned into the role of project director with another ATN multi-site study focused on HIV testing and linkage to care effort for Latinx adolescents and youth adults. When the study ended, I worked as an independent consultant for a few years before coming to Northwestern.

Why did you choose to work at Northwestern?

The <u>Center for Community Health</u> (CCH) announced a new position that would build an infrastructure for the center's

consultation requests and establish a new program — Stakeholder-Academic Resource Panels (ShARPs) custom panel sessions intended to create spaces for academics and community stakeholders to discuss research. Excited at the prospect of working on engagement efforts across a wide range of health topics and having the opportunity to build projects from the ground up, I decided to apply for the position. Two and half years later, here I am.

How do you help scientists at the medical school?

I help scientists think about the many different types of people that can help inform research design, implementation and dissemination. I also help scientists think about different strategies to engage stakeholders in ways that are meaningful and mutually beneficial. The work is not easy but it is extremely rewarding to be in spaces where these dialogues move people to work together and to change the way research work is done.

In November, Josefina Serrato, ShARP recruitment coordinator, and I hosted a ShARP for Namrantha Kandula, MD, MPH, associate professor and Swapna Dave, MPH, MBBS, research project manager, that included 13 panel members at the Skokie Village Hall. Dr. Kandula presented on the South Asian Healthy Lifestyle Initiative, a study that aims to reduce heart disease among South Asians. Asma Ali, PhD, of A.A. Associates, served as a community co-facilitator alongside me. Panel members offered feedback on ways to improve the relevance, practicality and potential value of the research study. We were excited to learn that the India Post and the India Tribune picked up the session.

It's important to note, my accomplishments to date are due in large part to my team in CCH. Over the past 10 years they have built a strong foundation of community engaged research programs and services at Northwestern.

What is your favorite part of the job?

I enjoy getting to work with so many different individuals throughout the university and from different community sectors, with diverse personal and professional backgrounds.

What exciting projects are you working on?

I'm working closely with <u>Keith Herzog</u>, assistant director of evaluation at NUCATS and <u>Mike Fagen, PhD, MPH</u>, associate professor of <u>Preventive Medicine</u> and the director of the Masters in Public Health Program and CCH staff to strengthen CCH's evaluation infrastructure so that the Center can continue to demonstrate the purpose and value of community-engaged research.

What do you like to do in your spare time?

I like to work out at OrangeTheory Fitness (the coaches are fun and extremely supportive!) and I like to read.

Connect with Grisel on LinkedIn.

Research in the News

Today, November 6

<u>Special Alzheimer's program helps couple deal with the disease</u> Lauren Dowden was quoted.

The New York Times, November 15

Amish mutation protects against diabetes and may extend life Doug Vaughan was quoted.

► This research was also featured in *Newsweek* and *The Guardian*

HealthDay, November 20

More patients are having a say in their medical care Jeffrey Linder was quoted.

► This research was also featured in U.S. News & World Report

U.S. News & World Report, November 22

U.S. News sits in as surgeons carry out an 8-person kidney exchange

Northwestern Memorial Hospital was mentioned.

Today, November 22

<u>Signs that your youngster might be at risk for food allergies</u> Ruchi Gupta was quoted.

U.S. News & World Report, November 27

Are there heart disease risks for teens moms? Marla Mendelson was quoted.

National Public Radio, November 27

<u>Light Therapy Might Help People With Bipolar Depression</u> Feinberg was mentioned.

Associated Press, November 29

Researchers use advanced technology to study child mummy Stuart Stock was quoted.

► This research was also featured in U.S. News & World Report, Chicago Tribune, The New York Times, Washington Post and USA Today

More media coverage available online.

Northwestern University NUCATS Clinical and Translational Sciences Institute

NUCATS Corner

Sex Cells: Discover Best Practices in Sex-Inclusive Research

The Women's Health Research Institute at Northwestern University invites you to attend the 2nd Annual Symposium on Sex Inclusion in Biomedical Research on January 25. This day-long symposium, on the Chicago campus, promotes the advancement of sexinclusive research within the basic, translational and clinical research fields. It fosters knowledge amongst interdisciplinary communities who currently conduct or are interested in sex-based research.

This year's theme, "A Spotlight on Autoimmunity," will feature keynote and plenary lectures from nationally recognized experts in sex-based immunology including Jayne Danska, Sabra Klein and Maureen Su. In addition, the symposium will feature a panel discussion on the state of sex-inclusive science, invited abstract presentations and a poster session.

Whether you are experienced in conducting sexinclusive research or would like to begin, the symposium gives you the opportunity to:

- Showcase your research <u>Submit an abstract</u> by December 18 for consideration for an oral or poster presentation.
- Enhance your grants Find out how to comply to the NIH sex-inclusion policy.
- Meet the experts Join nationally recognized experts in the field of sex-inclusion for engaging discussions.
- Create collaborations Network at the poster session and reception to find potential collaborators with expertise in sex-based research.
- Discover best practices Learn how to consider sex as a biological variable in your research design, analyses and reporting.

To learn more and register for the event, click here.

Sponsored Research



PI: Daniela Menichella, MD, PhD, assistant professor of Neurology in the Division of Neuromuscular Disease and of Pharmacology

Breakthroughs

Sponsor: National Institute of Neurological Disorders and Stroke

Title: "Cellular and Molecular Role of CXCR4 signaling in Painful Diabetic Neuropathy"

Diabetes affects 25.8 million people in the United States and neuropathic pain is a debilitating affliction present in 26 percent of diabetic patients, with substantial impact on the quality of life. Despite this significant impact and prevalence, current therapies for neuropathic pain are only partially effective and the molecular mechanisms underlying neuropathic pain in diabetes are not well understood.

Menichella's team has a long-term goal to elucidate the molecular mechanisms responsible for Painful Diabetic Neuropathy (PDN) in order to provide targets for the development of therapeutic agents for the effective treatment of this syndrome. The objective of this application is to identify the molecular cascade linking CXCR4/SDF-1 chemokine signaling to DRG nociceptor hyper-excitability, neuropathic pain and small fiber degeneration. The overall impact of this proposal is a better understanding of the molecular underpinnings of neuropathic pain and small fiber degeneration associated with diabetes. The proposed research will have a positive impact by identifying unique molecular targets for mechanism-based therapeutic development in PDN.

Read more about this project.



PI: Adam Sonabend, MD, assistant professor of Neurological Surgery

Sponsor: Office of the Director, National Institutes of Health

Title: "TOP2A effects on transcription in gliomas: implications for personalized therapy"

Glioblastomas (GBMs), the most common and malignant of all primary brain tumors, infiltrate the brain and are lethal. GBM can be diagnosed de novo or result from progression of lower-grade gliomas. All GBMs undergo the same non-curative treatment, including surgery, chemotherapy and radiation. Given that molecular characteristics are highly variable across GBMs, these tumors have been classified into subtypes based on gene expression patterns. These expression patterns and their underlying mechanisms might provide a unique tumoral vulnerability, a possibility not yet explored. Many transcription factors that control gene expression on proneural GBM subtype during glioma progression appear to be modulated by Topoisomerase IIA (TOP2A), an enzyme expressed by these tumors since early stages.

This application aims to study the role of TOP2A in transcriptional regulation in glioblastomas and explore its therapeutic targeting using intratumoral etoposide for this lethal form of brain cancer. Sonabend hypothesizes that TOP2A plays a vital role regulating gene expression in a subset of glioblastomas. His team will determine which subset of these tumors is regulated by TOP2A, which will provide an insight into tumoral vulnerability to etoposide, a drug that targets TOP2A. This information can be used as criteria to select patients for a future clinical trial of intratumoral etoposide for glioblastoma.

Read more about this project.



Welcome New Faculty

Lauren Balmert, PhD, joins as an assistant professor of Preventive Medicine in the Division of Biostatistics. Her scientific interests are primarily collaborative and include the application of biostatistics to urology, audiology and pediatric medicine. She is also particularly interested in methodology for time-to-event data. Previously, she was PhD candidate and graduate student scientist at the University of Pittsburgh Center for Occupational Biostatics and Epidemiology. Blamert earned her undergraduate degree from Fairfield University and her PhD in biostatistics from the University of Pittsburgh. She has published nine journal articles and has received numerous awards including the Outstanding Teaching Assistant Award from the University of Pittsburgh Graduate School of Public Health.

Joshua Rappoport

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Which honors are you most proud of and why?

I am most proud of the awards that we've won from the Office for Research every year since I've been at Northwestern. This demonstrates the continued excellence of our facility among a truly outstanding group of cores university-wide.

Who inspires you? Or, who are your mentors?

<u>Phil Hockberger, PhD</u>, in the Office for Research has been a fantastic mentor. He has shown me the best ways that core facilities can be run in an integrated model within a complex network of schools, departments and centers.

Scientifically, my postdoctoral advisor from The Rockefeller, Sandy Simon, PhD, really opened up my mind to the best application of the scientific method. In particular, microscopy can be prone to a search for a single pretty picture, but working with Sandy we always sought conclusions that were subject to rigorous statistical testing, rather than simply qualitative results.

Finally, there is a long list of scientists at Northwestern University and beyond that have served as mentors or role models, including Bob Goldman, PhD, and Volodya Gelfand, PhD, in the Department of Cell and Molecular Biology, John Heath, D.Phil, from the University of Birmingham, where I was previously a faculty member, and especially my PhD supervisor Ruth Abramson, MD, who unfortunately passed away while I was a postdoc.



Save the Date

The 14th Annual Lewis Landsberg Research Day
Thursday, April 5, 2018
1:00 p.m. to 5:00 p.m.
The Robert H. Lurie Medical Research
Northwestern Memorial Hospital's Feinberg Pavilion

This is a campus-wide event to promote faculty and trainee development through the sharing of exciting scientific discoveries and conversation with colleagues. Junior faculty are especially encouraged to submit abstracts and to network and exchange ideas with Feinberg faculty. Research Day also provides an opportunity to learn about the Research Cores and the full spectrum of support they provide for clinical and basic science research.

Funding

Distinguished Scientist Awards

More information

Sponsors: The Sontag Foundation **Submission deadline:** March 24

Upper amount: \$600,000 over a four-year period

Synopsis: The Distinguished Scientist Award seeks to provide career and research support to early career scientists who demonstrate outstanding promise for making scientific and medical breakthroughs in the field of brain cancer research.

Tau Pipeline Enabling Program

More information

Sponsors: The Alzheimer's Association

Submission deadline: January 5, Letter of Intent

Upper amount: \$750,000

Synopsis: The Tau Pipeline Enabling Program (T-PEP) seeks to accelerate the discovery of potential new therapies for tauopathies.

The intent of this program is to enrich the pipeline for therapy development by facilitating the translation of academia-derived ideas into practical application.

In short, it bridges the gap between innovative but resourceconstrained scientists and the larger pharmaceutical companies that are looking for drug candidates to be taken into human trials.

Precision Medicine Targeted Grant

More information

Sponsors: Pancreatic Cancer Action Network

Submission deadline: February 13

Upper amount: \$1,000,000

Synopsis: Applications for the current funding announcement are restricted to projects relevant to pancreatic ductal adenocarcinoma and can include treatments for resectable, locally advanced, metastatic or recurrent disease.

View more funding opportunities

How to Keep Current on Literature



Staying aware of current information in any field is a time-consuming undertaking. Our well-trod paths to trusted journals, society newsletters or email listservs are safe harbors in a turbulent sea of information. Beyond those resources, how do we find information sources that give us what we need, when we need it? How do we distinguish which sources to spend time on from those we decide to put aside? Anyone new to a field of research might need help finding the most current information in their field. Here are a few ideas to get started.

Web of Science's Hot and Highly Cited Papers

Using Web of Science, create a search strategy based on your research interests. Filter the results by "Hot Papers in Field" (papers in the top 0.1 percent in the past two months) and "Highly Cited in Field" (papers in the top 10 percent in the past 10 years), and set up a weekly search alert for your email address.

PubMed's "Latest Literature" and "Trending Articles" features

In 2016, PubMed rolled out the "Latest Literature" feature, which highlights newly indexed articles from highly accessed journals. Another enhancement is the "Trending Articles" feature, which highlights articles with a significant increase in daily views in the past two days compared to the previous baseline. You can also run a literature search in PubMed on a topic of interest to you, and use "Trending Articles" as a filter on the search results.

Scopus's "Follow this Author" feature

If you know the top scientists in your field, consider following those authors to receive alerts every time they publish a new paper that is indexed in Scopus. Simply use Scopus's

Author Search tab to find the correct person(s), and when in their Author details page, click on the "Follow this Author" button to receive emails on a periodic basis when this author publishes new articles. You can also choose the "Get citation alerts" button for whenever a paper cites one of the author's papers in Scopus.

BrowZine's "Bookcase" feature

From the <u>Galter Library homepage</u>, find the BrowZine link under our list of Popular Resources. BrowZine is a web or mobile app that allows you to access and browse e-journals from one interface. Once you sign into your free account, you can search for a journal and "add it to your bookshelf." When you login to your bookshelf on any device, this configuration will automatically sync to that device and display red bubbles indicating that you have new articles available in that journal.

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References:

Canese K. PubMed Homepage Enhanced. NLM Tech Bull. 2016 Sep-Oct;(412):e1. Retrieved from: https://www.nlm.nih.gov/pubs/techbull/so16/so16_pubmed_homepage_enhancement.html

My Bookshelf and BrowZine Account FAQ. Retrieved from: http://support.thirdiron.com/knowledgebase/articles/855504

High Impact Factor Research

Breakthroughs

Bao X, Siprashvili Z, Zarnegar BJ, Shenoy RM, Rios EJ, Nady N, Qu K, Mah A, Webster DE, Rubin AJ, Wozniak GG, Tao S, Wysocka J, Khavari PA. <u>CSNK1a1 Regulates PRMT1 to Maintain the Progenitor State in Self-Renewing Somatic Tissue</u>. *Developmental Cell*. 2017 Oct 23;43(2):227-239.e225.

Barefield DY, Puckelwartz MJ, Kim EY, Wilsbacher LD, Vo AH, Waters EA, Earley JU, Hadhazy M, Dellefave-Castillo L, Pesce LL, McNally EM. Experimental Modeling Supports a Role for MyBP-HL as a Novel Myofilament Component in Arrhythmia and Dilated Cardiomyopathy. Circulation. 2017 Oct;136(16):1477-1491.

Escobedo N, **Oliver G**. <u>The Lymphatic Vasculature: Its Role in Adipose Metabolism and Obesity</u>. *Cell Metabolism*. 2017 Oct;26(4):598-609.

Gadd S, Huff V, Walz AL, Ooms A, Armstrong AE, Gerhard DS, Smith MA, Auvil JMG, Meerzaman D, Chen QR, Hsu CH, Yan CH, Nguyen C, Hu Y, Hermida LC, Davidsen T, Gesuwan P, Ma Y, Zong ZS, Mungall AJ, Moore RA, Marra MA, Dome JS, Mullighan CG, Ma J, Wheeler DA, Hampton OA, Ross N, Gastier-Foster JM, Arold ST, Perlman EJ. A Children's Oncology Group and TARGET initiative exploring the genetic landscape of Wilms tumor. Nature Genetics. 2017 Oct;49(10):1487.

Kim J, Park DY, Bae H, Park DY, Kim D, Lee CK, Song S, Chung TY, Lim DH, Kubota Y, Hong YK, He YL, Augustin HG, **Oliver G**, Koh GY. <u>Impaired angiopoietin/Tie2 signaling compromises</u> <u>Schlemm's canal integrity and induces glaucoma</u>. *Journal of Clinical Investigation*. 2017 Oct;127(10):3877-3896.

Mehta MM, Weinberg SE, Chandel NS. Mitochondrial control of immunity: beyond ATP. Nature Reviews Immunology. 2017 Oct;17(10):608-620.

Morgan MAJ, Rickels RA, Collings CK, He X, Cao K, Herz HM, Cozzolino KA, Abshiru NA, Marshall SA, Rendleman EJ, Sze CC, Piunti A, Kelleher NL, Savas JN, Shilatifard A. A cryptic Tudor domain links BRWD2/PHIP to COMPASS-mediated histone H3K4 methylation. Genes & Development. 2017 Oct 01;31(19):2003-2014.

Motl RW, Sandroff BM, **Kwakkel G**, Dalgas U, Feinstein A, Heesen C, Feys P, Thompson AJ. <u>Exercise in patients with multiple sclerosis</u>. *Lancet Neurology*. 2017 Oct;16(10):848-856.

Pavel ME, Singh S, Strosberg JR, Bubuteishvili-Pacaud L, Degtyarev E, Neary MP, Carnaghi C, Tomasek J, Wolin E, Raderer M, Lahner H, Valle JW, Pommier R, Van Cutsem E, Tesselaar MET, Delle Fave G, Buzzoni R, Hunger M, Eriksson J, **Cella D**, Ricci JF, Fazio N, Kulke MH, Yao JC. <u>Health-related quality of life for everolimus versus placebo in patients with advanced, non-functional, well-differentiated gastrointestinal or lung neuroendocrine tumours (RADIANT-4): a multicentre, randomised, double-blind, placebocontrolled, phase 3 trial. *Lancet Oncology.* 2017 Oct;18(10):1411-1422.</u>

Reddy A, Zhang J, Davis NS, Moffitt AB, Love CL, Waldrop A, Leppa S, Pasanen A, Meriranta L, Karjalainen-Lindsberg ML, Norgaard P, Pedersen M, Gang AO, Hogdall E, Heavican TB, Lone W, Iqbal J, Qin Q, Li GJ, Kim SY, Healy J, Richards KL, Fedoriw Y, Bernal-Mizrachi L, Koff JL, Staton AD, Flowers CR, Paltiel O, Goldschmidt N, Calaminici M, Clear A, Gribben J, Nguyen E, Czader MB, Ondrejka SL, Collie A, Hsi ED, Tse E, Au-Yeung RKH, Kwong YL, Srivastava G, Choi WWL, Evens AM, Pilichowska M, Sengar M, Reddy N, Li SY, Chadburn A, Gordon LI, Jaffe ES, Levy S, Rempel R, Tzeng T, Happ LE, Dave T, Rajagopalan D, Datta J, Dunson DB, Dave SS. Genetic and Functional Drivers of Diffuse Large B Cell Lymphoma. Cell. 2017 Oct;171(2):481.

Sathiyamoorthy K, Jiang JS, **Mohl BS, Chen J,** Zhou ZH, **Longnecker R,** Jardetzky TS. <u>Inhibition of EBV-mediated membrane</u> <u>fusion by anti-gHgL antibodies</u>. *Proceedings of the National Academy of Sciences of the United States of America*. 2017 Oct;114(41):E8703-E8710.

Wolchok JD, Chiarion-Sileni V, Gonzalez R, Rutkowski P, Grob JJ, Cowey CL, Lao CD, Wagstaff J, Schadendorf D, Ferrucci PF, Smylie M, Dummer R, Hill A, Hogg D, Haanen J, Carlino MS, Bechter O, Maio M, Marquez-Rodas I, Guidoboni M, McArthur G, Lebbe C, Ascierto PA, Long GV, Cebon J, Sosman J, Postow MA, Callahan MK, Walker D, Rollin L, Bhore R, Hodi FS, Larkin J. Overall Survival with Combined Nivolumab and Ipilimumab in Advanced Melanoma.

New England Journal of Medicine. 2017 Oct 05;377(14):1345-1356.

Wong JJW, Young TA, Zhang JY, Liu SH, Leser GP, Komives EA, **Lamb RA**, Zhou ZH, Salafsky J, Jardetzky TS. <u>Monomeric ephrinB2 binding induces allosteric changes in Nipah virus G that precede its full activation</u>. *Nature Communications*. 2017 Oct;8:11.

Yoo SH, Kojima S, **Shimomura K**, Koike N, Buhr ED, Furukawa T, Ko CH, Gloston G, Ayoub C, Nohara K, Reyes BA, Tsuchiya Y, Yoo OJ, Yagita K, Lee C, Chen Z, Yamazaki S, Green CB, Takahashi JS. Period2 3 '-UTR and microRNA-24 regulate circadian rhythms by repressing PERIOD2 protein accumulation. Proceedings of the National Academy of Sciences of the United States of America. 2017 Oct;114(42):E8855-E8864.

Zha L, Jiang YD, Henke MT, Wilson MR, Wang JX, **Kelleher NL**, Balskus EP. <u>Colibactin assembly line enzymes use</u>
<u>S-adenosylmethionine to build a cyclopropane ring</u>. *Nature Chemical Biology*. 2017 Oct;13(10):1063.

Help Feinberg Track Journals

The Feinberg Research Office regularly tracks research published by Feinberg investigators. The citations are used on web pages, in newsletters and social media, for internal reporting and more. To more accurately track these journals, the Research Office asks that Feinberg investigators use the following institution name in the address field when publishing in peer-reviewed journals: "Northwestern University Feinberg School of Medicine."

Calendar

Friday, December 15

Aspergillus fumigatus Strain Specific Inflammatory Responses

Joshua Obar, PhD, Dartmouth Medical School, will present.

Time: Noon to 1:00 p.m.

Location: Prentice Women's Hospital, 3rd Floor, Canning

Auditorium, 250 E. Superior

Contact: Jamie Riley at jamie.riley@northwestern.edu

More information

Monday, December 18

Biostatistics Seminar

Brad Carlin, PhD, Head of the University of Minnesota's School of Public Heath's Division of Biostatistics, will present.

Time: 3 p.m. to 4:00 p.m.

Location: 680 N. Lake Shore Drive, Stamler Conference Room,

Suite 1400

Contact: Tameka Brannon at t-brannon@northwestern.edu

More information

Friday, January 4

The Role of Foxm 1 in Leukemogenesis

Zhijian Qian, PhD, associate professor, Department of Medicine, University of Illinois College of Medicine to present.

Time: 1:00 p.m. to 2:00 p.m.

Location: Robert H. Lurie Medical Research Center, Searle

Conference Room, 303 E. Superior

Contact: Lurie Cancer Center at cancer@northwestern.edu

More information

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NIH News

Registration Open for NIH Regional Seminar

The 2018 NIH Regional Seminar on Program Funding and Grants Administration will be held in Washington, D.C., May 2 to 4, steps away from the U.S. Capitol and Union Station. The NIH Regional Seminar offers a comprehensive program for the NIH extramural community about the NIH grants process and related policies, including such topics as fundamentals of the NIH, compliance, peer review, grant writing for success, pre-award and post-award issues for administrators and investigators, animal and human subject research and how to interact electronically with the NIH. Register through December 15, 2017, for discounted rates and save.

Webinar on Adverse Events in Research Facilities

Watch a webinar, hosted by Swapna Mohan, DVM, PhD, of the NIH's Office of Laboratory Animal Welfare, who talks about a variety of adverse events that can endanger the health and welfare of research animals. Mohan also provides steps that you can take to mitigate your risks and highlights some of the issues that have been reported. Read more about this topic in an article in the June issue of Lab Animal.

The 21st Century Cures Act

The Cures Act, or the 21st Century Cures Act, was signed into law on December 13, 2016. The legislation provides the NIH with critical tools and resources to advance biomedical research across the spectrum, from foundational basic research studies to advanced clinical trials of promising new therapies. On December 7, 2018, Francis Collins, MD, PhD, Director of the National Institutes of Health, appeared as a witness before the Senate Committee on Health, Education, Labor, and Pensions to highlight how the NIH is implementing some of the key provisions of the Cures Act. Read his full testimony.

NIH Research at Feinberg Highlighted in Campaign



United for Medical Research showcased three scientists at Feinberg whose work is supported by NIH funding. Almost 380,000 jobs across the United States were supported by NIH funding in 2016 alone. Read more about how the NIH contributes to economic activity and see Feinberg scientists featured online.