Breakthroughs

Feinberg School of Medicine Research Office

November 2018



Left: Lung tissue from a normal mouse. Right: Lung tissue from a mouse with a genetic deletion of a key epigenetic regulator protein (Uhrf1) within its regulatory T-cells. This leads to spontaneous severe inflammation of the lung and other organs.

Epigenetics: Landscape of Disease

By Will Doss

Imagine a marble, rolling down a hill. There are many paths the marble can take — many peaks and troughs guiding its descent to different places. As the marble moves down the hill, the paths and ultimate destinations available to the marble dwindle. The terrain drives where the marble lands.

This is how famed geneticist C.H. Waddington described his theory of "epigenetic landscape" for cell differentiation in 1957 — the marble is an uncommitted cell on the path of differentiation, the peaks and troughs are the pattern of gene expression that commits the cell to a certain identity. DNA methylation, a mechanism involved in a wide variety of epigenetic processes, wasn't discovered until 1975, but Waddington's initial premise held true.

Today, the study of epigenetics has taken off. In the last 20 years, laboratories across the world have been racing to identify molecular mechanisms of epigenetic regulation, finding they have an impact on more than just cell differentiation. Epigenetic



mechanisms play a role in a huge range of processes, including oncogenesis and immune response, and more are discovered every year.

At Northwestern, the Simpson Querrey Center for Epigenetics (SQE) leads the way, connecting the Northwestern academic and medical community to integrate the study of epigenetics into science and clinical care.

It's a living, breathing resource for scientists at Northwestern who want to learn more about changes in phenotype without a change in genotype, according to <u>Ali Shilatifard, PhD</u>, chair of <u>Biochemistry and Molecular Genetics</u>, the Robert Francis Furchgott Professor and director of the SQE.

"The main emphasis of this center is linking epigenetic discoveries — things that affect chromatin DNA and regulate gene expression — to human disease," said Shilatifard, who is also a professor of <u>Pediatrics</u>. "Our colleagues throughout the medical center and university need expertise in this area, and now they have a place to go."

A bi-weekly seminar called the Biochemistry Epigenetics and Metabolism Forum is a hub for the SQE, where members and non-members give updates on projects, share data and tout the use of core facilities co-sponsored by the center. There is also a monthly lecture series featuring experts in the field such

Epigenetics (continued from cover page)

as <u>Robert Roeder, PhD</u> (Rockefeller University), <u>Mike Levine, PhD</u> (Princeton University), <u>Martine Roussel, PhD</u> (St. Jude Children's Research Hospital) and <u>Lucy Godley, MD, PhD</u> (University of Chicago).

In addition, the SQE will hold its inaugural <u>symposium</u> on November 30, bringing together scientists and clinicians from across the world for a day of presentations, discussion and networking. The SQE also plans to offer courses that will give investigators the tools they need to conduct epigenetics research, Shilatifard said.

"For example, we are planning to offer courses on different methods of RNA sequencing and data analyses, how to use ChIPseq and related methodologies to identify functions of proteins that work on chromatin," said Shilatifard, whose own work using these techniques has defined how chromosomal translocations cause pediatric cancers and how this information can be used to treat cancers. "We want to teach investigators how to fish, instead of simply giving them the fish."

Pulmonary Patch-up

One area where epigenetics has been found to be influential is in immune response, specifically in lung repair.

Benjamin Singer, '07 MD, '11 GME, assistant professor of <u>Medicine</u> in the Division of <u>Pulmonary and Critical Care</u> and a member of the SQE, became interested in epigenetics' effect on immune response during a fellowship at Johns Hopkins University School of Medicine.

"The complex cell types involved in lung repair are highly regulated by epigenetic mechanisms," said Singer, who is also an assistant professor of Biochemistry and Molecular Genetics. "My main discovery was that by manipulating DNA methylation, we can actually encourage these cells to do their jobs better."

Now with his own laboratory at Northwestern, Singer has continued to investigate the topic. In one study, <u>published</u> in the *Journal of Biological Chemistry*, Singer took a detailed look at

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Learn more about Ali Shilatifard's research studying the epigenetic basis of cancer, and meet more of the scientists in the Department of Biochemistry and Molecular Genetics, in a series of videos <u>here</u>.

DNA methylation in mouse models of neonatal lung infection.

With help from the SQE, Singer used bioinformatics and computational tools to show that DNA methylation patterns play an important role in controlling T-cells that help repair the lung. A subsequent paper, <u>published</u> in the *Journal of Clinical Investigation Insight*, used an innovative sampling technique to measure DNA methylation patterns in human patients with lung failure. Singer found that the patterns in humans were very similar to what they saw in models, opening the door for one day using these patterns to predict treatment response.

"If you could define a part of the genome that has this methylation, you might be able to predict the outcome," Singer said. "One could draw blood from a patient, quickly assess the DNA methylation and estimate if this patient is likely to do poorly or to do well and respond to therapy."

There is even potential for a drug-based therapy, if scientists can identify an actionable drug target.

"If you can manipulate DNA methylation, you could help patients get off the ventilator and make it more likely that they would survive this horrible illness," Singer said.

These sampling and analyzing techniques, which will soon be expanded to a much larger group of patients as part of an <u>ongoing study</u> at Northwestern Medicine, are an example of how the SQE can help scientists at Northwestern.

"The SQE can affect research that spans from the atomic, molecular level all the way through application to patients," Singer said. "This can't be done at very many places — it makes this an incredible environment to do high-impact work."

Epigenetics (continued from page 2)

Onco-histones

One of the most popular areas of epigenetics is oncogenesis. SQE member <u>Amanda Saratsis</u>, <u>MD</u>, '14 <u>GME</u>, assistant professor of <u>Neurological Surgery</u>, became interested in diffuse intrinsic pontine glioma (DIPG), a rare and deadly pediatric tumor located in a part of the brainstem called the pons, during residency training at Georgetown University, when two groundbreaking papers discovered mutations in a protein called histone H3 in 80 percent of surveyed tumor samples.

"The presence of this histone mutation wreaks havoc on the epigenetic mechanisms of gene expression regulation in these tumors," Saratsis said.

Since then, Saratsis has made it her mission to learn more about these tumors, working with Shilatifard and other collaborators at Northwestern to find their source and shut them down. In a paper <u>published</u> last year in *Nature Medicine*, Saratsis, Shilatifard and colleagues found that the mutation in histone H3 leads to one amino acid being swapped out for another, causing a downstream cascade that leads to tumorpromoting gene expression in the brainstem.

A child's developing brain may be particularly susceptible to these epigenetic perturbations. For example, the genesis of these pontine tumors often coincides with a period of heavy myelination in the pons; the process by which neurons are insulated with a material called myelin. While myelin is needed to ensure information travels fast throughout the brain, the physiological signals that promote this normal process may also encourage DIPG cells to grow.

"We're still not 100 percent sure what the cell of origin is for DIPG, but we think the rapidly developing brainstem may provide a unique microenvironment for tumor cells to respond to normal signals with abnormal biology," Saratsis said.

In fact, epigenetic mechanisms may be more common in pediatric brain tumors than previously thought, Saratsis said.

"Now that we have this perspective, we're going back with fresh eyes and looking at these epigenetic processes, and we're finding abnormalities in pediatric brain tumors," Saratsis said. "They don't all have this histone H3 mutation, but they may have a different mutation that affects the same sort of process."

Collaboration with other SQE members is crucial, especially for studying a disease like DIPG. Because these tumors are deep in the brainstem, high-quality specimens are hard to come by, so Saratsis is working with the SQE to develop new biological



Magnetic resonance imaging of the brain demonstrating a large, infiltrative mass (round white structure) within the pons (brainstem), known as diffuse intrinsic pontine glioma (DIPG). Research has revealed epigenetic perturbations behind this kind of tumor development.

assays that can extract epigenetic information from archival tumor specimens or spinal fluid.

"The technology that the SQE provides allows us to approach these specimens that perhaps we would have no use for," Saratsis said. "How we process specimens, perform sequencing and then analyze that data has proven very challenging in the past, and now we're able to make gains like never before."

The field of epigenetics is in its infancy, but the knowledge base and scientific techniques continue to grow and improve. The top-to-bottom integration into both Singer's and Saratsis' research is something the SQE hopes to foster at Northwestern, galvanizing scientists across institutions and centers to produce solutions for patients.

"The beauty of Northwestern and the Simpson Querrey Center for Epigenetics is that we can go from basic chemistry, to biochemistry, to molecular genetics, into animals models and finally into the clinic, all at one institution," Shilatifard said.

Find more information about SQE education events and seminars <u>here</u>.

Seed Grants Support New Award Applications

The Office of Research provides seed grants of up to \$30,000 to initiate new applications for multi-investigator program project or center grants involving Feinberg faculty. The funds are intended to support new applications, preferably to the NIH. There is an expectation of casting a wide net, so research projects should involve at least two faculty members from outside the home department of the principal investigator.

This funding can be used to cover reasonable expenses for a retreat to bring together key faculty, staff and students, then to provide reagents for key preliminary experiments, costs for preparing the application and other reasonable expenses. Our centralized <u>research administration services group</u> can assist with staff support for the retreat and proposal preparation, if the principal investigator wishes.

In fiscal years 2015 to 2018, 11 seed commitments were made, totaling \$73,400. The majority of awards supported planning meetings and retreats related to programmatic grant applications, though pilot project funds and cost-sharing were each provided on one occasion. In addition to proposals and awards, outcomes have included collaborations, working groups, surveys, invited presentations, manuscripts, centers and a seminar series.

To date, 12 proposals have been submitted as a direct result of the seed funds, totaling \$36 million. Funding agencies included the NIH, Chicago Biomedical Consortium, Centers for Disease Control and Prevention, and United States Department of Agriculture. NIH funding mechanisms included R21, R01, P30 and P50.



To date, Feinberg investigators have received four awards as a direct result of seed funds, totaling \$19.3 million. This figure represents a return of \$263 for every dollar invested.

Success Story

<u>Richard D'Aquila, MD</u>, associate vice president of research and professor of



<u>Medicine</u> in the Division of <u>Infectious Diseases</u>, used Feinberg's seed funding to prepare an application that led to a \$9.4 million grant for the <u>Third Coast Center for AIDS Research</u>, now in its fourth year.

"The seed funding program was essential for beginning the growth of a highly trans-disciplinary, cross-campus collaboration that enabled a successful first-time application for an NIH P30. This NIH program requires that investigators in any and every field relevant to HIV research be included in the application and for the application to document how they would be served by the proposed center," D'Aquila explained.

"The initial retreat supported by seed funding was the first time many of the large group met and exchanged ideas for our mission and aims. It enabled a large and diverse team to start working together and supported temporary staffing essential for continuing meetings of several collaborative writing teams and the administrative tasks needed to assemble a large, complex application. I cannot imagine how we could have done this without the seed funding program."

Learn more about applying for seed funding here.

Update: Feinberg Scientific Images Contest

The randomly selected winner of the iPad is **Isabella Salamone**, a PhD candidate in the Driskill Graduate Program. All images are still under consideration for a gallery exhibit in the new Simpson Querrey Biomedical Research Center. More details will be available in the coming months.

Uncovering Pathogenesis of Lung Injury, With Clinical Impact

Ankit Bharat, MD, the Harold L. and Margaret N. Method Research Professor of Surgery



As both a thoracic surgeon and an active investigator, <u>Ankit</u> <u>Bharat</u>, <u>MD</u>, sees the importance of bench-to-bedside research first hand. Bharat, associate professor of <u>Surgery</u> in the Division of <u>Thoracic Surgery</u> and of <u>Medicine</u> in the Division of <u>Pulmonary and Critical Care</u>, leads a research laboratory focused on lung preservation, transplant

and translating discoveries in those areas into clinical impact.

Bharat is also a member of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University.

Q&A

What are your research interests?

Our research focuses on understanding the pathogenesis of lung injury, as well as the mechanisms of injury resolution, using models of lung transplantation and fibrosis, mimicking human disease. We use high-throughput genomic and transcriptomic techniques, as well as intravital imaging to determine the host immune response to injury mechanisms, such as ischemia-reperfusion and infections. We hope that by finding solutions to commonly encountered clinical problems in the context of lung biology, we can make a broad impact in patients with advanced lung disease and patients undergoing lung transplantation.

What is the ultimate goal of your research?

Our overarching goal is to develop novel areas of therapeutics in patients with advanced lung disease and for those undergoing lung transplantations. By modulating the host immune response, we can alter the lung disease biology and favorably impact patient outcomes.

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

We are fortunate to have a multidisciplinary research team with experienced collaborators from different divisions at Feinberg (including Pulmonary and Critical Care, <u>Rheumatology</u>, <u>Allergy and Immunology</u>, and <u>Organ Transplantation</u>) as well as at the McCormick School of Engineering. We also work closely with investigators at Washington University School of Medicine and the Norton Thoracic Institute in Phoenix.

Where have you recently published papers?

Our research has been recently published in *Science Translational Medicine*, the *Journal of Clinical Investigation, Journal of Immunology* and *American Journal of Respiratory & Critical Care Medicine*. Our <u>discovery</u> that Mollicutes cause fatal hyperammonemia in humans was featured as one of the cover stories on sciencemag.org. Our <u>discovery</u> of resident pulmonary non-classical monocytes and their sentinel role in initiating lung ischemia-reperfusion injury leading to the lethal syndrome of primary graft dysfunction, the predominant cause of mortality following lung transplantation, was selected as the cover of *Science Translational Medicine*. Recently, we <u>discovered</u> a new role for the spleen in the education of monocytes, enabling them to permeabilize host endothelium, thereby allowing neutrophils to extravasate into the interstitial space and initiate inflammation. This work for published in the *Journal of Clinical Investigation*.

What do you enjoy about teaching and mentoring young scientists in the lab?

I particularly enjoy getting the trainees excited about the research they are involved with. We try to ask research questions in our lab that have high clinical relevance. Being active in the surgical field and having translated some of our findings to patient care, I feel fortunate to be able to explain the clinical impact of the work to our trainees. The motivation they derive from this is immensely gratifying. I hope that the trainees maintain that drive and a keen passion towards transforming the lives of our patients, even after finishing their training in the lab.

How is your research funded?

Our research is predominantly funded through the NIH (K08 and R01 award). Additionally, our research has been funded by the American Association of Thoracic Surgeons, American Lung Association, LUNGevity Foundation, Thoracic Surgery Foundation, International Heart and Lung Transplant Society and the Society of University Surgeons.

Staying Active in and Outside the Laboratory Kosta Nicolozakes, Medical Scientist Training Program



Kosta Nicolozakes, a fourthyear student in the Medical Scientist Training Program (MSTP), studies shoulder instability in the laboratories of Eric Perreault, PhD, professor of Biomedical Engineering and Physical Medicine and Rehabilitation, and Amee Sietz, PT, PhD, associate professor of Physical Therapy and Human Movement Sciences.



Where is your hometown? Wooster, Ohio.

What is your research focus?

I conduct my research in the Neuromuscular Control Laboratory of Eric Perreault, PhD, at the Shirley Ryan AbilityLab. I'm also fortunate to train under Amee Seitz, PT, PhD, a clinicianscientist, and take advantage of a collaboration between Eric's position in Biomedical Engineering and Amee's in Physical Therapy. Both of these mentors offer valuable training and have given me immense freedom to design an independent project balancing their engineering and clinical expertise.

In my current research, I'm looking at ways to determine why certain individuals with loose shoulders are in pain and some stay asymptomatic. This project has taken me down the road of developing some instrumented techniques to try and improve the assessments physicians and therapists are able to utilize when evaluating how loose a patient's shoulder is.

My research background is rooted in sports medicine, so I'm thrilled to have been able to design a sports-inspired project in a more rehabilitation-focused environment at the Shirley Ryan AbilityLab.

Why did you choose Feinberg?

When I was applying to MSTPs four years ago, my "ideal" landing spot was a prominent Midwestern academic institution (as I was born and raised an Ohio boy); Northwestern immediately vaulted to the top of the list.

The advice I received from colleagues and mentors about where to attend had a unifying message: Choose a program that wants you as you. During my admissions interview, I found that interactions with the current MSTP students were remarkably natural. The additional conversations with faculty, including my current research mentor, contained sincere interest in my skillset and research goals. These connections with students and faculty sold me on Feinberg.

Additional resources at Feinberg — such as the close connection to the Shirley Ryan AbilityLab (formerly the Rehabilitation Institute of Chicago) and the outstanding Chicago community Feinberg lives in — added substantial reinforcement to my decision.

What have you found most rewarding about Feinberg?

I truly believe an institution is a product of its people, and Feinberg has some of the best people I've had the pleasure to work with. When applying to schools, institutions can become objectified behind a cloak of rankings, hospital statistics and research infrastructure. The incredible individuals at Feinberg were a welcome addition to my training that I already knew was going to be medically and scientifically sound.

My participation in multiple initiatives at Feinberg has allowed me to not only meet but cultivate relationships with deans, directors, students and staff; every individual has uniquely impacted my experience. I often reflect on Dean Wayne's words surrounding the impact our graduates make as residents at other institutions: They are coveted as much for being exceptional people as they are for being exceptionally trained clinicians. Her sentiment summarizes my time at Feinberg, and I'm excited for class after class that gets to experience this culture.

How do you maintain balance with interests outside of the laboratory?

I love the Chicago community and have been lucky to involve myself in organizations both within and outside of Feinberg. I have an extensive music background, so the recent formation of the <u>Northwestern Medical Orchestra</u> offered a beautiful opportunity to continue my participation in a musical ensemble. Relationships at Feinberg have also connected me with medical volunteering for the Chicago Marathon, and that work has been an exciting and unique opportunity to realize some of my sports medicine clinical interests.

I'm very active in the large Chicagoland Greek Orthodox community. Recently, I've been working with some national initiatives to research and improve young adult involvement and connection within the church. Finally, my Ohio State and Pittsburgh fandom is no secret here in Chicago, and I've loved the opportunity to see my "home teams" play in my new "home town." I've seen the Buckeyes repeatedly play at Northwestern, and while I've never actually seen the Pirates victorious at Wrigley (0-7), a trip to Milwaukee this summer helped temporarily satisfy that void with a win.

Providing Administrative Expertise to Move Research Forward Elizabeth Pugh, Department Administrator, Preventive Medicine



Q&A

Where are you originally from?

Waukesha, Wisconsin, which is a suburb of Milwaukee. Yes, this means I am a Packers fan for life!

What is your educational background?

I received a bachelor's degree in business administration

from the University of Wisconsin-Madison. I worked in the undergraduate office at the business school, which piqued my interest in working in higher education. I was very close to all the staff and really enjoyed helping faculty and students.

Please tell us about your professional background.

I wanted to obtain a master's degree and decided to pursue a position at the University of Illinois at Chicago (UIC) in the College of Dentistry for the tuition benefit. It turns out I really enjoyed higher education and stayed at UIC for 15 years and obtained two master's degrees — in public administration and in healthcare administration. Obviously, I love to learn and knew I was meant to work in administration. Besides the College of Dentistry, I worked at the School of Public Health, Human Resources and the Research Resources Center. Almost all of my positions have been as a generalist (finance, HR and operations) in administrative and academic units.

Why did you choose to work at Northwestern?

I knew several people who worked at Northwestern and had positive and enriching experiences. I was contacted via LinkedIn about a position in Life Sciences at the Weinberg College of Arts and Sciences. I missed working with faculty and was really excited about the prospect of being involved with research again. I recently accepted a position at Feinberg to work with one of the most inspiring leaders at Northwestern, <u>Donald</u> <u>Lloyd-Jones, MD, ScM</u>, chair of <u>Preventive Medicine</u>.

How do you help scientists at the medical school?

I help provide administrative support for Feinberg faculty, so they are able to focus on their research and have the funding to do so.

What is your favorite part of the job?

I love working with dynamic and appreciative faculty, mentoring staff to make process improvements and implement the Department of Preventive Medicine's vision.

What exciting projects are you working on?

Several! I am reorganizing the administrative structure, balancing the budget and planning a faculty retreat to form the department's vision for the next five years. I have also had the pleasure of working on the work tasks committee for the staff engagement survey.

What do you like to do in your spare time?

I love to travel, ride motorcycles — both track and on the street, and long-distance cycling.

Anything else we should know about you? I like to laugh. It's a great stress reliever.



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Research in the News

San Francisco Chronicle, October 5

Half of Antibiotics Given With No Infection Noted Jeffrey Linder, MD, MPH, was guoted

▶ This research was also featured in *WebMD* and *HealthDay*.

National Public Radio, October 8

Some Apps May Help Curb Insomnia, Others Just Put You to Sleep

Jason Ong, PhD, was quoted.

Reuters, October 10

World's Most Innovative Universities | 2018 Brain tumor SPORE and NEST (Newborn Essential Solutions and Technologies) grants noted.

HealthDay, October 11

<u>Diabetes Drug Might Help Shield the Heart From Smog's III</u> <u>Effects</u> Scott Budinger, MD, was quoted.

U.S. News & World Report, October 23

Yes, Your Cat Can Tell if You're Out All Night Daniel Dombeck, PhD, was quoted. ► This research was also featured in USA Today.

Chicago Tribune, October 24

Hormonal Changes Might Lead to Hernias in Aging Men Serdar Bulun, MD, was quoted.

This research was also featured in HealthDay.

MSN, October 25

This Secret Sleep Trick Will Help You Lose Weight Ivy Cheung Mason, PhD candidate, was quoted.

More media coverage available online.



NUCATS Corner

Meaningfully Engage Communities, Patients and Stakeholders in Your Research

The <u>Center for Community Health</u> (CCH) catalyzes and supports meaningful engagement of communities, patients and stakeholders across the research spectrum to improve health and health equity. CCH offers a new vision for engaging communities and other stakeholders that enables research to improve the health and healthcare of Chicago and beyond. CCH facilitates community and population health research through:

Workshops, Seminars and Team Training: The CCH and its two programs, the Alliance for Research in Chicagoland Communities and the Practice-Based Research Program, provide training, learning opportunities, toolkits and other resources.

Funding Opportunities: CCH provides a variety of funding opportunities, including the NUCATS/ARCC Seed Grant Program for community-based research partnerships.

<u>Consultations, Proposal Review and Support</u>: CCH offers access to faculty, professional staff and experienced community partners who provide expertise and guidance related to the unique methodological and practical challenges of the research process. Consultations may be one-on-one or via our innovative group-based Stakeholder Academic Resource Panels.

Patient and Stakeholder Engagement: CCH can help investigators identify and actively engage patients, clinicians and other stakeholders to ensure that research answers questions important to stakeholders, studies are implemented efficiently and results are shared effectively.

For more information, contact the Center for Community Health at <u>cch@northwestern.edu</u> or sign up for a consultation <u>here</u>. Feinberg School of Medicine Research Office Breakthroughs

Sponsored Research



PI: Jane Wu, MD, PhD, professor of Neurology in the Division of Neuromuscular Disease

Sponsor: National Institute of Neurological Disorders and Stroke

Title: The Role of Mitochondria in TDP-43 Proteinopathy

Recent data indicate that about 50 percent of brain samples from patients affected by Alzheimer's disease (AD) show TDP-43 pathology. While it is well established that mitochondrial dysfunction contributes to AD pathogenesis, only recently have scientists demonstrated that enhancing mitochondrial proteostasis reduces amyloid beta misfolding and neurotoxicity, providing a new avenue for therapeutic development in AD and related dementia. It remains unresolved whether mitochondria protect against or contribute to TDP-43 induced neurodegeneration, especially events critical for cognitive impairment.

Building on solid preliminary data, Wu's team proposes using an integrated approach combining molecular, biochemical, cell biological assays and animal models together with patient samples and patient iPSC-derived neurons to systematically investigate the role of mitochondrial damage in TDP-43 related neurodegeneration. The study will elucidate pathogenic mechanisms and help in future development of therapeutic strategies for Alzheimer's disease, AD-related dementia and other neurodegenerative diseases with TDP-43 pathology.



PI: Irina Balyasnikova, PhD, associate professor of Neurological Surgery

Sponsor: National Institute of Neurological Disorders and Stroke

Title: Genetic Approaches to Optimize CAR T-cells for Glioblastoma Therapy

Genetically modified T-cells expressing chimeric antigen receptors (CARs) have the potential to serve as a unique cytotoxic tool to specifically target glioblastoma (GBM).

Balyasnikova's group has developed a single-chain variable fragment specific for IL13R α 2, a GBM-associated tumor antigen, and has generated an IL13R α 2-CAR. In previous research, IL13R α 2-CAR T-cells only recognized IL13R α 2-positive glioma cells and had anti-glioma activity in preclinical xenograft and immune-competent animal models. However, tumors eventually recurred, paralleling the situation in humans.

Collaborating with a team at St. Jude Children's Research Hospitals led by Stephen Gottschalk, MD, Balyasnikova's group hypothesizes that IL13R α 2-CAR T-cells can be further genetically engineered to optimize their anti-GBM activity by enhancing their persistence, targeting multiple tumor antigens and improving their trafficking to tumor sites. While the lab will use its data to justify the development of a future clinical study using optimized IL13R α 2-CAR T-cells for patients with GBMs, their modified approach to T-cell therapy could be applicable to a broad range of solid tumors.

Read more about this project.

Read more about this project.



Welcome New Faculty

Andrea Graham, PhD, joins us as assistant professor of <u>Medical Social Sciences</u> and <u>Preventive Medicine</u>, and her position is housed in the <u>Center for Behavioral</u> <u>Intervention Technologies</u>. Her research focuses on designing, testing and implementing digital technologies for screening, preventing and treating eating disorders and obesity among youth and adults. She is also interested in the implementation of evidence-based tools into clinical practice, including understanding barriers such as costs that impact adoption and sustainability. Graham earned her PhD in clinical psychology from Washington University in St. Louis and completed a postdoctoral fellowship in health services research at the University of Chicago. During her fellowship, she received an F32 National Research Service Award from the Eunice Kennedy Shriver National Institute

of Child Health and Human Development to conduct an economic evaluation of a family-based behavioral intervention for pediatric obesity. She has published 39 peer-reviewed papers and is currently principal investigator on a grant from the National Institute of Diabetes and Digestive and Kidney Diseases to design and test a mobile app for adults with obesity and binge eating.

Nicolozakes (continued from page 6)

What are your plans after graduation?

After completing my PhD and MD training, I plan to apply to a residency program in either physical medicine and rehabilitation or orthopaedic surgery. Both offer unique routes towards my long-term goal of clinical and scientific work in sports medicine. The location of my laboratory in the Shirley Ryan AbilityLab and the subsequent exposure to PM&R clinicians has absolutely biased me towards this route, but I believe both specialties fit quite well with my interests. Hopefully, in a decade or so, I'll have a position at a big academic center where I can seamlessly continue my musculoskeletal research and begin treating athletes.

Latest Podcast Episodes



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Chronic Pain and the Placebo Effect with A. Vania Apkarian, PhD. Listen <u>here</u>.

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Funding

Reproductive Medicine Collaborative Clinical Trials Program

More information

Sponsors: Eunice Kennedy Shriver National Institute of Child Health and Human Development Letter of Intent Due: December 18 Submission Deadline: January 18 Upper Amount: \$2.5 M per year over a max project period of five years Synopsis: The purpose of this opportunity is to develop a multi-site

project designed to conduct clinical trials that investigate problems in reproductive medicine, including female and male infertility, gynecologic and male reproductive system diseases, and disorders that impact fertility. Collaborative R01 clinical trial required.

Fc-Dependent Mechanisms of Antibody-Mediated Killing

More information

Sponsor: National Institute of Allergy and Infectious Diseases Letter of Intent: January 2

Submission Deadlines: February 1

Amount: \$300,000 in direct costs per budget period with a max period of five years

Synopsis: Three to five awards in fiscal year 2020 will support research focused on elucidating mechanisms of Fc-dependent, antibody-mediated killing of infected or aberrant cells, or antibody-mediated therapeutic ablation of cells implicated in immune pathologies, including autoimmune and allergic diseases. Studies supported by this funding opportunity are expected to define variables that affect efficiencies of antibody-dependent cellular cytotoxicity and/or antibody-dependent cell-mediated phagocytosis, both in vitro and in vivo. U01 clinical trial not allowed.

A Census of Cells and Circuits in the Aging Brain

More information

Sponsor: National Institute of Aging Letter of Intent Due: February 8

Submission Deadline: March 8

Amount: \$2.5 M intended to fund two to three awards

Synopsis: This grant, which builds on and aligns with BRAIN Initiative efforts, will support pilot studies aimed to establish molecular, anatomical and functional cell and circuit census data from selected brain regions of young and old C57BL/6J mice. This research will inform a design for a comprehensive characterization of cells and circuits in the brain across the lifespan, including the generation of a comprehensive 3D brain cell reference atlas of the aging mouse brain. R01 clinical trial not allowed.

View more funding opportunities

Promoting Your Work to a Broad Audience



By Karen Gutzman, digital innovations specialist, and Patty Smith, research impact librarian

Much of science communication happens online, where vast amounts of information are consumed and dialogues shift at lightning speeds. Engaging with this environment can feel intimidating, but the rewards are high: discover new audiences to discuss your work, find your unique voice among the masses and increase your influence in your field. Whenever you have a new publication coming out, keep a few simple steps in mind to help you navigate the online environment, promote your work and engage with a broader audience.

Increase Accessibility to Your Work

Consider creating a collection of items that support an upcoming or newly published article — data, code, protocols or methodologies, any presentations — and make those items available in <u>DigitalHub</u> (Northwestern Medicine's open access repository) to accompany your published paper. DigitalHub makes your work more discoverable because it is indexed by major search engines, including Google, so your work will show up in search results. DigitalHub also gives each uploaded item a unique Digital Object Identifier, or DOI, which makes it possible to properly cite and track use of your work.

Keep Your Online Presence Updated

The plethora of online profiles makes keeping them up-todate incredibly time consuming. Instead, select a few that you use often and invest your energy in those. Once a new paper comes out, consider updating your <u>ORCiD profile</u> and your <u>Google Scholar profile</u>. It also might be a good time to make sure your <u>Feinberg faculty profile</u> has captured your new publication, or that your <u>LinkedIn profile</u> has all your correct information. Finally, consider updating any versions of your CV or biosketch that might be impacted by your new publication.

Share on Social Networks

Social media is interactive, fast-moving and very brief in its character allowances, which makes it an appealing method of communication for some. Before discussing your publication on social media, consider writing a lay summary providing a short account of your research for non-specialized audiences. Lay summaries should answer the questions, "What is your research about?" and "Why is it important?"¹ in plain language (devoid of jargon or complicated terminology) and should be easy to read by most audiences. These summaries are a

great format for sending out on Twitter, Facebook or relevant listservs along with a link to your publication.

Engage in Discussions

There are some topics worth expanding upon that don't easily lend themselves to the brevity required on social media. In those cases, blogging is a great option for communication. On your own blog (or as a guest on a highly-trafficked blog) you can write about your research findings or discuss new directions in your field. Blogs are a great way to allow for comments and engage with your audience.

In addition, blogging will help you craft your elevator speech, a brief description of your research and why someone might be interested. There are many tip and tricks, but most often it helps to think about how you would talk about your work with a stranger sitting next to you.

Take Advantage of Feinberg's Resources

Feinberg's Office of Communications offers a wide array of resources, tips and ideas. See their website on <u>Media</u> <u>Relations and Training</u> to share news with the Feinberg community and find tips for conducting a successful interview.

Promoting Your Work: A Checklist

- 1. Upload your scholarly outputs to DigitalHub.
- 2. Update your online profiles: ORCiD, University, Google Scholar, LinkedIn.
- 3. Write a plain language summary and share any links to your work on Twitter or by email.
- 4. Write blog posts for your own blog or as a guest blogger on your research findings.
- 5. Practice an elevator speech to communicate your research with non-specialized audiences.

Galter Library endeavors to provide exceptional resources and services to support the information needs of Northwestern Medicine. Be sure to visit us <u>online</u> or in person. If you need individualized support, contact your <u>liaison librarian</u>.

¹Ellen L. Spotlight on: explaining your work in plain language. Kudos [blog post]. 2015 Dec 4. Available at: <u>https://blog.growkudos.</u> com/2015/12/04/explain-your-work-the-kudos-way/

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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, November 16

Physiology Seminar

Temporal lobe epilepsy is common but can be difficult to treat, and the cause is largely unknown. Guest speaker, Paul Buckmaster, DVM, PhD, professor of Comparative Medicine and of Neurology and Neurological Sciences at Stanford Medicine, will address this in his presentation titled "Mechanisms of Epilepsy."

Time:	Noon to 1:00 p.m.
Location:	Ward Building 303 E. Chicago St., Room 5-230
Contact:	d-daviston@northwestern.edu

More information

Tuesday, November 20

Microbiology-Immunology Lecture

Jun Huang, PhD, assistant professor of Molecular Engineering at the University of Chicago, will present "T-Cell Recognition and Differentiation." This seminar will discuss recent work on pMHC dodecamer technology development, CD28 as the primary target for PD-1-mediated inhibition and the role of histone methyltransferase EZH2 in Tfh cell differentiation.

Time:Noon to 1:00 p.m.Location:Robert H. Lurie Medical Research Center
Baldwin Auditorium, 303 E. Superior St.

Contact:

chyung-ru-wang@northwestern.edu

More information

Tuesday, December 4

Institute for Public Health and Medicine Population Health Forum

This inaugural event will include a keynote by Sandro Galea, MD, MPH, DrPH, dean and Robert A. Knox Professor at Boston University School of Public Health. Galea's work is focused on the intersection of social and psychiatric epidemiology with a focus on behavioral health consequences of trauma. The day will also include a research poster session, panel discussion and breakout sessions.

Time: 9:00 a.m. to 3:00 p.m.

Location: Robert H. Lurie Medical Research Center 303 E. Superior St.

Contact: <u>ipham@northwestern.edu</u>

More information

More research events here.

NIH News

Grant Application Submission: Tips for Success Videos

The NIH has released short new videos to help make the grant application submission a success. Quickly learn how to access application forms, ensure your application is a good fit for an announcement and make an important final check of your application after submitting. Access these tips for success and other useful tutorials on the application process <u>here</u>.

Data Sharing Policy: Share Your Voice

A blog post by Carrie Wolinetz, PhD, NIH associate director for science policy, and Michael Lauer, MD, NIH deputy director for extramural research, centers on the importance of data management and sharing relative to the NIH's role as a biomedical research agency. "Data sharing is a means to an end, not itself an end goal and, as such, needs to be done thoughtfully, in a way that fulfills the vision and mission of NIH and continues the advancement of treatments for disease and improvement of human health," write Wolinetz and Lauer.

The NIH's effort to improve data management and sharing processes has long been at the forefront. In recent years, a request on <u>Strategies for NIH Data Management</u>, <u>Sharing and</u> <u>Citation</u> was released, and in 2017 a joint workshop with the National Science Foundation focused on the value of data sharing. This month, the NIH released a <u>notice</u> that seeks public input on key policy provisions, including the definition of scientific data, the elements of required data management and sharing plans, and optimal timing/phasing for a new data management and sharing policy.

Share your thoughts <u>here</u> by December 10. Feedback will help inform the development of a draft NIH policy for data management and sharing.

Bayh-Dole Act Policy Requirements and Amendments

Recipients of NIH-funded research awards are required to report all inventions that result from NIH-funded projects. The Bayh-Dole Act is a patent and invention policy that allows funding recipients to retain ownership of inventions made under federally-funded research grants or programs, as well as manage the patenting and licensing for them. The NIH implemented new regulations under this act, applicable to all new, renewed and continued awards beginning on or after October 1, 2018. Review a summary of new policy requirements <u>here</u>.

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