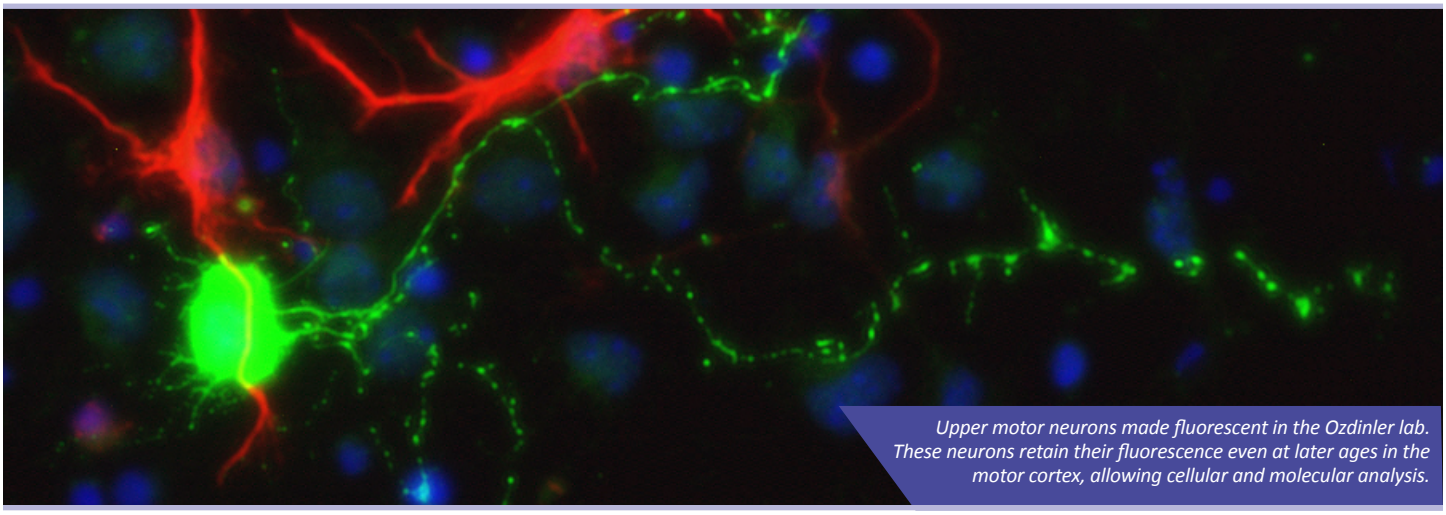
Breakthroughs

Feinberg School of Medicine Research Office

August 2018



Upper motor neurons made fluorescent in the Ozdinler lab. These neurons retain their fluorescence even at later ages in the motor cortex, allowing cellular and molecular analysis.

Basic Science: the Foundation for ALS Care

By Will Doss

Amyotrophic lateral sclerosis, or ALS, has been a tough nut to crack.

Over the decades, investigators at Feinberg and across the globe have identified rare genes that cause ALS to run in families, leading to the creation of disease models that faithfully recapitulate aspects of the human disease in mice and other experimental platforms. But a disease-modifying treatment has remained elusive.

Still, all of this work has generated an explosion of information about how mutated proteins injure nerve cells and hint at unifying theories to explain the underlying cause of ALS. And it holds the promise of developing new and powerful treatments, according to Robert Kalb, MD, the Les Turner Professor and director of the Les Turner ALS Center. **(Listen to an interview with Kalb in our podcast series here.)**

Kalb believes that the road to a transformative therapy is paved with incremental discoveries, a philosophy that guides investigation in his own laboratory and others under the Les Turner banner.

"Ultimately, it's going to come down to better understanding of basic physiology and how the disease-causing proteins corrupt the normal operation of nerve cells," said Kalb. He believes the mechanisms of cellular waste disposal may be one root cause of dysfunction in ALS.

"Cells are constantly making misfolded proteins, and they're very effective at recognizing that garbage and getting rid of it," said Kalb, who's also a professor of Neurology in the Division of Neuromuscular Disease. "It turns out that several of the genetic mutations that cause familial ALS are in that protein degradation pathway — there are many reasons to think that the most effective treatments on the near horizon will be targeting cellular trash disposal pathways."

To turn ideas into discoveries, and eventually treatments, investigators in the Les Turner ALS Center are working to uncover the genetic causes of ALS and define the mechanisms of degeneration in a variety of neurons.

"The laboratories and methods they use all have distinct advantages, so they fit together like pieces of a puzzle," Kalb said. "You need people that are devoted to basic science, and I think we have that here."

Decoding the Disease

Teepu Siddique, MD, the Les Turner ALS Foundation/Herbert C. Wenske Foundation Professor, has been at the forefront of ALS research for 30 years. In fact, Siddique and his collaborators discovered the first cause of ALS, linking mutations in the SOD1 gene to the disease, and they developed the first animal model for ALS, now used by investigators all over the world.

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Northwestern Medicine®

ALS Cure *(continued from cover page)*

Since then, the Siddique team has discovered mutations in UBQLN2, SQSTM1, ALS2, ALS5, CHCHD10 and others in familial cases of ALS. They found damaging ubiquilin2 and p62 protein aggregations in motor neurons — it was the first time a cause for ALS could be directly linked to the mechanism of disease defects in protein recycling of damaged proteins, but the impact of ubiquilin2 and p62 goes further, according to Siddique.

"When we looked at a large number of autopsy cases of all forms of ALS and ALS dementia patients, we found virtually all of them had protein aggregations in motor neurons decorated with ubiquilin2 and p62, irrespective of cause or family history. This tells you that these proteins have relevance to sporadic disease, not just familial disease — it's also a universal pathology of ALS and ALS/dementia," said Siddique, also a professor of Cell and Molecular Biology.

He further showed that p62 and other genetic causes of ALS can cause dementia, muscle, bone and eye diseases. "This helped break the paradigm that ALS is only a motor neuron degeneration. We know now that ALS-causing mechanisms contribute to a wider spectrum of disease, affecting several organ systems."

Early Warning

Another laboratory in the Les Turner ALS Center, led by Pembe Hande Ozdinler, PhD, associate professor of Neurology in Neuromuscular Disease, focuses on neuronal degeneration itself.

Ozdinler specializes in the degeneration of corticospinal motor neurons, also known as upper motor neurons. Previously, little was known about these neurons, as they proved difficult to identify, isolate and study. Ozdinler's laboratory pioneered in their labeling, isolation and cellular investigation, and subsequently discovered that upper motor neurons are among the first neurons to show evidence of degeneration in ALS — a canary in a coal mine.

"These neurons become vulnerable up to six months before you see any symptoms in patients, so we developed ways to make them visible, to make them stand out," she said. "We've now developed and characterized five different models in which upper motor neurons degenerate."

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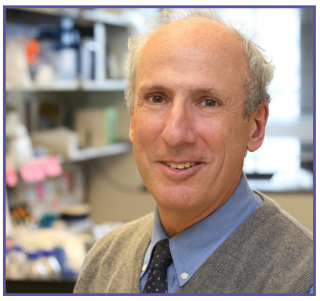


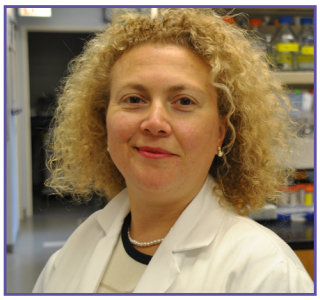

Clockwise, from top left: Robert Kalb, MD; Teepu Siddique, MD; Pembe Hande Ozdinler, PhD; Evangelos Kiskinis, PhD.

Further investigation has revealed endoplasmic reticulum stress is a major factor for degeneration, and now Ozdinler is developing novel biomarkers that can detect that degeneration.

"We are lucky because certain proteins are secreted and can be detected in the blood," she said. "Those are potential early detection biomarkers, or even biomarkers that could tell us what stage the disease is at before symptoms appear."

In addition, Ozdinler advocates considering the health of corticospinal motor neurons in clinical trials of ALS drugs and is developing a novel drug discovery platform which includes the neurons' survival as a read-out. This is important as current trials often just look at the health of the spinal motor neurons, she said.

"When corticospinal motor neurons die, the whole circuitry is affected," Ozdinler said. "If we want to build effective and long-term solutions, we need to consider the health of brain motor neurons as well."

Isolating Mutations

While other laboratories in the Les Turner ALS Center use mouse models, Evangelos Kiskinis, PhD, assistant professor of Neurology in Neuromuscular Disease, uses a unique patient-derived stem cell model, allowing for direct study and manipulation of motor neurons with disease.

For example, Kiskinis and his team can produce motor neurons from patients and compare them with ones generated from healthy control individuals, looking for disease-related phenotypes or screen for potential therapeutic compounds. In cases where a disease-causing mutation is present, they can use CRISPR-Cas9 gene editing to reverse it, creating a stem cell line identical to the patient's cells, but without the mutation — an isogenic control line.

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Wertheim Named Associate Director for MSTP Admissions

Jason Wertheim, MD, PhD, vice chair for research in the Department of Surgery, has been named associate director for admissions for the Medical Scientist Training Program (MSTP).

"I am very honored and thrilled to work with our physician-scientists in training and prospective students in the Medical Scientist Training Program," said Wertheim, who is also the Edward G. Elcock Professor of Surgical Research and associate professor of Surgery in the Division of Organ Transplantation.

The MSTP prepares students for careers as physician-scientists with a dual MD/PhD degree. The program, which enrolls up to 15 students each year, consists of an integrated seven- to eight-year course of study.

"Jason, as a former MSTP student, is familiar with the MD/PhD program and has shown great insight and understanding of the training process," said Hossein Ardehali, MD, PhD, director of the MSTP and professor of Medicine in the Division of Cardiology. "He has been involved in MSTP admissions for a number of years and will now chair the Admissions Committee. Given his background and commitment to the program, I am confident that he will play a major role in recruiting top students to Northwestern's MSTP."

Jason Wertheim, MD, PhD

Wertheim is a clinical transplant surgeon and leads a laboratory focused on tissue engineering and organ regeneration. He is a member of the National Institutes of Health's (Re)Building-a-kidney consortium. His research group uses cell biology and bioengineering to develop liver, kidney and blood vessel tissue as a cutting-edge solution to organ shortage.

Feinberg Entrepreneurs Learn About Commercialization

This summer, more than a dozen Feinberg entrepreneurs participated in a four-week mentorship program called INVOForward to learn how to move their health information technologies toward commercialization and, ultimately, use their innovative ideas to improve human health.

INVOForward first launched in September 2017 with a goal to help entrepreneurial teams across Northwestern identify their products' market fit and fine-tune their business value proposition. This summer's cohort concentrated on health information technologies.

Over the four-week period, the teams each conducted 30 interviews with various stakeholders, researched pricing and regulatory strategy, and learned the landscape of their intellectual property and competition. The program also included office hour support, virtual classes on topics ranging from competitive analysis to conducting a customer discovery interview, and a final pitch presentation.

"An increasing number of scientists are becoming interested in the innovation lifecycle and the ultimate impact on patients, as well as the journey of commercialization and how it can connect to translational funding, commercialization resources or entrepreneurial support," said Dimitra Georganopoulou, PhD, director of commercialization at INVO, Northwestern's Innovation and New Ventures Office.

In the fall, INVOForward will kick off its third program, with a cohort of teams focused on therapeutics. Read more here.

ALS Care *(continued from page 2)*

"This allows us to test whether a phenotype or defect in a motor neuron is caused by that particular mutation," Kiskinis said. He can also use these stem cells in other ways, such as combining them with a new technique called optopatch to measure electricity in cells en masse.

Kiskinis created patient-derived spinal cord motor neurons with ALS and measured the electrical patterns of hundreds of cells at once, finding the ALS neurons were hyper-excitable under normal conditions, but became under-excited when prompted to fire rapidly.

"The excitability changes observed in these patient neurons most likely represent the early steps in the disease process," he said. "The fact that these changes are detectable in stem cell-derived neurons offers the hope that interventions that affect excitability could affect disease progression before symptoms begin."

Looking Forward

The fight against ALS is a marathon, not a sprint. The goal of a disease-modifying treatment is still out of reach, but a deep commitment to basic science is the approach that can move the needle in a concrete way, according to Kalb.

"You have to understand the underlying basic biology," Kalb said. "That's where the answers will come from."

Unraveling DNA Virus Biology

Derek Walsh, PhD, associate professor of Microbiology-Immunology

In his laboratory, Derek Walsh, PhD, associate professor of Microbiology-Immunology, focuses on two key research areas: 1) cell signaling and protein synthesis during poxvirus infection and 2) microtubule regulation during herpesvirus infection.

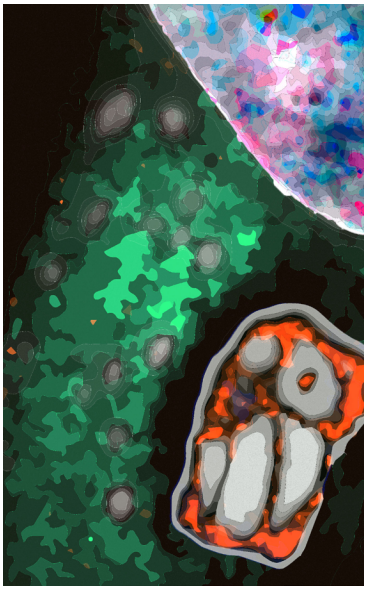
His work has uncovered new regulatory processes in the fields of cell signaling, translational control and microtubule regulation that are critical to infection by a number of viruses. "Moreover, by exploiting viruses as genetic tools to dissect basic biological processes, my lab has helped provide insights into more fundamental aspects of cell signaling and translational control," said Walsh, also a member of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University.

Walsh, who joined Northwestern in 2014, earned his doctoral degree in biotechnology from Dublin City University and completed postdoctoral fellowships at Columbia University and New York University.

Q&A

What are your research interests?

Our lab is interested in how large DNA viruses usurp different host cell functions. We primarily work on two very different topics. The first is how poxviruses take control of their host's protein synthesis machinery in order to make viral proteins, both by manipulating upstream signaling pathways and by directly targeting host translation factors and ribosomes. The second is how herpesviruses — particularly herpes simplex virus type 1 (HSV-1) and human cytomegalovirus (HCMV) — exploit microtubule networks to infect and then completely remodel the host cell in order to replicate and spread.



Above: During poxvirus infection, dysregulated mTOR (orange) localizes at the host-cell golgi network resulting in degradation of the DNA sensor, cGAS (green).

Although we study viruses, as master manipulators of host processes, they end up teaching us a lot of fascinating and totally unexpected things about basic cell biology — even across different species. For example, we recently found that poxviruses modify our ribosomes so that they function more like plant ribosomes. It turns out that this is because poxviruses make strange mRNAs that are more like plant mRNAs. For that reason, I'm never sure whether to call ourselves virologists or cell biologists. I guess we are both.

What is the ultimate goal of your research?

Our primary goal is to try to understand some of the fine mechanistic details behind how poxviruses and herpesviruses manipulate specific host processes, as a means of contributing to our cumulative understanding of infection.

Most of the time our work would be considered hardcore basic research in virology with applications to cell biology. But now and then we stumble onto something that might be unexpectedly translational. For example, based on what many people would view as an extremely specialized focus on how the ends of microtubules are regulated during HCMV infection, in collaboration with a group at the University of Illinois at Chicago, we recently developed small peptides that can interfere with this process and inhibit HCMV replication. These proteins have such a specialized function in cells, yet the virus requires them, so the inhibitory peptides are not toxic and could one day form the basis of a new virus inhibitor. We have filed a joint invention disclosure on this, with the hope of testing its therapeutic potential down the line.

Nobody can predict where the next therapeutics will come from, which is why continued support for what seems like very basic research is so important.

How does your research advance medical science and knowledge?

Our research is helping to reveal how several medically important viruses replicate and cause disease. Poxviruses, for example, include the variola virus that caused smallpox,

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Investigating Psychotherapies to Reduce Symptom Burden in Patients With Gastrointestinal Disorders

Livia Guadagnoli, Clinical Psychology PhD Program

Livia Guadagnoli, a third-year student in the Clinical Psychology PhD Program, studies the role of psychological processes in the onset and maintenance of gastrointestinal disorders in the laboratory of Laurie Keefer, PhD, adjunct associate professor of Medicine in the Division of Gastroenterology and Hepatology and of Psychiatry and Behavioral Sciences.

Q&A

What is your hometown?
My hometown is in southern Connecticut in a town called Trumbull. I loved growing up in Connecticut. It's really beautiful, has great food and is only about an hour and a half outside of New York City. I grew up eating "New Haven-style" pizza, so moving to Chicago and trying deep dish was quite the experience for me. I enjoy a slice of deep dish every now and then, but Pepe's white clam pizza will always be my favorite!

What are your research interests?
Broadly, I'm interested in the field of psychogastroenterology, which focuses on the role of psychological processes in the onset and maintenance of gastrointestinal disorders and application of brain-gut psychotherapies to reduce symptom burden. Specifically, I'm interested in psychophysiology and the impact of symptom perception on autonomic nervous system processes. My line of research is primarily in individuals with esophageal disorders and evaluating the relationship between esophageal hypervigilance, or the increased awareness of esophageal sensations, and the body's physiological response. Hypervigilant individuals can develop fear towards even benign esophageal sensations, which activates the body's threat system, exacerbates symptom perception and perpetuates this fear. I hope to develop ways to intervene and break this cycle!

What exciting projects are you working on?
I am getting ready to propose my dissertation, which is focused on characterizing esophageal hypervigilance in patients with gastroesophageal reflux disease. I'm interested in the relationship between esophageal hypervigilance and heart rate variability, as well as other psychological factors, such as illness acceptance and resilience, that may impact hypervigilance.

The Division of Gastroenterology and Hepatology was recently awarded a program project grant that includes three R01s — one of which is focused on evaluating the role of psychological factors in esophageal motility disorders. In addition to my dissertation, my primary focus in the next year will be to work on this project. I helped write the psychophysiological portion, so I'm really excited to be able to contribute to something that I had a role in developing.

What attracted you to the PhD program?
I love the interdisciplinary nature of the Clinical Psychology PhD Program. I knew I wanted to specialize in health psychology when I was applying to graduate programs, so the fact that our program was housed within a medical setting was ideal. My research lab, which is a psychology lab, is in the Division of Gastroenterology and Hepatology. I have the opportunity to interact with gastroenterologists, basic scientists and GI psychologists who are all doing GI-related research. Clinically, it's also such a unique experience — I'm able to see a GI patient for psychotherapy down the hall from their gastroenterologist!

What has been your best experience at Feinberg?
Spending time with my cohort has created relationships and memories I will have forever. There's seven of us, and we are very close. They are some of the most intelligent, driven and passionate women I've ever met! As the years progress, schedules have gotten busier, and it's harder to see each other. However, we make it a point to set up happy hours or fun events to go to together. I feel so lucky to be able to go through grad school with their support, and I look forward to the future with them as my colleagues.

How would you describe the faculty at Feinberg?
The faculty treat you like junior faculty, so they definitely challenge you and have high expectations, but are always there to help. In my experience, the faculty are always willing to collaborate or provide guidance on an area, even if they don't work directly with you. I reached out to a faculty member in a different department who had similar interests as me. He gave me advice on my dissertation, and now he's on my dissertation committee!

What are your plans for after graduation?
I plan to complete a postdoctoral fellowship and continue to pursue a career as a GI psychologist. I would love to be in an academic medical setting where I can work as a scientist-practitioner.

Connect with Livia on Linkedin.

Supporting Feinberg's Basic Science Research

Pamela Shaw, MSLIS, MS, Biosciences and Bioinformatics Librarian
Galter Health Sciences Library

Q&A

Tell us about yourself.
I was born in northern Indiana, and I have worked in medical schools in the Chicago area since graduating college in 1986, so I've been in the greater Chicagoland area for most of my life. I attended Oberlin College, where I received my undergraduate degree in psychobiology — a degree that is virtually equivalent to neuroscience. I worked in neuroscience research laboratories for almost 20 years as a research technician and lab manager: seven years at Loyola University Stritch School of Medicine, followed by more than ten years here at Feinberg in the laboratory of M.-Marsel Mesulam, MD, director of the Mesulam Cognitive Neurology and Alzheimer's Disease Center (CNADC). During my last two years in Dr. Mesulam's lab, I completed the University of Illinois' library and information sciences online master's program. I then got a job at the Galter Health Sciences Library in January of 2006, after which I completed a master's in computational biology and bioinformatics from Northwestern in 2010.

What is it like to work at Northwestern?
I really love working at Northwestern. I like the Chicago location of the medical school, and Northwestern's employee benefits and recognition are very generous. When I worked in Dr. Mesulam's lab, I was proud of the research done in the CNADC, but I was not familiar with many other departments' research pursuits. Now that I work in the library, I'm exposed to more research conducted at Feinberg, and I'm impressed by the quality and depth of our clinical and basic science investigators' work. I've also stayed all these years because my colleagues and supervisors are so fantastic. I learn from my colleagues every day. I am also given great freedom to direct my priorities and projects by my direct supervisor, Linda O'Dwyer, MA, MSLIS, and my director, Kristi Holmes, PhD.

How has your job changed since you first started working at Northwestern?
Since joining Galter Library, my job has changed subtly throughout the years. I was initially hired to support the information needs of basic scientists, because of my experience as a basic science lab tech, but I eventually began providing literature search services for some clinical departments, as well. Now I am back to primarily supporting basic scientists and have more time and freedom to offer training in computational biology and bioinformatics tools and databases, which is in line with my position's core responsibilities. I also have taken on the role of NIH Public Access Compliance Reporter (PACR) for the university. In this role, I assist NIH-funded investigators with ensuring that publications supported by their NIH grants are deposited to PubMed Central in compliance with the NIH Public Access policy passed in 2008. I'm happy to provide this support, in order to assist the Office for Sponsored Research (OSR) — I can answer investigators' questions about this policy, taking some of the burden for this topic off of our hard-working grant officers at the OSR.

How do you help scientists and/or research students at the medical school?
My director has called me the "Swiss Army librarian." I provide support in traditional librarian roles such as literature searches, but I also provide support as the PACR, and I arrange workshops and seminars on many topics in computational biology. More recently, I have begun to turn my attention to providing support for Feinberg scientists regarding research data management, in partnership with our data scientist, Matthew Carson, and data librarian, Sara Gonzales.

What exciting projects are you working on?
One of my favorite recent projects has been the establishment of the Computational Skills for Informatics series, which I've affectionately nicknamed "CSI Chicago." These are workshops hosted in the library and taught by a diverse set of instructors, including myself, faculty from Feinberg departments and members of NUIT's Research Computing Services staff. My partnership with NUIT Research Computing on this series has been one of the most satisfying partnerships I've developed over the years. We've been able to host workshops on a great variety of topics, from reproducible research to basic command line skills, to RNA-Seq analysis pipelines on Quest.

What do you like to do in your spare time?
I'm trying to improve my computer coding skills and my statistical knowledge in my free time. I like to watch nature and science television such as National Geographic, Discovery and the Science Channel. Every five to ten years, I try to travel to the mountains of the American West to hike and camp. My favorite places are Glacier, Yellowstone and the Tetons national parks.

Anything else we should know about you?
I happily admit that I love all things "science." While I am most comfortable with biology, genomics and neuroscience, I like to read about physics and astronomy, too. I'm also not ashamed of the fact that I'm very close to what people picture as the stereotype of a librarian: from my glasses to my closet full of cardigans to my ownership of multiple cats.

Connect with Pamela on LinkedIn.

Research in the News

The New York Times, June 14

From a Pediatrician, Lessons for Dads-to-Be
Craig Garfield, MD, was quoted.
▶ This research was also featured in *U.S. News & World Report.*

Chicago Tribune, June 27

New treatment lowers risk for death from aggressive prostate cancer by over 70 percent, study finds
Maha Hussain, MD, was quoted.
▶ This research was also featured in *HealthDay.*

The Washington Post, June 11

Why straight parents struggle to talk to their LGBTQ kids about sex and how to make it easier
Michael Newcomb, PhD, was quoted.

Reuters, July 2

People with allergies often leave life-saving epinephrine at home
Ruchi Gupta, MD, MPH, was quoted.

HealthDay, July 9

When Parents Do Time, Kids Pay the Price
Nia Heard-Garris, MD, MSc, was quoted.
▶ This research was also featured in *Chicago Tonight.*

Crain's Chicago Business, July 12

Northwestern researchers on a big breakthrough: Slowing cancer cell growth
Karl Scheidt, PhD, was quoted.

WebMD, July 16

Eczema Can Dramatically Hurt Quality of Life
Jonathan Silverberg, MD, PhD, MPH, was quoted.
▶ This research was also featured in *HealthDay.*

HealthDay, July 17

Food Allergies Less Severe in Infants: Study
Waheeda Samady, MD, and Ruchi Gupta, MD, MPH, were quoted.

More media coverage available online.

Northwestern University
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NUCATS Corner

NUCATS at Your Service

NUCATS provides investigators, participants and stakeholders in the research continuum with an extensive array of resources, consultative services and expertise in order to accelerate transformative scientific discoveries from the lab to patients and the community. It is our goal to continually increase the quality, safety, efficiency, speed and impact of innovative clinical and translational research.

Through our centers and programs, we provide resources and expertise to assist investigators and their research teams across all the phases of clinical and translational research. We offer services to address your clinical research needs, including support with regulatory needs, study participant recruitment, study coordination, and budgeting and finance. We provide informatics and biostatistical services. We work proactively to create meaningful partnerships between investigators and community stakeholders. We offer educational and career development training programs that help investigators and research staff gain the skills they need to perform sound clinical and translational research. Additionally, we provide funding to accelerate your research, and we assist with the commercialization of drugs and devices.

Discover how NUCATS can help accelerate your research.

Listen to the *Breakthroughs* Podcast

Check out our latest episodes featuring Feinberg investigators including:

- Katherine Wisner, MD, on medication and mental health during pregnancy
- Robert Kalb, MD, on what causes ALS
- Brian Mustanski, PhD, on improving LGBTQ health

Sponsored Research

PI: Gordon Shepherd, MD, PhD, associate professor of Physiology

Sponsor: National Institute of Neurological Disorders and Stroke

Title: Synaptic Circuit Organization of Motor Cortex

Sensory-guided movements of the arms and hands are essential for many activities of daily living, and pathological processes that impair the cortical circuits mediating these behaviors are a common cause of disability. To better understand and treat these disorders, it will be important to understand the cellular mechanisms in these circuits.

Shepherd's team previously elucidated many aspects of the circuit organization of primary motor cortex (M1) neurons in the forelimb area of mouse neocortex. However, a fundamental question remains poorly understood: How are forelimb M1 neurons integrated into functional synaptic circuits with the cells and circuits of primary somatosensory cortex (S1)?

In this research, investigators will test a series of predictions about the cellular organization of the forelimb S1-M1 circuit. Their overall aim is to determine the cellular basis for key long-range excitatory circuit connections that mediate communication between forelimb S1 and M1, and between these areas and somatosensory and motor nuclei in the thalamus.

Read more about this project.

PI: Robert Vassar, PhD, professor of Neurology in the Division of Behavioral Neurology and of Cell and Molecular Biology

Sponsor: National Institute on Aging

Title: Molecular and Cellular Mechanisms of the UNC5C Netrin Receptor In Alzheimer's Disease Pathogenesis

The mechanism of neuron death in Alzheimer's disease is enigmatic; however, a newly discovered mutation in the gene for UNC5C — a rare coding mutation called T835M — increases the vulnerability of neurons to Alzheimer's-associated stresses.

Vassar's team will investigate their hypothesis that UNC5C T835M predisposes to late onset Alzheimer's by making neurons more vulnerable to cell death induced by pathogenic amyloid beta and tau proteins. The investigators will define cell death pathways in mouse models of amyloid beta and tau pathology crossed to knockin mice in which UNC5C T835M is expressed endogenously; identify cell death pathways in human induced pluripotent stem cell neurons generated from UNC5C T835M patient fibroblasts; and use mass spectrometry-based proteomics to determine the comprehensive UNC5C T835M cell death proteome.

The team hopes to determine the mechanism of UNC5C-associated neuron death and design strategies to prevent neuron death as a proof of concept for new therapies.

Read more about this project.

Welcome New Faculty

Judd Hultquist, PhD, joins us as an assistant professor of Medicine in the Division of Infectious Diseases. His research focuses on mapping the functional plasticity in host-pathogen interactions in primary models of disease. Leveraging expertise in primary cell modeling, proteomic profiling and functional genomics, his research group studies the changing landscape of protein-protein interactions, post-translational modifications, gene expression profiles and functional dependencies that unfold during the course of viral infection. His goal is to strengthen the bridge from big data to targeted discovery to clinical application for the development of personalized, host-driven therapies and the betterment of human health.

Hultquist earned his PhD in molecular biology and virology from the University of Minnesota before serving as a postdoctoral fellow in systems biology at the J. David Gladstone Institutes in San Francisco. He has published more than 20 primary research articles, including landmark studies in *Nature* and *Cell*, and is the currently principal investigator on a K22 grant funded by the National Institutes of Health investigating the genetic determinants of HIV latency establishment and maintenance. He is the recipient of numerous awards, honors, and fellowships for his research and academic achievements and has participated in several outreach efforts to raise awareness of the ongoing fight against the AIDS epidemic. Watch his latest video for the American Foundation for AIDS Research Epic Voices project here.

Walsh

(continued from page 3)

a disease that killed more people than any other human pathogen combined and ushered in the era of vaccines. We work on vaccinia virus, a variola-like poxvirus that was used in the global vaccine campaign against smallpox. Although smallpox was eradicated (in my opinion the biggest medical milestone of the last century), new zoonotic poxviruses are adapting to infect humans in the same way variola did, and these pose a serious future threat that we need to prepare for proactively.

In addition, poxviruses are now widely used as vaccine and gene therapy vectors, as well as oncolytics (viruses capable of killing cancer cells), so we need to understand them well. By contrast, HCMV is widespread in the human population and is a leading cause of congenital birth defects — yet there is no vaccine or cure. Clearly, understanding the basics of how these viruses replicate is of fundamental importance to the field of medical sciences.

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

We are a relatively small team. Of our two graduate students, Colleen Furey works on the role of microtubules during HSV-1 infection of different natural target cell types, while Madeline Rollins works on how poxviruses manipulate host ribosomes to mimic plant translation strategies. Of our three postdoctoral fellows, Nathan Meade, PhD, works on how poxviruses control the metabolic sensor mTOR; Stephen DiGiuseppe, PhD, works on how poxviruses alter ribosome function; and Dean Procter, PhD, works on how HCMV uses microtubules to remodel host cells. I consider myself fortunate as a PI that they all share my intrigue and passion for research, which makes for a fun yet very focused and productive group.

Where have you recently published papers?

We have had a run of good luck with our publications in the past year or so. Our last poxvirus papers were published in *Nature*, *Cell Reports* and *Cell*. Our HCMV paper, published this year in *Developmental Cell*, ended up as the cover image for the April 9 issue. We also have a long-standing collaboration with the laboratory of Mojgan Naghavi, PhD, which does some really cool work on HIV, and we have published some collaborative papers with that team recently in *Nature Communications*.

How is your research funded?

We are very fortunate to be currently funded by the National Institutes of Health, through the National Institute of Allergy and Infectious Diseases and the National Institute of General Medical Sciences. We also receive important internal support from NUCATS and the Dean's Office, and some of our projects were developed initially through invaluable support from the Third Coast Center for AIDS Research.

Funding

HIV Drug Resistance: Genotype-Phenotype-Outcome Correlations (R01 Clinical Trial Not Allowed)

More information

Sponsors: National Institute of Allergy and Infectious Diseases
Letter of Intent Due: November 5
Submission Deadline: December 5
Amount: $500,000 per year, for five years

Synopsis: The purpose of this funding opportunity is to support studies that will evaluate HIV drug resistance and its relationship to treatment success. Applications are sought proposing studies of genotype/phenotype correlations in diverse subtypes, the relationship between drug resistance mutations present in minority variant viral populations and treatment outcomes, and on the reasons for the discordance between genotype and treatment success or failure. Laboratory evaluations of samples with clinical correlates in patients on recommended regimens are encouraged.

Late Stage Clinical Trials for the Spectrum of Alzheimer's Disease and Age-related Cognitive Decline (R01 Clinical Trial Required)

More Information

Sponsors: National Institute of Aging
Submission Deadline: Standard dates apply
Upper Amount: $3.125M

Synopsis: This funding opportunity encourages R01 grant applications that propose to develop and implement late stage (Phase II/III, III) clinical trials of promising pharmacological and non-pharmacological interventions in individuals with age-related cognitive decline and across the Alzheimer's disease spectrum from pre-symptomatic to more severe stages of disease.

Modular R01s in Cancer Control and Population Sciences (R01 Clinical Trial Optional)

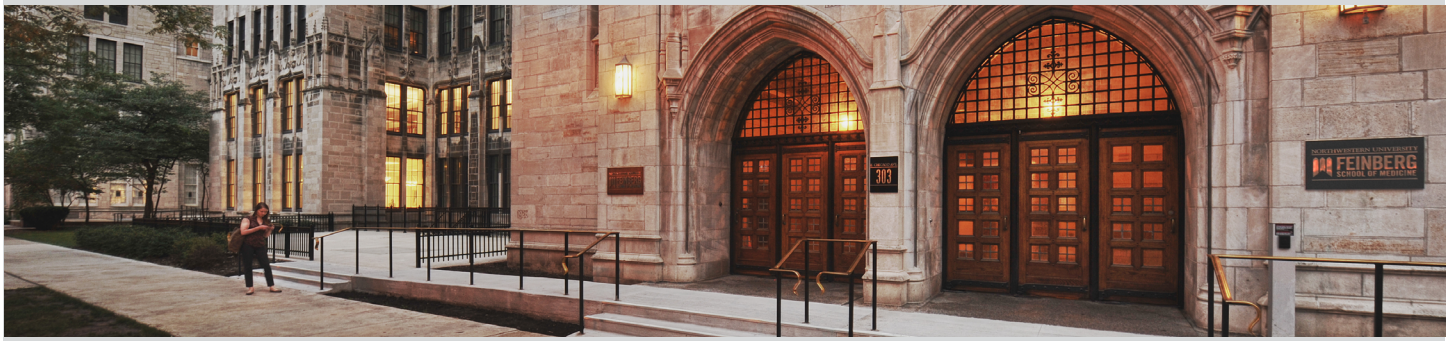
More Information

Sponsors: National Cancer Institute
Submission Deadline: November 7
Upper Amount: $250,000 in direct costs for a maximum project period of five years

Synopsis: Applications for research in cancer control and population sciences are encouraged. The overarching goal is to provide support to promote research efforts on novel scientific ideas that have the potential to substantially advance cancer research in statistical and analytic methods, epidemiology, cancer survivorship, cancer-related behaviors and behavioral interventions, health care delivery and implementation science.

View more funding opportunities

Reusing Scholarly Content: A Discussion of Copyright, Fair Use and Licenses



By Mary Anne Zmaczynski and Karen Gutzman

Copyright, fair use and licenses are terms frequently mentioned in academic work, but not easily understood. Copyright protects content creators and gives them the right to say how and when their work can be used or transformed to create something new. Licenses, or permissions, help content creators establish reuse options for works as they are created, encouraging easy sharing. Creative Commons is a well-known organization that helps content creators both protect and share their work with others. Fair use allows content creators to use works still under copyright for the purpose of education and criticism. By reviewing how content will be reused, you can determine if you need to pay any fees to the owner of the material before using it.

Copyright, Licensing and Fair Use in Practice

Copyright Scenario: You have some figures that you previously published in a journal article that you'd like to reuse in a new book chapter. Can you use the figures from your published article? Do you need to gain permission to use them? And if so, from whom?

While authors are starting to negotiate terms of reuse into their contracts with publishers, traditionally ownership and copyright of content is transferred to the publisher of the journal upon publication. Therefore, in order to reuse something, you must seek permission from the copyright holder, usually the publisher. The Copyright Clearance Center manages this process for hundreds of journals in an easy-to-use online format. Individuals can search for a journal, enter information about how they will use the content, obtain an estimate and then purchase the rights. For journals not managed through the Copyright Clearance Center, check the owning journal's homepage and look for "author guidelines" specifically on "copyright, reuse or permissions." You may need to email the owning journal directly to find out whether you can reuse it.

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Many images online are not in the public domain; instead they're online because the copyright holder has placed them online, or because the copyright holder has used a license, often called a Creative Commons License, to explain how someone may copy, distribute and make some uses of their work. To find images to use in your presentations, consider:

- Using websites devoted to images in the public domain or ones that have a Creative Commons Zero license, such as Pixnio, Unsplash or Wikimedia Commons
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Once you are sure you've properly followed the licenses provided by the image creators, then you may consider uploading your presentation to DigitalHub, so that it can be made openly available to a larger audience.

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If possible, you should cite the video and any other media on a presentation slide or in the course materials. Use the Fair Use Principles to evaluate the use of media in an educational setting: 1) purpose and character of the use; 2) nature of the copyrighted work; 3) amount used; and 4) effect on the market for the work. For more detail, see the Fair Use Checklist from Cornell University.

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Whenever you reuse content, you should, at minimum, cite others' work. Use these links to learn how to cite an image or photograph using APA style or NLM style, or check out these online videos on using APA style or NLM style. Contact your liaison librarian for assistance in finding copyright, licensing and fair use guidelines.

High-Impact Factor Research

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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

Wednesday, August 15

State of Sexual and Gender Minority Health Symposium

The Institute for Sexual and Gender Minority Health and Wellbeing (ISGMH) presents: "Illuminating the Intersections of Race and LGBTQ Health." The symposium centers on the intersection between racial and ethnic minorities, and sexual and gender minority populations, identifying areas where research can improve the health and well-being of minority populations.

Time: **2:00 p.m. to 5:30 p.m.**

Location: **Arthur J. Rubloff Building**
Aspen Hall
375 E. Chicago Ave.

Contact: **bethann.hamilton@northwestern.edu**

More information

Friday, August 17

Allergy and Immunology Seminar Series

Kathleen Sullivan, MD, PhD, chief of the Division of Allergy and Immunology at the Children's Hospital of Philadelphia.

Time: **Noon to 1 p.m.**

Location: **Prentice Women's Hospital**
Canning Auditorium
250 E. Superior St., 3rd Floor

Contact: **jamie.riley@northwestern.edu**

More information

Save the Date: Friday, September 21

Feinberg Medical Education Day

An annual celebration of outstanding teaching and scholarship by faculty, housestaff and students. The conference will feature workshops, innovative didactic presentations, awards for teaching and educational research and a keynote lecture by Richard K. Reznick, MD, MEd, dean, Faculty of Health Sciences, Queen's University.

Time: **9:15 a.m. to 5:00 p.m.**

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

Contact: **j-langland@northwestern.edu**

More information

NIH News

NIH Application Resubmission Policy

NIH's resubmission policy has not changed, but the latest policy notice highlights some important points:

- Only a single resubmission (A1) of an original application (A0) will be accepted
- An A0 application may be submitted following an unsuccessful A0 or A1 application, with a few exceptions
- What happens when switching funding opportunity announcements between the A0 and A1 applications
- Generally a change of activity code (e.g., R01) between the A0 and A1 is not allowed, with one exception

Read the policy for details.

All About Grants Podcast

The latest episode of the NIH's *All About Grants* podcast discusses the grant application's two-level peer review process. Sally Amero, PhD, NIH review policy officer, and Rebekah Rasooly, PhD, director at the National Institute of Nursing Research, weigh in how advisory councils fit in this process, the general award decision-making process and more. Listen to the 10-minute recording or read the transcript here.

Expiring NIH Appropriations

With the end of the fiscal year approaching on September 30, it is important for NIH grant recipients to carefully monitor and review the terms and conditions of their award. The NIH funds most grants and cooperative agreements in 12-month increments, or budget periods. Each budget period is funded with dollars appropriated for that specific fiscal year in which the award is made. These funds are only available until the end of the fifth fiscal year after the funds are awarded. At the end of five years, any remaining balances are canceled and returned to the Treasury.

To learn more about how you can avoid your funds from expiring, watch the Q&A panel here featuring Michelle Bulls, director of the NIH Office of Policy for Extramural Research Administration, and Alan Whatley, lead accountant in the NIH Office of Financial Management.

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