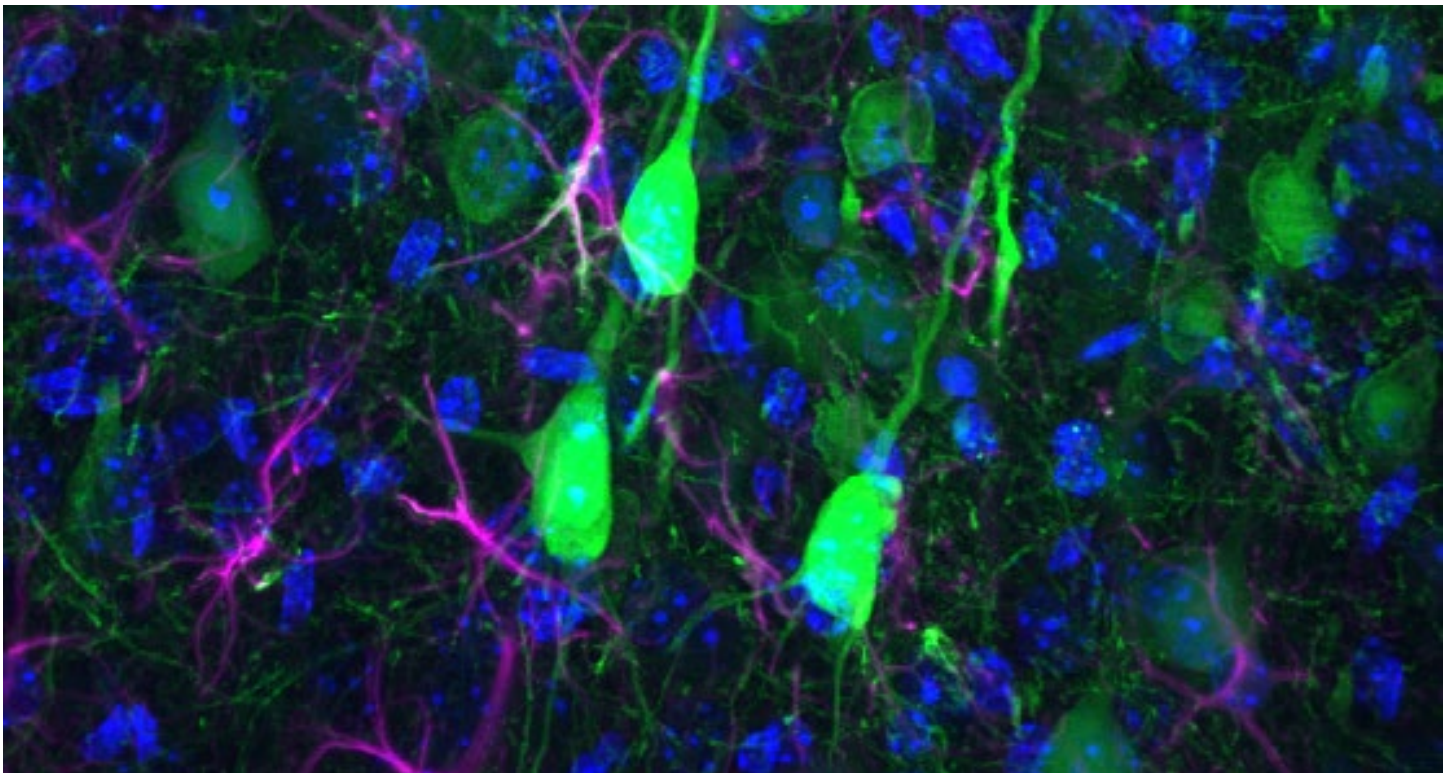
Breakthroughs

Feinberg School of Medicine Research Office

April 2014



Thanks to neon, motor neurons associated with ALS glow green, making it easy for scientist to track what goes wrong and causes their death. Photo credit: Ozdinler lab.

Upper Motor Neurons Take Center Stage in Ozdinler Lab

Where others see mice, P. Hande Ozdinler, PhD, assistant professor of Neurology, sees cortical spinal motor neurons (CSMN).

"They act as the spokesperson for the initiation of movement," said Ozdinler, director of one of two Les Turner amyotrophic lateral sclerosis (ALS) laboratories at Northwestern. "These cells are responsible for collecting, integrating, and translating signals from the brain before transmitting the information to the spinal cord, which then initiates a voluntary physical action by the body."

CSMN degeneration has an immense impact on motor neuron circuitry and is one of the underlying causes of numerous neurodegenerative diseases. An invited review article published in March by Ozdinler in *Frontiers in Neuroanatomy* explores the role of CSMNs in health and disease.

Her emphasis on CSMNs—the upper motor neurons that originate in the cerebral cortex—has garnered substantial support, most recently in the form of nearly $3 million from the National Institutes of Health, Les Turner ALS Foundation, and ALS Association. The grants, and backing from Dimitri Krainc, MD, department chair, have led to expanded lab space from the Office of the Dean, new equipment, and the addition of two postdoctoral fellows, two students, and one technician.

For Ozdinler, the journey to become an ALS researcher began

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Upper Motor Neurons Take Center Stage

(continued from cover page)

in her native country, Turkey. After completing an undergraduate degree and master's degree in molecular biology and genetics in her homeland, she came to the United States and earner her PhD in cell biology, anatomy, and neuroscience at Louisiana State University Health Sciences Center. Her interests in neuroscience and cell biology led her to Harvard Medical School, where she trained under the direction of Jeffrey Macklis, MD, a world-renowned expert on stem cell biology, and the first scientist to identify the molecular controls directing differentiation of corticospinal motor neurons.

Recent findings, like those published in the January issue of *Science* linking cellular pathologies of cortical spinal motor neurons to common neurodegenerative diseases, reinforce Ozdinler's belief that her work will impact scientific understanding well beyond ALS.

"Historically, investigators have limited themselves by the notion of disease, focusing on Alzheimer's or Parkinson's, or ALS. But it's not really the disease that we should be concerned with, it's the vulnerable neuron, the connectivity, the circuitry of the brain," said Ozdinler, a member of the Cognitive Neurology and Alzheimer's Disease Center and Northwestern University Interdepartmental Neuroscience Program. "The problem with neurodegeneration is that the moment we see the symptom, it's mostly too late."

To combat this, Ozdinler's lab is undertaking a novel approach in an effort to reveal some early detection markers, not only for ALS, but for hereditary spastic paraplegia, Parkinson's, and many other diseases. The study is working with models at such an early point in life that no symptoms of the disease are present. Instead, scientists will be exploring the genetic changes taking place at the motor neuron level.

The thesis of Ozinler's review published in *Drug Discovery Today* at the end of last year hinged on the recognition that it's not just keeping mice, but motor neurons, alive that will be crucial for translating biological findings to human health.

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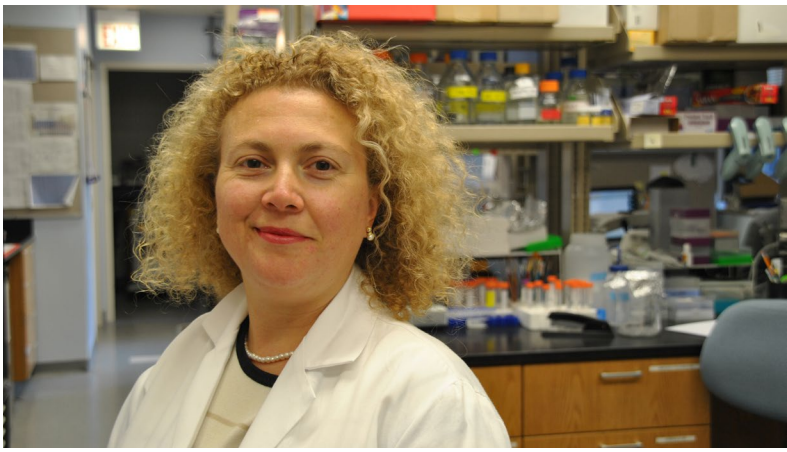


P. Hande Ozdinler, PhD, garnered substantial support, most recently in the form of nearly $3 million from the National Institutes of Health, Les Turner ALS Foundation, and ALS Association.

"Renewed attention and the increasing ability to study motor neurons will be a big component in moving clinical trials for ALS forward," Ozdinler said. "This paradigm shift has created an internal energy that will undoubtedly lead to new knowledge."

CSMNs have been largely ignored by scientists because the only way to study them involved a difficult surgical process beyond the scope of most. In 2013, Ozdinler found a solution in UCHL1. She cloned the gene with a fluorescence molecule, creating a mouse whose upper motor neurons shine green. She then mated it with an ALS mouse model to produce a new preclinical version of the disease with fluorescent motor neurons in the brain.

"I think the field has realized the importance of making these neurons neon because although we understood their importance to a certain degree, a major limitation was that we didn't have a way to make them seen," Ozdinler said. "We have sent animal models around the world, and for the first time, together with our collaborators, we might understand the underlying cellular mechanisms that are important in health and disease.

"I see disease as a large coin," said Ozdinler, also a member of the Robert H. Lurie Comprehensive Cancer Center. "One side has all of these neurodegenerative diseases interlinked, and on the other side is cancer. When we explored genes that are related to neurodegeneration we were amazed to find that overexpression of some lead to cancer in many forms, while mutations result in very early neurodegeneration."

UCHL1 is a good example of a gene that may sit at the crossroads. Ozdinler recently explored the idea in a review article published in *Cell Biochemistry and Biophysics*.

"The collaborations we've established and the novel tools, applications and knowledge recently generated in our lab could be extremely significant in the fight against neurodegeneration," Ozdinler said. "By moving upper motor neurons to center stage, it not only uniquely positions our team, but also provides exceptional strength to Northwestern's push for new discoveries."

Tenth Annual Research Day Celebrates Science, Energizes Campus

The 10th Annual Lewis Landsberg Research Day, held April 3, featured a record-setting number of posters. The 324 presenters—a 50 percent increase since 2011—represented nearly every medical school department and celebrated the work of faculty, fellows, residents, and students from Feinberg's graduate, medical, and physician-scientist programs.

"If you want to see what the future of Northwestern Medicine will look like, it's happening here, right now, as students, junior trainees, and faculty share ideas and form the foundations of inquiry that will become tomorrow's high-impact discoveries," said Eric G. Neilson, MD, vice president for Medical Affairs and Lewis Landsberg Dean.

Neilson welcomed attendees to Hughes Auditorium during an opening ceremony that featured keynote speaker William Pao, MD, PhD, professor of medicine, cancer biology, and pathology at Vanderbilt University. His presentation, "Defining Clinically Relevant Molecular Subsets of Solid Tumors," focused on cancer mutations and their significance.

"Over the past decade or more we have identified mutations in tumors, which not only induce the formation of tumors, but their sustained signaling leads to a particular Achilles' heel that can be targeted with new therapies," said Pao, director of the Division of Hematology/Oncology and Personalized Cancer Medicine at the Vanderbilt-Ingram Cancer Center. "We are all excited because the molecular sub-setting has led to progress in terms of overall cancer survivability."

The opening session also saw the Tripartite Legacy Faculty Prize awarded to Lee Jampol, MD, Louis Feinberg, MD, Professor of Ophthalmology. Jampol, a member of the Feinberg faculty since 1983, was honored for his emphasis on research, mentoring, and national leadership in macula and retinal diseases.

2014 Research Day poster competition winners.

Faculty Mentor of the Year awards were announced for Ram Yogev, MD, professor of Pediatrics-Infectious Diseases, and D. Mark Courtney, MD, associate professor of Emergency Medicine.

At the day's conclusion, awards were announced for 13 individual presenters. More than 30 judges, comprised of senior Feinberg faculty, evaluated abstracts and posters based on potential contributions to the advancement of medical science and healthcare. In addition, the Alliance for Research in Chicagoland Communities presented the second annual Community Engaged Research Partnership Award to the Collaboration to Improve Chronic Disease Outcomes for Chicago Public Schools Students.

Read more and watch a Research Day video.

2014 Research Day Winners

Basic Science Research
- First place: Shuang Zhang, BS, student in the Driskill Graduate Program in Life Sciences
- Second place: Andrea Murmann, PhD, research assistant professor of Medicine
- Third place: Daniela Menichella, MD, PhD, assistant professor of Neurology

Clinical Research
- First place: David Klein, MS, medical student
- Second place: Kevin Shih, BA, medical student
- Third place: Shreya Shah, BS, medical student

Public Health and Social Sciences Research
- First place: Paul Jansson, MS, medical student
- Second place: Tao Gao, MD, research associate
- Third place: Elizabeth Peoples, BA, research assistant

Women's Health Research

Basic Science
- First place: Suzanne Schauwecker, student in the Medical Scientist Training Program
- Second place: Andrea Murmann, PhD, research assistant professor of Medicine

Clinical Research and Public Health and Social Sciences
- First place: Rebecca Lin, MD, resident in Pathology
- Second place: David Walega, MD, MSCI, associate professor in Anesthesiology

Community-Engaged Research Partnership Award
- Collaboration to Improve Chronic Disease Outcomes for Chicago Public Schools Students

Complete list of winners, PIs, and project titles.

Faculty Profile: Michael Markl, PhD

Associate Professor in Radiology/McCormick School of Engineering

Approximately one to two of every 100 Americans have a bicuspid aortic valve, which can lead to life-threatening complications such as aneurysm and rupture. Interested in the underlying mechanisms of cardiovascular diseases, Michael Markl, PhD, associate professor in Radiology/McCormick School of Engineering, recently published paper in *Circulation* investigating aortic blood flow in patients with a bicuspid aortic valve.

"The underlying mechanism that promotes the development of such aortic pathologies, whether it is genetic in origin or related to changes in blood flow through the bicuspid valve, and which patients are at highest risk is still the topic of ongoing debate," Markl said. "In our study, we used a new Magnetic Resonance Imaging (MRI) technique, 4D flow MRI, to explore the impact of the presence and type of bicuspid aortic valve on 3D blood flow in the heart."

Q&A

What are your research interests?

A central objective of my research is to develop multi-parametric imaging techniques that can afford a better understanding of the underlying mechanisms of cardiovascular disease development and the impact of therapy. The purpose of this approach is to merge different functional aspects of each anatomical region into a more complete picture of local and global anatomy and function of the heart muscle, valve systems, ventricular chambers and vessels throughout the human body. In this context, my research group has been instrumental in establishing '4D Flow MRI' for the comprehensive assessment of cerebro- and cardiovascular hemodynamics. Further interests include the development, validation and application of novel imaging tools for the evaluation of structure and function of the heart.

What is the ultimate goal of your research?

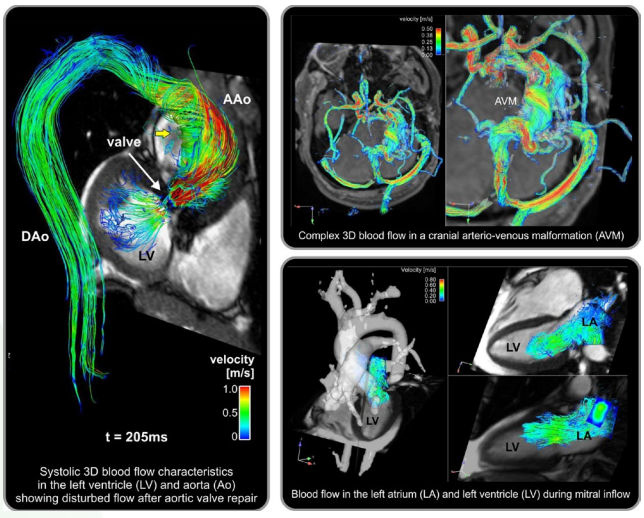
The transfer of novel magnetic resonance (MR) methods into clinical studies and ultimately clinical applications is one of the key objectives of current and future research. To achieve these aims, interactions between basic scientists, engineers, industry partners, and clinicians are essential to enable this type of translational research. The ultimate goal is to develop clinical applications that can provide new insights and a better understanding of the specific relationships between disease, therapy, intervention, and functional changes within the heart and vascular system, critical for improving therapy management in a patient.

What types of collaborations are you engaged in across campus?

This is a challenge for all research studies assembling the multi-disciplinary expertise that is needed to recruit and identify patients, implement advanced MR imaging within a clinical setting, and develop the data analysis to derive advanced metrics of disease morphology and physiology. Northwestern University provided a very fertile environment to successfully assemble such a team. For our research we closely work with investigators with expertise in radiology, cardiology, cardiac surgery, neurology, computer science, imaging physics, biomedical and mechanical engineering, as well as preventive medicine, industrial engineering and management sciences, and others.

How is your research funded?

Since my arrival at Northwestern University in April 2011, I have built a very active research group with 10 scientists and clinical investigators at the graduate, postdoctoral, and junior faculty level. In addition, I have brought together investigators from multi-



Three-dimensional blood flow in the aorta, heart, and brain is shown using a new imaging technique, 4D flow Magnetic Resonance Imaging.

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Student Profile: Theanne Griffith

Northwestern University Interdepartmental Neuroscience Program

Theanne Griffith, a fourth-year graduate student in the Northwestern University Interdepartmental Neuroscience Program (NUIN) studies the role of kainate receptors in neuronal function in the laboratory of Geoffrey Swanson, PhD, associate professor in Pharmacology. Last year she was awarded a two-year predoctoral fellowship by the American Heart Association.

Before beginning her doctoral training, Griffith spent two years doing research at the Pontifical Catholic University of Chile in Santiago, where she investigated the neuroprotective effects of a St. John's wort derivative in a model of Alzheimer's disease. She received her undergraduate degree from Smith College in Massachusetts as a dual neuroscience and Spanish major.

Q&A

What is your hometown?
I am from Alexandria, Virginia.

What are your research interests?
I'm currently in Geoffrey Swanson's lab, and the primary focus is to investigate kainate receptors, which are a excitatory receptors in the brain. These receptors are important for maintaining the balance between excitation and inhibition in the brain. They are involved in different disease states such as epilepsy, pain, stroke, and migraines.

A couple of years ago, these receptors were shown to associate with an auxiliary subunit consisting of two proteins, called Neto 1 and Neto 2. These subunits drastically altered the function of kainate receptors, so the goal of my research is to understand the structural basis of that interaction. We utilize several different approaches to address this research question, including patch-clamp electrophysiology, confocal microscopy, and biochemical/molecular techniques.

Kainate receptors have been very difficult to target due to overlap in their pharmacological profiles with other excitatory receptors. The idea behind my project is to identify important amino acid residues and key sites not only in the Neto proteins but also in the Kainate receptors, so that chemists can design drugs to target those sites and modulate kainate receptor function in diseases in which they are involved.

How did you choose this research project?
Neuroscience fascinates me because there is so much to know and so many questions to ask. I've always been interested in structure-function relationships, so I am excited to work on this project where I can study one particular protein and one other protein and try to understand how they fit together.

What do you like to do outside of the lab?
Science outreach is definitely one of my big passions. In my first year, I was active in the Junior Science Club. I am involved in science outreach with the brain fair for Brain Awareness Week. Last year I went to five sessions to do mini-lectures and activities for students at an elementary school in the Uptown neighborhood. In my life, I had very easy access to science education, and no one ever deterred me, but that is not the case for everyone. I don't think anyone should be excluded from being able to learn about science or miss the opportunity to learn whether they like it or not, especially in underprivileged socioeconomic communities.

Michael Markl, PhD
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ple disciplines, which enabled me to quickly translate ideas and innovative MR imaging techniques into novel clinical applications. Based on these accomplishments, my research group has received significant grant support, including two five-year NIH R01 grants as well as several American Heart Association awards, including pre- and post-doctoral fellowships and a scientist development grant.

Which honors are you most proud of and why?
As a highlight of my career to date, I have recently been selected for the Distinguished Investigator Award of the Academy of Radiology Research. This prestigious honor recognizes individuals for their accomplishments in the field of imaging research. Past recipients have gone on to introduce new technologies to the field that have fundamentally impacted patient care.

Staff Profile: Michael Moore, PhD

Invention Manager, INVO

Where are you originally from?
I grew up in Schiller Park, Illinois.

What is your educational background?
I went from high school at St. Ignatius in Chicago to the University of Illinois at Urbana-Champaign where I received a Bachelor of Science degree in biochemistry. Afterwards I went directly to grad school and received a master's degree and doctorate degree in biochemistry from the University of California–San Diego, where I studied in Susan Taylor's lab characterizing the catalytic subunit of Protein Kinase A.

Please tell us about your professional background.
I started at Northwestern University's Innovation and New Ventures Office (INVO) pretty much out of graduate school, with a stint as a stay-at-home dad with my twin sons in between. My original position at INVO was created for someone with a technical background that would gain experience in the office on the patent and licensing aspects of the job. After gaining that experience, I was promoted to my current position.

Why did you choose to work at Northwestern?
My specific position was appealing because it would give me the opportunity to work in a field where academic research meets the commercial world, while allowing me to make use of my biochemistry education.

Being from the Chicago area, I know how admired Northwestern is in our community, and it is great to be a part of that tradition and to work toward promoting its mission. Now, I don't know about "Chicago's Big Ten Team," but that's the Illini in me.

What is your role within INVO?
I work with investigators to assess how or if their research could move forward on a commercial path. This involves assessing the patentability of an invention, the strength of a potential patent, and the likelihood of finding a commercial partner to license that invention/patent. I work with patent counsel to seek patent protection for those inventions where appropriate, engage with companies to promote Northwestern University inventions, and am also responsible for negotiating license agreements for those inventions I manage.

How do you personally help investigators at Feinberg?
My responsibilities help me promote INVO's mission, which is to foster a culture of innovation and help facilitate moving the research done here at Northwestern out to benefit the public. This can often be accomplished by disseminating the information to the scientific community, but in those instances where a significant investment is necessary to get a product on the market, patenting, and licensing is going to be required.

What is your favorite part of the job?
There are a number of cool things about my job. On the science side, I like the diversity of inventions and inventors I get to work with, and that I am constantly learning new things. I also like negotiating license agreements where you have to understand the other side's perspective and work to find creative solutions to come to an agreement that protects Northwestern's interests while allowing the licensee to be successful.

What do you like to do in your spare time?
I've been coaching my sons' soccer and basketball teams for our park district the last few years, which I'm not great at, but really enjoy. I like rollerblading and completed my first skate marathon last year. I've also run several half and two full marathons with my wife over the last few years.

Is there anything happening at INVO this spring that Feinberg investigators should be aware of?
You can always keep up with INVO by visiting our website. This spring we have a commercialization clinic in early May, and we're also gearing up for our Innovation to Commercialization summer internship program, I2C. Feinberg is funding the participation of two students in this program which we are very excited about.

NU Medical Device Startup Receives Venture Championship Award

Innoblative Designs, Inc., a Northwestern University startup, won "Best Written Business Plan" and was an overall runner-up at the Oregon New Venture Championship in April. The startup commercializes a radiofrequency ablation probe that uses heat to remove residual cancer cells after a breast lumpectomy. The device was invented by David Mahvi, MD, professor of Surgery-Surgical Oncology and McCormick School of Engineering and surgical resident Daniel McCarthy, MD, MBA, MEM.

The company was started by Northwestern graduate students. The team includes Oyinlolu Adeyanju, PhD and medical scientist training program student from Feinberg, Tyler Wanke, a graduate student at Feinberg, Kellogg and McCormick, Brian Robillard and Curtis Wang, both students at McCormick, and Jason Sandler, a student at Kellogg and the law school.

Research in the News

Chicago Tribune March 31
Drowsiness a danger on road as well as rails
Phyllis Zee was quoted.

The Wall Street Journal March 27
Do you take statins? If not, you may have to
Neil Stone was interviewed.

- Stone was also quoted in *USA Today,* Reuters, CNBC, *The Washington Post*, and more.

US News & World Report March 24
Targeted radiation might help fight advanced breast cancer: study
Robert Lewandowski's research was featured.

- Lewandowski's research was also featured on Yahoo! News, Web MD, and more.

Crain's Chicago Business March 24
Printed tissue could ease transplant shortages
Ramille Shah and Katherine Barsness were quoted.

TIME Magazine March 17
Fat-heart disease findings confusing, enticing
Brian Hitsman was quoted.

- Hitsman was also quoted in Reuters, Yahoo! News, and more.

NY Times March 12
Quitting smoking linked to improved mood
Linda Van Horn was quoted.

- Van Horn was also quoted in FOX News, *Health Magazine*, *Chicago Tribune* and more.

NBC News March 6
Expert help on how to manage insomnia
Kelly Baron was quoted.

Popular Science March 5
New wearable device could protect against HIV and pregnancy?
Patrick Kiser's research was featured.

- Kiser's research was also featured on CNN, The Daily Beast, Voice of America, FOX News, Self Magazine, New Scientist, Yahoo! News, and more.

Washington Post March 4
Alzheimer's buddy program pairs patients, students
Darby Morhardt's research was featured.

- Morhardt's research was also featured in ABC News, FOX News, Yahoo! News, and more.

More media coverage available online.

Northwestern University
NUCATS
Clinical and Translational Sciences Institute

NUCATS Corner

Participate in Northwestern University Clinical Research

Are you interested in contributing to our understanding of human health and behavior? After learning more about current research studies you may decide to become a participant in research at Northwestern University by calling 1-855-NU-STUDY or by emailing us at nustudy@northwestern.edu.

If you're interested in specific areas of research, we can assist you and discuss your options. If there are no studies currently available, you may elect to participate in the general research registry so we can notify you for future research opportunities. Also, visit the Northwestern University Registry to learn about other research registry options. If eligible, you may be contacted for future research opportunities. Healthy participants, as well as those with diagnosed diseases, are encouraged to register if interested.

If you are a faculty or staff member looking for help with conducting clinical research, please contact one of our Research Navigators for further assistance.

Unlocking the Genome

The Genomics Core Facility was featured in Northwestern University's Office for Research newsletter recently, in the story "Unlocking the Genome."

Last year, the core moved from separate lab spaces in the Ward and Tarry buildings into a single laboratory in Tarry specifically designed to support genomics research.

The Core's DNA extraction service recently received accreditation from the College of American Pathologists. With this accreditation, it joins an elite group of internationally recognized facilities that meet the highest standards in laboratory practices. Read more.

Sponsored Research

PI: Atsushi Kato, PhD
Assistant Professor of Medicine-Allergy and Immunology

Sponsor: National Institute of Allergy and Infectious Diseases

Title: "Role of Thymic Stromal Lymphopoietin in Chronic Rhinosinusitis"

Chronic rhinosinusitis (CRS) is a heterogeneous disease characterized by local inflammation of the upper airways and sinuses that are unresponsive to antibiotic therapy and which persists for at least 12 weeks. It is one of the most common chronic diseases in adults in the U.S., affects more than 10 million Americans, and has a severe impact on patients' quality of life and healthcare costs. Due to poor responses to medical therapy, more than 250,000 surgical procedures are performed annually in the U.S.

CRS is clinically classified into CRS with nasal polyps (CRSwNP) and CRS without nasal polyps (CRSsNP). Both forms are characterized by intense inflammatory cell infiltration which drives symptoms of the disease, but CRSwNP is the more severe form of the two and is associated more closely with clinical complaints of nasal obstruction and olfactory loss. Although CRSwNP is known to be characterized by Th2-related inflammation including eosinophilia, the mechanisms underlying the amplification of Th2-related inflammation in patients with CRSwNP have not been identified.

My laboratory has focused on an epithelial cytokine, TSLP (thymic stromal lymphopoietin), that is an IL-7-like cytokine molecule now recognized as an important regulator of Th2-related inflammation. TSLP stimulates dendritic cells (DCs) to induce naive CD4+ T cell differentiation into Th2 cells. TSLP can also activate mast cells and group 2 innate lymphoid cells (ILC2) to produce Th2 cytokines, including IL-5 and IL-13.

Considerable evidence now implicates TSLP in the pathogenesis of several Th2-related inflammatory diseases, including atopic dermatitis and bronchial asthma. We therefore hypothesized that TSLP is over expressed in patients with CRSwNP and TSLP controls the initiation and amplification of Th2-related inflammation in the patients. We initially discovered that TSLP mRNA and TSLP activity were significantly elevated in nasal polyps of patients with CRSwNP. Importantly, levels of TSLP in tissues significantly and positively correlated with levels of Th2 cytokines and markers of eosinophilia. This suggests that TSLP may be a key factor in the amplification of Th2-related inflammation in CRSwNP.

In addition, we have identified a novel metabolic pathway of TSLP in nasal polyps. At least one of the TSLP metabolites demonstrated functional activity on DCs and mast cells. Importantly, this mechanism can occur in humans but not in rodents. These results suggest that human studies are necessary to understand the molecular mechanisms of TSLP-related inflammation in human diseases.

In our proposed project, we will investigate the metabolic mechanisms of TSLP in humans and identify interactions between the different forms of TSLP and the inflammatory cells that express the TSLP receptor. Understanding the functional activity of TSLP and its metabolites, and their interaction with inflammatory cells, could provide key information as to whether TSLP is a novel therapeutic target for not only CRSwNP but also other Th2-related diseases.

PI: Chonghui Cheng, MD, PhD
Assistant Professor in Medicine-Hematology/Oncology

Sponsor: National Cancer Institute

Project: Investigating the mechanisms of CD44s splice isoform in breast cancer metastasis

Tumor metastasis is the major cause of cancer-related death in most types of human cancers including breast cancer. The long-term goal of our research is to better understand molecular mechanisms of alternative splicing underlying breast cancer metastasis, thereby identifying potential therapeutic targets for the treatment of tumor metastasis. In the awarded project we will investigate the mechanisms of a positive feedback loop involving the CD44s splice isoform and Akt activation that is responsible for breast tumor metastasis.

The cell surface molecule CD44 is comprised of a family of proteins that are generated by alternative splicing. Inclusion of different combinations of variable exons generates CD44v. Conversely, exclusion of all of the variable exons produces CD44s. CD44 can be viewed as a sensor for extracellular cues. By forming co-receptor complexes with receptor tyrosine kinases (RTKs) and their growth factors, CD44 augments growth factor-stimulated RTK signaling. Our previous studies showed that CD44v and CD44s act on different signaling cascades: CD44s activates Akt signaling that is critical for promoting cell survival, while CD44v, on the other hand, promotes Ras/MAPK signaling resulting in a cell proliferative state. We recently reported that the CD44s isoform plays an essential role in epithelial-mesenchymal transition (EMT), a developmental process that is abnormally activated in tumor metastasis. We also found that depletion of CD44 by shRNA inhibits breast tumor metastasis

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Sponsored Research

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in animals and that CD44s expression is upregulated in high-grade patient breast tumor specimens. These results suggest a critical role for CD44s in breast cancer metastasis. Mechanistically, we have shown that CD44s potentiates Akt activation and promotes cell survival. We also found that CD44s-dependent Akt signaling upregulates hyaluronic acid synthase 2 (HAS2) expression. Importantly, the HAS2 product, hyaluronic acid (HA), is a ligand that binds to CD44 and facilitates CD44s-mediated Akt activation. These observations led us to hypothesize that a positive feedback loop couples CD44s and Akt signaling, resulting in sustained Akt activation and promoting breast cancer metastasis.

In this award, we will test our hypothesis using biochemical and molecular biology approaches combined with animal models and patient sample analyses. Successfully accomplishing this project will define a novel mechanism of a positive feedback loop that promotes breast tumor metastasis. Intervening this positive feedback loop could offer an exciting new therapeutic approach for the treatment of metastatic breast cancer.

"Gadgets, Widgets, and Apps - Oh My! Clinical Research in the Information Age and Beyond," Feinberg's Fifth Annual Clinical Research Symposium, will take place on Friday, May 16 in the Daniel Hale Williams Auditorium (McGaw Pavilion) from 8 a.m. to noon. The event is sponsored by the Northwestern Advisory Council for Clinical Research.

Presentations include "Using Technology to Foster Health Lifestyle Change," by Bonnie Spring, PhD, and "Use of Technology and Social Media in Conducting Research with LBGT Youth: Challenges, Ethical Considerations, and Opportunities for Innovation," by Brian Mustanski, PhD, and Michael Newcomb, PhD.

The event is free, but registration is required. Learn more.

Funding

Evaluation of AHRQ Initiative to Accelerate the Dissemination and Implementation of PCOR Findings Into Primary Care (R01)

More information

Sponsor: United States Department of Health and Human Services, Agency for Healthcare Research and Quality (AHRQ)

Submission deadline: June 3 (LOI May 23)
Upper Amount: $14 million

Synopsis: AHRQ invites applications to conduct a rigorous external evaluation of an AHRQ grant-funded initiative to disseminate and implement patient-centered outcomes research (PCOR) findings to improve heart health and to improve the capacity of primary care practices to implement PCOR findings into practice.

Advanced Neural Prosthetics Research and Development (U01)

More information

Sponsor: United States Department of Health and Human Services, National Institutes of Health

Submission deadline: June 5
Upper Amount: $5 Million

Synopsis: The purpose of this award is to encourage applications to pursue translational and pilot clinical studies for neural prosthetics. The program will utilize the cooperative agreement mechanism to enable support for milestone-driven projects for the development and demonstration of clinically-useful neural prosthetic devices. Activities supported in this program include implementation of clinical prototype devices, preclinical safety and efficacy testing, design verification and validation activities, pursuit of regulatory approval for clinical study, and proof-of-concept or pilot clinical studies.

View more funding opportunities

High Impact Factor Research

February 2014

Allen NB, **Siddique J, Wilkins JT**, Shay C, Lewis CE, Goff DC, Jacobs DR Jr, **Liu K**, **Lloyd-Jones D**. Blood pressure trajectories in early adulthood and subclinical atherosclerosis in middle age. *JAMA- Journal of the American Medical Association*. 2014 Feb 5;311(5):490-7.

Bhattacharyya S, Yu H, **Mim C**, **Matouschek A**. Regulated protein turnover: snapshots of the proteasome in action. *Nature Reviews Molecular & Cell Biology*. 2014 Feb;15(2):122-33.

Cohen R, Buttke DE, Asano A, Mukai C, Nelson JL, **Ren D**, **Miller RJ**, Cohen-Kutner M, Atlas D, Travis AJ. Lipid modulation of calcium flux through CaV2.3 regulates acrosome exocytosis and fertilization. *Developmental Cell.* 2014 Feb 10;28(3):310-21.

Olanow CW, Kieburtz K, Odin P, Espay AJ, Standaert DG, Fernandez HH, **Vanagunas A**, Othman AA, Widnell KL, Robieson WZ, Pritchett Y, Chatamra K, Benesh J, Lenz RA, Antonini A; LCIG Horizon Study Group. Continuous intrajejunal infusion of levodopa-carbidopa intestinal gel for patients with advanced Parkinson's disease: a randomised, controlled, double-blind, double-dummy study. *Lancet Neurology*. 2014 Feb;13(2):141-9.

Zhao J, **Weng X**, **Bagchi S**, **Wang CR**. Polyclonal type II natural killer T cells require PLZF and SAP for their development and contribute to CpG-mediated antitumor response. *Proceedings of the National Academy of Sciences USA*. 2014 Feb 18;111(7):2674-9.

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."

Welcome New Faculty

Tamara Isakova, MD, joins as assistant professor of Medicine-Nephrology.

She most recently was assistant professor of medicine in the Divison of Nephrology and Hypertension at the University of Miami Miller School of Medicine and a staff nephrologist at Jackson Memorial Health System in Miami. She received her Doctor of Medicine degree from SUNY Downstate Medical Center College of Medicine, and her Master of Medical Sciences Degree in clinical and physiological investigation from Harvard Medical School. She completed her internship and residency in medicine and clinical fellowship in nephrology at Massachusetts General Hospital, where she also completed a research fellowship in nephrology.

Isakova's main research interest is the examination of pathophysiological triggers that initiate mineral metabolism abnormalities in patients with chronic kidney disease.

Ryne Estabrook, PhD, joins as assistant professor of Medical Social Sciences.

Most recently, he served as a postdoctoral fellow in psychiatry at the Virginia Institute for Psychiatric and Behavioral Genetics at Virgina Commonwealth University in Richmond. He earned his master's and doctorate degree in psychology, with a concentration on quantiative psychology, from the University of Virginia, in Charlottesville, where he then became an adjunct professor of psychology.

Estabrook's research focuses on intraindividual variability, lifespan development, and the creation of new statistical methods, including the study of interindividual differences in intraindividual variability, interindividual differences in change and development, alternative approaches to factorial and measurement invariance, and terminal change.

Calendar

Tuesday, April 15

Pathology Department Mayberry Lecture

"Membrane organelles, cytoskeleton, and metabolism in cell organization and function," presented by Jennifer Lippincott-Schwartz, PhD, National Institutes of Health.

Time: 4 to 5 p.m.

Location: Lurie Research Center — Hughes
303 E. Superior St. (Chicago campus)

Contact: kgreen@northwestern.edu
More information

Tuesday, April 22

Lectures in Life Sciences

"Mechanisms responsible for insulin resistance in type 2 diabetes and the metabolic syndrome," presented by Gerald Shulman, MD, PhD, Yale University .

Time: 3 to 4 p.m.

Location: Lurie Research Center — Baldwin
303 E. Superior St. (Chicago campus)

Contact: h-ardehali@northwestern.edu
More information

Tuesday, April 29

Microbiology-Immunology Seminars

"Bacterial adaptations to life in the stomach," presented by Nina Salama, PhD, Fred Hutchinson Research Cancer Center.

Time: Noon to 1 p.m.

Location: Lurie Research Center — Baldwin
303 E. Superior St. (Chicago campus)

Contact: m-mandel@northwestern.edu
More information

More Events
Event organizers are encouraged to submit calendar items on Plan-It Purple for consideration. Please contact the Research Office with further questions.

NIH News

The National Institutes of Health (NIH) has announced the launch of the Big Data to Knowledge (BD2K) initiative. The intiative's mission is to enable biomedical scientists to capitalize more fully on big data being generated by those research communities. "The future of biomedical research depends upon our ability to support a research ecosystem that leverages the flood of biomedical data, strengthens the research workforce through diversity, and attracts the next generation of researchers," said NIH Director Francis Collins MD, PhD. "I'm grateful to the experts, both inside NIH and from the broader biomedical research community, who have given these matters extensive thought and made it possible for NIH to put forward actions designed to benefit our entire research community for years to come."

Dr. Sally Rockey, deputy director of NIH for Extramural Research, posted a blog entry concerning a survey NIH is conducting in association with the National Council of University Research Administrators (NCURA) on postdoc benefits.

Jocelyn Kaiser of *Science* recently reported, "New data show that after remaining more or less steady for a decade, the number of investigators with National Institutes of Health (NIH) funding dropped sharply last year by at least 500 researchers and as many as 1,000. Although not a big surprise—it came the same year that NIH's budget took a five percent cut—the decline suggests that a long-anticipated contraction in the number of labs supported by NIH may have finally begun." The article cited an analysis by Jeremy Berg, PhD, and published by the American Society for Biochemistry and Molecular Biology (ASBMB). A commentary in the *Wall Street Journal,* "How to Reverse the Graying of Scientific Research," by Ronald J. Daniels and Paul Rothman, MD, of Johns Hopkins, also cited the ASBMB analysis.

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