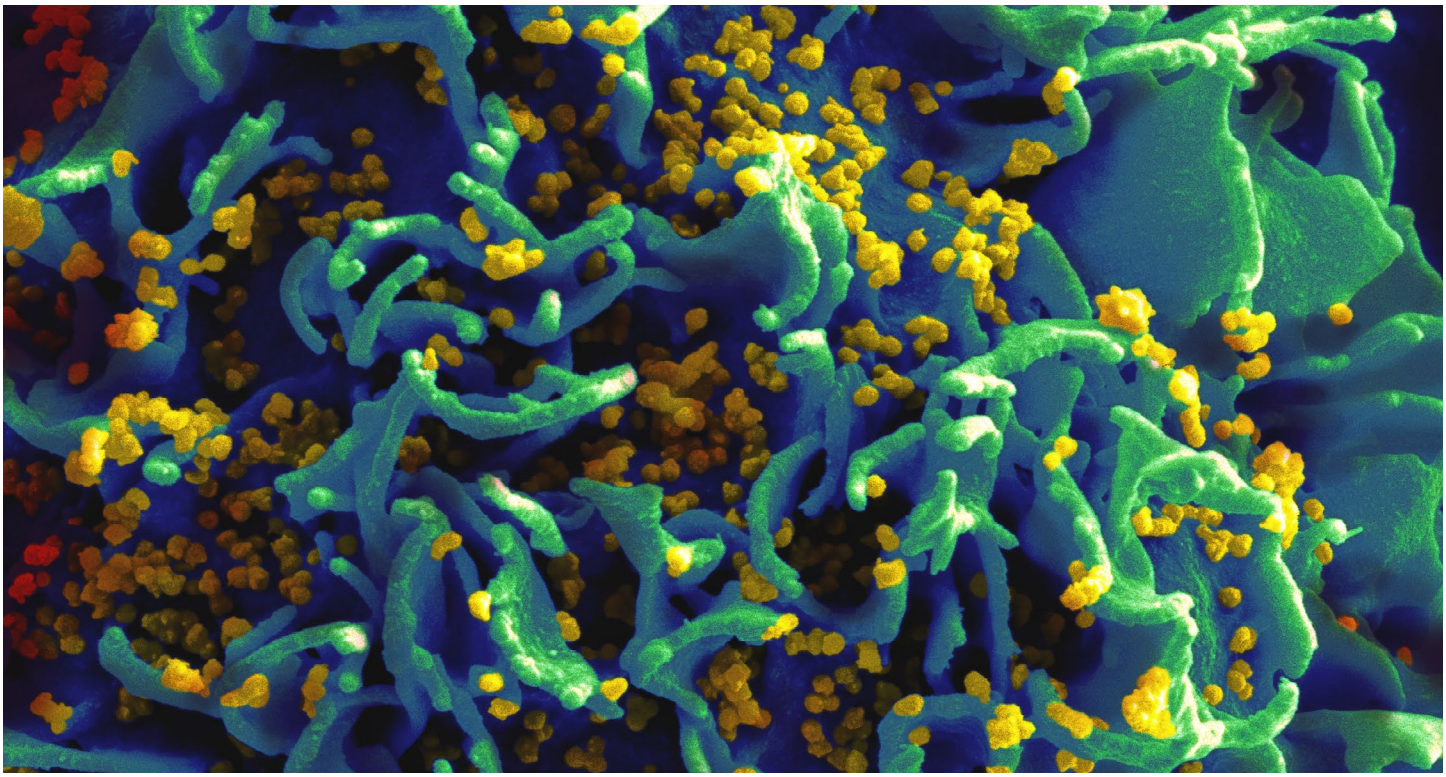
Breakthroughs

Feinberg School of Medicine Research Office

November 2014



Scanning electron micrograph of HIV particles infecting a human T cell. Source: National Institute of Allergy and Infectious Diseases (NIAID)

HIV Research Expands at Feinberg

Scientists at Feinberg are attacking HIV from all sides in an effort to understand, prevent, and cure the virus that affects more than 35 million worldwide.

Richard D'Aquila, MD, professor in Medicine-Infectious Diseases and director of Northwestern University Feinberg School of Medicine's HIV Translational Research Center (HTRC), focuses on finding a cure. His lab is working to develop new treatments to replace lifelong antiretroviral therapy (ART), which stops HIV from spreading within the body and slowly harming immune defenses.

"ART does not cure HIV," emphasizes D'Aquila. "If it's stopped at any time, the HIV infection rebounds within three weeks from a small number of cells where it is dormant in the body."

Currently, patients must faithfully use ART every day for life in order to continue to receive its protection. But there are rare exceptions to this system: Some patients, called "controllers," stay healthy without treatment by spontaneously keeping the virus at low levels, with fewer dormant cells. Scientists at HTRC discovered that these special patients have higher levels of APOBEC3 proteins compared to others.

"Our clinical research is now testing the hypothesis that APOBEC3 defenses decrease soon after HIV is acquired in most people, but not in controllers," said D'Aquila. "If confirmed, the next step will be to try to boost APOBEC3 levels in recently infected subjects who are not controllers to see if that will keep HIV at low levels."

(continued on page 2)

Northwestern Medicine®

HIV Research Expands at Feinberg

(continued from cover page)

These labs are also studying candidate molecules that boost APOBEC3 and target other cellular processes that make HIV dormant in the early months of infection.

Meanwhile, Thomas Hope, PhD, professor in Cell and Molecular Biology and Obstetrics and Gynecology, has concentrated recent research on understanding if and how antibodies and mucus in the female reproductive tract could interact to protect against HIV acquisition.

In October, Hope published a paper showing that the entire female reproductive tract is susceptible to HIV infection, not just the cervix, a finding that broadens the target for HIV prevention strategies.

Earlier this year, Patrick Kiser, PhD, associate professor in Obstetrics and Gynecology and Biomedical Engineering at the McCormick School of Engineering, developed a first-of-its-kind intravaginal ring that protects women from HIV, sexually transmitted disease, and pregnancy for up to three months at a time. The device delivers a common antiretroviral drug called tenofovir and a contraceptive simultaneously.

Promising clinical trials testing the ring with tenofovir are almost done; trials using the ring with both the anti-HIV drug and the contraception will begin soon.

"We continue to make modifications of the rings to improve their design and manufacturing," said Kiser.

All of these efforts by scientists in the Feinberg community have the potential to help patients worldwide. Robert Murphy, MD, '81, '84 GME, director of the Center for Global Health, oversees several research training grants to empower scientists in Africa so they can also contribute to HIV knowledge.

CONTENTS

Northwestern's HIV research team includes, from left to right: Patrick Kiser, PhD; Richard D'Aquila, MD; Brian Mustanski, PhD; and Thomas Hope, PhD. Many other faculty members are working to end HIV.

"We're giving people in affected countries the tools to figure out the best ways to tackle these epidemics from home," said Murphy.

For example, through the Medical Education Partnership Initiative in Nigeria (MEPIN), Murphy and other Feinberg faculty are helping six medical schools modernize their curriculums so that their students can develop needed clinical, translational, and laboratory research skills – including how to apply for international funding to conduct the research.

Back in Chicago, Ram Yogev, MD, '77 GME, and Ellen Chadwick, MD, '82, '85 GME, both professors in Pediatrics-Infectious Diseases, lead the Pediatric HIV Program at Ann & Robert H. Lurie Children's Hospital, which they formed in 1987.

"Our studies have reduced the rate of mother-to-child HIV transmission to less than 2 percent and exponentially lengthened the life expectancy and improved the quality of life for HIV-infected children and adolescents," said Chadwick. She is co-chair of a multinational study investigating whether early intensive treatment of HIV-infected newborns can achieve HIV remission after stopping antiretroviral therapy when patients are two to four years old, through the NIH-funded International Maternal, Pediatric and Adolescent AIDS Clinical Trials (IMPAACT) Network.

Steven Wolinsky, MD, '82 GME, chief of Infectious Diseases, has received more than $37 million in grant funding since 2009 for HIV projects. Among them is the Multicenter AIDS Cohort Study. Feinberg has been one of four clinical research sites throughout the 30-year history of the prospective study, which has tracked thousands of men who report sex with men (MSM) in the United States. Wolinsky's group uses genome sequencing to explore the molecular basis of the disease.

Brian Mustanski, PhD, associate professor in Medical Social Sciences and Psychiatry and Behavioral Sciences, and director

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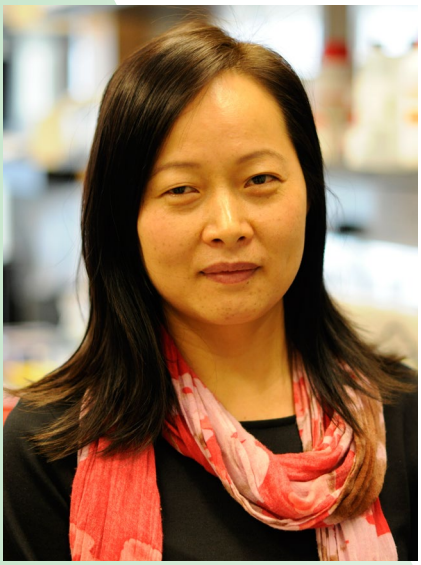
Faculty Profile: Jindan Yu, MD, PhD

Associate Professor of Medicine-Hematology/Oncology



Two challenges scientists face in prostate cancer research are distinguishing indolent from aggressive tumors, and effectively treating late stages of the disease. Jindan Yu, MD, PhD, associate professor of Medicine-Hematology/Oncology, takes on these challenges using genomics and bioinformatics to better understand the progression of prostate cancer and to develop diagnostic tools and treatment strategies.

Since joining Northwestern University Feinberg School of Medicine as an assistant professor in 2009, Yu's lab has published several studies including a recent paper in *Nature Communications*. She found that protein FOXA1 inhibits the function of androgen receptors and is a tumor suppressor under androgen-depleted conditions. Androgens are a group of hormones that play a role in male traits and reproductive activity.

Last year Yu won the Fifth Annual Early Career Professor Award from Agilent Technologies, a laboratory equipment company, for her outstanding potential for future research.

Q&A

What are your research interests?

I am interested in understanding the molecular mechanisms underlying oncogenic progression. In particular, our research focuses on genomic and epigenomic regulations of prostate cancer. We work on how transcription factors, such as FOXA1, alter epigenetic modifications and regulate gene expression. A main emphasis is on how these proteins change the transcriptional program mediated by the androgen receptor, a critical driver of prostate cancer progression.

We utilize high-throughput approaches including next-generation sequencing techniques to map the genomic landscapes of transcription factors, histone modifications, DNA methylation or hydroxymethylation, and RNA methylations, and how these are disturbed by oncogenic factors. We are keen to understand how cancer initiation and progression are regulated at the systems level by examining genome-wide profiles. Through these approaches, we aim to pinpoint the most critical genes and pathways. We then use molecular and biochemical approaches to investigate changes in key signal transduction pathways and use functional assays and mouse models to determine how these perturbations lead to tumorigenesis.

What is the ultimate goal of your research?

Our goal is to identify novel cancer-specific events to understand the underlying molecular mechanisms and to translate these research findings from laboratory to the bedside for patient treatment. Through understanding the genomics and epigenomics of prostate cancer, we pursue translational research to define novel diagnostic/prognostic biomarkers by examining gene expression in primary specimens and determining their associations with clinical outcomes. By characterizing the essential oncogenic pathways of cancer, we investigate novel therapeutics strategies for the treatment of late-stage castration-resistant prostate cancer.

What types of collaborations are you engaged in across campus?

The environment at Feinberg and the Robert H. Lurie Comprehensive Cancer Center has cultivated a number of collaborations. I work closely with investigators of the prostate cancer SPORE program including William Catalona, MD, Timothy Kuzel, MD, Ximing Yang, MD, PhD, Sarki Abdulkadir, MD, PhD, Raymond Bergan, MD, Robin Leikin, PhD, and Chung Lee, PhD. These collaborations have already led to several publications and grants. Very recently, we together submitted a SPORE renewal application along with investigators from the University of Chicago and Northshore Health System.

In addition, there are frequent discussions and collaborations with the labs of the Division of Hematology and Oncology, including Jonathan Licht, MD, John Crispino, PhD, Marcus Peter, PhD, and Chonghui Cheng, MD, PhD, and with other investigators sharing common research interests, such as Debabrata Chakravarti, PhD, and Ann Harris, PhD. We also collaborate with Shad Thaxton, MD, PhD, for nanoparticle delivery of siRNA for prostate cancer treatment. Within the Northwestern environment, there are frequent discussions with many other investigators across campus, and new collaborations are continuously being formed, which are essential for the success of our research program.

(continued on page 4)

Jindan Yu, MD, PhD
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How is your research funded?
Currently, my laboratory is funded by a National Institutes of Health R01 grant to study the role of tumor suppressor gene NOV in prostate cancer. Our research on androgen receptor and transcriptional regulation is supported by a Research Scholar Award from the American Cancer Society. Our epigenetic projects involving DNA methylation/hydroxymethylation and RNA methylation are funded, respectively, by a Department of Defense Idea Development Award and an Exploration-Hypothesis Development Award. My research is also actively supported by the prostate cancer SPORE grant and an Agilent Early Career Professor Award.

Who are your mentors?
I am very fortunate to have had many great mentors over the years. I did postdoctoral training in the laboratory of Arul Chinnaiyan, MD, PhD, at the University of Michigan, where I learned the skills essential for my work today. I am deeply touched by his passion for translational cancer research and am truly inspired by the way Dr. Chinnaiyan does science, manages his team, and interacts with colleagues. He is my role model and life-time mentor.

I was also extremely fortunate to have Jonathan Licht, MD, as my current mentor. I am always amazed by the broad knowledge and seemingly endless energy Dr. Licht has. His high enthusiasm for science is almost contagious to me. We share common interests in genomic and epigenomic research, and discussions with Dr. Licht have always been constructive and inspiring. It is safe to say that I would not be where I am today without these two critical mentors.

HIV Research Expands at Feinberg
(continued from page 2)

of the IMPACT LGBT Health and Development Program, leads a program of translational HIV prevention research focused on the population most at risk for HIV infection: young gay and bisexual men, particularly African Americans.

Mustanski's work includes epidemiological studies on HIV prevalence in this group; longitudinal cohort studies to identify the developmental trajectories of HIV, associated health issues, and biopsychosocial risk and protective factors; plus randomized clinical trials that test new HIV prevention approaches.

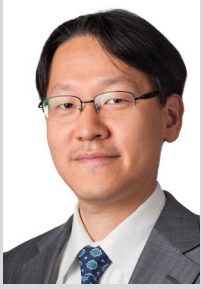
"Many of these prevention approaches use new media and technology, such as online and text messaging technologies," he said.

This year he won an $8.7 million NIH grant for a study to identify and understand the connections between sexually transmitted infections, substance use, and romantic relationship patterns over time among young MSM in Chicago.

With Mustanski, Robert Garofalo, MD, MPH, professor in Pediatrics-Adolescent Medicine and Preventive Medicine, D'Aquila and the HIV Translational Research Center hope to collaborate to bring effective therapies to members of this population.

"The plan is to start pilot clinical trials of the most promising new drug candidates from the HTRC or other laboratories, along with current ART," said D'Aquila. "The ultimate goal is a 'functional cure' after a year or so of treatment, which means that HIV will never rebound off ART."

Welcome New Faculty

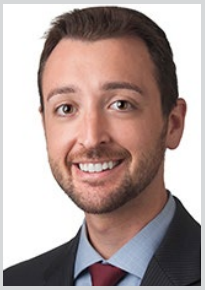


Young Kwang Chae, MD, MPH, MBA, joins as assistant professor of Medicine-Hematology/Oncology.

Chae was most recently a hematology and oncology fellow and clinical specialist in internal medicine at University of Texas M.D. Anderson Cancer Center, in Houston. He earned his Doctor of Medicine degree at Seoul National Academy in South Korea, and master's degrees in public health and business administration from Johns Hopkins University in Baltimore, Maryland.

His research interests are personalized cancer therapy, precision medicine, early phase clinical trials, first-in-human study, novel combination cancer therapy, targeted therapy, immunotherapy, biomarker studies, novel drug development, novel drug delivery systems, adaptive clinical trials design, cell signaling pathways, and immune checkpoint pathways.

Chae has served as author or co-author on more than 30 peer reviewed journal articles.



Stephen A. VanHaerents, MD, joins as instructor of Neurology.

VanHaerents most recently completed a fellowship in neurophysiology/EEG and residency in neurology at Beth Israel Deaconess Medical Center and Harvard Medical School. Prior, he completed an internship in internal medicine at William Beaumont Hospital in Michigan. He earned his Doctor of Medicine degree from Wayne State University School of Medicine in Detroit.

His clinical research interests include neurostimulation, early detection and treatment of non-convulsive status epilepticus, and treatment of refractory epilepsy.

Staff Profile: Peggy Murphy, MLS

Librarian and Communications Manager, Stanley Manne Children's Research Institute

Where are you originally from?

I grew up in New York, first in the Bronx as a young child then in Westchester County until I was 12. My family moved to St. Charles, Illinois where I spent the remainder of my childhood.

What is your educational background?

I completed a double major at Knox College in Galesburg, Illinois. My first major was biology—I was interested in prairie restoration and managing natural areas. Then I fell in love with ceramics and completed an art major. After being in the workforce for nine years, I went to library school at the University of Michigan (U of M), where I was fortunate enough to work in a natural sciences library. The highlight was spending a summer as the librarian at the U of M field station in northern lower Michigan. That was awesome.

Please tell us about your professional background.

After college graduation, I became a lab technician at the University of Chicago. My area of specialization was tissue and cell culture. I moved to Birmingham, Alabama and worked in labs at the University of Alabama at Birmingham, culminating in a position as a laboratory manager in the Division of Radiation Oncology.

Following my MILS (Master of Information and Library Science), I accepted an offer from the University of Illinois at Chicago in the Library of the Health Sciences. Being a new graduate, I learned a great deal. I then came to Children's Memorial Hospital, worked in the Brennemann Library, and transitioned over to the Pritzker Research Library. Other than a brief stint at St. Jude Children's Research Hospital, I have been at Lurie Children's for most of my library career.

Why did you choose to work at the Stanley Manne Children's Research Institute?

It seemed that the position of librarian at the research institute was the perfect mix for someone with my background. I had worked in laboratories, and subsequently helped scientists with their information needs. I felt I could speak the language of science and understand it, and thus be more effective. I also have a strong belief that scientific research in general is a noble pursuit, and I am proud to be involved in it in any capacity.

What is your role within the Institute?

I began as the research librarian, performing literature searches, retrieving articles and books, building the library collection, and setting up systems to serve the information needs of the scientists, staff and students here. About ten years ago, the research institute's president and scientific director, Mary J.C. Hendrix, PhD, asked me to check the references in a grant she was submitting. I sent her back the document with edits of the text. I think she recognized a burgeoning editor, and asked if I would be interested in producing our newsletter, *InTouch*. After that I began managing the Research Institute annual report projects, wrote press releases, and updated news on the website. I am now responsible for the Institute's website, library, and communications.

How do you help scientists at the medical school?

I continue to do literature searches, build the library's collections in our research areas, and train on biomedical literature databases, EndNote and other databases/programs. I answer reference questions; everything from "What are the best journals I should submit my article to?" to "Who are other experts in my field?" to "How do I format citations in my publication?" I help them access journals and databases. I try to alert them to funding opportunities in their areas. In my role as communications manager, I broadcast their research accomplishments, honors and other information of note to the larger community.

What is your favorite part of the job?

Even though it's not my area of expertise, I love working on the website and troubleshooting the content management systems that we use.

What exciting projects are you working on?

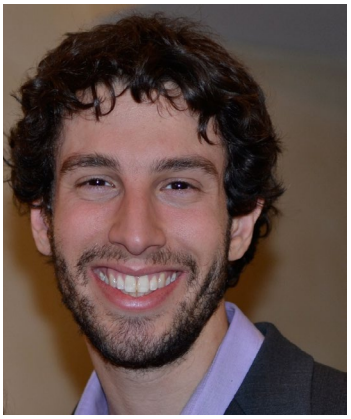
The research institute website will soon be integrated into the Lurie Children's website. It just makes sense in terms of consistency and information flow. I have been tasked with overseeing the project. Our marketing and communications team – Tina Tsinonis and Anne McElherne – has been fabulous about sharing time and expertise to make this transition happen in a logical, comprehensive and thoroughly researched way to deliver a much improved user experience.

What do you like to do in your spare time?

I love to quilt, make functional pottery (such as mugs and bowls), garden, hang out with my very entertaining pets, including my husband, and watch ridiculously stupid movies. Whenever possible, my husband and I take motorcycle trips to the countryside in Illinois, Indiana, Michigan, and Wisconsin. We have a cabin in a very remote area of southern Indiana, where we are visited by an extremely friendly mutt that we have named "Bear" because he looks like a dog-bear.

Student Profile: Josh Glaser

Northwestern University Interdepartmental Neuroscience Program



Josh Glaser, a third-year PhD student in the Northwestern University Interdepartmental Neuroscience Program (NUIN), studies computational methods in neuroscience to understand large data sets in the laboratory of Konrad Kording, PhD, associate professor of Physical Medicine & Rehabilitation and Physiology.

Glaser received his bachelor's degree in physics and mathematics from the University of Illinois–Urbana Champaign. From a young age he was always curious about science, and after his first research experience as an undergraduate student, he knew he wanted to earn a doctorate degree to pursue a career in research.

Q&A

What is your hometown?
I grew up in Skokie, Illinois.

What are your research interests?
It is an extremely exciting time to be involved in neuroscience, as the field is entering an age of "big data," where thousands of neurons are being recorded from simultaneously. My main research interest is applying computational methods to neuroscience in order to understand these large and complex data sets. In particular, I am interested in discovering how large ensembles of neurons encode and transmit information.

The ability to accurately make sense of extremely large data sets will be important to the advancement of our knowledge in all topics of neuroscience and our understanding of neurological disorders.

What exciting projects are you working on?
Through Konrad Kording's lab, I am involved in an exciting collaboration to understand and develop new technologies that could lead to large-scale neural recording. We have been statistically analyzing the capabilities of these technologies, developing algorithms for them, and soon we will start analyzing data.

I am also involved in an exciting collaboration with the lab of Mark Segraves, PhD, associate professor of Neurobiology. In this project, we are aiming to understand the neural basis for how we decide where to look next. There are many visual features that we are more likely to look at, such as very salient objects. We want to know how these features are encoded in the brain.

Why did you choose Northwestern?
As an undergraduate, I participated in a summer internship in neural engineering program at Northwestern. Over that summer, I worked in Konrad Kording's lab and had contact with many other helpful Northwestern professors. I had a very positive experience, which made me want to pursue a neuroscience PhD, and ultimately return to Konrad's lab and Northwestern.

What has been your best experience at Feinberg?
The people, both in my NUIN classes and in my lab. Being surrounded by so many friendly, positive people has probably been the most important factor in making graduate school such an enjoyable experience so far.

How would you describe the faculty at Feinberg?
The faculty have been very friendly and helpful. They are always willing to make time for students.

What do you do in your free time?
I like to spend time with friends and family. I also enjoy outdoor activities and sports, such as biking, hiking, kayaking, soccer, and basketball.

What are your plans for after graduation?
I plan to stay in academia and do a postdoc. I hope to continue doing research that applies quantitative methods to neuroscience.

Contractor Named New NUIN Director

Anis Contractor, PhD, associate professor of Physiology, has been named director of graduate studies for the Northwestern University Interdepartmental Neuroscience (NUIN) graduate program. Leadership of the program changes every three years. Dave McLean, PhD, assistant professor of Neurobiology, has been named associate director and Sally McIver will remain assistant director.

NUIN is comprised of 159 faculty members spread over 18 departments on both campuses. More than 150 students are enrolled in the PhD program.

Research in the News

***US News & World Report* October 30**
Eczema tied to bone fracture risk in study
Jonathan Silverberg's research was featured.

***The New York Times* October 29**
This is your brain on drugs
Hans Breiter's research was featured.

***USA Today* October 24**
Some worry doctors will stop helping Ebola patients
Robert Murphy was quoted.

- Murphy was also quoted this month in *Chicago Tribune, New York Daily News, Boston Herald, Arizona Sun, Modern Healthcare, Education Week,* Yahoo! News, and on FOX Chicago, ABC Chicago, CBS Chicago, WGN Radio, the NPR Blog, and more.

***Chicago Tribune* October 24**
2011 ALS 'breakthrough' recirculates hope on social media
Teepu Siddique's research was featured.

***TIME Magazine* October 23**
6 medical breakthroughs that matter
Seema Khan's research was featured.

***Chicago Tribune* October 20**
3D-printed hearts, iPad mini tablets and surgery inside tiny ears
Kathy Barsness' research was featured.

CNN (National) October 19
U.S. public 'very worried' about Ebola
Mark Reinecke was quoted.

***The New York Times* October 16**
Treating depression before it becomes postpartum
Katherine Wisner was quoted.

Huffington Post October 16
Eczema: Studies for new treatment
Amy Paller's research was featured.

***US News & World Report* October 14**
Could a blood test one day detect depression?
Eva Redei's research was featured.

***New York Magazine* October 7**
Ebola fears are triggering mass hypochondria
Catherine Belling was quoted.

More media coverage available online.

Northwestern University
NUCATS
Clinical and Translational Sciences Institute

NUCATS Corner

NUCATS Offers Linkage to Evanston Computing via Weekly Office Hours

Northwestern University Information Technology (NUIT) provides advanced computing, visualization, storage, network, and grid resources to University researchers. Due to distance, it has sometimes been difficult for potential clients on the Chicago campus to link to these services located on the Evanston campus, but that is no longer the case.

NUIT Research Computing is now hosting drop-in office hours every Thursday from 10 a.m. to Noon at the NUCATS Institute to help Northwestern faculty, staff, and students understand the available tools and how they can benefit from them. They can provide advice on the development, porting, debugging, or optimization of applications, assist in the development of visualization content and tools, aid in determining technical specifications and budgeting for research grant proposals, and much more.

Regardless of your data size or discipline, NUIT supports a wide spectrum of data from social sciences and humanities, to biomedical and life sciences. Their services can mitigate risk, free up your time and help you rethink how to do data analysis in a meaningful way.

Users of Quest, a large-scale shared high performance computing system, and those interested in learning more are encouraged to schedule a consultation with a NUIT research computing consultant at the NUCATS Institute today.

Sponsored Research

PI: Karen Ridge, PhD
Associate Professor of Medicine-Pulmonary and Cell and Molecular Biology

Sponsor: National Heart, Lung, and Blood Institute

Title: "Role of Vimentin in Influenza A-Induced Acute Lung Injury"

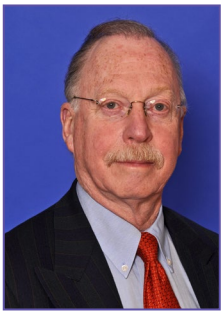
Influenza A virus is a highly contagious virus that causes upper and lower respiratory tract infections resulting in 200,000 hospitalizations and 36,000 deaths in the United States annually, and new influenza strains generate recurring epidemics and pandemics with significant attributable morbidity and mortality.

Most of the mortality associated with influenza A infection is attributable to development of the acute respiratory distress syndrome (ARDS). Acute lung injury (ALI) and ARDS are defined by damage to the alveolar epithelium and endothelium, which allows the exudation of protein-rich fluid into the alveolar space.

In preliminary data, Ridge and colleagues show that vimentin, a type III intermediate filament protein, is required for the activation of the NLRP3 inflammasome. The group provided preliminary data that vimentin-/- mice are protected from lung viral pneumonia following infection with influenza A virus (IAV). Increasing evidence from Ridge's group and others suggests that these filamentous cytoskeleton structures play key roles in signal transduction pathways and provide a scaffold for the formation and activation of protein complexes, such as the NRLP3 inflammasome. Ridge shows that NLRP3 interacts with vimentin and that this protein-protein interaction is required for the processing and maturation of pro-IL- 1[unreadable] into biologically active IL 1[unreadable]. Additionally, they provide preliminary data showing that vimentin is required for the interaction and translocation of NOD2 to the outer mitochondrial membrane, which results in the NOD2-mediated activation of IRF3 and release of interferon- from the IAV- infected cells.

Based on these preliminary data, Ridge hypothesizes that vimentin acts as scaffold for the assembly and activation of the NLRP3 inflammasome, and that NOD2 protein interaction with vimentin is required for the activation of IRF3 signaling. Her group has formulated three interrelated specific aims to study the regulation of vimentin intermediate filaments in both in vivo and in vitro models of influenza A-induced lung injury:

The first aim is to determine the mechanism by which vimentin contributes to activation of NLR proteins during influenza A virus-induced acute lung injury. The second is to define the protein domain(s) in vimentin required for interaction with and activation of the NLRP3 inflammasome. The third is to determine whether the interaction between vimentin and NOD2 is required for the activation of IRF3 and the release of interferon from the IAV-infected cells.



PI: Robert Lavker, PhD
Jack W. Graffin, MD, Research Professor and Professor of Dermatology

Sponsor: National Eye Institute

Title: "The Role of MicroRNAs in Corneal Epithelial Homeostasis"

The anterior surface of the eye functions as a barrier to the external environment and protects the delicate underlying structures from injury, in part, through the elaboration of the limbal and corneal epithelia. As self-renewing tissues, these epithelia are governed by stem cells, which play a crucial role in tissue homeostasis, regeneration, transplantation, gene therapy, and in the pathogenesis of several anterior ocular surface diseases.

Equally important for proper vision is the need for corneal transparency, which is achieved through avascularity. It is well-accepted that the limbal epithelium is the site f the corneal epithelial stem cells; however, major questions remain unresolved concerning how the limbal epithelium is regulated. Likewise, the understanding of factors that control angiogenesis is incomplete.

microRNAS (miRNAs) are a major class of regulatory molecules that are part of the RNAi silencing machinery. While some studies have been directed towards deciphering the roles of miRNAs in the corneal epithelium, little is known about the miRNA signature in the stem cell-enriched limbal epithelium.

Lavker's team recently discovered that miRs-103/107 are limbal-preferred. Furthermore, they have evidence that miRs-103/107 function to insure proper limbal epithelial cell-cell contact, autophagy and impact on cell cycle quiescence. Until recently, it was believed that miR-184, the most abundant corneal epithelial miRNA, functioned to attenuate miR-205, which insured proper cell migration and cell survival. Evidence now exists that miR-184 may directly prevent corneal epithelial angiogenesis.

Proper vision requires both a stabile limbal epithelial and corneal clarity; therefore Lavker has proposed to focus on the

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Sponsored Research

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roles of miRs-103/107 in assuring the integrity of the limbal epithelium, and how miR-184 functions to maintain corneal avascularity.

To accomplish these goals, Lavker and colleagues will capitalize on the ability to elucidate miRNA target proteins and modulate miRNA and target protein levels in submerged cultures of human limbal and corneal epithelial keratinocytes and human microvascular endothelial cells. They will manipulate these cultured cells to form either 3-D organotypic rafts, or endothelial tubes, which mimic the in vivo tissues. They will assess the functional consequences of such miRNA and protein modulations with a combination of biochemical, molecular biological, cell biological, and physiological approaches.

By focusing on the biology of these miRNAs and their target proteins, the proposal represents a novel approach to understand how the limbal epithelium is regulated and what contributes to the maintenance of corneal avascularity. Such knowledge has relevance to stem cell biology and clinically to ex vivo corneal epithelial transplantation. This proposal also has clinical implications beyond just corneal avascularity and may impact pathological retinal angiogenesis. Ultimately these studies will provide rationales for the development of innovative treatment regimens focused on the use of either inhibitors of specific miRNAs or their targets, or delivery of miRNAs in patients with diseases that affect the ocular anterior segmental epithelia.

IRB Brown Bag: Chicago Campus

Join Northwestern University's Institutional Review Board (IRB) for a brown bag session on the Chicago campus titled, "New Electronic IRB Submission Process." The session takes place from Noon to 1 p.m. on Wednesday, November 19, in the Robert H. Lurie Medical Research Center's Baldwin Auditorium. It is free and open to all faculty, staff, and students.

In addition to the brown bag, IRB mainatains Chicago campus drop-in office hours in two locations. The locations are at the IRB office in Rubloff (420 E. Superior St.), room 730, on the second Tuesday of each month from 1 to 3 p.m., and at the Rehabilitation Institute of Chicago (345 E. Superior St.), room 1429, on the first and third Wednesday of every month. An office hours calendar is available online.

Funding

NIDDK Program Projects (P01)

More information

Sponsor: Department of Health and Human Sciences, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)

Submission deadline: January 25 (January 7 for AIDS)
Upper Amount: $6.25 million

Synopsis: New biologic knowledge will come from both sole investigators following their vision and from teams of scientists sharing their expertise. Some complex biomedical problems require a multidisciplinary vantage point to discover an innovative solution. The P01 program project award supports research that has multiple distinct but synergistic projects built around a unifying central theme relevant to the NIDDK. The proposed programs should address scientific areas relevant to the NIDDK mission including diabetes, endocrine and metabolic diseases, digestive diseases and nutrition, and kidney, urologic and hematologic diseases, as well as new approaches to prevent, treat and cure these diseases, including clinical research.

Research to Action: Assessing and Addressing Community Exposures to Environmental Contaminants (R01)

More information

Sponsor: Department of Health and Human Sciences (HHS), National Institutes of Health (NIH)

Submission deadline: February 5
Upper Amount: $2.5 million

Synopsis: This opportunity encourages applications using community-engaged research methods to investigate the potential health risks of environmental exposures of concern to the community and to implement an environmental public health action plan based on research findings. The overall goal is to support changes to prevent or reduce exposure to harmful environmental exposures and improve the health of a community.

View more funding opportunities

High Impact Factor Research

September 2014

Adair JE, Johnston SK, Mrugala MM, Beard BC, **Guyman LA**, **Baldock AL**, **Bridge CA**, **Hawkins-Daarud A**, Gori JL, Born DE, Gonzalez-Cuyar LF, Silbergeld DL, **Rockne RC**, Storer BE, Rockhill JK, **Swanson KR**, Kiem HP. Gene therapy enhances chemotherapy tolerance and efficacy in glioblastoma patients. *Journal of Clinical Investigation*. 2014 Sep 2;124(9):4082-92.

Bruns AM, Leser GP, **Lamb RA**, **Horvath CM**. The Innate Immune Sensor LGP2 Activates Antiviral Signaling by Regulating MDA5-RNA Interaction and Filament Assembly. *Molecular Cell*. 2014 Sep 4;55(5):771-81.

Feng H, Lopez GY, **Kim CK**, **Alvarez A**, Duncan CG, Nishikawa R, Nagane M, Su AJ, Auron PE, Hedberg ML, Wang L, **Raizer JJ, Kessler JA**, **Parsa AT**, Gao WQ, Kim SH, Minata M, Nakano I, Grandis JR, McLendon RE, Bigner DD, Lin HK, Furnari FB, Cavenee WK, **Hu B**, Yan H, **Cheng SY**. EGFR phosphorylation of DCBLD2 recruits TRAF6 and stimulates AKT-promoted tumorigenesis. *Journal of Clinical Investigation*. 2014 Sep 2;124(9):3741-56. doi: 10.1172/JCI73093.

Fizazi K, Scher HI, Miller K, Basch E, Sternberg CN, **Cella D**, Forer D, Hirmand M, de Bono JS. Effect of enzalutamide on time to first skeletal-related event, pain, and quality of life in men with castration-resistant prostate cancer: results from the randomised, phase 3 AFFIRM trial. *Lancet Oncology*. 2014 Sep;15(10):1147-56.

Kushner RF, Ryan DH. Assessment and lifestyle management of patients with obesity: clinical recommendations from systematic reviews. *JAMA-Journal of the American Medical Association*. 2014 Sep 3;312(9):943-52.

Stefka AT, Feehley T, Tripathi P, **Qiu J**, McCoy K, Mazmanian SK, Tjota MY, Seo GY, Cao S, Theriault BR, Antonopoulos DA, **Zhou L**, Chang EB, Fu YX, Nagler CR. Commensal bacteria protect against food allergen sensitization. *Proceedings of the National Academy of Sciences U S A*. 2014 Sep 9;111(36):13145-50.

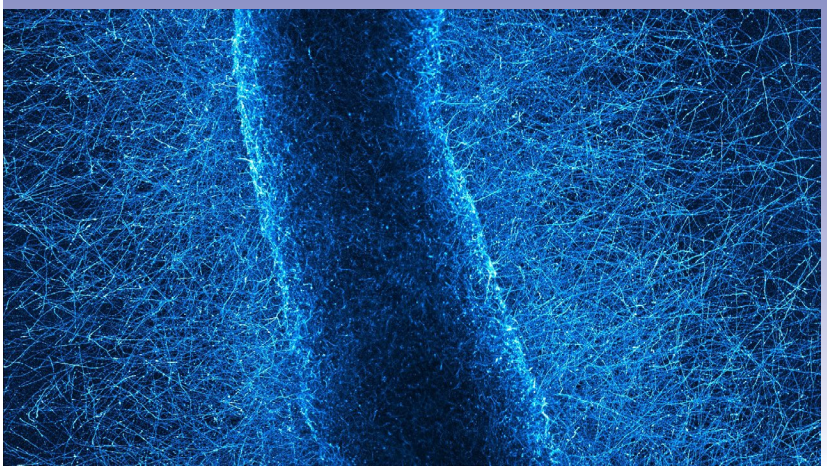
Tell RW, **Horvath CM**. Bioinformatic analysis reveals a pattern of STAT3-associated gene expression specific to basal-like breast cancers in human tumors. *Proceedings of the National Academy of Sciences U S A*. 2014 Sep 2;111(35):12787-92.

Wang DH, Tiwari A, Kim ME, Clemons NJ, Regmi NL, Hodges WA, Berman DM, Montgomery EA, Watkins DN, Zhang X, Zhang Q, **Jie C,** Spechler SJ, Souza RF. Hedgehog signaling regulates FOXA2 in esophageal embryogenesis and Barrett's metaplasia. *Journal of Clinical Investigation*. 2014 Sep 2;124(9):3767-80.

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."

Scientific Images Contest Winners



"Neurons in Nanofiber Gel," by Simpson Querrey Institute for BioNanotechnology postdoctoral fellow Shantanu Sur, won second place in Northwestern University's Science in Society 2014 Scientific Images Contest.

In this image, the neurons from a mouse embryo have been encapsulated in a nanofiber matrix (vertical cylinder), and then allowed to grow embedded in a block of collagen gel. After a few days of culture, these neurons (blue lines) grew out of the nanofiber matrix into the surrounding collagen gel.

See all the contest winners on the Science and Society Facebook page.

Calendar

Wednesday, November 12

Lurie Cancer Center Grand Rounds

"Bone Marrow Matrix Enivronment: Regulation of Platelet Production in Physiologic and Pathologic Conditions," by Alessandra Balduini, MD, Tufts University.

Time: Noon to 1 p.m.
Location: Lurie Medical Research Building — Searle
303 E. Superior St. (Chicago campus)
Contact: cancer@northwestern.edu
More information

Tuesday, November 18

Early Stage Drug Discovery Workshop

Presented by Northwestern's Center for Molecular Innovation and Drug Discovery. Registration required.

Time: 9:30 to 11:30 a.m.
Location: Lurie Medical Research Building — Searle
303 E. Superior St. (Chicago campus)
Contact: t-fraterrigo@northwestern.edu
More information

Tuesday, November 18

Manus Krauff, MD, Lecture

"Epigenetic Mechanisms of Stem Cell Aging and Rejuvenation," by Thomas A. Rando, MD, PhD, Stanford University School of Medicine and Palo Alto VA Medical Center.

Time: 4 to 7 p.m.
Location: Lurie Medical Research Building — Hughes
303 E. Superior St. (Chicago campus)
Contact: angela.mccoy@northwestern.edu
More information

Thursday, November 20

Endocrine Grand Rounds

"Metabolic Regulation by Post-Translational Protein Modifications and Sirtuins," by Matthew Hirschey, PhD, Duke University.

Time: 4 to 5 p.m.
Location: Lurie Medical Research Building — Searle
303 E. Superior St. (Chicago campus)
Contact: billy.phillips@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

Early Independence Awards

The 2015 National Institutes of Health (NIH) Director's Early Independence Awards have been announced. This initiative allows exceptional junior scientists to accelerate their transition to an independent research career by effectively skipping the traditional postdoctoral training. Letters of intent are due by December 30, and applications are due by January 30, 2015. Full details, including who qualifies and how to apply, are available on the NIH website.

Type 5 Progress Reports Reminder

As of October 17, NIH requires grantees to submit all type five progress reports using the Research Performance Progress Report (RPPR) module in eRA Commons. Annual progress reports submitted in any format other than the RPPR will not be processed by the NIH and will require resubmission through the RPPR. For additional information and links to related announcements and resources, visit NIH Guide Notice NOT-OD-15-014.

NIH Operates Under a Continuing Resolution

The Department of Health and Human Services, including NIH, operates under the Continuing Appropriations Act, 2015 (H.J.Res. 124) signed by President Obama on September 19. This act continues government operations through December 11 at 99.9 percent of the FY 2014 enacted level.

New Informational NIH YouTube Videos

NIH has continued to uploaded informational videos to YouTube:

"Systems Science at NIH," presented by Patricia Mabry, OBSSR and David Clark, NIDCR.

"ASSIST Overview," a high-level overview for using ASSIST to submit multi-project applications to NIH.

"NIH e-Sub Top 10," ten simple tips to avoid common errors and successfully submit electronic grant applications to NIH.

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