Breakthroughs

Feinberg School of Medicine Research Office

March 2014

"The flu fights every effort we make, mutating to survive in the face of our efforts to keep people alive," says Michael Ison, MD. Illustration: Influenza virus.

Scientists Working to Uncover, Combat Flu's Deadly Secrets

As deadly variants of avian flu emerge in Shanghai, scientists in Chicago are preparing for what could become the world's next pandemic.

"By early February, there were more cases of novel influenza strain H7N9 (avian flu) in the world's largest city than last year, when it was first discovered in humans," said Michael Ison, MD, associate professor of Medicine-Infectious Diseases and Surgery-Organ Transplantation. "It's a concerning situation because once there's evidence that it can spread from person to person, the potential for pandemic increases dramatically."

As co-chair of the antiviral section of a forthcoming revision to the Infectious Disease Society of America's (IDSA) treatment guidelines for influenza, Ison is helping create the nation's future plan of defense.

"Antivirals are the cornerstone of treatment," said Ison, a member of the Comprehensive Transplant Center. "We don't know when the seasonal virus might develop resistance to Tamiflu and Relenza, but we do know that we don't currently have any other approved treatment regimens."

Created in the months before the 2009 H1N1 "swine flu" pandemic, the IDSA guidelines are an evidence-based set of recommendations, assembled with contributions from many sources, including the IIDSA, Centers for Disease Control and Prevention (CDC) and the American Academy of Pediatrics.

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Uncovering Flu's Deadly Secrets

(continued from cover page)

"Because of the '09 pandemic, there was a new and significant body of knowledge that was recognized as vital to our future plans," Ison said. "In this edition, we've prepared specific guidance for any future pandemic outbreak, and are working to address a host of considerations that we didn't tackle previously."

The 2015 IDSA guidelines will rely on scientific investigation and expert opinion where data is limited.

"As we learn more about how the virus works and causes disease in humans, we may be able to modulate the course of illness in individual patients," Ison said. "As a physician-scientist, the overall goal remains to minimize the impact of the flu by keeping people alive and allowing them to do what they want to be doing."

New Treatments

Ison is also working to create new therapeutic options. He was lead investigator of the phase II and one of two lead investigators of current phase III studies of Peramivir, a drug currently being evaluated by the Food and Drug Administration (FDA) for approval.

Peramivir was used prior to FDA approval in 2009 as part of the nation's Emergency Use Authorization plan because it can be delivered to individuals too sick to ingest oral or inhaled medication. As potentially the first FDA-approved intravenous treatment option to fight influenza, the drug could play a large role in future flu outbreaks.

Ison recently published a study in *Antiviral Therapy* that demonstrated daily use of Peramivir was associated with clinical improvement during the pandemic.

Ison is also part of a collaborative project investigating the management of influenza over a range of clinical severity, from otherwise healthy adults, to patients at risk of severe influenza and those hospitalized with severe influenza. The studies are supported by the National Institutes of Health.

"These studies were designed not only to investigate novel antiviral strategies, namely plasma and antiviral combinations, but also to investigate the effect of various therapies on quantitative virology," Ison said. "With this data, we hope to advocate for quantitative virology to become an acceptable endpoint for studies of immunocompromised patients and those with severe influenza, where clinical endpoints have proven unreliable."

Michael Ison, MD, associate professor of Medicine-Infectious Diseases and Surgery-Organ Transplantation, is the protocol co-chair of an NIAID-funded study evaluating effectiveness of newly designed antiviral therapies.

New Connections

While Ison's research focuses on immunocompromised and hospitalized individuals, Kathryn Radigan, MD, instructor of Medicine-Pulmonary and Critical Care, explores the relationship between obesity and influenza survival.

Using an early career investigator award from the American Thoracic Society Foundation, Radigan is incorporating sophisticated genetic models to help answer mechanistic questions with respect to leptin signaling.

Leptin is a hormone made by fat tissue that acts on the brain to regulate appetite and body weight. Radigan's preliminary experiments have shown a link between a deficiency of the hormone and obesity. She also found evidence in preclinical animal models that such a deficiency may impair viral clearance and worsen lung injury following influenza infection.

"Patients with obesity experienced significant mortality during 2009's H1N1 outbreak," Radigan said. "These studies may identify novel targets for therapeutic drug development in influenza A-infected patients."

Influenza A has most recently been associated with avian and swine flu. According to the CDC, the vast majority of 2013-14 flu cases involve H1N1, and nearly half of all adults hospitalized with influenza were obese.

Radigan is also investigating ways to develop a better mouse model of influenza.

"We know that the route of inoculation is critical in designing mouse models to study influenza infection in humans," Radigan said. "We have definitive data showing intratracheal inoculation of influenza virus is a more reliable method of administration of the virus compared to intranasal inoculation. This may help scientists develop more accurate mouse models in the future."

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2014 Dixon Translational Research Grants Announced

Northwestern Memorial Foundation and the Northwestern University Clinical and Translational Sciences (NUCATS) Institute recently announced the 2014 Dixon Translational Research Grant awardees in the Innovation and Young Investigator Award categories. The Dixon Translational Research Grants are awarded to Northwestern investigators for highly innovative, multi-disciplinary clinical and translational research collaborations that accelerate the identification and implementation of new treatments to improve human health.

Young Investigator Awards

William Funk, PhD, assistant professor of Preventive Medicine-Cancer Epidemiology and Prevention, will research the use of adductomics for identifying early detection biomarkers for ovarian cancer.

Sarika Jain, MD, assistant professor of Medicine- Hematology and Oncology, will investigate intratumoral injection of clostridium novyi-NT spores in advanced breast cancer.

Matthew Maas, MD, assistant professor of Neurology and Anesthesiology, aims to test the hypothesis that circadian dysfunction is associated with poor neurologic outcomes, thus establishing a physiologic mechanism for the harm seen in conjunction with delirium and a potential target of novel therapies.

Raja Mutharasan, MD, assistant professor of Medicine- Cardiology, has invented a new gold nanotechnology-based test called the AuraChol test to improve cardiovascular risk assessment. The AuraChol test will be compared to the laboratory standard test, the cellular reverse cholesterol transport assay.

Amisha Wallia, MD, MS, instructor of Medicine- Endocrinology and in the Institute for Public Health and Medicine (IPHAM), will evaluate glucose control following islet cell transplant.

Innovation Awards

Timothy Carrol, PhD, professor of Radiology and in the McCormick School of Engineering, will study imaging of cerebral oxygen extraction fraction (OEF) in patients who have had a stroke or symptoms related to the narrowing of blood vessels in the brain.

Brian Layden, MD, PhD, assistant professor of Medicine- Endocrinology, will explore a novel Type 2 diabetes treatment biased agonists for free fatty acid receptor 2 (FFAR2).

Kristin Swanson, PhD, professor of Neurological Surgery and in the McCormick School of Engineering, will study patient-specific mathematical modeling of pediatric high-grade gliomas.

Jason Wertheim, MD, PhD, assistant professor of Surgery- Organ Transplantation and in the McCormick School of Engineering, will investigate the development of a small caliber vascular graft using a tissue engineering strategy.

More information about the awardees and their projects is available on the NUCATS website.

Research Day: Save the Date

The 10th annual Lewis Landsberg Research Day takes place Thursday, April 3, from 1 to 5 p.m. in the Robert H. Lurie Medical Research Building's John Hughes Auditorium and in Northwestern Memorial Hospital's 3rd Floor Conference Center in the Feinberg Pavilion.

This year's event will feature keynote speaker William Pao, MD, PhD, professor of Medicine, Cancer, Biology, and Pathology and director of the Division of Hematology/Oncology at Vanderbilt University, and director of personalized cancer medicine at Vanderbilt-Ingram Cancer Center.

The keynote program will begin at 1 p.m., and will also feature Feinberg's Mentor of the Year Awards and the Tripartite Award. The poster session will begin at 2:15 p.m., and poster awards will be presented at 4:15 p.m. Visit the Research Day website for a complete listing of events and locations.

Faculty Profile: Elizabeth Eklund, MD

Professor of Medicine– Hematology and Oncology

Elizabeth Eklund, MD, professor of Medicine- Hematology and Oncology, and her team discovered a potentially new approach to treating Fanconi anemia, a rare bone marrow disorder. Recently published in the *Journal of Clinical Investigation*, the study showed that current solutions to treat infections in these patients may accelerate bone marrow failure and leukemia.

"This study suggests that protecting Fanconi anemia patients from repeated infections might delay bone marrow failure or progression to leukemia," says Eklund, also a member of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University. "Currently, these patients are given bone marrow stimulating growth factors when they develop infection. Our data suggests that these growth factors may be a part of the problem."

Q&A

What are your research interests?

My main research interest is to understand how uncommitted stem cells in bone marrow become fully functional infection-fighting white blood cells. This process, which is referred to as myelopoiesis, is driven by growth factor signaling and gene regulation events that must be completed correctly, or bone marrow failure or leukemia may result.

I have been especially interested in identifying key processes that control cell division, program cell death, and acquire functional competence during myelopoiesis. These events tend to be strictly regulated and relevant to a switch from normal to leukemic blood cell development.

What is the ultimate goal of your research?

The goal of my research is to use our studies of the molecular mechanisms of myelopoiesis to develop novel translational approaches to leukemia. This is greatly facilitated by the opportunity to collaborate with other scientists here at Northwestern University, including leukemia researchers, individuals in high throughput screening and drug discovery, and translational clinical investigators. This multi-disciplinary approach is necessary to take observations from basic biology into patient care.

How did you become interested in this area of research?

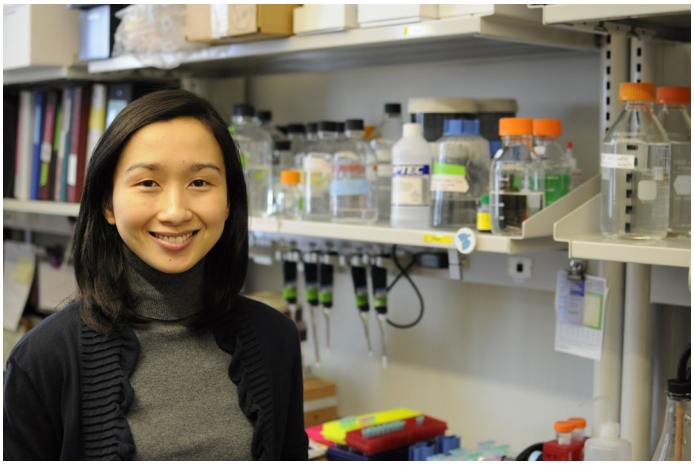
I became interested in the process whereby uncommitted stem cells become mature cells with a highly specific function as an undergraduate. Specifically, I took courses as part of the honors track in biological sciences at University of Illinois at Champaign-Urbana that emphasized the biochemistry and molecular biology of developmental processes. Later, as a fellow in Hematology/Oncology at Indiana University, I was able to see how these basic questions and scientific approaches were highly applicable to the leukemia problem.

How is your research funded?

My research has been funded by the National Institutes of Health (NIH) and the U.S. Department of Veteran Affairs (VA). I was fortunate to be awarded NIH career development grants early in my career; this enabled me to develop a program that obtained R01 support. I also had the opportunity to obtain funding through the VA. This source of support has provided a clinical connection for my research through the years. I have benefited from the Translational Research Program through the Leukemia and Lymphoma Society. These awards are specifically designed to transition from a basic laboratory observation to a clinical trial. I recently obtained support for a completely new area of investigation through the Fanconi Anemia Research Fund. This grant has opened up a whole new area of investigations and collaborations relevant to bone marrow failure, immune deficiency, and leukemia.

Student Profile: Kamonwan "Pear" Fish

Driskill Graduate Training Program in Life Sciences



Kamonwan "Pear" Fish, a native of Thailand, graduated from Chulalongkorn University in 2006 with a degree in veterinary sciences. She soon discovered that clinical practice was not what she enjoyed most. Upon immigrating to the U.S., she tried different career paths, including pharmacy, but ultimately decided that research is her passion, and applied to Northwestern University's dual-degree PhD and MPH program.

Q&A

Where are you originally from?
I grew up in a small town in the Northeastern part of Thailand.

What is your educational and professional background?
After finishing high school, I went to a veterinary school in Bangkok. (Thailand adopts the British higher education system, whereby high school graduates enroll directly in professional degree programs without going through bachelor's degree programs).

After awhile, I learned that clinical practice is just not quite what I wanted to do. After finishing veterinary school, I immigrated to the U.S. and got my first job in a Pharmacy department at the University of Wisconsin-Madison Hospital. It was a good first job experience to adapt myself in American culture, but I felt I needed something more challenging.

Someone I knew back home told me that my alma mater received contract funding from the U.S. to investigate avian influenza outbreaks in Thailand. I did a summer research project back in Thailand, and become convinced that I do really like research. I went to veterinary school when I was 17 and decided to pursue a research career when I was 26. It took me a long time to figure it out.

Why did you choose Northwestern?
The PhD-MPH dual degree program is a very unique opportunity, a good combination of degrees. I chose Northwestern specifically because of it.

What are your research interests?
The Epstein-Barr virus (EBV) has been associated with certain cancers, but the mechanisms of how the virus causes tumor growth is not yet understood. I study how a specific viral protein from EBV can disrupt cell function and speed up tumor growth.

EBV produces several proteins during infection, and the combination of these viral products promotes replication of infected cells. In healthy individuals, the immune system can prevent uncontrolled cell replication caused by EBV. When people have compromised immune systems, such as patients infected with HIV or transplant patients who undergo immunosuppressive therapy, they lose the ability to regulate the expression of EBV products and develop cancers with greater incidence than in healthy people. In certain types of cancers, EBV and the activation of oncogenes together drive cancer development.

The viral protein I am studying is interesting because the protein by itself doesn't cause much of a problem to the cells. But when there is an increased activity of oncogene (a gene that causes cancer), they are like partners in crime, together creating very fast tumor growth.

What do you hope to do in the future?
Moving forward, I would like to understand how this protein helps degrade a tumor suppressor. We think that the viral protein causes rapid cell proliferation because it promotes the degradation of this tumor suppressor. I hope to figure out how to target this protein in EBV-associated cancer.

If we could inhibit or intercept how the virus disrupts the cell physiology, then we would be able to find some novel target that could specifically treat EBV-associated malignancies or cancers.

What do you like to do in your free time?
I like to try out different restaurants in Chicago area. I like few Thai restaurants in Chicago, but the most authentic Thai place (in my opinion) is near Western Brown line station called Rosded.

I also follow European soccer. I hope I can go to see the World Cup final one day.

Staff Profile: Rosa Pico

Division Administrator 3, Feinberg Cardiovascular Research Institute

Where are you originally from?
I was originally born in Guadalajara, Jalisco, Mexico, but came to Chicago as an infant. So I would say that I consider my hometown to be the Windy City.

What is your educational background?
Believe it or not, I originally wanted to teach middle school students English literature. So I ventured into the wonderful world of the middle school classroom. It was an experience of great joy and compassion, but after receiving my bachelor's degree, I realized that teaching was not for me. I wanted to focus on administration and finance. That in turn led me to pursue my master's degree from the University of Illinois.

Please tell us about your professional background.
I started my professional career at the University of Illinois working for the Jane Addams College of Social Work. After two years there, I transitioned into a business administrator role for The Department of Disability and Human Development's Center on Health Promotion (CHP). I spent seven years at CHP and finally decided I was ready for a change. This was back in 2007, and it was in 2007 that I joined Northwestern.

Why did you choose to work at Northwestern?
It was the prestige of Northwestern that led me to apply for a position here. I was excited to join the ranks of so many talented people.

What is your role at the medical school?
Currently, I am a division administrator for the Division of Nephrology and the Feinberg Cardiovascular Research Institute.

How do you personally help investigators at Feinberg?
In general my role is to help investigators navigate the ever-changing medical school landscape. I help keep research and clinical spending on track, but most importantly, I ensure that investigators have the information they need to make the most informed decisions. Sometimes this is related to finance, grants, personnel, space, etc. My goal is to help ensure that faculty have the resources they need to continue to further our tripartite mission. I certainly cannot do this alone. I have a team of phenomenal staff that help support the research mission as well.

What is your favorite part of the job?
My favorite part of the job is having the opportunity to collaborate with leaders in the field of research. I also enjoy the opportunity to collaborate with my colleagues at Northwestern Medical Group, Northwestern Memorial Hospital, and the Ann & Robert H. Lurie Children's Hospital of Chicago. It makes my job that much more exciting.

What do you like to do in your spare time?
I am an avid yogi! I practice Bikram yoga several times a week and try to do two back-to-back sessions (that's three hours) on Saturdays and Sundays.

Anything else we should know about you?
Most people are shocked to learn that I rode a motorcycle across the U.S. on a 2,000 mile road trip. It was the most amazing experience of my life!

Navdeep Chandel, PhD, Susan Quaggin, MD, and Jacob Sznajder, MD, were among the attendees at Quaggin's recent investiture.

Investing in Science

In recent months, investitures were held for Susan Quaggin, MD, the Charles Horace Mayo, MD, Professor of Medicine, chief of the Division of Nephrology/Hypertension, professor of Nephrology, and director of the Feinberg Cardiovascular Research Institute; Dimitri Krainc, MD, PhD, the Aaron Montgomery Ward Professor of Neurology chair of the Ken and Ruth Davee Department of Neurology; and Andrew Parsa, MD, PhD, the Michael J. Marchese Professor of Neurological Surgery and chair of the Department of Neurological Surgery.

Photos from these events are posted to Feinberg's Flickr page and available for download.

Research in the News

US News & World Report February 21
Modern war wounds can devastate vets' sexual, emotional health
Chris Gonzalez's research was featured.

NPR February 19
Sit more, and you're more likely to be disabled after age 60
Dorothy Dunlop's research was featured.

- Dunlop's research was also featured in CBS News, NBC News, FOX News, WGN News, *TIME*, *US News & World Report*, *USA Today*, *Los Angeles Times*, *Chicago Tribune*, Reuters, UPI, Yahoo! Shine, Huffington Post, *Scientific American*, *International Business News*, *Toronto Star, Irish Health*, and more.

Los Angeles Times February 14
As marijuana laws change, health risks of pot use are weighed
Richard Miller was quoted.

FOX News February 14
New models help address kidney organ donation shortages
John Friedewald was quoted.

60 Minutes (CBS News) February 9
Sex matters: Drugs can affect sexes differently
Melina Kibbe was interviewed.

CNN February 6
'Biggest Loser' winner: Too thin?
Robert Kushner was quoted.

NPR February 4
Higher blood pressure at 18 means hardening arteries at 40
Norrina Allen's research was featured.

- Allen's research was also featured on FOX News, WebMD, Voice of America News, *US News & World Report*, and more.

USA Today February 4
Your brain often edits that trip down memory lane
Joel Voss' research was featured.

- Voss' research was also featured on NPR, in the Los Angeles Times, FOX News, and more.

New York Times February 3
As peanut allergies rise, trying to determine a cause
Ruchi Gupta was quoted.

More media coverage available online.

Northwestern University
NUCATS
Clinical and Translational Sciences Institute

NUCATS Corner

NUCATS Institute Provides Training to Onboard New Clinical Research Staff

Are you onboarding new staff members in your research area and need to get them up to speed on the basics of clinical research?

Are you new to the clinical research coordinator role and seeking a fast, thorough introduction to the process of running a clinical trial?

The Northwestern University Clinical and Translational Sciences (NUCATS) Institute offers research staff training programs, both live and online, to assist you. Course topics include: Clinical Research Coordinator Basic Training (Live and Online), Introduction to Clinical Research, Human Subjects Protections, Good Clinical Practice, Clinical Research Billing, and Research Misconduct.

Contact the NUCATS Institute and enroll today!

New Online MPH Program at Feinberg

Starting in summer 2014, Northwestern University's Program in Public Health will offer a four-quarter, intensive Masters in Public Health (MPH).

Northwestern has long provided the opportunity for healthcare professionals and those working in public health and medical research to pursue an MPH degree through a part-time, evening program on its Chicago campus.

This new full-time program is designed for health professionals, medical students, post-doctoral trainees and public health workers who wish to complete the MPH degree in one year.

Sponsored Research

PI: Paul Schumacker, PhD, Professor in Pediatrics-Neonatology, Cell and Molecular Biology, and Medicine- Pulmonary

Sponsor: National Heart, Lung, and Blood Institute

Title: "Metabolic Regulation of Pulmonary Vascular Remodeling"

Pulmonary hypertension is a disease where the pressure is increased in the pulmonary arteries that deliver blood flow to the lungs. Pulmonary hypertension can result from a variety of causes that include genetic factors, heart disease, disorders in the coagulation system, connective tissue diseases, and even parasitic infections. In rare cases known as idiopathic pulmonary hypertension, the cause cannot be identified.

The most common cause of pulmonary hypertension is chronic lung disease, especially chronic obstructive pulmonary disease (COPD).

The principal function of the lung is to permit gas exchange between blood and air. In healthy lungs, cyclic breathing assures that the airspaces throughout the lung are well ventilated and maintain high oxygen levels. However, in chronic lung diseases the ventilation in regions of the lung is partially obstructed due to airway disease. For example, in patients with COPD, airway disease limits the delivery of ventilation to some lung regions. Consequently, the oxygen concentration falls in those regions—a condition known as alveolar hypoxia.

In the lung, alveolar hypoxia triggers constriction of small pulmonary arteries. This helps to improve the efficiency of gas exchange by redistributing blood flow toward better oxygenated regions. This works well when disease affects only small regions of the lung. However, in COPD the majority of the lung may remain hypoxic, so the vasoconstriction causes the pulmonary artery pressure to increase. When that condition is sustained for many weeks, the pulmonary artery wall thickens and the vessels remodel, causing sustained pulmonary hypertension. In some patients this condition worsens progressively and leads to heart failure.

In collaboration with Navdeep Chandel, PhD, this project tests the hypothesis that mitochondria in the pulmonary artery cells act as O2 sensors that detect alveolar hypoxia and trigger the arterial wall remodeling. Previous studies have shown that the immediate vasoconstriction during acute hypoxia is activated by these organelles. While mitochondria are generally viewed as the energy generators of the cell, they also act as hypoxia sensors by releasing low levels of reactive oxygen species (ROS)—most notably hydrogen peroxide—to the cytosol. These ROS signals trigger an increase in intracellular calcium ions that cause constriction. This project is now testing whether the same ROS signals also trigger the remodeling of the pulmonary arteries during prolonged alveolar hypoxia. If so, then targeted antioxidant compounds could prove to be an effective treatment for pulmonary hypertension.

Cells in the pulmonary arteries of patients with pulmonary hypertension acquire cancer-like properties, such as increased proliferation and a shift toward glucose metabolism and away from mitochondrial metabolism. Another question being tested in this project is whether interventions that shift the cells back toward mitochondrial metabolism can prevent the remodeling behavior that contributes to progressive pulmonary hypertension.

Finally, cells undergoing replication use an energy sensing system to monitor the availability of nutrients. This system assures that cells lacking sufficient energy supplies will stop growing. This project will test the hypothesis that therapeutic activation of this sensor, known as AMP Kinase, can prevent the development of pulmonary hypertension. By activating this sensor in the pulmonary artery, proliferation and cell growth could be inhibited by causing the cells think that energy supplies are critically low. Importantly, drugs already used safely for the treatment of diabetes can turn on this response, giving promise to the possibility that a novel therapy could soon appear.

Overall, this exciting project seeks to manipulate the upstream signals that orchestrate the growth and proliferation of pulmonary artery cells, potentially leading to the identification of novel therapies to treat this debilitating illness, for which few effective therapies exist.

PI: Bin Zhang, MD, PhD, Associate Professor in Medicine-Hematology/Oncology and Microbiology-Immunology

Sponsor: National Cancer Institute

Project: CD73 and Tumor Immunity

The promises of cancer immunotherapy have not been translated into clinical successes because immune-suppressive mechanisms that act in cancer patients can block effective anti-tumor immunity. Therefore, to eradicate cancers by immunotherapy, tumor-induced immunosuppression must be overcome.

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Sponsored Research

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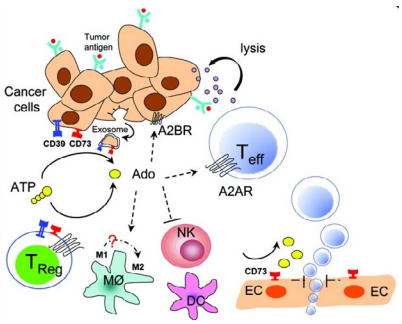
Zhang's lab has recently demonstrated a novel tumor-intrinsic immunosuppressive mechanism whereby tumor-derived CD73 functions as an ecto-enzyme to produce extracellular adenosine, which limits anti-tumor T cell immunity to promote tumor growth via adenosine receptor (AR) signaling. They also found that CD73 expression in malignant cancers was closely associated with poor immune status of tumor infiltrating effector T cells.

This exciting preliminary data using CD73 siRNA-treated tumor cells and CD73-/- mice indicated that ablation of both tumor and host CD73 synergistically inhibited tumor growth in a T cell-dependent manner. A similar anti-tumor effect was observed by pharmacological blockade of CD73 using the selective inhibitor α,β-methylene adenosine 5'-diphosphate (APCP).

Thus, Zhang hypothesizes that both tumor and host CD73 through their enzymatic activity prevent tumor destruction by incoming anti-tumor T cells. He plans to further clarify the mechanisms of tumor protection by which CD73 expression on either tumor cells or host cells impacts anti-tumor T cell responses. Because endogenous anti-tumor immunity, even if restored, is often insufficient and transient, targeted CD73 cancer therapy may not be optimal unless combined with other forms of immuno-therapy, such as adoptive T cell transfer or DC vaccines. Several immunogenic tumors will be tested to assess the efficacy of endogenous and adoptively transferred anti-tumor CD8+ T cell immunity in combination with CD73 ablation. Finally, to establish the translational relevance of targeted CD73 therapy, Zhang will explore the preclinical potential of inhibiting CD73 using APCP or an anti-CD73 monoclonal antibody (mAb) combined with T cell therapy.

By the completion of these studies, Zhang will gain insight into the immunosuppressive mechanisms of CD73 in the cancer microenvironment and, more importantly, validate a novel and feasible strategy of cancer treatment. This therapeutic approach may enhance chemotherapy and particularly T cell-based therapy by enhancing the adaptive immune response machinery, which may increase the function of tumor-infiltrating CD8+ T lymphocytes, and subsequently lead to improved survival in cancer patients.



Immune actions of CD73-generated adenosine in the tumor microenvironment. CD73 has distinct roles in hematopoietic and nonhematopoietic cells in limiting antitumor T cell immunity through its etco-enzymatic activity.
(2012 Oncoimmunity)

Funding

Advancing Patient Safety Implementation Through Safe Medication Use Research (R18)

More information

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

Submission deadline: May 25

Upper Amount: $1.5 million

Synopsis: AHRQ is addressing patient safety and medication research by focusing on safe usage of medications. This centers on how medications move through the health care system and how the process can be improved so patients are not harmed, while health care delivery is improved. This opportunity will fund investigative research demonstration projects that examine the effective implementation of processes, policies, and behaviors that support safe use of medication as well as its sustainment and dissemination.

Advances in Patient Safety Through Simulation Research (R18)

More information

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

Submission deadline: May 25

Upper Amount: $1.05 Million

Synopsis: AHRQ is interested in funding a diverse set of projects that develop, test, and evaluate various simulation approaches for the purpose of improving the safe delivery of health care. Applications that address a variety of simulation techniques, clinical settings, provider groups, priority populations, patient conditions, and threats to safety are welcomed.

2013 LRI Distinguished Innovator Awards

More information

Sponsor: Lupus Research Institute

Submission deadline: May 16

Upper Amount: $1 million

Synopsis: LRI Distinguished Innovator Awards provide outstanding scientists with substantial support for up to four years to conduct novel research into the fundamental causes of systemic lupus erythematosus and so provide new directions towards a cure.

View more funding opportunities

High Impact Factor Research

January 2014

Auyeung E, Li TI, Senesi AJ, Schmucker AL, Pals BC, de la Cruz MO, **Mirkin CA**. DNA-mediated nanoparticle crystallization into Wulff polyhedra. *Nature*. 2014 Jan 2;505(7481):73-7.

Dose M, Emmanuel AO, Chaumeil J, Zhang J, Sun T, Germar K, Aghajani K, Davis EM, Keerthivasan S, Bredemeyer AL, Sleckman BP, **Rosen ST**, Skok JA, Le Beau MM, Georgopoulos K, Gounari F. β-Catenin induces T-cell transformation by promoting genomic instability. *Proceedings of the National Academy of Sciences U S A*. 2014 Jan 7;111(1):391-6.

Frilling A, Modlin IM, Kidd M, Russell C, Breitenstein S, **Salem R**, Kwekkeboom D, Lau WY, Klersy C, Vilgrain V, Davidson B, Siegler M, Caplin M, Solcia E, Schilsky R; Working Group on Neuroendocrine Liver Metastases. Recommendations for management of patients with neuroendocrine liver metastases. *Lancet Oncology*. 2014 Jan;15(1):e8-21.

Getts DR, **Terry RL**, **Getts MT**, Deffrasnes C, Müller M, van Vreden C, Ashhurst TM, Chami B, **McCarthy D**, Wu H, Ma J, **Martin A**, Shae LD, Witting P, **Kansas GS**, Kühn J, Hafezi W, Campbell IL, Reilly D, Say J, Brown L, White MY, Cordwell SJ, Chadban SJ, **Thorp EB**, Bao S, **Miller SD**, King NJ. Therapeutic inflammatory monocyte modulation using immune-modifying microparticles. *Science Translational Medicine*. 2014 Jan 15;6(219):219ra7.

Glasauer A, Sena LA, Diebold LP, Mazar AP, Chandel NS. Targeting SOD1 reduces experimental non–small-cell lung cancer. *Journal of Clinical Investigation*. 2014 Jan 2;124(1):117-28.

Mc Donald J, Krainc D. Alzheimer gene APOE ε4 linked to brain development in infants. *JAMA- Journal of the American Medical Association*. 2014 Jan 15;311(3):298-9.

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

Orin Bloch, MD, joins as the Khatib Professor of Neurological Surgery and assistant professor of Neurology, and a neurosurgeon at Northwestern Memorial Hospital.

He received his bachelor's degree in bioengineering from the University of Pennsylvania and his medical degree from the University of California, San Francisco. He completed an internship in general surgery and a residency in neurological surgery at the University of California, San Francisco, followed by a fellowship in surgical neuro-oncology and skull base tumor surgery at UCSF.

Bloch's research interests are focused on identifying mechanisms of immunoresistance in brain tumors to enhance the efficacy of immunotherapy. He has published more than 40 peer-reviewed journal articles, and has research funding from the Howard Hughes Medical Institute, the National Cancer Institute, and the National Institute of Neurological Disorders and Stroke.

Congcong He, PhD, joins as assistant professor of Cell and Molecular Biology.

She received her Bachelor of Science degree from Zhejiang University in China and her doctorate degree from the University of Michigan, Ann Arbor. She completed a postdoctoral research fellowship in the Department of Internal Medicine at the University of Texas Southwestern Medical Center in Dallas, where she later served as an instructor.

He seeks to understand the molecular mechanisms of mammalian autophagy and its functions in regulating metabolism and preventing metabolic diseases, using animal models and molecular and cell biology approaches. She has published more than 15 articles in peer-reviewed journals, and has research funding from the National Institutes of Health.

Calendar

Tuesday, March 18

Lectures in Life Sciences

"Role of E2F Proteins in Tumoregenesis," presented by Jacqueline A. Lees, PhD, Koch Institute for Integrative Cancer Research.

Time: 4 to 5 p.m.

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

Contact: j-crispino@northwestern.edu
More information

Wednesday, March 19

Center for Molecular Innovation and Drug Discovery Symposium

"Protein-Protein Interactions: A Promising Avenue for Drug Discovery," sessions presented by Andrew Binkowski, PhD, Biosciences Division, Argonne National Laboratory and fellow, Computation Institute, University of Chicago and Andrew Souers, PhD, Oncology Discovery, AbbVie. Registration required.

Time: 10 a.m. to 1 p.m.

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

Contact: drugdiscovery@northwestern.edu
More information and to register

Thursday, March 27

IPHAM Seminar Series

"Role of Improvement Science in Global Health," presented by Lisa Hirschhorn, MD, Department of Global Health & Social Science, Harvard Medical School.

Time: Noon to 1 p.m.

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

Contact: e-curran@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 Institute of General Medical Sciences has posted a request for information soliciting input on planned extramural training activities relevant to data reproducibility. Comments are due by February 28.

National Institute of General Medical Sciences (NIGMS) director Jon R. Lorsch, Ph.D., has a new post on the *NIGMS Feedback Loop* blog about funding trends and factors affecting the success rate.

NIH deputy director Sally Rockey posted about "Fiscal Policies and More for 2014" on the NIH *Rock Talk* blog. "I am particularly grateful that NIH was able to recover a significant portion of the funds lost due to sequestration, which should bring our budget situation back on track not only for this year, but hopefully into the future," she notes.

New investigator R01 due dates for spring 2014 have been announced by NIH.

NIH director Francis S. Collins and principal deputy director Lawrence A. Tabak wrote in Nature about the NIH's plan to significantly enhance reproducibility, stating, "A growing chorus of concern, from scientists and laypeople, contends that the complex system for ensuring the reproducibility of biomedical research is failing and is in need of restructuring."

Science Insider reported that NIH has partnered with 10 pharmaceutical companies to study four diseases: Alzheimer's disease, Type 2 diabetes, rheumatoid arthritis, and lupus. The unprecedented $230 million partnership will span five years. Said director Collins, "The goal is to cut down on the more than 95% failure rate for drug candidates. As a result, it now takes some 10 years and more than $1 billion to develop a successful drug. By combining forces, companies and academics hope to cut costs and speed things up by sorting through a wealth of new genomic and molecular data on disease biology to find the most promising new drug targets."

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