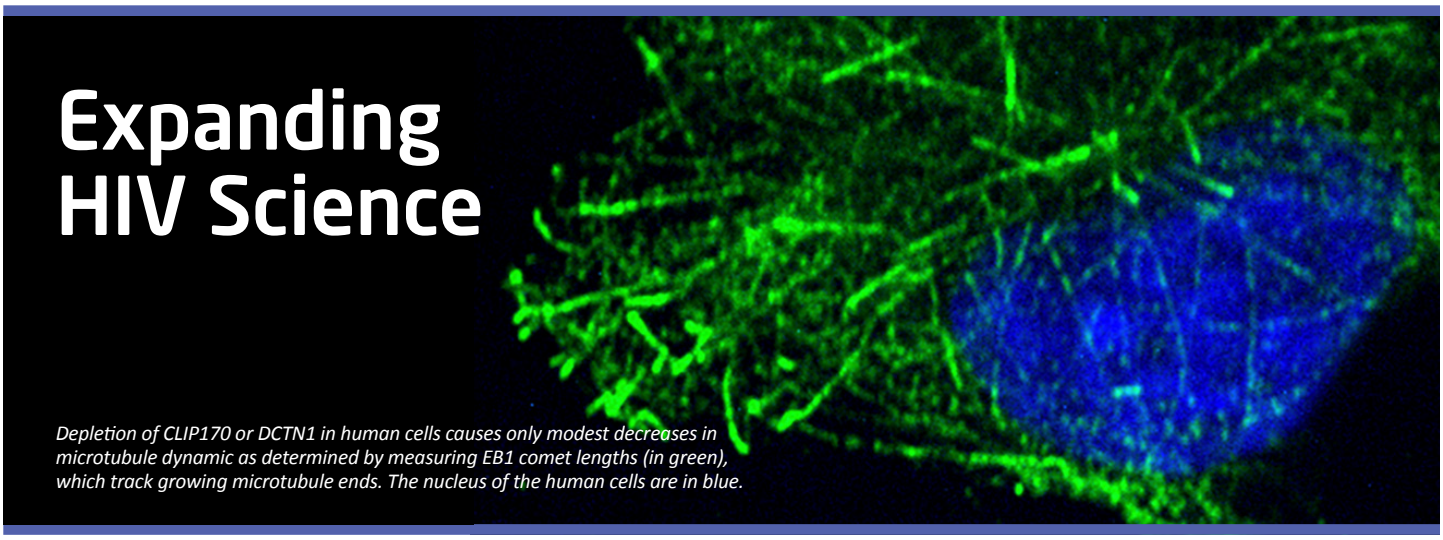
Breakthroughs

Feinberg School of Medicine Research Office

April 2022

Expanding HIV Science



Depletion of CLIP170 or DCTN1 in human cells causes only modest decreases in microtubule dynamic as determined by measuring EB1 comet lengths (in green), which track growing microtubule ends. The nucleus of the human cells are in blue.

By Will Doss

As far as viruses go, human immunodeficiency virus (HIV) is quite simple. About 100,000 times smaller than a red blood cell, the virus expresses just a dozen proteins, yet it can establish a lifelong infection that, if left untreated, causes acquired immunodeficiency syndrome (AIDS) and death. At Feinberg, HIV science ranges from examining microscopic mechanisms of initial infection to trials of treatments, all geared toward the goal of ending one of the world's largest pandemics.

"It's been amazing to see science and medicine work to produce these improvements," said Thomas Hope, PhD, professor of Cell and Developmental Biology and of Obstetrics and Gynecology. "We are seeing a new generation of scientists enter the field, and those new perspectives will help us solve this problem."

Identifying Microscopic Mechanisms

Many viruses exploit microtubule filaments in host cells, traveling along these "highways" to reach the virus's preferred replication site within a cell. Mojgan Naghavi, PhD, professor of Microbiology-Immunology, has shown that HIV uses some unusual strategies to do so; an HIV capsid mimics a central microtubule regulator to control its transport and disassembly (commonly called uncoating), according to recent studies published in *The EMBO Journal* and *Proceedings of the National Academy of Sciences* (PNAS). This allows the virus to coordinate transport, uncoating and converting its RNA genome to a DNA form on the way to the nucleus, where it then integrates into the host cell genome.

"More refined drugs targeting highly specialized microtubule regulators could potentially be an attractive approach for development of new, non-toxic therapeutic strategies to treat HIV," Naghavi said.

This mechanism is one example of how HIV "hijacks" native processes in cells and uses them to replicate and spread. HIV is remarkably resourceful, according to Judd Hultquist, PhD, assistant professor of Medicine in the Division of Infectious Diseases, who studies how the virus manipulates host cell machinery to replicate.

In a recent study published in *Nature Communications,* Hultquist and his collaborators used a CRISPR-Cas9 gene-editing approach to ablate over 400 different genes in CD4+ T-cells isolated from human blood donors. By challenging these cells with HIV in the lab, they were able to identify 86 host factors that the virus uses to replicate. While nearly half of

Northwestern Medicine®

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Expanding HIV Science *(continued from cover page)*

these have been studied previously, the other half represent new targets for mechanistic study, Hultquist said.

Studying the myriad ways in which HIV infects cells and alters their normal functioning is critical for developing better treatments and an eventual cure, according to Hultquist.

"If we're going to build a drug with curative potential, it has to be able to eliminate or disable the virus in all of the places it may be lurking throughout the body," Hultquist said.

The persistence of the virus is the main reason efforts to cure HIV have so far proven unsuccessful, according to Hope. Even with antiretroviral therapy (ART) that can reduce levels of virus to undetectable levels, as soon as somebody stops taking those medications, the virus can bounce back. Hope has spent the last two years searching for HIV "reservoirs," the locations in the body where the virus remains even after treatment.

"Everyone looks in the blood, but the virus is only detected in the blood about a week or so after infection," Hope said. "To find a cure, we need to find these reservoirs where infection is happening first and where the virus is hiding out."

Developing Better Treatment

The last three decades have seen significant improvements in treatment options for HIV, but life expectancy for people with HIV is still shorter compared to other people. Due to a phenomenon of premature aging, people with HIV experience high rates of cardiovascular disease, dementia and bone loss.

Frank Palella, MD, the Potocsnak Family – C.S.C. Professor of Medicine in the Division of Infectious Diseases, was recently named associate director of Northwestern's new Potocsnak Longevity Institute and director of the institute's Potocsnak Center for Aging and HIV. The institute will address the special needs of people aging with HIV through research, education and patient care, according to Palella.

Northwestern is also involved in improving therapies. The classic three-drug ART regimen worked well, but advancements in the medications themselves now allow for a two-drug regimen. Babafemi Taiwo, MBBS, the Gene Stollerman Professor of Medicine and chief of Infectious Diseases in the Department of Medicine, led the AIDS Clinical trial Group (ACTG) study published in the journal *Clinical Infectious Disease* that first showed efficacy of this new treatment strategy.

"This heralds a shift in the three-drug paradigm as a way to lower lifetime exposure to these medications," Taiwo said. "We know this can be done successfully without compromising suppression."

Increasing the duration of these treatments is another priority, as most regimens require daily medication that can complicate adherence or serve as a constant reminder of one's HIV infection. Current efforts include long-acting pre-exposure prophylaxis or ART that could mitigate these issues and increase treatment adherence.

Future of HIV

The COVID-19 pandemic forced science and medicine to marshal collective resources against an emerging threat, which could pay dividends for infectious diseases beyond COVID-19. Of particular interest are advancements such as the mRNA vaccines, which have proven effective against SARS-CoV-2, but are yet to be tested against a virus that mutates and changes as rapidly as HIV, according to Hultquist.

"The pandemic loosened up the wheels in terms of getting these big ideas tested and tried," Hultquist said. "It also precipitated a historic investment in virus research, and this has enabled us to bring together scientists across diverse disciplines who may have never even thought about viruses before, and here we all are working towards one common goal."

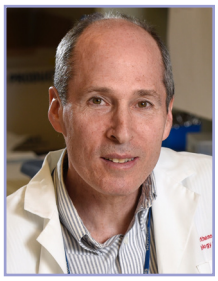
Further, several patients with HIV have received stem cell transplants to treat cancer and have been cured of the virus. While this treatment is unfeasible on a larger scale, it provides a blueprint for how scientists might one day design a cure for HIV, according to Taiwo.

"We're learning a lot from these patients," Taiwo said. "We now know biological markers of cure, and we have a general strategy. But most importantly, we know it's possible."

Hope, Naghavi and Taiwo are members of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University.

CONTENTS

Groundbreaking Molecular Neuroscientist to Receive 2022 Nemmers Prize in Medical Science



Jeremy Nathans, MD, PhD, an investigator at the Howard Hughes Medical Institute and a professor at Johns Hopkins University School of Medicine, known for his landmark discoveries into the molecular mechanisms of visual system development, function and disease, is the recipient of the 2022 Mechthild Esser Nemmers Prize in Medical Science at Northwestern University.

The Mechthild Esser Nemmers Prize in Medical Science, which carries a $200,000 stipend, is given to a physician-scientist whose body of research exhibits outstanding achievement in their discipline as demonstrated by works of lasting significance. A jury of distinguished scientists from around the country made the final selection.

Nathans, the Samuel Theobald Professor of the Wilmer Eye Institute at Johns Hopkins Medicine, has devoted his career to studying the vertebrate visual system.

"I am humbled to be in the same company as the previous Nemmers Prize winners," Nathans said. "And I am delighted to have this opportunity to strengthen my ties to colleagues at Northwestern University's Feinberg School of Medicine."

In connection with this award, Nathans will deliver a public lecture and participate in other scholarly activities at Feinberg in the coming year.

"Dr. Nathans is one of the greatest molecular neuroscientists in the world, whose remarkable work has transformed our understanding of vision," said Eric G. Neilson, MD, vice president for Medical Affairs and Lewis Landsberg Dean. "He is an exceptional physician-scientist who has inspired many others, and we are thrilled to honor his scientific accomplishments and contributions to improving human health."

Nathans' Accomplishments

Nathans, preeminent among molecular neuroscientists, identified genes encoding human light receptors (visual pigments) in rods and cones, as well as the mechanisms regulating the expression of these sensory receptors. This work led to his elucidation of the molecular basis of inherited variation in human color variation, including the variations that are referred to as "color-blindness."

His laboratory went on to genetically engineer mice, so that instead of seeing with only two-color receptors, as mice normally do, they were able to see with three color receptors, as primates do — suggesting, in the evolution of sensory systems, that the brain has innate plasticity, allowing it to process information from novel sensory inputs unencountered previously. This work suggests that genetic alterations at the receptor level may be the driving force in the evolution of many sensory systems and led to his elucidating the molecular basis of inherited variation in human color vision associated with color blindness.

Other studies from the Nathans laboratory have elucidated the genetics of inherited forms of retinitis pigmentosa and macular degeneration. Nathans' work on Frizzled receptors and Norrin/Wnt ligands identify the key role of this signaling pathway in retinal vascular development and in maintaining the integrity of the blood-retina and blood-brain barriers as well as the way in which defects in this pathway cause inherited retinal vascular disorders.

Nathans serves on the editorial board of *Proceedings of the National Academy of Sciences,* and he serves on the scientific advisory boards of The Foundation Fighting Blindness, the RYR1 Foundation, the Klingenstein Philanthropies, and the Life Sciences Research Foundation. A member of the National Academy of Medicine since 2011, his work has been recognized with numerous awards, including the Edward M. Scolnick Prize in Neuroscience by the McGovern Institute at the Massachusetts Institute of Technology and the 2013 Arthur Kornberg and Paul Berg Lifetime Achievement Award in Biomedical Sciences from Stanford University School of Medicine.

Nathans received his Doctorate Degree in Biochemistry from Stanford University School of Medicine in 1985, and then his Doctor of Medicine degree in 1987. Previously, he earned a Bachelor of Science at Massachusetts Institute of Technology. Following his studies at Stanford, he completed a postdoctoral fellowship at Genentech, Inc.

About the Nemmers Prizes

One of five Nemmers Prizes awarded by the University, the Mechthild Esser Nemmers Prize in Medical Science is made possible by a generous gift by the late Erwin Esser Nemmers and the late Frederic Esser Nemmers. It is the fourth Nemmers Prize to be established by Northwestern University and joins the Erwin Plein Nemmers Prize in Economics, the Frederic Esser Nemmers Prize in Mathematics, the Michael Ludwig Nemmers Prize in Music Composition and the Nemmers Prize in Earth Sciences, established in 2016. The awards are given every other year.

In 2016, the inaugural award was presented to Huda Zoghbi, MD, a Howard Hughes Medical Institute investigator and professor at Baylor College of Medicine, whose research has focused on Rett syndrome and other neurological disorders.

Stuart Orkin, MD, an investigator of the Howard Hughes Medical Institute at Boston Children's Hospital and Dana-Farber Cancer Institute and a professor at Harvard Medical School, a pioneering hematologist known for his landmark discoveries into blood cell development and the genetic basis of blood disorders, was awarded the 2018 prize.

Learn more.

Graduate Student/Post-Doc Events and Opportunities

Northwestern Women in Medicine: Celebrating our Voices

Friday, April 22
8 a.m. to 4:30 p.m.

Women physicians face unique challenges and obstacles throughout their professional careers. These challenges may affect leadership development and opportunities for women in medicine resulting in a gender gap in the governance of academic medical centers. This is the fourth annual symposium, and will help to identify the obstacles that contribute to gender inequity, shed light on gender disparities and share experiences and tools to overcome the barriers that exist.

Hybrid: In person and online
More information

Fourth Thursday Oasis

Thursday, April 28
7 p.m.

Come experience midweek worship and fellowship. We will have praise and worship music with Exposition of the Blessed Sacrament. Confession will be available.

Religious Life Center, Level M
Abbot Hall
710 N. DuSable Lake Shore Drive, Chicago
More information

First Annual Pathogen Genomics Symposium: Genes, Genomes and Infection

Wednesday, May 4
9 a.m. to 5:30 p.m.

Join us for a full day of scholarly events, including a series of sequential workshops, poster session and a keynote address followed by a series of research overview talks.

Simpson Querrey Biomedical Research Center – Potocsnak Family Atrium
303 E. Superior St., Chicago
More information

A Site of Struggle: American Art Against Anti-Black Violence

Now through July 10
12 p.m. to 8 p.m.

This exhibit foregrounds African Americans as active shapers of visual culture and highlights how art has been used to protest, process, mourn and memorialize anti-Black violence.

Mary and Leigh Block Museum of Art
40 Arts Circle Drive, Evanston
More information

Research in the News

***The New York Times,* March 1**

The coronavirus invades cells in the penis and testicles of monkeys, researchers discover
Thomas Hope, PhD, was featured.

***Reuters,* March 1**

Texas investigating parents of transgender youth for child abuse
Brian Mustanski, PhD, was featured.

***NBC News,* March 14**

Lasting depression and anxiety can follow a severe case of COVID, study finds
Marc Sala, MD, was featured.

***CNN,* March 17**

Sleeping with even a small amount of light may harm your health, study says
Phyllis Zee, MD, PhD, was featured.

***US News & World Report,* March 23**

Moderna says its low-dose COVID shots work for kids under 6
Bill Muller, MD, PhD, was featured.

***Chicago Tribune,* March 24**

Northwestern performs rare double lung transplant on patient with terminal lung cancer
Ankit Bharat, MBBS, and Young Chae, MD, MPH, MBA, were featured.

Improving Diagnosis, Care and Outcomes for Acutely Ill and Injured Pediatric Patients

Todd Florin, MD, MSCE, associate professor of Pediatrics in the Division of Emergency Medicine

Todd Florin, MD, MSCE, is an associate professor of Pediatrics in the Division of Emergency Medicine. He is also an attending physician and director of research in the Division of Emergency Medicine at Ann & Robert H. Lurie Children's Hospital, and director of the Grainger Research Program in Pediatric Emergency Medicine Research at Lurie Children's.

What are your research interests?

I am a clinical epidemiologist and trialist with a focus on improving the diagnosis and management of children with respiratory infections in the acute care setting. Specifically, I am interested in the risk stratification of children with pneumonia and how we can use risk stratification tools to target therapeutic approaches.

During my early faculty years, I led a prospective cohort study called Catalyzing Ambulatory Research in Pneumonia Etiology and Diagnostic Innovations in Emergency Medicine (CARPE DIEM) that enrolled more than 1,140 children with suspected pneumonia who presented to the emergency department (ED). During this work, we collected extensive clinical data linked to a biorepository of blood, urine and nasopharyngeal specimens with the goal of examining how clinical factors and biomarkers can be used to improve diagnosis and risk stratification.

I have expanded this work globally as the co-PI of a prospective cohort study of more than 2,500 children with pneumonia enrolled in 69 EDs across 19 countries as part of the Pediatric Emergency Research Network (PERN), a global consortium of pediatric emergency research networks. Given the challenges of COVID-19 and in collaboration with investigators from University of Calgary and UC Davis, we have leveraged this global infrastructure in PERN to study a host of important topics in pediatric COVID-19, including risk stratification, comparative effectiveness of pediatric therapies and post-COVID conditions.

What is the goal of your research?

Ultimately, it is my hope that our work will bring new strategies into the acute care setting for children with respiratory infections that will result in more accurate and targeted diagnosis and management based on patient-specific risk. Pediatric lower respiratory infections represent a heterogeneous group of diseases, with similar and overlapping presentations. It is therefore challenging for clinicians to determine exactly which children require antibiotics or need to be treated in the hospital. The goal is to ensure that those children at greatest risk for complications or severe disease receive early, targeted therapies, while avoiding unnecessary antibiotics, hospitalizations and other resource use in those who do not require them.

How did you become interested in this area of research?

My interest in this field started as a pediatric resident and pediatric emergency medicine fellow at the Children's Hospital of Philadelphia. Like most impactful clinical research, it began with observations at the bedside as I cared for children with respiratory infections. I was struck by the variation in management for these children, both across individuals and institutions.

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

Collaboration is the most exciting and powerful part of clinical research, in my opinion. Research is challenging and only by incorporating many different and diverse perspectives can we together tackle these very difficult and important questions. I feel fortunate to be part of such a supportive and collaborative community within Lurie Children's, the Stanley Manne Children's Research Institute and Northwestern University.

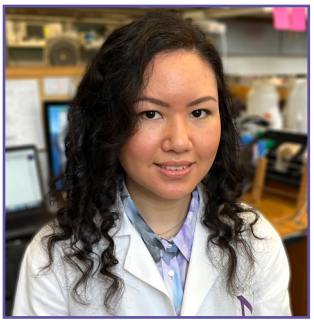
Within our community, I have had productive collaborations with teams within the Smith Child Health Outcomes, Research, and Evaluation (SCHORE) Center to evaluate parent and clinician perspectives on antibiotic use in pediatric pneumonia. Additionally, I work to foster multidisciplinary work within our ED, with strong collaborations with Orthopaedic Surgery, Infectious Diseases, Critical Care, and Allergy and Immunology, among others, at Lurie Children's.

How is your research funded?

My research has been funded by a variety of sources. Most has come from the National Institute of Allergy and Infectious Diseases and the National Heart, Lung, and Blood Institute. I have also received foundation funding from the Gerber Foundation and the Academic Pediatric Association, in addition to philanthropic funding that allows this work to move forward.

Macrophage Metabolism and Heart Failure

Vanessa Hayashi, Driskill Graduate Program in Life Sciences



Vanessa Hayashi, a student in the Driskill Graduate Program in Life Sciences (DGP), studies transendothelial migration in the laboratory of William A. Muller, MD, PhD, the Janardan K. Reddy, MD Professor of Pathology.

Where is your hometown?
I am half-Japanese and half-Panamanian. I've lived in five countries and have actually been in the U.S. the longest. I consider Osaka, Japan, my hometown on paper, but I make wherever I currently am my home in my heart.

What attracted you to your program?
I was attracted to the Driskill Graduate Program in Life Sciences (DGP) because it allowed me to choose a thesis laboratory from a comprehensive list with varied disciplines. I rotated through laboratories that studied metabolism, cancer and inflammation — not every graduate program allows that opportunity.

What are your research interests?
After my rotations in the first year, I was interested in inflammation. I joined the Muller laboratory in the Department of Pathology, which studies transendothelial migration, the step when the majority of circulating white blood cells commit to leaving the blood vessels in order to reach the site of inflammation. We study this step both in vitro and in vivo, using different models that are each relevant to diseases that are caused by dysregulated inflammation. My goal is to learn more about ongoing research and contribute through my own research.

What are you currently working on?
I am trying to figure out the mechanism by which a synthetic peptide blocks transendothelial migration, which is an important step in inflammation. The preliminary data suggest that this peptide blocks a specific step in transendothelial migration in endothelial cells that is critical for efficient transmigration in both human and mouse models of acute inflammation. Our hope is that we will be able to develop this peptide into therapies for diseases such as heart attack and stroke, whose prognosis is worsened by the uncontrolled inflammation that follows the initial damage from hypoxia.

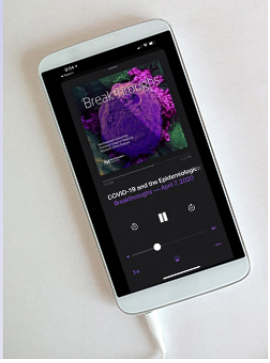
What has been your best experience at Feinberg?
My best experience has been meeting like-minded individuals through my cohort and thesis lab. I really value connections with people, because graduate-level study is challenging, but having people that support me and believe in me helps me feel like I can keep pressing on. Moreover, there are so many people that can give me advice based on their professional experience and teach me what they would have wanted to know at my age. I believe those kinds of interactions are the greatest appeal of graduate school, but Feinberg has a particularly collaborative and supportive environment that invites people to reach out.

What do you do in your free time?
When I am not writing grants or presentations, I like to spend my time writing fiction and sharing it with people who enjoy reading. I have always felt the advantages of the internet allowing us to connect with people from around the world, but this is especially true for writers like myself. It allows us to have an audience that provides unbiased feedback, which is truly valuable when one wants to improve in the craft.

What are your plans for after graduation?
I plan to work as a postdoctoral fellow after I finish my PhD, and then follow this with a tenure track faculty position. This career goal combines two things that I love: research and teaching. I love the intellectual challenge of biomedical research — solving puzzles that provide new data to help humankind. Yet, as much as I enjoy doing benchwork science, I want to dedicate as much of my life as possible to the mentorship of new students and researchers. Professors at my undergraduate institution and faculty at Feinberg inspired me and keep inspiring me to continue in this field, and I desire nothing more than to be a similar figure for the future generation of scientists.

Podcast: Pet Dogs Advance Glioblastoma Research

Amy Heimberger, MD, is the Jean Malnati Miller Professor of Brain Tumor Research and professor of Neurological Surgery. In this episode of *Breakthroughs*, Heimberger describes her part in a Phase I clinical trial at the Texas A&M College of Veterinary Medicine & Biomedical Sciences Veterinary Medical Teaching Hospital. Investigators injected an immunotherapy drug known as a STING (STimulator of INterferon Genes) agonist directly into the glioblastoma tumors of six dogs. This new study in canine glioblastoma could lead to more effective human glioblastoma clinical trials. Listen to the episode here.



Ethics of Organ Transplantation and Donation

Jefferson Uriarte, research project coordinator at the Center for Health Services and Outcomes Research

Jefferson Uriarte, research project coordinator at the Center for Health Services and Outcomes Research (CSHOR) within the Institute for Public Health and Medicine (IPHAM), helps conduct research on the ethics of organ transplantation and donation.

Where are you originally from?
I am originally from Lima, Peru. I immigrated to the United States when I was nine years old. Since then, I have lived in St. Louis, Missouri.

What is your educational background?
I graduated from Loyola University Chicago in 2014 where I double majored in psychology and international studies. As an undergraduate student, I was a Ronald E. McNair Scholar which exposed me to academic research and motivated me to pursue graduate studies. I am currently completing a Master of Arts in cultural and educational policy at Loyola University Chicago.

Please tell us about your professional background.
After completing my undergraduate studies, I spent a few years as an educator in Texas, where I taught pre-K, kindergarten and 3rd grade. With hopes of pursuing a PhD in the future, I returned to Chicago to enhance my research experience. Prior to joining Northwestern, I worked as a research assistant for the Children Adapting to Stress and Adversity Lab at Loyola University and the Center for Decision Research at the University of Chicago.

Why do you enjoy working at Northwestern?
I have gotten to know so many amazing people. Although some have left Northwestern to pursue other interests, I am happy that I've been able to maintain these friendships. Further, one of my favorite restaurants, Cafecito, is just a few blocks away from our downtown campus. I definitely recommend it.

How do you help scientists at the medical school?
I am a research coordinator working alongside Elisa Gordon, PhD, MPH, in the Center for Health Services and Outcomes Research. As a research coordinator, I manage three federally-funded research projects and ensure studies are conducted in accordance with IRB policies, while also contributing to the development of manuscripts for publication. Further, I have had the pleasure and opportunity to mentor undergraduate and medical students who are interested in academic research.

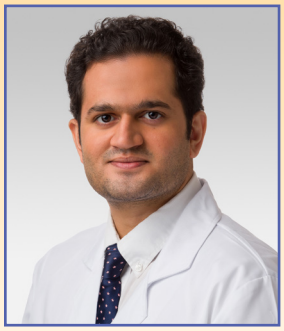
What is your favorite part of the job?
My favorite part of working at Northwestern has been all the opportunities I've had to develop as a researcher. I've been fortunate to work alongside and learn from some amazing people. I've had the chance to improve my analytical and writing skills while being involved in every aspect of academic research.

What are you currently working on?
Our research projects focus on the ethics of organ transplantation and donation, as well as health disparities in healthcare access and outcomes. One of our studies examined public opinion and perceptions of vascular composite allotransplantation (e.g., hand and face transplants) through focus groups. We hope to report our findings in the near future.

What do you like to do in your spare time?
In my spare time, I enjoy spending time with friends and family (specially my dog, Tobias). I love reading fantasy books. I am a huge fan of Brandon Sanderson and Patrick Rothfuss; both are amazing authors. I also enjoy training for and competing in powerlifting competitions. Although I haven't competed since 2019, I hope to make my comeback this year.

New Faculty

Niraj K. Shenoy, MD, PhD, MS, joined as the associate professor in the Department of Medicine (Hematology and Oncology) in September 2021. Shenoy specializes in genitourinary malignancies. His lab is interested in understanding and targeting the interactions between aberrant metabolism, epigenetic dysregulation, immune evasion and hypoxia signaling in cancer. While clear cell renal cancer constitutes a large focus of his research program, he also undertakes select projects in other malignancies. Prior to coming to Northwestern, he was assistant professor at the Albert Einstein College of Medicine.



NUCATS Corner
Clinical and Translational Sciences Institute

New Feinberg Pilot Funding Page Launched

A new webpage provides a comprehensive look at pilot and seed grant funding available throughout the medical school. The searchable database currently features nearly 30 opportunities.

This new webpage is curated and managed by the Northwestern University Clinical and Translational Sciences (NUCATS) Institute. Please email Roger Anderson to add an opportunity.

"Pilot awards and seed grants allow researchers to test the most promising new ideas, thereby enabling new NIH grant applications and future success," says Richard D'Aquila, MD, director of the NUCATS Institute. "The generation of pilot data is a critical step in getting research studies off the ground and many amazing discoveries can trace a line back to one of these early funding opportunities."

The NUCATS Institute annually supports more than $1 million in pilot research funding that seeds new NIH applications.

Research Workforce Conference Set for April 28-29

Please join Chicago's NUCATS-funded funded research institutions as they host the annual Enhancing Quality in the Translational Research Workforce (EQuaTR) conference.

The 2022 EQuaTR conference offers the opportunity for clinical research staff to learn from leaders in the field, gaining practical knowledge on current trends and issues in clinical research. EQuaTR is presented by the NUCATS Institute, the Institute for Translational Medicine and the UIC Center for Clinical and Translational Science.

This year's event will take place the mornings of April 28 and April 29. The application deadline for this well-attended virtual event is April 22.

NIH News

New Scientific Data Sharing Website

A new NIH Scientific Data Sharing website has launched. Launched in April, the new site houses the latest NIH news and updates. This will be an extremely valuable resource especially as we prepare for the new NIH Data Sharing Policy effective January 25, 2023. This website will further help researchers understand which NIH policies apply to their research, how to share and submit data, and how to access data from NIH supported repositories.

Research Methods Resources: Stepped-Wedge Group Randomized Trials and More

The NIH Research Methods Resources (RMR) website was developed as one in a series of initiatives to enhance the quality, accountability, and transparency – in short, the rigor – of NIH-supported clinical trials. Investigators can now find helpful resources for stepped wedge group or cluster-randomized trials and more than fifteen other study designs and methodological issues on the RMR website. The information provided represents current thinking among biostatisticians and other methodologists at the NIH regarding best practices for issues that may arise when working with different study designs.

New NIH All About Grants Podcast Page Available for Your Viewing and Listening Pleasure

Over 50 podcasts are available on various parts of the grants process, from application to closeout. NIH shares tips for preparing applications, advice for new and early career scientists, peer review, post-award activities and more. The podcast explores subjects including safety plans for conference applications, basic experimental studies with humans, financial conflicts of interest, considering alternatives to animals and research misconduct. The NIH All About Grants podcast is a great resource for investigators, fellows, students, research administrators and others interested in the application and award process.

Podcast: Advancing Mental Health Research

Sachin Patel, MD, PhD, is the new chair and Lizzie Gilman Professor of Psychiatry and Behavioral Sciences at Feinberg and psychiatrist-in-chief at Northwestern Memorial Hospital's Norman and Ida Stone Institute of Psychiatry. In this episode, he talks about the current mental health crisis in this country, and his research and vision for the department. Patel will be launching a new Center for Psychiatric Neuroscience, which is aimed at bringing together basic translational neuroscientists that have a goal of understanding and deepening the understanding of physiological mechanisms that underlie mental illness. Listen to the episode here.

Sponsored Research

PI: Sergey Troyanovsky, PhD, **professor of** Dermatology **and of** Cell and Developmental Biology

Sponsor: National Institute of Arthritis and Musculoskeletal and Skin Diseases

Title: Cadherin Clusters and Actin Filaments

Cadherin clustering is a unique molecular process that mediates and controls cell-cell adhesion. In addition, it also regulates the actin cytoskeleton, polarity, proliferation, and apparently other structures and signaling pathways. Cadherin clusters reinforce weak individual adhesive bonds and generate functional cell-cell adhesion links. By connecting to F-actin, they determine the overall organization and dynamics of the actin cytoskeleton. Finally, they provide specific structural scaffolds for various signaling pathways. Despite such incredibly important functions, which obviously play out in nearly every aspect of tissue morphogenesis, the molecular mechanisms and regulation of cadherin clustering remains to be studied.

Our work will shed light on how cadherin clusters form and how they participate in such a diverse array of cellular mechanisms. Work done under this proposal in previous years showed that adherens junctions (AJs), the major cell-cell adhesion structures in vertebrates, consist of numerous transient but highly adhesive cadherin nanoclusters. The short lifetime of each cluster makes AJs adhesive and flexible at the same time. The continuous generation of these clusters is apparently based on a remarkable reaction —cooperative binding of the cadherin-associated protein α-catenin to actin filaments. The assembly-disassembly cycles of both cadherin clusters and associated F-actin are tightly coupled thereby synchronizing cadherin and actin dynamics in adjacent cells. Finally, we found that cadherin clusters could be structurally diversified by cadherin/catenin-bound proteins. Diversification of cadherin clustering is based on the fact that each of these proteins provides specific modes of lateral cadherin-cadherin interactions. A variety of these interactions results in formation of an array of distinct clusters, each of which might have particular functions.

The advances in understanding cadherin clustering allowed to come up with this proposal, which includes determining 1) the role of cadherin in clustering and function of two proteins: signaling protein Erbin and adaptor protein PLEKHA5; 2) molecular mechanisms interconnecting extracellular cadherin binding events with α-catenin-binding to F-actin; and 3) the role of cadherin clustering in some examples of tissue morphogenesis.

Read more

PI: Daniela Ladner, MD, MPH, **professor of** Surgery **in the Division of** Organ Transplantation **and of** Medical Social Sciences; **director of Northwestern University Transplant Outcomes Research Collaborative** (NUTORC).

Sponsor: National Institute of Diabetes, Digestive and Kidney Diseases

Title: Natural History, Risk Prediction and Cost of Cirrhosis in Insured Americans

Cirrhosis is a leading cause of mortality in the U.S., diagnosed in 1.5-9.4 million Americans and is associated with high morbidity leading to hospitalizations and high mortality. Every year, 5-7 percent of patients with cirrhosis experience life-threatening decompensating events, such as ascites, hepatic encephalopathy (HE) and gastrointestinal bleeding (GIB), dropping the life expectancy from 12 years to less than two years. Also, 1-8 percent develop hepatocellular carcinoma (HCC), which is associated with high mortality. The challenge is to accurately predict those patients who are likely to develop decompensating events and which patients are likely to die. Accurate risk stratification of persons with cirrhosis will allow for early identification and prioritization for guideline recommended care and emerging therapies (for example, statins).

Several predictive models exist but none of them adequately answer this question. Furthermore, no longitudinal cost of care analyses and cost prediction has been performed in the U.S. for people with cirrhosis. The care of patients with cirrhosis is complex, often involving costly recurrent hospitalizations and procedures. In 2015, the hospital costs alone associated with cirrhosis were reported to be $16.3 billion. Our proposed research will analyze a large national administrative health payer with detailed information on diagnoses, procedures, laboratory tests, medications, in- and outpatient care, as well as standardized costs for insured Americans between 2011 and the present.

Such a large population-based cirrhosis cohort, which includes cost data, offers a unique and unprecedented opportunity to study disease progression, develop highly accurate prediction models and study costs. The following are our aims: 1) describe the natural history of cirrhosis over time in a large longitudinal cohort of insured Americans with liver cirrhosis in the United States; 1.1) data preparation and variable transformation; 1.2) adjudicate potentially risk-relevant covariates by a cirrhosis stakeholder panel; 1.3) describe the natural history of cirrhosis; 2) predict the risk of decompensation, hospitalization and death in patients with cirrhosis using a large longitudinal administrative dataset; 2.1) model the risk of decompensation; 2.2) model the risk of hospitalization; 2.3) merge data with the National Death Index and model the risk of death; 3) predict costs associated with all aspects of care in patients with liver cirrhosis; 3.1) ascertain standardized cost stratified by state/phenotypes of liver cirrhosis; and 3.2) model the cost of care over time.

Read more

Funding

The Feinberg School of Medicine has increased seed funding up to $50,000 for application preparation to initiate new multi-investigator program project or center grant applications involving Feinberg faculty. Learn more on the website here.

Spinal Cord Injury Research on the Translational Spectrum

More information

Sponsors: Craig H. Neilsen Foundation

Letter of intent: June 10

Invited full proposals: November 11

Upper amount: postdoctoral fellowships (up to $150K), two-year pilot research grants for new investigators (up to $300K), and three-year senior research grants (up to $600K)

The Spinal Cord Injury Research on the Translational Spectrum focuses on research designed to improve understanding and advance the current treatment of acute and chronic spinal cord injury. The goal of this grant is to address gaps in the field and advance novel approaches to improving function after spinal cord injury. Grants support research projects that include but are not limited to: neuroprotection of the pathological mechanisms that occur after spinal cord injury, pharmacological therapies to improve function after spinal cord injury, testing of innovative rehabilitation strategies and devices in person with spinal cord injuries, and the effects of spinal cord injuries and novel interventions on sensory and motor function.

Young Investigator Awards – Prostate Cancer

More information

Sponsors: Prostate Cancer Foundation

Submission deadline: April 25

Upper amount: $250,000

The Prostate Cancer Foundation funds research with the goal of ending death and suffering from metastatic prostate cancer. Funds from the Young Investigator Awards may be used innovatively and flexibly to advance the career and research efforts of awardees. Applications are sought from early-career basic scientists, medical oncologists, pathologists, urologists, radiologists, radiation oncologists, public health experts, bioinformaticians, bioengineers or professionals from any other field that could contribute to the end of prostate cancer. Applications from those traditionally under-represented in science and medicine are highly encouraged.

Daymon Runyon-Rachleff Innovation Awards

More information

Sponsors: Daymon Runyon Cancer Research Foundation

Submission deadline: July 1

Upper amount: $800,000 total over four years

The Innovation Award is designed to provide support for the next generation of creative thinkers with 'high-risk' 'high-reward' ideas that have the potential to impact our approaches to prevention, diagnosis or treatment of cancer. This is a two-year award with the potential to be renewed for an additional two years.

National Centers for Translational Research in Reproduction and Infertility (Clinical Trial Optional)

More information

Sponsors: National Institutes of Health

Letter of intent: June 28

Submission deadline: July 28

Upper amount: $1.1 million/year (maximum project period is five years)

This funding opportunity encourages research in reproductive sciences. It is becoming apparent that non-genetic factors are involved in fertility and diseases of reproductive health. This funding should focus on research involving multi-component reproduction and infertility research. Applications that address the 'omic' (e.g., genomic, epigenomic, proteomic, metabolic) bases of reproductive health and fertility will be strongly encouraged. Particular emphasis will be on applications that go beyond correlative studies to address possible causality and contributions of variants to inherited reproductive health.

If you are interested in NIH funding opportunities, sign up for the weekly email here.

Finding Expertise and Being Found

By Kristi Holmes, PhD, Director, Galter Health Sciences Library

One of the most important aspects of modern biomedical research is its collaborative nature which regularly requires finding and connecting with different expertise and perspectives. Identifying and connecting with expertise outside of one's own discipline can be challenging, but it is an essential skill. Here are a few strategies for finding expertise and being found that can help support dissemination, networking and successful collaboration.

Publication Databases

Finding Expertise: Publication databases such as PubMed and Scopus allow users to search for concepts that can be limited to target specific timeframes or geographic regions. Leveraging publication data can be helpful if your collaboration requires regular access to a specialized instrument, if you are looking for a speaker from a particular geographic region, or if you are student looking for a mentor in a specific topic area. As terminologies can differ across disciplines, do your homework or consult with your Liaison Librarian to understand if there are keywords that can help your search be more effective.

Being Found: There are steps you can take to enhance discoverability through your published works. Optimize article titles to be clear, concise and declarative. Incorporate both natural language keywords as well as Medical Subject Heading (MeSH) terms. Use the MeSH on Demand tool from the National Library of Medicine to help identify MeSH terms in your abstract or manuscript, as well as articles similar to your submitted text. If possible, repeat significant keywords or phrases (and their synonyms), as the document is considered more relevant if a given term is used more frequently. Likewise, include any unique identifiers in the abstract to link to datasets or files (genes, proteins, structures, etc.) deposited in public databases.

Scholarly Profiles

Finding Expertise: Feinberg Faculty Profiles help faculty document work and career accomplishments and is an excellent resource for finding expertise right here on campus. Searchers can enter keywords or terms related to methods or instrumentation (e.g., "artificial intelligence"), or even professional activities such as service or memberships (e.g. "National Academies").

Being Found: The Office of Faculty Affairs offers several reasons why an accurate and robust faculty profile is important, including improved visibility to prospective collaborators, mentees and media; informing donors and funding organizations about your work; and focusing your "findability" on specific topics that you wish to highlight. Regardless of the platform, be sure to regularly curate your online scholarly identity in these various profiles to ensure that the content represents you, your work and your active scholarly efforts.

Your Online Presence

Finding Expertise: Many people are comfortable with doing a quick search on Google and you can leverage the power of the platform by optimizing your search. Twitter is increasingly used by academics to communicate about personal and professional interests and can be a good way to find expertise. Twitter can be searched by keywords or a relevant hashtag (e.g., #massspec or #meded). Filter your search by popular tweets, people tweeting or most recent results to refine your results.

Being Found: Keep your profiles up-to-date and acknowledge your funding on all work to enhance your discoverability and meet requirements. Deposit scholarly works into DigitalHub to ensure that they are findable, and register for an Open Researcher and Contributor ID (ORCID), a persistent digital identifier which can connect with your professional information including your Northwestern NetID (ORCID Enrollment). Use this ID to share your information with other systems, ensuring you get recognition for all your contributions, saving you time and hassle and reducing the risk of errors.

How Can We Support You?

Finding expertise and *being found* depends on the discoverability of disseminated work. Effective dissemination takes planning and our Department of Research Assessment and Communications provides a wide range of services and resources to support you. For questions or support on these or other topics, please contact your Liaison Librarian.

High-Impact Factor Research

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(continued on next page)

High-Impact Factor Research

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Featured Core

NUCATS Center for Clinical Research

The Northwestern University Clinical and Translational Sciences (NUCATS) Institute's Center for Clinical Research (CCR) supports Northwestern clinical and translational scientists, trainees and staff by providing resources, services and guidance specific to the needs of each investigator and study. CCR aims to accelerate study start-up, increase investigator and study coordinator satisfaction and improve financial outcomes.

Specifically, CCR provides regulatory and financial support for teams, provides clinical trial support at the Robert H. Lurie Comprehensive Cancer Center of Northwestern University and Northwestern Memorial Hospital Clinical Research Units, as well as remotely through mobile nurse support, and offers a range of recruitment and retention tools.

Investigators who know which CCR services they would like to use are encouraged to complete the CCR intake form. The center also offers virtual studio consultation to learn how CCR and other NUCATS services can help with research projects as investigators plan their grant submissions.

Contact:
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