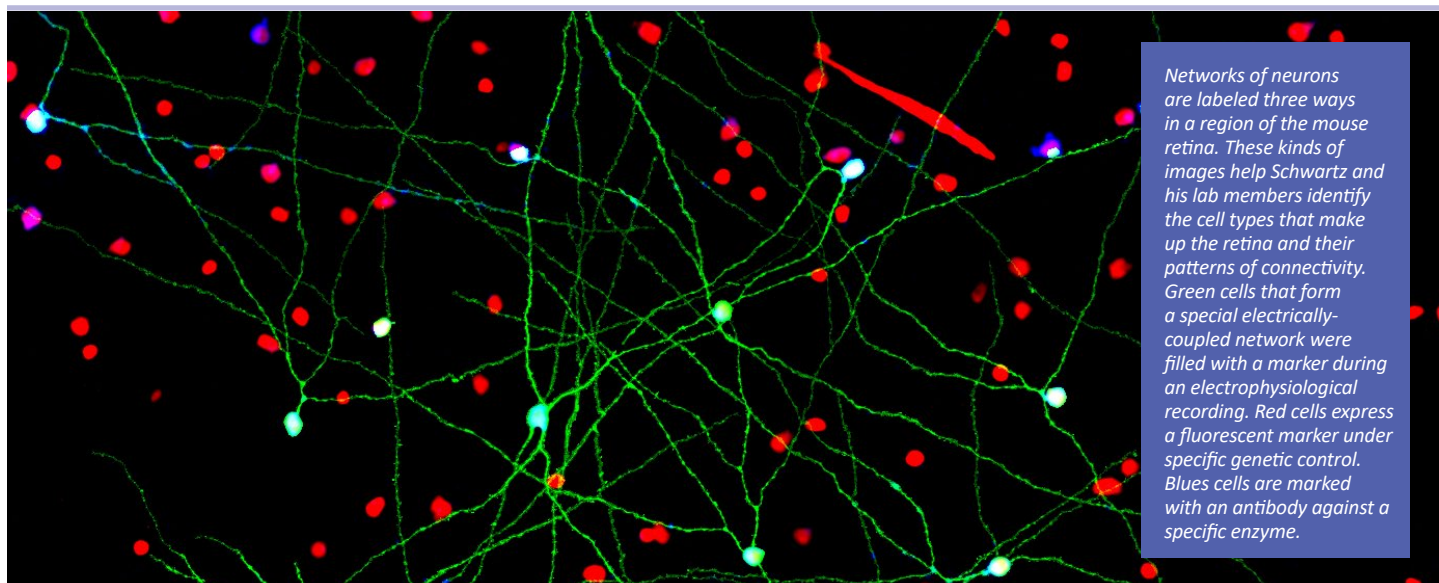


# Breakthroughs

Feinberg School of Medicine Research Office

June 2019



Networks of neurons are labeled three ways in a region of the mouse retina. These kinds of images help Schwartz and his lab members identify the cell types that make up the retina and their patterns of connectivity. Green cells that form a special electrically-coupled network were filled with a marker during an electrophysiological recording. Red cells express a fluorescent marker under specific genetic control. Blues cells are marked with an antibody against a specific enzyme.

## Mapping the Visual System, From Photoreceptors to Brain

By Emily Ayshford

The retina, commonly thought of as a device that takes a “snapshot” of the visual world for further processing by the brain, is now known to be a complex network of cells and synapses that sorts and packages different aspects of the visual scene for transmission to dozens of areas of the brain.

Not only does the retina process images, it also serves as a key part of the central nervous system, helping to regulate everything from daily hormonal oscillations to circadian rhythms.

With advances in technology and genetics, Northwestern investigators are conducting basic science research to understand just how the retina works in concert with the brain.

This understanding could ultimately lead to novel treatments for many diseases that lead to blindness, including macular degeneration and diabetic neuropathy.

“The best and most successful treatments of today and in the

future are going to depend on a very precise understanding of different cell types, and how those cells communicate with each other and the brain,” said [Nicholas Volpe, MD](#), the George W. and Edwina S. Tarry Professor of [Ophthalmology](#) and chair of the department. “We’re working to understand exactly what each type of retinal neuron does, what cells it synapses with, how this informs vision processing and ultimately how we might replace or repair damaged cells.”

### Mapping Out Retinal Cells

At the heart of much of this area’s research are retinal ganglion cells — the neurons located near the inner surface of the retina. There are about 50 known types of these cells, which transmit information from the retina to more than 50 areas in the brain. [Greg Schwartz, PhD](#), assistant professor of Ophthalmology and [Physiology](#), is working to definitively classify all types of ganglion cells, using the latest technologies and techniques to figure out where they go, and what they do.

Retinas are particularly interesting to study because they can survive — and continue to function — for many hours outside of the body. That allows Schwartz to use techniques like

## Mapping *(continued from cover page)*

electrophysiology to study the mouse retina ex vivo. By placing the retina on a slide and showing it movies, he can record the spikes in the ganglion cells that travel down the optic nerve (and ultimately in the brain) to better understand how different visual cues affect different cells. Some ganglion cells are motion-sensitive, while others respond to visual cues like edges or colors.

Schwartz hopes to identify each retinal ganglion cell's function, genetic signature, and how it is connected to targets in the brain, and after years of research, he estimates that he and other investigators are about 90 percent there. He [recently discovered one cell](#) that is likely involved in eye growth, which could ultimately lead to new ways of preventing and treating myopia (nearsightedness).

"We have a real chance of solving the entire retina, of understanding it on a level that we are not close to understanding in the rest of the brain," he said.

### How Retinal Cells Use Proteins Differently

Beyond visual cues, retinas provide the brain with key information that regulates other behaviors, such as our sleep/wake cycles. One subset of these cells, called intrinsically photosensitive retinal ganglion cells, may hold the key to understanding these behaviors.

[Tiffany Schmidt, PhD](#), assistant professor of [Neurobiology](#) at Weinberg, studies these cells in genetic mouse models. She, too, uses electrophysiology to study how retinal cells respond to movies on a slide versus how the animal with the same genetic disposition behaves in response to the same movies.

Schmidt recently found that when she removed a protein called melanopsin from retinal cells, the cells could not see contrast as well. This was puzzling because melanopsin was only thought to detect the brightness of environmental light, not image features. She and her group eventually discovered that intrinsically photosensitive retinal ganglion cells all use

melanopsin in different ways, depending on the behavior. Some cells use them for contrast, while others use the protein to regulate sleep/wake cycles.

"These cells are all using this protein in unique, specialized ways," she said. Next, she wants to map how the intrinsically photosensitive retinal ganglion cells are connected to different brain areas to influence these very different behaviors.

"I'm really interested in how we take in information from our environment and how it affects our behavior," she said. "The visual system is a great model for studying this."

### Following the Signal

But retinal ganglion cells are just one step in a long chain of connections from the eye to the brain.

[Steven DeVries, MD, PhD](#), is interested in the first step — how the cone photoreceptor synapse enables the cone to signal to the next neurons in line, the retinal bipolar cells.

To do this, he uses the ground squirrel as a model — since it has a nearly all-cone retina — and records the signals that flow from the cone to the bipolar cell across the synapse. He is also working to grow 3D ground squirrel retinas from stem cells to better understand the proteins expressed in the synapse.

"We want to understand why this synapse has such an unorthodox design and how it functions to support vision," said DeVries, who is the David Shoch, MD, PhD, Professor of Ophthalmology.

DeVries is also collaborating with [Yongling Zhu, PhD](#), assistant professor of Ophthalmology and Physiology, on a project in which retinal ganglion cells are infected with rabies virus. Because the rabies virus spreads rapidly across synapses in the brain, including in the retina, it is a unique tool to understand neuron connections. Rabies allows them to identify the amacrine cells (in the inner retina) and bipolar cells that talk with each type of ganglion cell.

"We want to be able to follow the visual signal as it goes through the retina and into the brain," said DeVries. "That's the holy grail — to take a piece of the nervous system and have a complete description of how that works."

DeVries is equally excited about the clinical possibilities of this knowledge. "Clinicians and scientists are using the same techniques in different ways and developing insights together," he said.

That sort of basic science to translational science is key in the Department of Ophthalmology, according to Volpe.

"We are really of the mindset that when we figure out how these cells communicate with each other, we will be able to make meaningful contributions to reverse vision-affecting diseases," Volpe said.

## CONTENTS

<a href="#">Global Health</a>	3
<a href="#">Faculty Profile: Daniela Matei, MD</a>	4
<a href="#">Student Profile: Warren McGee</a>	5
<a href="#">Staff Profile: Megan Connolly</a>	6
<a href="#">In the News, NUCATS Corner, Podcast</a>	7
<a href="#">Sponsored Research and New Faculty</a>	8
<a href="#">Funding</a>	9
<a href="#">Galter Library Connection</a>	10
<a href="#">High-Impact Factor Research</a>	11
<a href="#">Featured Core and NIH News</a>	12

# Global Health, Elevated: A New Feinberg Institute Launches

By Will Doss

On March 27, approximately 60 members of Northwestern University Feinberg School of Medicine's Center for Global Health gathered for a retreat in Wieboldt Hall to discuss plans for the evolution of a new institute focused on global health with expanded objectives, enhanced collaborations and a renewed mission.

Now, building on the international work of numerous faculty across Northwestern and unifying programs such as the center — until now embedded within the Institute for Public Health and Medicine (IPHAM) — and the Global Health Initiative Fund, Northwestern has established a new [Institute for Global Health](#) that aims to improve health in middle- and lower-income countries around the world and deepens the medical school's commitment to solving health problems worldwide.

This new institute will continue strengthening connections throughout Northwestern, according to [Robert Murphy, MD, '81 '84 GME](#), the John Philip Phair Professor of [Infectious Diseases](#) and executive director of the new institute.

"There are big pressing needs worldwide; our objective is to help the citizens of these areas through technology and training," said Murphy, also a professor of Biomedical Engineering at the McCormick School of Engineering. "The broader structure of an institute fits better with the multi-disciplinary nature of what we're doing."

[Robert Havey, '80 MD, '81 '83 GME](#), clinical professor of [Medicine](#) in the Division of [General Medicine and Geriatrics](#), and director and founder of the [Global Health Initiative Fund](#), will serve as deputy director of the Institute for Global Health.

"The majority of people on this planet have poor access to even basic healthcare, creating both a humanitarian crisis and a critical threat to the social and economic stability of the world," Havey said. "Northwestern's Institute for Global Health will expand upon the work started by the Global Health Initiative and the Center for Global Health, reaching across the university to find innovative and sustainable solutions. Our work will affect the lives of people everywhere, from the streets of Chicago to the villages of sub-Saharan Africa, making it possible for billions of people to live healthy and productive lives."

The institute's guiding principles will align with the United Nation's Millennium Development Goals — eight objectives which range from halving extreme poverty to halting the spread of HIV/AIDS, tuberculosis, malaria and other diseases. While older models of global health relied on mission trips or exporting Western-style care to lower-income countries, that approach has fallen out of favor, according to Murphy.



"The whole idea that there's nobody taking care of people in these countries is just not true — they have doctors and facilities, but their doctors may not have great resources," Murphy said.

Instead, Northwestern focuses on nurturing local health and research infrastructures in low- and middle-income countries. For example: One current project, a collaboration with Northwestern Biomedical Engineering, is soliciting proposals from universities all across Africa for devices that can improve management of HIV/AIDS.

This kind of project can help jump-start development cycles, according to Murphy, and develop Northwestern expertise to gird similar projects against the potential pitfalls of later project development.

"It may give you enough for a prototype, so they can continue to raise funds and get into the next steps," Murphy said. "We want to train people to be able to meet their millennium development goals themselves."

The new institute will continue to offer a variety of educational opportunities for students and trainees, including the HBNU [Fogarty Global Health Training Program](#) and the [McGaw Global Health Clinical Scholars Program](#). "This is the logical growth of a successful Center for Global Health. We've expanded over the last 10 years, and now have many centers and a wealth of expertise," Murphy said. "It's time to really grow and become a top-ranked international institute."

Read more about the new Institute for Global Health [here](#). Faculty interested in joining the institute can visit the institute website and fill out a [request for membership](#).



# Fighting Ovarian Cancer

Daniela Matei, MD, Diana, Princess of Wales Professor of Cancer Research



Matei, also a professor of [Medicine](#) in the Division of [Hematology and Oncology](#) and of [Obstetrics and Gynecology](#) in the Division of [Gynecologic Oncology](#), studies how ovarian cancer grows and devises treatments that exploit weaknesses unique to the cancer. Ovarian cancer is more deadly than other reproductive cancers: Women with ovarian cancer often have few or mild symptoms until the disease is in an advanced stage, and therefore difficult to treat.

While Matei is relatively new to Feinberg, she has already established a wide network of colleagues reflecting her interdisciplinary work and has published in high-profile journals, including a study in the *New England Journal of Medicine* that could change the way women are treated for later stage endometrial cancer. Listen to our podcast about the study [here](#).

## Q&A

### What are your research interests?

My laboratory studies mechanisms of metastasis and novel therapeutics for ovarian cancer. The general theme is translation between bench and clinic, with laboratory research forming the foundation for clinical experiments.

A new focus of research in the laboratory is the characterization of unique traits and therapeutic vulnerabilities of cancer stem cells. We recently defined the metabolome of cancer stem cells as being enriched in unsaturated fatty acids which are generated in situ and provide distinct energetic substrate for these rare cells' survival. We are dissecting the mechanisms by which the unsaturated fatty acids fuel cancer "stemness" and are studying whether targeting lipid desaturases could eliminate cancer stem cells residual after chemotherapy.

Additionally, the laboratory is studying DNA and RNA methylation as a key regulator of response to DNA damage. Some of our laboratory findings were translated to the clinic by using DNA methyl transferase inhibitors to re-sensitize platinum-resistant ovarian tumors to chemotherapy, or, more recently, to immunotherapy. We characterized the genome and epigenome of platinum resistant ovarian tumors using specimens collected from clinical trials designed and conducted by our group. An ongoing investigator-initiated clinical trial at Northwestern University uses a DNA hypomethylating agent as a priming agent for immune checkpoint inhibitor therapy in women with platinum resistant ovarian cancer.

I have also been engaged in clinical research and serve as the principal investigator of many clinical trials testing novel therapies for ovarian cancer, including several cooperative group and National Cancer Institute-sponsored trials for gynecologic cancer.

### What is the ultimate goal of your research?

The ultimate goal is to improve the outlook of women with chemotherapy-resistant ovarian cancer by bringing new treatments developed in the laboratory. If we could benefit one patient, all the effort would have been worthwhile. Fortunately, I think, we have already reached that goal.

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

I am a relatively new investigator at Northwestern, having started in January 2016. I found the community of investigators in the [Robert H. Lurie Comprehensive Cancer Center of Northwestern University](#) to be especially welcoming and in the short time that I have been here, I have established many collaborations, who are helping re-shape my research interests. For example, by collaborating with [Dr. Bin Zhang](#) in the Department of [Medicine](#), we have expanded our reach to evaluate the impact of epigenetic modifiers on the immune landscape of tumors. Together, we have been successful obtaining new funding from the Department of Defense to allow studying tumor biopsies from women enrolled in a clinical trial using a novel hypomethylating agent in combination with an immune checkpoint inhibitor.

I'm also collaborating with [Dr. Vadim Backman](#) in the [Center for Physical Genomics and Engineering](#), [Dr. Marcus Peter](#) in the Department of Medicine and [Dr. Ramana Davuluri](#) in the Department of [Preventive Medicine](#) and Northwestern University Clinical and Translational Sciences Institute ([NUCATS](#)). We are developing a new project characterizing transcription regulation in cancer stem cells. I also have active long-distance collaborations,

*continued on page 9*

# "Computer to Bench": At the Interface of Bioinformatics and Molecular Biology

Warren McGee, Medical Scientist Training Program



Warren McGee, an eighth-year student in the Medical Scientist Training Program ([MSTP](#)), investigates improving RNA-Sequencing data analysis in the laboratory of [Jane Wu, MD, PhD](#), a professor of [Neurology](#) and the Dr. Charles L. Mix Research Professor of Neurology and Psychiatry.

## Q&A

### Where is your hometown?

My family moved around quite a bit while I was growing up. I lived in West Virginia for most of my childhood but spent time in Evanston and California before that. In high school, my family moved to Western Springs, a suburb west of Chicago. My family has lived there ever since. Despite all of the moving, I consider greater Chicagoland area to be my home.

### What are your research interests?

I am primarily interested in the interface between bioinformatics and molecular biology. Bioinformatics (the "dry lab") provides powerful ways to sift through large amounts of data and identify pathways or genes that are likely to be critical for many important questions, including (A) understanding the pathogenesis of a disease, (B) predicting the treatment response or prognosis of a patient, or (C) predicting which patients might be at risk for a disease.

Ultimately, though, bioinformatics tools can only provide predictions — and all predictions need to be tested against reality. This is where molecular biology and other "wet lab" disciplines can help see which predictions hold up and which require further refinement. Physician-scientists tend to operate in a cycle of "bedside-to-bench" and "bench-to-bedside"; they allow clinical observations to drive important research questions. These, in turn, generate new discoveries that improve patient care. Similarly, I'm interested in the "computer-to-bench" and "bench-to-computer" cycle: allowing new predictions from bioinformatics to drive new discoveries at the bench, and conversely allowing new methods and discoveries at the bench to drive innovation with bioinformatics methods.

### What exciting projects are you working on?

My most exciting work has been related to improving how we analyze RNA-Sequencing (RNA-Seq) data. This work came as a direct result of the "bench-to-computer-to-bench" cycle. The bioinformatics field tends to think of RNA-Seq data as "count data" (this much of gene one, this much of gene two, etc.), when in reality it is "compositional data," where the units are

percentages and the only information available is relative (this percent of gene one, this percent of gene two, etc.). This has important implications for interpreting the results that come from RNA-Seq experiments, with current methods producing potentially misleading results, sometimes dramatically so. [Our work](#) advocates for broader adoption of using "exogenous spike-in" RNAs as a way to normalize data, allowing for an "apples-to-apples" comparison across samples.

Much of the remaining work I've been doing in the lab is applying this new RNA-Seq analysis method to our own datasets and the datasets of others, and bringing the new insights it reveals to the bench for validation.

### What attracted you to the MD/PhD program?

I have been interested in medicine since I was a kid; I honestly had "cancer researcher" as a potential career in a fifth-grade autobiography project. In college, while I was discerning whether medicine would be my career, I was given my first opportunity to do research in a lab. I absolutely loved the discovery process! As I progressed, I noticed a clear dichotomy between the clinical world and the research world, and felt at the time that I would have to choose one or the other. In the midst of this, I was introduced to the MD/PhD program as a possibility. Why choose one, when you can pursue both? After having gone through a large portion of my training, it is clear that MD/PhD-trained physician-scientists are unique chimeras — not fully in the clinical world or the research world, but a hybrid of both and serving as a bridge between.

### What has been your best experience at Feinberg?

Over my many years at Feinberg, the best experience has been witnessing the chain of mentorship and cooperation among students. I have received outstanding mentorship from faculty and students further along in their journey. I, in turn, have been blessed to have opportunities to mentor students who are earlier on in their training, whether through review sessions, tutoring or just conversations. In addition, a core value of the Feinberg curriculum related to the team-based philosophy is fostering cooperation among the students..

### What are your plans for after graduation?

I am just finishing my PhD, so I have two more years of medical school to complete. I am in the process of discerning what specialty to pursue, but I know for certain that I want to bring my status as a bridge between the clinical and research worlds, and between the dry lab and wet lab worlds, to bear on pursuing the dream of "precision medicine": giving each patient the best care possible for them as an individual.

# Overseeing Regulatory Requirements for Research Studies

Megan Connolly, Research Coordinator, Women's Health Research Institute



## Q&A

### Where are you originally from?

I was born and raised in a northwest suburb of Chicago called Rolling Meadows.

### What is your educational background?

I graduated with a bachelor's degree in business administration, with a concentration in healthcare management. I am currently working on my master's degree in health services administration.

### Please tell us about your professional background.

Prior to working at Northwestern University, I was an assistant office manager at a private OB/GYN practice for five years. I started my career at Northwestern Medicine as an administrative assistant, and now I am a research coordinator in the [Department of Obstetrics and Gynecology](#).

### Why do you enjoy working at Northwestern?

I enjoy the atmosphere and energy that Northwestern exudes. There are always exciting new science and medical advances taking place, which motivate and inspire me to work hard and strive for success.

### How do you help scientists at the medical school?

I am responsible for overseeing all the regulatory requirements for human subject research studies. It is also my responsibility to educate and inform patients about the various research studies that are available to them, obtain proper informed consent and perform data collection.

### What is your favorite part of the job?

Although I am not on the clinical side, I love being able to connect and communicate with patients.

### What exciting projects are you working on?

I am working on several exciting research studies, but the two I am most excited about are looking at the reproductive health of patients with hematologic malignancies. The first study is investigating reproductive health and the impact of tyrosine kinase inhibitors on female patients with chronic myelogenous leukemia (CML). There have been promising laboratory studies indicating that tyrosine kinase inhibitors can protect the ovaries from some of the harmful effects of chemotherapy and radiation. The second study looks at the effects of therapies on male and female patients with hematologic malignancies. Our goal is to identify patients who have an increased risk of infertility, and to develop strategies to prevent these negative impacts.

### What do you like to do in your spare time?

I love going to the Chicago Riverwalk. It's my favorite place to go and wander in the city. It has amazing views and is a great place for a nice run, or just to hang out with family and friends. I also love doing yoga. It is great for my mental and physical health.

### Anything else we should know about you?

I am a two-time cancer survivor of Hodgkin's Lymphoma. I was fortunate enough to be treated here at Northwestern, so I am extremely grateful to be working here and giving back to the institution that saved my life. This past year I was able to be a patient advocate and testify for HB2617 in Springfield. This bill helps patients who are at risk of becoming infertile as a result of medical treatment. The bill mandates that insurance companies cover fertility preservation for these patients at risk. This past summer HB2617 passed, and went into effect January 1, 2019. [Read more about HB2617.](#)

# Research in the News

## **NBC News, May 1**

[Why do people love coffee and beer? It's the buzz, not the taste, study finds](#)

Marilyn Cornelis, PhD, was quoted.

► This research was also featured in *Yahoo! News*.

## **Reuters, May 2**

[Happiness training may ease dementia caregivers' anxiety, depression](#)

Judith Moskowitz, PhD, was quoted.

► This research was also featured on *National Public Radio*.

## **HealthDay, May 6**

[Many Kids With Chronic Illness Are Still Happy: Study](#)

Courtney Blackwell, PhD, was quoted.

► This research was also featured in *U.S. News & World Report*.

## **TIME, May 6**

[Heart Problems Are Killing More Americans—Even Younger Ones. Here's How to Reduce Your Risk](#)

Sadiya Khan, MD, MSc, was quoted.

► This research was also featured in *CNN*, *U.S. News & World Report* and *HealthDay*.

## **U.S. News & World Report, May 7**

[2 Illinois Universities Launch Twins Research Project](#)

► This research was also featured in *Chicago Tribune*, *U.S.* and *HealthDay*.

## **The New York Times, May 20**

[A.I. Took a Test to Detect Lung Cancer. It Got an A.](#)

Mozziyar Etemadi, MD, PhD, was quoted.

► This research was also featured in *Yahoo! News*.

## **HealthDay, May 21**

[Cholesterol Levels Improving Among U.S. Kids](#)

Amanda Perak, MD, MS, was quoted.

► This research was also featured in *WebMD*.

[More media coverage available online.](#)



## NUCATS Corner

### Access Research Design and Analysis Training for Study Coordinators

The NUCATS Research Design and Analysis Methods Program (RAMP) for Study Coordinators provides study coordinators and other interested study team members training on the primary components of health research design and analysis.

The in-person workshops have now been converted into online modules that can be accessed at any time. Study coordinators or other interested study team members can work their way through the RAMP for Study Coordinators program at their own pace and cover topics such as:

- *Data Along the Research Path: Trace research data from study design through publication*
- *The Mysterious Math of Medical Research: Dispel the mystery behind statistical summaries of research data*
- *Patient Reported Outcomes – Measuring Subjective Experience: Explore the systematic query of subjective experience using PROs*
- *Day-to-Day Statistical Issues in Clinical Trials: Survey statistical concepts underlying Phase I, II and III clinical trials*

For more information and to access the modules, visit [nucats.northwestern.edu/education-and-career-development/research-staff-development/ramp.html](http://nucats.northwestern.edu/education-and-career-development/research-staff-development/ramp.html).

## Latest Podcast Episodes

Subscribe to our podcast and rate it [here](#).



Heart Failure Deaths on the Rise in Younger People with Sadiya Khan, MD, Msc: Listen [here](#).

Changes to Endometrial Cancer Treatment with Daniela Matei, MD: Listen [here](#).



# Sponsored Research



**PI: Thomas Hope, PhD, professor of Cell and Molecular Biology, of Obstetrics and Gynecology, and at the McCormick School of Engineering**

**Sponsor: National Institute of Allergy and Infectious Diseases**

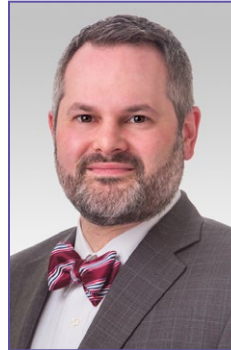
**Title: Characterizing Mucosal Changes in the FRT Leading to Increased HIV Acquisition**

The mucosal system of the female reproductive tract (FRT) is multifactorial, combining epithelial and mucus barriers, a highly specialized immunology, the microbiome and hormonal fluctuations to protect this complex and essential organ from attack by pathogens such as HIV. Perturbation of any of the components of this system has the potential to decrease barrier function while potentially increasing a woman's vulnerability to HIV sexual acquisition.

Recent studies have revealed that an increase in the presence of multiple pro-inflammatory cytokines are a strong signature of increased HIV acquisition in women. This increased inflammatory environment is consistent with the dysfunction of normal mucosal barrier function. A number of factors have been implicated in this inflammatory state including hormones, the microbiome and epithelial barrier disruption. However, the origin of these inflammatory cytokines and the mechanism of how they are related to increased HIV acquisition is not understood. To advance HIV prevention science, we need a better understanding of the FRT mucosal system.

In this project, Hope's team will examine hysterectomy derived cervical tissues and mucus donated by high-risk populations in Nairobi, Kenya, to gain insight into the changes in the mucosal system that alters epithelial and mucus barrier function. They will also examine how antibodies can potentially enhance the mucus barrier function, potentially revealing a novel strategy for HIV vaccine development.

[Read more about this project.](#)



**PI: Andrew Naidech, MD, MSPH, professor of Neurology, Anesthesiology, Medical Social Sciences, Neurological Surgery and Preventive Medicine**

**Sponsor: National Institute of Neurological Disorders and Stroke**

**Title: Hemostasis, Hematoma Expansion and Outcomes After Intracerebral Hemorrhage**

Intracerebral hemorrhage (ICH) is the most morbid form of stroke and has no treatment approved by the FDA. Hematoma expansion (HE) — interval growth of the hematoma — is a proximate cause of worse patient outcomes and death as larger hematomas displace brain tissue. Preventing HE is a promising strategy to improve outcomes for patients with ICH.

Our relative inability to predict HE, however, has impeded the development of effective treatment strategies for ICH, and several clinical trials have been unsuccessful. Even when HE has been reduced, our ability to detect a benefit is hampered by relatively insensitive patient outcomes.

This proposal will resolve two roadblocks that prevent the development of effective treatments for ICH, the most morbid form of stroke. Three comprehensive stroke centers will partner to prospectively enroll patients with ICH, measure hemostasis, measure HE and record patient outcomes with state-of-the-art assessments, including the NIH Patient Reported Outcomes Measurement Information System (PROMIS) and NIH Toolbox.

The project will determine how platelet activity, activation of coagulation, and fibrinolysis predict HE, and how HE, in turn, affect patient outcomes.

[Read more about this project.](#)



## Welcome New Faculty

[Lee Cooper, PhD](#), joins as an associate professor of [Pathology](#). His research focuses on computational pathology and developing machine-learning software to provide accurate predictions of clinical outcomes and quantitative histologic measurements. His lab develops new algorithms to extract information from genomic and imaging datasets, and creates software infrastructure that enables investigators to interact with large and complex datasets using predictive algorithms. His goal is to improve the information used in clinical interventions and to provide investigators with insights into disease biology. He has received over \$7.3M in funding as a principal investigator from the NCI, NIBIB, NINDS, NLM and industry sources. He received his PhD in electrical engineering from Ohio State University in 2009.



## Ovarian Cancer

(continued from page 4)

with Drs. Ji-Xin Cheng at Boston University, Kenneth Nephew at Indiana University and David Nolte at Purdue University. The concept of team science is more important than ever, with cross-cutting research themes and intersecting technologies being the forces that drive science going forward.

### How is your research funded?

My laboratory has received research funding from the National Cancer Institute, Department of Defense, U.S. Department of Veterans Affairs and other private cancer foundations such as the Ovarian Cancer Research Alliance, V-foundation, and others. Together with other clinical investigators in the Lurie Cancer Center, we were awarded a LAPS grant from the NCI this year to fund clinical research related to cooperative group trials.

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

I am very fortunate to be leading a group of engaged young scientists. [Dr. Horacio Cardenas](#) has been with me for almost 10 years and he is the mentor who welcomes students and keeps them on task — the glue that keeps the lab together. [Dr. Hao Huang](#) and Yinu Wang are promising junior investigators who lead the efforts on epigenetic alterations in platinum resistant ovarian cancer models and in cancer stem cells. Two very productive graduate students, Yaqi Zhao and Guangyuan Zhang, bring technical precision, curiosity and strong analytic tools to the team.

Last, but not least, we welcome physicians in training to get a taste of laboratory work and incorporate this knowledge in the way they approach clinical practice in the future. For example, Dr. Mathew Cowan, a fellow in gynecologic oncology, completed his research project in the lab, helping develop a new methodology to identify immune cells subpopulation in the tumor microenvironment.

### Where have you recently published papers?

Our work describing alterations in lipid metabolism in cancer stem cells was [published](#) in *Cell Stem Cell* in 2017. We publish consistently in American Association for Cancer Research (AACR) journals, such as *Cancer Research*, *Clinical Cancer Research* and *Molecular Cancer Therapeutics*.

This year, I am the lead author on a standard of care changing paper published in the *New England Journal of Medicine*. This paper presents results of a randomized international phase III trial that compared chemo-radiotherapy to chemotherapy for the treatment of locally advanced endometrial cancer. The results of NRG-GOG 0258 indicate that the combined modality regimen did not result in an improvement in recurrence-free survival, and that chemotherapy alone remains the standard of care for stage III uterine cancer.

The study confirms that chemotherapy alone should be the preferred treatment approach for this patient population, avoiding the long term toxicities associated with radiotherapy.

# Funding

## Melanoma Research Program (MRP) Translational Research Award

[More information](#)

**Sponsor:** Department of Defense Melanoma Research Program

**Proposal Due:** July 26

**Submission Deadline:** Proposal is required; application submission is by invitation only.

**Upper Amount:** \$600,000

**Synopsis:** The MRP Translational Research Award supports hypothesis-driven, translational, high-impact research and encourages applications with mature research projects that specifically focus on critical scientific or clinical melanoma issues. Important factors under consideration will be: continuity of research, clinical applicability and leveraging of clinical samples from clinical trials and/or biorepositories. The award will support identifying scientific outcomes through rigorous, robust research that are translatable toward treatment and/or preventive strategies. Research proposed should aim to accelerate promising findings toward clinical applicability and leverage research results to maximize impact. Proposed studies should focus on the commonalities in melanoma research to advance the understanding of the field.

## Drug Screening with Biofabricated 3-D Skin Disease Tissue Models (U18 Clinical Trial Not Allowed)

[More information](#)

**Sponsor:** National Center for Advancing Translational Sciences (NCATS)

**Letter of Intent Due:** July 1

**Submission Deadline:** July 31

**Amount:** \$400,000

**Synopsis:** The purpose of this funding opportunity is to build on existing research under the NCATS Pilot Program for Collaborative Drug Discovery Research Using Bioprinted Skin Tissue ([RFA-TR-17-007](#)) and utilize physiologically-relevant and validated 3-D biofabricated skin disease tissue models in multi-well drug screening platforms. The award will support intramural-extramural collaborations to implement the use of 3-D biofabricated skin tissue models and provide evidence of success for 3-D drug screening platforms.

## Workshops on the Use of Adolescent Brain Cognitive Development (ABCD) Data (R25 Clinical Trial Not Allowed)

[More information](#)

**Sponsor:** National Institute on Drug Abuse (NIDA) and National Institute of Mental Health (NIMH)

**Letter of Intent Due:** September 17

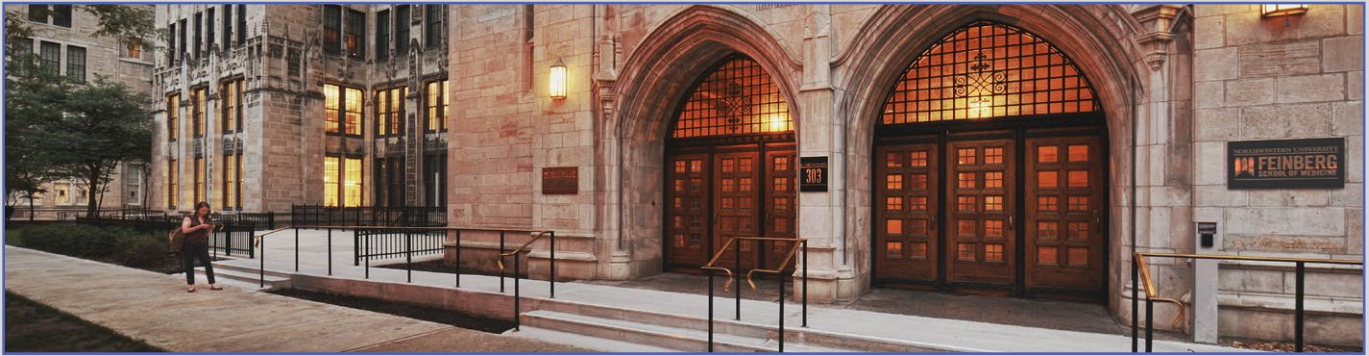
**Submission Deadline:** October 17

**Upper Amount:** \$300,000

**Synopsis:** The goal of this program is to support educational activities that complement and/or enhance the training of a workforce to meet the nation's biomedical, behavioral and clinical research needs in the use of ABCD data. This funding will support creative educational activities with a primary focus on courses for skills development. In particular, NIDA/NIMH are interested in supporting short-term workshops that will allow participants to explore the hands-on use of ABCD data, through cooperative or competitive approaches.

[View more funding opportunities](#)

# Evaluating Research with Critical Appraisal



By Eileen Wafford, Research Librarian

Critical appraisal (CA) is an integral step in the Evidence-Based Medicine process. CA requires readers to systematically examine a research article to assess the validity of the research methodology, identify bias and evaluate the results and interpretations. Need help with CA resources? Galter Health Sciences Library & Learning Center has you covered.

## PICO and the Research Question

PICO is a framework designed to help you create a well-built question. Identifying the research question and PICO components early in the appraisal process makes it easier to pinpoint important concepts and gauge the potential relevancy of an article. The following questions can help you evaluate a study using PICO.

### P- Population or Problem

- What are important characteristics and demographic information about the patients, population or problem under investigation?
- Did the authors discuss the [sample size](#) and assignment of participants?

### I - Intervention

- Did the authors explicitly state the intervention (treatment, procedure, diagnostic test or prognostic factors) of interest?

### C – Comparator

- If applicable, did the authors state the comparison treatment or mention a placebo?

### O – Outcome

- Did the authors clearly state the [primary and secondary outcomes](#) of interest and describe how they measured the outcomes?
- Did the author address potential confounders?

## Question Type and Study Design

With the key concepts and the research question identified, check to see if the investigators used an appropriate [study design for that type of question](#). As the study design shapes all aspects of the study, an inappropriate study design is a major indicator of flawed research.

There are several classification systems based on the Levels of Evidence hierarchy with recommendations on which types of studies are appropriate for a research question. The Centre

for Evidence-Based Medicine (CEBM) presents a [levels of evidence table](#) that guides you on the types of studies that are appropriate for a question.

Like many levels of evidence hierarchies, the CEBM Levels of Evidence offers recommendations and not requirements. As readers, you must evaluate the content of the article to determine the quality of the data and reliability of the results.

## Understanding the Results

Evaluating the results of a research study can be the most intimidating part of critical appraisal. Simply put, the results section is where the authors provide quantitative and descriptive information about the outcomes in the study.

As we appraise the results, we should see data that reports:

- Estimates: values that convey the strength of associations or relationships observed in the investigation. These values might include the relative risk, odds ratio or sensitivity and specificity in diagnostic test studies.
- Inference: values such as confidence intervals, p-value and type I or type II errors that give readers an idea of the strength of the estimates and the ability to draw conclusions (or inferences) about the larger population.
- Adjustment: data generated by models such as stratification, analysis of covariance, multivariate models and logistic regression which address the effects of confounding variables.

Galter Library offers many [resources](#) to help readers understand issues that may affect the [transparency or reproducibility of research findings](#).

## Critical Appraisal Checklists

Several organizations have developed checklists to help readers critically appraise published studies. These checklists present criteria for evaluating the methodological quality of studies, including the research question, study design and results. View checklists provided by [CEBM](#), the [Joanna Briggs Institute](#), and other organizations on our [Tools for Reviewers](#) page.

Ultimately, readers must weigh the strengths and weaknesses of a study and determine its usefulness to your setting whether it is research, clinical or something in between. The tools listed above and available on the [Reporting Research and Evaluating Studies](#) GalterGuide can aid in the critical appraisal of medical research. Galter Library also offers a class on this, so check our [classes schedule](#) for the next one on the calendar.

# High-Impact Factor Research

Amsterdam SH, Stanev TK, Zhou Q, Lou AJ, Bergeron H, Darancet P, **Hersam MC**, Stern NP, Marks TJ. [Electronic Coupling in Metallophthalocyanine-Transition Metal Dichalcogenide Mixed-Dimensional Heterojunctions](#). *ACS Nano*. 2019 Apr 23;13(4):4183-4190.

Bentley AR, Sung YJ, Brown MR, et al. (including **Liu K**). [Multi-ancestry genome-wide gene-smoking interaction study of 387,272 individuals identifies new loci associated with serum lipids](#). *Nature Genetics*. 2019 Apr;51(4):636.

**Carota IA, Kenig-Kozloysky Y, Onay T, Scott R, Thomson BR, Souma T, Bartlett CS, Li YY, Procissi D, Ramirez V, Yamaguchi S, Tarjus A, Tanna CE, Li CJ, Eremina V, Vestweber D, Nadipupo SS, Breyer MD, Quaggin SE**. [Targeting VE-PTP phosphatase protects the kidney from diabetic injury](#). *Journal of Experimental Medicine*. 2019 Apr;216(4):936-949.

Curry SJ, Krist AH, Owens DK, Barry MJ, Cabana M, Caughey AB, Doubeni CA, Epling JW, Kemper AR, Kubik M, Landefeld CS, Mangione CM, Pbert L, Silverstein M, **Simon MA**, Tseng CW, Wong JB, Force USPST. [Screening for Elevated Blood Lead Levels in Children and Pregnant Women US Preventive Services Task Force Recommendation Statement](#). *JAMA-Journal of the American Medical Association*. 2019 Apr;321(15):1502-1509.

Franzmeier N, Rubinski A, Neitzel J, et al. (including **Mesulam MM, Mesulam MM, Rogalski E, Lipowski K, Weintraub S**). [The BIN1 rs744373 SNP is associated with increased tau-PET levels and impaired memory](#). *Nature Communications*. 2019 Apr;10:12.

Garrett-Bakelman FE, Darshi M, Green SJ, et al. (including **Turek FW**). [The NASA Twins Study: A multidimensional analysis of a year-long human spaceflight](#). *Science*. 2019 Apr;364(6436):144.

Gladstein S, Almossalha LM, Cherkezyan L, Chandler JE, Eshein A, Eid A, Zhang D, Wu WL, Bauer GM, Stephens AD, Morochnik S, Subramanian H, Marko JF, **Ameer GA, Szleifer I, Backman V**. [Multimodal interference-based imaging of nanoscale structure and macromolecular motion uncovers UV induced cellular paroxysm](#). *Nature Communications*. 2019 Apr;10:15.

Kiraly B, Liu X, Wang L, Zhang Z, Mannix AJ, Fisher BL, Yakobson BI, **Hersam MC**, Guisinger NP. [Borophene Synthesis on Au\(111\)](#). *ACS Nano*. 2019 Apr 23;13(4):3816-3822.

Kuppermann N, Dayan PS, Levine DA, Vitale M, Tzimenatos L, Tunik MG, Saunders M, Ruddy RM, Roosevelt G, Rogers AJ, **Powell EC**, Nigrovic LE, Muenzer J, Linakis JG, Grisanti K, Jaffe DM, Hoyle JD, Greenberg R, Gattu R, Cruz AT, Crain EF, Cohen DM, Brayer A, Borgialli D, Bonsu B, Browne L, Blumberg S, Bennett JE, Atabaki SM, Anders J, **Alpern ER**, Miller B, Casper TC, Dean JM, Ramilo O, Mahajan P, Pecarn. [A Clinical Prediction Rule to Identify Febrile Infants 60 Days and Younger at Low Risk for Serious Bacterial Infections](#). *JAMA Pediatrics*. 2019 Apr;173(4):342-351.

Liu XL, Wang LQ, Li SW, Rahn MS, Yakobson BI, **Hersam MC**. [Geometric imaging of borophene polymorphs with functionalized probes](#). *Nature Communications*. 2019 Apr;10:7.

Ng K, **Nimeiri HS**, McCleary NJ, Abrams TA, Yurgelun MB, Cleary JM, Robinson DA, Schrag D, Miksad R, Bullock AJ, Allen J, Zuckerman D, Chan E, Chan JA, Wolpin BM, Constantine M, Weckstein DJ, Faggen MA, Thomas CA, Kournioti C, Yuan C, Ganser C, Wilkinson B, Mackintosh C, Zheng H, Hollis BW, Meyerhardt JA, Fuchs CS. [Effect of High-Dose vs Standard-Dose Vitamin D-3 Supplementation on Progression-Free Survival Among Patients With Advanced or Metastatic Colorectal Cancer The SUNSHINE Randomized Clinical Trial](#). *JAMA-Journal of the American Medical Association*. 2019 Apr;321(14):1370-1379.

**Rodriguez AE**, Ducker GS, **Billingham LK, Martinez CA**, Mainolfi N, Suri V, Friedman A, Manfredi MG, **Weinberg SE**, Rabinowitz JD, **Chandel NS**. [Serine Metabolism Supports Macrophage IL-1 beta Production](#). *Cell Metabolism*. 2019 Apr;29(4):1003.

Tombal B, Saad F, Penson D, **Hussain M**, Sternberg CN, Morlock R, Ramaswamy K, Ivanescu C, Attard G. [Patient-reported outcomes following enzalutamide or placebo in men with non-metastatic, castration-resistant prostate cancer \(PROSPER\): a multicentre, randomised, double-blind, phase 3 trial](#). *Lancet Oncology*. 2019 Apr;20(4):556-569.

Waikar SS, **Srivastava A**, Palsson R, Shafi T, Hsu CY, Sharma K, Lash JP, Chen J, He J, Lieske J, Xie DW, Zhang XM, Feldman HI, Curhan GC, Appel LJ, Go AS, Kusek JW, Rao P, Rahman M, Townsend RR, Chronic Renal Insufficiency C. [Association of Urinary Oxalate Excretion With the Risk of Chronic Kidney Disease Progression](#). *JAMA Internal Medicine*. 2019 Apr;179(4):542-551.

**Yamawaki N, Li XJ, Lambot L, Ren LY, Radulovic J, Shepherd GMG**. [Long-range inhibitory intersection of a retrosplenial thalamocortical circuit by apical tuft-targeting CA1 neurons](#). *Nature Neuroscience*. 2019 Apr;22(4):618.

Zhao W, Wang X, Deik AA, Hanna DB, Wang T, Haberlen SA, **Shah SJ**, Lazar JM, Hodis HN, Landay AL, Yu B, Gustafson D, Anastos K, Post WS, Clish CB, Kaplan RC, Qi Q. [Elevated Plasma Ceramides Are Associated With Antiretroviral Therapy Use and Progression of Carotid Artery Atherosclerosis in HIV Infection](#). *Circulation*. 2019 Apr 23;139(17):2003-2011.

*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."*



# Featured Core

## Pathology Core Facility

The Pathology Core Facility (PCF) is a centralized, comprehensive core laboratory providing histology, immunohistochemistry, molecular analysis and microscopic evaluation services for human tissue-based studies. PCF is accredited by the College of American Pathologists (CAP) and certified through Clinical Laboratory Improvement Amendments (CLIA) with the capability to serve integral marker studies that require biomarker-based treatment arm assignment. In addition to core laboratory services, PCF performs procurement of fresh biospecimens for clinical trials and biobanking. It facilitates basic, translational and clinical research at Northwestern, with laboratories located at the downtown Chicago campus.

### Services Offered:

- Histology
- ImmunoHistoChemistry
- Bio Repository
- Molecular Pathology
- Digital Pathology (Microscopy)
- Clinical Trials Unit (CTU)
- Equipment use and training

### General Contact

Demirkan B. Gürsel, MSc, MS Law, PhD  
Scientific Director  
(312) 503-0324 (office)  
(240) 529-3666 (cell)  
(312) 503-1148 (fax)

### Location

Olson Pavilion, 8th Floor  
Room 8-419  
710 North Fairbanks Court  
Chicago, IL 60611

## Follow Feinberg Social Media



## NIH News

### NIH Inclusion Data by Research and Disease Category Now Available Online

For over two decades, NIH has required investigators to include women, members of racial and ethnic minority groups and children in their work unless there is an acceptable scientific or ethical rationale for their exclusion. Now, for the first time, select inclusion data on sex, gender, race and ethnicity are publicly available for various research, condition and disease areas. Public reporting by NIH Research, Condition and Disease Classification (RCDC) category is aimed at helping ensure that women and minorities are appropriately included in biomedical research across a diverse array of diseases and conditions. This data set can be accessed on the new [NIH RCDC Inclusion Statistics Report webpage](#).

### First Look at Outcomes for NIH Loan Repayment Program

[NIH Loan Repayment Programs \(LRPs\)](#) were designed to recruit and retain early-stage investigators into biomedical or biobehavioral research careers by repaying up to \$35,000 annually of a researcher's qualified educational debt in return for a commitment to engage in NIH mission-relevant research. Since its launch in 1988, LRPs have funded more than 25,000 awards totaling \$950 million.

Until recently not much was known about the benefits of LRPs beyond the obvious educational debt repayment benefit. The NIH Office of Extramural Research's Division of Loan Repayment recently analyzed programmatic outcomes of LRPs by comparing individuals who applied and received an award against those who applied and did not receive an award from 2003-2009. Results indicate that individuals who received an award had higher levels of "research persistence" — a cumulative measure of grant or fellowship applications, receiving grant or fellowship awards and publications. When looking at research persistence over a 14-year period, LRP-funded individuals demonstrated nearly double the increase in productivity compared to their unfunded peers.

To learn more about NIH Loan Repayment Programs, click [here](#) to visit their website. Individuals interested in applying, mark your calendars for the next application cycle, which will reopen September 1, 2019.