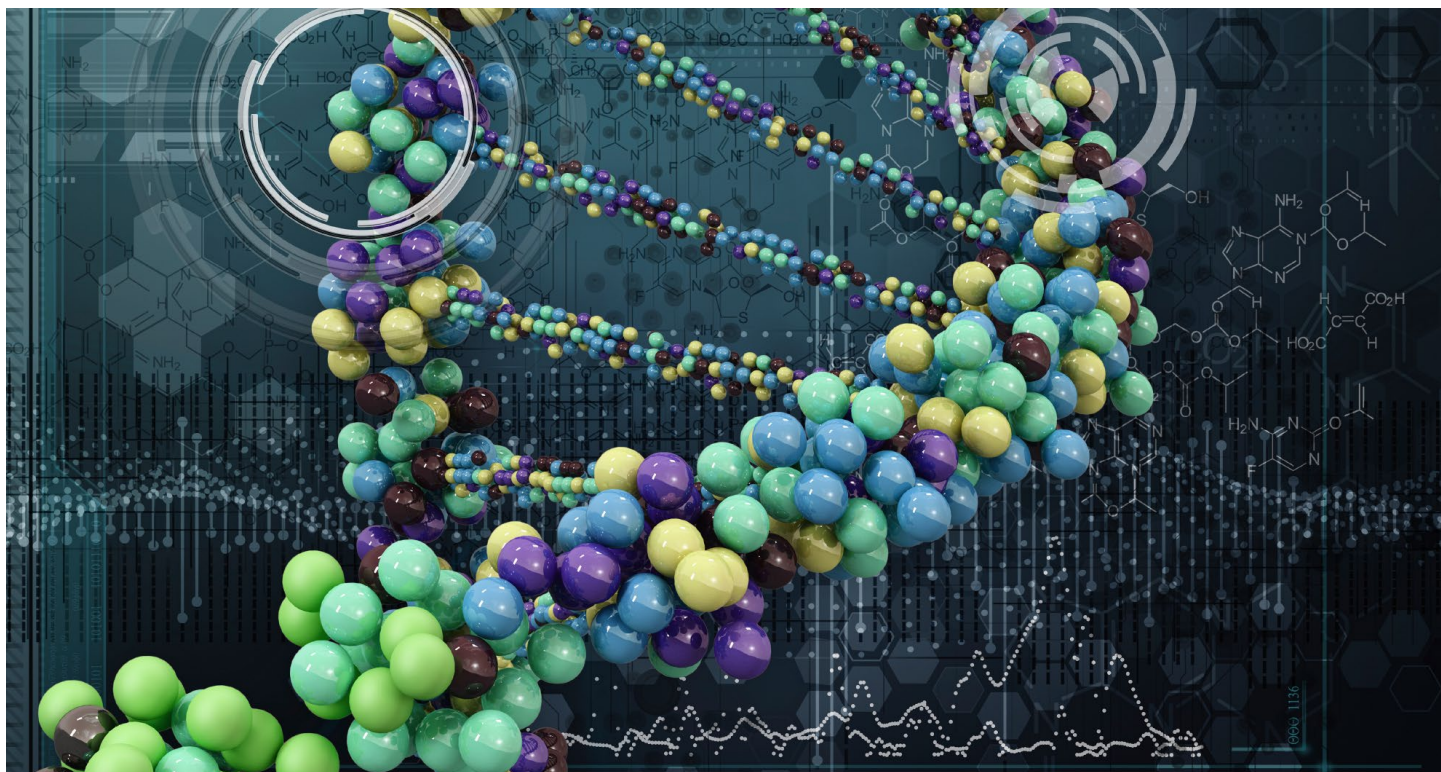


# Breakthroughs

Feinberg School of Medicine Research Office

December 2014



*Scientists seek to solve healthcare problems by studying medical and health information, such as segmenting cancer patients based on DNA sequencing data.*

## Solving Healthcare Problems with Informatics

**At Feinberg, data scientists seek to cure healthcare problems by studying medical and health information.**

“Our division serves as a catalyst for informatics activities across the medical school,” says [Justin Starren, MD, PhD](#), chief of the [Division of Health and Biomedical Informatics](#) in the Department of Preventive Medicine. “We are creating a department not for where informatics is today, but for where it will be in five to 10 years.”

Starren started the division in 2011 and has since added multiple faculty members whose diverse specialties range from natural language processing to translational and health informatics. As the division has grown, biomedical informatics collaborations have expanded into departments and centers such as Phar-

macology, Biological Chemistry, and the Center for Genetic Medicine. Additionally, the division has established an Advanced Bioinformatics and Bio-Computation Core (ABBC) led by Ramana Davuluri, PhD, open to all Feinberg investigators ([see page 3](#)).

Here’s a look at three of the division’s investigators.

### **Biomedical Natural Language Processing**

Analyzing and interpreting medical literature, text, and speech allows [Siddhartha Jonnalagadda, PhD](#), assistant professor in Preventive Medicine-Health and Biomedical Informatics, to create advanced algorithms designed to enhance the functionality of clinical knowledge systems such as electronic health records.

With funding from National Library of Medicine grants, he is im-

*(continued on page 2)*

## Solving Healthcare Problems with Data

(continued from cover page)

plementing text mining algorithms that summarize information from biomedical literature that clinicians could use at the point of care. Jonnalagadda has also teamed with the [Bluhm Cardio-vascular Institute](#) to extract biomedical concepts and associations found in clinical notes for use in clinical trial enrollment.

"Identifying which patients meet clinical trials criteria could save a lot of time, identify more patients, and gather more evidence," he says. "The research has significant impact in improving the quality of patient care, and minimizing costs and medical errors."

Jonnalagadda's work extends beyond electronic health records: since joining Feinberg in 2013, he published a method he developed to automatically rate journals for a given clinical topic, such as congestive heart failure. Quality of information on topics across journals varies, he says, so he created a formula based on a variety of metrics which can rate any journal in relation to its importance to the given topic. This formula can yield a reliable list of prioritized journals, which can support a clinician's decision-making and potentially decrease medical errors.

**Translational Bioinformatics and Cancer Genomics**

[Ramana Davuluri, PhD](#), professor in Preventive Medicine-Health and Biomedical Informatics, applies integrative informatics and next-generation sequencing techniques to create classification systems for deadly tumors that could aid in better diagnosis and treatment plans for patients. His research is supported by the National Library of Medicine.

"Cancer is a complex disease, which varies from one individual patient to another. Our goal is to place cancer patients into homogenous groups using sequencing data," he says. "If we can group patients based on the genomic information of their cancer, one treatment might work for one group, whereas a different treatment regimen might work for another group."

Davuluri, who collaborates with basic science and clinical research groups, envisions informatics playing a bigger role in



From left: Siddhartha Jonnalagadda, PhD, Ramana Davuluri, PhD, and Nicholas Soulakis, PhD, use healthcare data to yield important insights in the Division of Health and Bioinformatics.

clinical research and practice.

"Molecular understanding of tumor heterogeneity, or diversity, is key to personalized medicine and effective cancer treatments," he says. "We are developing novel computational methods that can accurately integrate genetic and epigenetic signatures, derived using multiple experimental platforms, for predicting patient outcomes based on genomic information. Soon cancer genome sequencing will be routinely used in clinical practice, making it possible in principle to tailor treatments to each patient."

**Healthcare Informatics**

[Nicholas Soulakis, PhD](#), knows that five out of eight employees at Northwestern Memorial Hospital in some way interact with a heart failure patient. Soulakis, assistant professor in Preventive Medicine-Health and Biomedical Informatics, uses epidemiologic surveillance methods to monitor community disease trends.

After coming to Feinberg last spring, he shifted from examining infectious diseases to cardiovascular disease such as congestive heart failure. With the data he collects, researchers and community health providers can create programs and targeted messaging to address these health issues. His research is funded by the National Library of Medicine.

"Collaborating with [Abel Kho, MD](#) (Medicine-General Internal Medicine and Geriatrics, and Preventive Medicine- Health and Biomedical Informatics), and [Ron Ackermann, MD, MPH](#) (Medicine-General Internal Medicine and Geriatrics, Center for Community Health, and Medical Social Sciences) and others, I started to understand the role that Northwestern plays in providing preventive care to the community," Soulakis says. "Now I want to understand how well Northwestern provides that care."

He uses algorithms to track quality and safety programs by analyzing networks of providers using a composite indicator of patient outcomes and cost to attribute value to collaborative care. Soulakis then applies this information to change how care is structured and understand how environments effect how teams work. He is applying these tools to the development of the new Northwestern Medicine Lake Forest Hospital.

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## Save the Date

# 11th Annual Lewis Landsberg Research Day Thursday, April 2, 2015

Research Day is a campus-wide event to promote faculty and trainee development through the sharing of exciting research and conversation with colleagues. The day features a number of speakers, awards, and the largest poster session at Northwestern.

The 2015 event will take place on Northwestern University's Chicago campus on Thursday, April 2, 2015, from 1 to 5 p.m.



## 2015 Research Day Keynote Speaker

**Elaine Fuchs, PhD, Investigator, Howard Hughes Medical Institute**

**Rebecca C. Lancefield Professor**

**Robin Chemers Neustein Laboratory of Mammalian Cell Biology and Development  
The Rockefeller University**

Elaine Fuchs, PhD, is interested in understanding the molecular mechanisms underlying the ability of skin stem cells to produce the epidermis and its appendages, including hair follicles and sweat and oil glands. She utilizes mammalian epithelial stem cell culture and mouse genetics as model systems. Her studies bridge an understanding of the normal biology of skin stem cells with an understanding of how these processes are transiently altered during wound healing, and how they go awry in human diseases of the skin—including genetic diseases, skin cancers, and proinflammatory disorders.

[Read more about Elaine Fuchs, PhD.](#)

## Introducing the Advanced Bioinformatics and Bio-Computation Core

Biomedical informatics support continues to be one of the most-requested services among researchers as biomedical research generates more datasets and as researchers become interested in analyzing publicly-available datasets.

Housed within the Northwestern University Clinical and Translational Sciences Institute, the Advanced Bioinformatics and Bio-Computation Core ([ABBC](#)) meets this demand, providing big data and computation support.

"The core faculty and staff works in collaboration with Feinberg investigators to help them generate data and results for single investigator and multi-PI large grants," says core director Ramana Davuluri, PhD. "Without the right skills, researchers will end up finding patterns that mean nothing and missing those that are true breakthroughs."

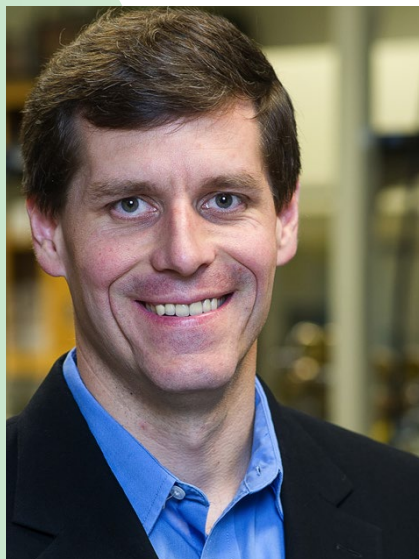
Services offered by the ABBC include data integration and analysis, predictive modeling, and data management. The core also provides consultation services to organize, store, and query genomic and proteomic data.

In data integration and analysis, core staff provides efficient and effective ways to create connections across data types, such as data in genomics and similar fields; multiscale data; and multiple platform data including microarray and NextGen sequencing.

Finally, core staff will also collaborate with investigators in predictive modeling to create new biomedical information. Examples of data creation include biomarker identification and molecular subtyping based on transcriptome and genomic data.

# Experimental Materials with Biomedical Applications

Mark Hersam, PhD, Professor of Medicine-Pulmonary, McCormick School of Engineering, and the Weinberg College of Arts and Sciences



In September, materials scientist [Mark Hersam, PhD](#), professor in Medicine-Pulmonary, the McCormick School of Engineering, and the Weinberg College of Arts and Sciences, received an impressive nod to his research career when he was named a [MacArthur Fellow](#). The five-year, \$625,000 unrestricted grant goes to exceptionally creative, dedicated individuals.

Since joining Northwestern University in 2000, Hersam has indeed proven dedicated to his crafts: investigating nanomaterials and teaching. His approach to research is interdisciplinary, drawing on techniques from materials science, physics, engineering, and chemistry. He is a leading experimentalist in hybrid organic-inorganic materials, with a focus on the study of the electrical and optical properties of carbon and related nanomaterials.

In addition to his faculty appointments, Hersam is director of Northwestern's Materials Research Center and a member of the [Robert H. Lurie Comprehensive Cancer Center](#) of Northwestern University.

## Q&A

### What are your research interests?

My laboratory is interested in the preparation, characterization, and application of one-dimensional and two-dimensional nanomaterials such as carbon nanotubes and graphene, respectively. One of the unique attributes of nanomaterials (compared to bulk macroscopic materials) is that their properties depend upon size. Consequently, strategies for controlling structure at or near the atomic scale allow new properties to be realized. The size-dependence of properties also implies that the purity of nanomaterials needs to be exceptionally high in order to realize reproducible performance in applications. Consequently, much of our work is focused on developing scalable purification methods.

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

Ultimately, we want to realize atomically precise, high purity nanomaterials in sufficient quantities to impact real-world applications. Examples of applications that we are actively pursuing include electronics, solar cells, and batteries. We have worked extensively with collaborators at Feinberg on methods for minimizing the toxicity of nanomaterials, thus opening possibilities for biomedical applications such as imaging contrast agents, sensors, and drug delivery vehicles.

### How does your research advance medical science and knowledge?

The purity of our nanomaterials coupled with our ability to tailor the surface chemistry of nanomaterials allows toxicity to be minimized and thus facilitates the development of biomedical applications.

### What types of collaborations are you engaged in across campus?

We collaborate extensively across campus (and at other institutions) with faculty members in chemistry, molecular biosciences, physics, engineering, and medicine. Specific examples in the Northwestern University Feinberg School of Medicine include [Scott Budinger, MD](#), [Gokhan Mutlu, MD](#), [Harris Perlman, PhD](#), and [Ramille Shah, PhD](#).

### How is your research funded?

We are funded by several federal and nonfederal sources including the National Science Foundation, Department of Energy, Office of Naval Research, NASA, and the W. M. Keck Foundation.

### Where have you recently published papers?

We regularly publish in the following journals: *Nature Nanotechnology*, *Nature Chemistry*, *Nature Communications*, *Nano Letters*, *Advanced Materials*, and *ACS Nano*.

### Which honors are you most proud of and why?

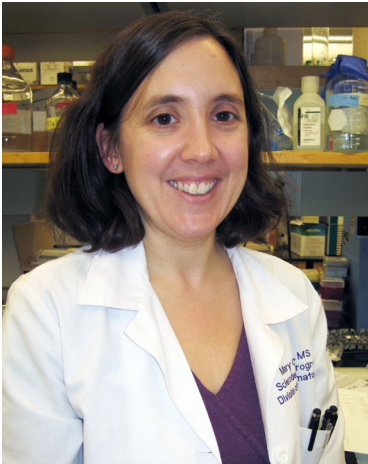
I am most proud of being named Teacher of the Year in the Department of Materials Science and Engineering on six separate occasions. I believe that a professor's number one job is to be an educator, and thus teaching honors have high personal meaning to me.

### What do you enjoy about teaching/mentoring young scientists in the lab?

Young people bring many desirable attributes to a laboratory: ambition, urgency, creativity, and nearly endless energy. Working with young scientists hopefully helps keep me young and is certainly my favorite part of being a professor.

# Coordinating Research, Coordinating Care

## Mary Carns, Northwestern Scleroderma Program



### Where are you originally from?

I was born in Cleveland, Ohio, but moved to Rochester, Minnesota in high school.

### What is your educational background?

I have a bachelor's degree in biology and sociology-anthropology from Knox College in Galesburg, Illinois, and I received my master's degree in Human Development and Family

Studies from the University of Wisconsin-Madison.

### Please tell us about your professional background.

I originally started my career as a crisis nursery counselor for parents in need of emergency child care at Lutheran Social Services in Duluth, Minnesota. I decided to make a career change to move into clinical research a little more than 10 years ago, and started at Northwestern University as a research coordinator for the [NUgene Project](#) in the [Center for Genetic Medicine](#). NUGene is a large DNA biorepository with associated clinical information designed to be used by many researchers for genetic studies. I had developed a love of human genetics in college, so was thrilled to be working on developing such a unique resource.

After three and a half years at NUGene, I worked briefly for [David Mohr, PhD](#), in the Department of Preventive Medicine as Coordinator of the Stress in Multiple Sclerosis ([SIMS](#)) study. This multi-site study (Northwestern, University of California-San Francisco, and Evergreen Medical Center near Seattle) examined the correlation between stress and multiple sclerosis (MS), and sought to determine if cognitive behavioral therapy (CBT) could help to reduce the number of new brain lesions, frequency of exacerbations, and progression of disability for people with MS. I was excited to take on the challenge of managing a large-scale study aimed at trying to improve health outcomes through an intervention such as CBT.

[John Varga, MD](#), John and Nancy Hughes Distinguished Professor of Rheumatology and professor of Dermatology, later recruited me to coordinate the newly developed [Scleroderma Program](#) in the Division of Rheumatology at Northwestern.

### Why did you choose to work at Northwestern?

I am attracted to Northwestern's vibrant community of professionals from many disciplines and backgrounds. In the last 10 years, I have had the privilege to work with and get to know

fellow coordinators, physicians, scientists, technicians, nurses, schedulers, administrators, and phlebotomists who have a true passion for their work. Northwestern is a leader in research and patient care because of the dedication of these many employees, and I feel honored to be working among them.

### What is your role within the Scleroderma Program?

As program coordinator, I manage scleroderma clinical and translational research, preparing study submissions for the IRB, obtaining patient consent, and overseeing sample and data collection and storage. I also arrange new patient visits to the program, and ensure coordination of visits with our multidisciplinary team of physicians.

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

I love working with patients! Because the program is relatively small, I have the chance to really get to know patients and their families, and have the opportunity to provide some support during a difficult time. I have learned that a friendly smile and a listening ear can really put people at ease. I am happiest at the end of a work day when I know that something seemingly small, such as coordinating rheumatology and pulmonary visits for the same day for a patient driving several hours to Northwestern, has made a patient's day that much better.

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

I spend nearly all of my spare time with my husband, Ben Rowland, and children, Erin, age four, and Aidan, 18 months. Our favorite weekend activity is taking a long walk at the Chicago Botanic Garden; I think we have about 50 different photos of my daughter posing on the "Cuddly Lion" statue, at the entrance to the English Walled Garden!

## eNOTIS Basics and Policy Training Update

On Wednesday, January 28, 2015, the Northwestern University Clinical and Translational Sciences Institute (NUCATS) will host a discussion and demonstration of eNOTIS so that users can become familiar with the system. Topics that will be covered include logging in participants, creating budgets for studies, and policy clarification on background and usage of eNOTIS.

The session takes place Wednesday, January 28, 2015, from 10 to 11 a.m. in the Rubloff Building, on the 11th floor.

[Add it to your calendar with PlanIt Purple.](#)



# Deconstructing How the Brain Processes Odors

James Howard, NUIN PhD Student



James Howard, a PhD student in the Northwestern University Interdepartmental Neuroscience Program ([NUIN](#)) recently published an [article](#) in *Neuron* which found that distinct regions of the human brain encode an odor's molecules not only altogether in a mixture, but also as individual parts.

Howard studies in the laboratory of senior author [Jay Gottfried, MD, PhD](#),

associate professor in the Ken and Ruth Davee Department of [Neurology](#).

## Q&A

### What was the goal of this research?

Most natural scents contain dozens of molecular components, but we perceive them together as one unified object—say, peanut butter. We wanted to deconstruct one of these natural odors to determine what molecules make up that smell, and then to determine how the brain breaks down this information, from the molecules individually and the whole odor mixture.

We were inspired by previous studies that suggest specific odor molecules within a mixture drive behavior in animals—for instance, particular molecules within a flower's scent mixture prompt flight and feeding in moths.

### What is the key finding?

These findings provide the first evidence that the human brain can engage object-level and component-level mechanisms to process a natural food odor mixture, implying that both modes work simultaneously to guide odor-related behavior.

### Tell us about the research.

We used a common food odor—peanut butter—to test the idea. Using functional magnetic resonance imaging (fMRI) to measure brain activity, we had study participants sniff 14 individual molecular components of the food odor, the whole food odor, and a control, banana. Participants rated each one for pleasantness and intensity.

We did this both before and after a lunch of peanut butter on crackers to examine the sensory-specific satiety effect, which holds that food odor pleasantness tends to decrease after you've consumed the food to satiety. Participants rated the peanut butter odor, as well as a handful of its molecular components, as less pleasant after eating lots of peanut butter. Likewise, we looked for differences in fMRI activity in certain areas of the brain after lunch.

We then analyzed the fMRI activity in seven brain regions associated with odor and reward value processing. Whole mixture processing involved the posterior piriform cortex, the central smell-processing center, a finding that replicated previous studies.

Our really novel finding was that the amygdala, a part of the brain that's typically involved in processing emotions or salience of stimuli, is processing individual components of the mixture; not just what they are, but how good they smell.

This suggests that another region, the orbitofrontal cortex, integrates all of the mixture and component information.

### How can this finding be applied to future research?

These findings could apply to future research on controlling appetite.

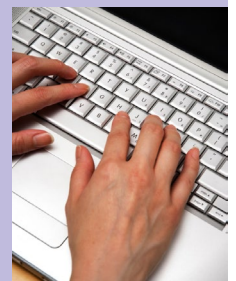
If there are certain molecules that seem to be more relevant for processing the value of a food odor, adding or removing these components could affect feeding behavior. Smells of food odors are really powerful to help you start or finish eating.

## Center for Community Health Manuscript Writing Retreat

Turn conference abstracts into papers, plan for possible papers, make progress on drafts, or finish revisions.

On Friday, January 23, 2015, the Center for Community Health will host dedicated space and time for attendees to focus on their own manuscripts. Two different rooms will be available in the Rubloff Building; one will be a quiet space dedicated to writing and the second will allow for some noise to talk.

Faculty and staff will be on hand to share publishing experience, answer questions, and provide guidance as needed. Refreshments will be provided. [Learn more and RSVP here.](#)



# Research in the News

**Mashable November 30**

10 times science ruled in 2014

Eva Redei's research was featured.

**Yahoo! News November 27**

How to win at sleep

Phyllis Zee's research was referenced.

**TIME Magazine November 23**

Your lungs: A user's manual

Ravi Kalhan was quoted.

**CBS Chicago November 21**

Doctors urge CPS to help students adopt better sleep habits

Phyllis Zee was quoted.

**FOX News November 18**

Merck's Zetia cuts heart attack, stroke risk in long-awaited study

Neil Stone was quoted.

**CBS News (National) November 17**

Many teens suffer cyber dating abuse

Brian Mustanski was quoted.

**Boston Globe November 17**

Taking daily aspirin fails to prevent heart deaths

Philip Greenland was quoted.

**My FOX Chicago November 16**

Vitamin D deficiency linked to 3 cancers

Adam Murphy's research was quoted.

**The Washington Post November 14**

National Children's Study may be stopped for cost and research methods

Jane Holl was quoted.

**National Geographic November 7**

Why it's crucial to get more women into science

Teresa Woodruff was quoted.

**The New York Times November 5**

The eczema and broken bone connection

Jonathan Silverberg's research was featured.

[More media coverage](#) available online.

Northwestern University

# NUCATS

Clinical and Translational Sciences Institute

## NUCATS Corner

### Clinical and Translational Research Studio Consultations

**Connect early and often.** The [NUCATS Institute](#) offers clinical and translational research studio consultations to investigators who are in the planning stages of a new program or center grant at Northwestern University and affiliate institutions.

A studio brings together leadership from NUCATS and affiliates to identify relevant resources that can help support and enhance grant submissions. The intent of a studio is to provide investigators with dedicated space and time to receive multidisciplinary guidance from clinical and translational science experts and leverage existing NIH-supported infrastructure through the NUCATS Institute in order to be more competitive for federal funding.

As a result of NUCATS studios, research teams have been able to take advantage of in-kind or heavily subsidized existing NUCATS resources and services in:

- Training and career development
- Clinical research coordinator and regulatory support
- Stakeholder engagement, dissemination and implementation
- Epidemiologic, biostatistical, and informatics support for study design and analysis
- Access to the Northwestern Medicine Enterprise Data Warehouse
- Pilot and voucher funding

Use of these existing NUCATS resources has helped avoid infrastructure duplication and freed up direct grant dollars for investment in scientific aims.

If you'd like NUCATS to help you organize a studio, please contact one of the Institute's Research Navigators by [requesting a consultation](#). Learn more about [when you should connect with NUCATS](#).

# Sponsored Research



**PI: Tamara Isakova, MD, MMSc**  
**Assistant Professor of**  
**Medicine-Nephrology**

**Sponsor: National Institute of Diabetes,**  
**Digestive, and Kidney Diseases (NIDDK)**

**Title: "Impact of Phosphate and FGF23**  
**Reduction on Intermediate End Points**  
**in CKD"**

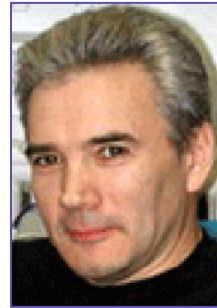
Disordered mineral metabolism is a near-universal complication of chronic kidney disease (CKD) that is strongly linked to cardiovascular disease (CVD), CKD progression, fractures, and death. Phosphate excess induces arterial calcification, an important phenotype of CVD in CKD. Elevated fibroblast growth factor 23 (FGF23) maintains serum phosphate in the normal range in CKD, but FGF23 excess contributes to left ventricular hypertrophy (LVH). Together, the effects of phosphate and FGF23 excess on the cardiovascular system promote CVD events and death.

Dietary phosphate absorption is a modifiable determinant of these levels. In animals, a high phosphate diet promotes kidney failure, and, in preliminary data, raises phosphate and FGF23 levels and induces LVH. Reducing dietary phosphate absorption with phosphate binders, low phosphate diets, or the nicotinamide precursor, niacin, lowers phosphate and FGF23 levels in pilot studies of CKD stage three to four patients. Thus, targeting phosphate and FGF23 excess may represent a novel therapeutic paradigm to improve outcomes in CKD. A roadblock to advancing this approach is the lack of evidence on the effects of phosphate and FGF23 reduction on intermediate end points in CKD.

The NIDDK-supported COMBINE study of 200 CKD stage three to four patients provides a unique opportunity to fill this gap. The parent study will test whether combining nicotinamide and lanthanum carbonate will lower serum phosphate and FGF23 levels. The ancillary study will enrich the parent study by adding assessments of bone and mineral metabolism and surrogate measures of CVD and renal risks at baseline, at nine, and 18 months post-randomization.

By obtaining these assessments of bone turnover markers and mineral metabolites, the team will test whether active therapy will blunt the slope of parathyroid hormone (PTH) rise, attenuate the decline of calcitriol and klotho levels, and improve bone turnover markers. They will use serial measures of cardiac magnetic resonance imaging (MRI) and CVD biomarkers to test whether active therapy will reduce or blunt the increase in LV mass, attenuate LV diastolic dysfunction, and reduce levels of CVD biomarkers. Finally, using serial serologic testing and gadolinium-free blood oxygenation level dependent MRI and diffusion-weighted MRI to monitor changes in intra-renal oxygenation and fibrosis, they will test whether active therapy

will blunt the slope of decline in glomerular filtration rate and the rise in proteinuria and inflammatory markers, improve intra-renal oxygenation and stabilize or reduce progression of renal fibrosis.



**PI: Donald R. McCrimmon, PhD**  
**Professor of Physiology and**  
**Anesthesiology**  
**Associate Chair of Physiology**

**Sponsor: National Heart, Lung, and**  
**Blood Institute**

**Title: "CNS Pathways Integrating Respira-**  
**tory and Metabolic Control"**

The central nervous system's (CNS) control of breathing is remarkably adept at homeostatically regulating arterial blood gas levels and acid-base status within narrow limits, despite marked changes in metabolism. Identifying the CNS mechanisms underlying this control has been a long-held fundamental challenge in respiratory biology and medicine. While a great deal has been learned about the neuronal circuitry involved in generating and elaborating the basic breathing rhythm to various respiratory muscles, little is understood with respect to the identity of the central pathways and associated neurotransmitters that match ventilation to metabolism.

This tight relationship between ventilation and metabolism is disrupted in a subgroup of obese individuals with obesity hypoventilation syndrome (OHS). Individuals with OHS have a body mass index  $>30\text{kg/m}^2$ , an elevated arterial partial pressure of  $\text{CO}_2$  ( $\text{PCO}_2$ ), and hypoxemia (low oxygen in arterial blood) during wakefulness. Epidemiologic studies suggest that up to about 30 percent of severely obese patients have OHS. OHS patients have a reduced respiratory drive and a blunted ventilatory response to a  $\text{CO}_2$  challenge.

Several lines of research suggest that resistance to the action of leptin, a cytokine hormone that is produced in large part by adipocytes, is responsible for the reduced ventilatory drive. For example, OHS symptoms are largely reproduced in a mouse model of obesity (the ob/ob mouse) that fails to produce leptin: these mice are obese and hypoventilate. Intriguingly, administering leptin to these mice normalizes ventilation and arterial  $\text{PCO}_2$ . Body weight is also returned to normal but more slowly than the correction in  $\text{PaCO}_2$ , a finding that suggests that leptin actively "stimulates" breathing. It also suggests that identification of the neuronal pathways by which leptin stimulates breathing along with their associated transmitters and peptide neuromodulators would provide an opportunity for development of targeted pharmacotherapies for OHS.

*(continued on page 9)*



## Sponsored Research

(continued from page 8)

However, multiple nuclei within the CNS contain leptin receptor-expressing neurons (termed ObRb neurons), and there is almost no evidence as to which of these groups are involved in the stimulation of breathing.

A team including McCrimmon, [Marco Martina, MD, PhD](#), [Gabriella Sekerka, MVD, CSc](#), [Kevin McKenna, PhD](#), and [Gordon Shepherd, MD, PhD](#), has obtained preliminary results implicating several brainstem and hypothalamic nuclei in a leptin-modulated hierarchical, respiratory control system. They are currently employing an optogenetic approach in which Cre-LoxP technology is used to insert a light sensitive ion channel selectively into neurons that express the leptin receptor. With this approach, both excitatory (channelrhodopsin-2; ChR2) and inhibitory (halorhodopsin or archaerhodopsin) actuators will be used. At the behavioral level, activation of individual groups of ObRb neurons expressing ChR2 will identify the extent to which activation of a particular neuronal group mimics the respiratory response to systemic leptin. Conversely, optogenetic inhibition of a cell group while attempting to stimulate breathing with a systemic leptin administration will help determine whether a particular neuronal group is required for leptin-mediated respiratory stimulation.

The neuronal pathways by which individual groups of leptin receptor-expressing cells communicate with the known circuits generating respiratory rhythm will also be determined. Once specific ObRb cell groups are linked with respiratory stimulation, the pathways connecting them to neurons known to be involved in generating the basic respiratory pattern will be identified using standard neuroanatomical tract-tracing techniques, along with a novel transynaptic viral tracing method, in which an injected virus crosses only 1 synapse to specify leptin-activated mono- and poly-synaptic pathways stimulating breathing. The peptide transmitters contained within these pathways will be identified immunohistochemically.

Finally, the impact of synaptic input from leptin-activated pathways onto respiratory pattern generating neurons in the brainstem will be determined ex-vivo. The effects of the immunohistochemically identified neurotransmitters and peptide neuromodulators on the electrophysiological properties of neurons generating the respiratory pattern will be identified in acute slices of brain tissue and their molecular mechanisms investigated.

The combined studies will systematically identify CNS ObRb neuronal groups that stimulate breathing in response to systemic leptin administration. Additionally, paucisynaptic pathways mediating this influence will be revealed as will the identity of their peptide transmitters. Finally, associated cellular/molecular mechanisms contributing to a stimulation of breathing will be defined. The findings could form the basis for the development of pharmacotherapies for OHS patients.

## Funding

### Outcome Measures for Use in Treatment Trials for Individuals With Intellectual and Developmental Disabilities (R01)

[More information](#)

**Sponsor:** Department of Health and Human Services, National Institutes of Health

**Submission deadline:** February 5

**Upper Amount:** \$2,499,996

**Synopsis:** This funding opportunity announcement encourages applications from institutions and organizations that propose to develop informative outcome measures for use in clinical trials for individuals with intellectual and developmental disabilities (IDD). This opportunity will address a significant need in the field, one that is especially apparent in efforts to develop pharmacological treatments for these populations. This FOA will focus ongoing clinical and translational research on a neglected area essential for therapy and pharmacological treatment development.

### Type 1 Diabetes Complications IMPACT Award (DP3)

[More information](#)

**Sponsor:** Department of Health and Human Services, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases

**Submission deadline:** February 19

**Upper Amount:** \$2 million

**Synopsis:** The goal of this initiative is to support creative research projects that address major obstacles to development and testing of new therapeutic approaches for type 1 diabetes complications. This funding opportunity announcement solicits research focused on defining biomarkers that can be used to track the onset, progression, and extent of tissue damage that develops over time in people with type 1 diabetes. It also solicits research to develop approaches to regenerate damaged tissue. Proposed studies should be designed to address major unmet needs and/or compelling opportunities that have the potential to dramatically advance the field.

[View more funding opportunities](#)

# High Impact Factor Research

## October 2014

Al Olama AA, et. al. (includes **Murphy AB**). [A meta-analysis of 87,040 individuals identifies 23 new susceptibility loci for prostate cancer](#). *Nature Genetics*. 2014 Oct;46(10):1103-9.

Ceco E, Bogdanovich S, Gardner B, Miller T, DeJesus A, Earley JU, Hadhazy M, Smith LR, Barton ER, Molkentin JD, **McNally EM**. [Targeting latent TGF \$\beta\$  release in muscular dystrophy](#). *Science Translational Medicine*. 2014 Oct 22;6(259):259ra144.

De Vos M, Smits J, **Woodruff TK**. [Fertility preservation in women with cancer](#). *Lancet*. 2014 Oct 4;384(9950):1302-10.

Gorrie GH, **Fecto F**, Radzicki D, Weiss C, Shi Y, Dong H, Zhai H, Fu R, Liu E, Li S, Arrat H, Bigio EH, Disterhoft JF, Martina M, Mugnaini E, Siddique T, Deng HX. [Dendritic spinopathy in transgenic mice expressing ALS/dementia-linked mutant UBQLN2](#). *Proceedings of the National Academy of Sciences U S A*. 2014 Oct 7;111(40):14524-9.

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## Help Feinberg Track Journals

The Feinberg Research Office regularly tracks research published by Feinberg investigators. The citations are used on web pages, in newsletters and social media, for internal reporting, and more. To more accurately track these journals, the Research Office asks that Feinberg investigators use the following institution name in the address field when publishing in peer-reviewed journals: "Northwestern University Feinberg School of Medicine."

## Welcome New Faculty



**David M. Condon, MBA, PhD**, joins as instructor in Medical Social Sciences. He earned his Doctor of Philosophy degree in personality psychology and Master of Science degree in psychology at Northwestern University. He earned a Master of Business Administration degree from University of Chicago.

Condon's research focuses on the assessment of individual differences across multiple domains (e.g., affective, cognitive, and conative) and the manifestation of these differences on life outcomes, with a focus on individual difference (personality) variables that predict health outcomes, creative achievement and entrepreneurial behaviors.

# Calendar

Friday, January 9

## Illinois Brain, Behavior, and Immunity Meeting

Keynote speakers are John F. Sheridan, PhD, The Ohio State University, and Mark Opp, PhD, University of Washington.

**Time:** All day, Friday, January 9 and Saturday, January 10

**Location:** Lurie Medical Research Building — Hughes  
303 E. Superior St. (Chicago campus)

**Contact:** [ilbbmeeting@gmail.com](mailto:ilbbmeeting@gmail.com)

[More information](#)

Tuesday, January 13

## Lectures in Life Sciences

“Determinants of Vascular Wall Development and Homeostasis,”  
by Hal Deitz, MD, Howard Hughes Medical Institute and Johns  
Hopkins School of Medicine.

**Time:** 4 to 5 p.m.

**Location:** Lurie Medical Research Building — Hughes  
303 E. Superior St. (Chicago campus)

**Contact:** [h-ardehali@northwestern.edu](mailto:h-ardehali@northwestern.edu)

[More information](#)

Friday, January 16

## Department of Physiology Seminar

“GABAergic Control of Striatal Projection Neurons,” by Stefano  
Vicini, PhD, Georgetown University.

**Time:** 4 to 7 p.m.

**Location:** Ward Building — Room 5-230  
303 E. Chicago Ave. (Chicago campus)

**Contact:** [d-daviston@northwestern.edu](mailto:d-daviston@northwestern.edu)

[More information](#)

Monday, January 26

## CRS Minisymposium on Reproductive Biology

The keynote speaker is Richard L. Stouffer, PhD, Oregon Health and  
Science University.

**Time:** 10 a.m. to 6 p.m.

**Location:** Lurie Medical Research Building — Baldwin  
303 E. Superior St. (Chicago campus)

**Contact:** [f-murdoch@northwestern.edu](mailto:f-murdoch@northwestern.edu)

[More information](#)

### More Events

Event organizers are encouraged to submit calendar items on  
[Plan-It Purple](#) for consideration. Please contact the [Research  
Office](#) with further questions.

## NIH News

### Departments Rank High in List of NIH Funding

Eight departments at Feinberg rank in the top 10 in their  
discipline in a list of National Institutes of Health (NIH)  
funding to medical schools, with an additional three depart-  
ments in the top 20, according to a recent report.

The rankings, calculated by the Blue Ridge Institute for Med-  
ical Research, include grants awarded between October 1,  
2013 and September 30, 2014. These rankings typically do  
not include contracts or other specialized mechanisms.

“Our faculty represent top scientists, physician-scientists  
and innovators in their fields who rely on NIH support,”  
said Eric G. Neilson, MD, vice president for Medical Affairs  
and Lewis Landsberg Dean. “These rankings reflect their  
successful pursuit of scientific discovery, conducted as they  
mentor and train the next generation to likewise join bio-  
medical research enterprise.”

The rankings record overall funding to medical schools, as  
well as funding divided by academic department. The ten  
departments at Feinberg that rank among the top 20 in  
their area are: Obstetrics and Gynecology (3), Dermatology  
(4), Public Health—Preventive Medicine and Medical Social  
Sciences (4), Urology (4), Physiology (4), Physical Medicine  
and Rehabilitation (4), Neurology (8), Internal Medicine and  
Geriatrics (19), Otolaryngology (19), and Cell and Molecular  
Biology (20). Another department, Neurological Surgery, will  
rank 15th after the NIH issues grant assignment corrections.

“Our faculty continue to outperform our peers in securing  
NIH funding in a national environment where NIH funding  
has been essentially flat for the past decade,” said Rex  
Chisholm, PhD, vice dean of Scientific Affairs and Graduate  
Education. “This is a reflection of the innovative research  
our faculty perform.”

In the last decade, the NIH – the largest funder of medical  
research in the world – only funded about one in six of the  
grant applications it received. Overall, Blue Ridge ranked  
Feinberg 22nd for NIH funding among all medical schools in  
the United States, higher than any medical school in Illinois.

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