CMIDD a Catalyst for Drug Discovery

In the 100,000 hours it often takes to move a drug from concept to chemical intervention, Raymond Bergan, MD, professor of medicine-hematology/oncology and preventive medicine, sees a decade of inefficiencies.

“Since the ’50s it has taken 10 years to go through the drug-discovery pipeline, and it still takes that long today. What has continued to change is the cost, which has risen exponentially,” said Bergan, co-director of the Center for Molecular Innovation and Drug Discovery (CMIDD). “If the center can help implement a more powerful and reliable approach to reduce the time and cost, we could produce 100 Lyrica-like breakthroughs.”

Based primarily in Evanston and comprised of scientists with expertise in assay development, high throughput screening, molecular modeling, medicinal chemistry, and compound purification, CMIDD is a collaborative research platform bridging the gap between biologists and chemists.

Founded in 2007, the center has made it possible for Northwestern University Feinberg School of Medicine scientists to apply for more than $100 million in drug-discovery related funding. Today, CMIDD has a library of more than 70,000 small molecules and has begun developing an internal collection of compounds created by Northwestern scientists for use in basic and translational research projects.

The center also administers two cores – ChemCore and the High Throughput Analysis Lab (HTAL) – which are shared resources of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University.

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HTAL’s main purpose is to provide academic and industrial researchers with the ability to rapidly conduct large-volume tests in an effort to identify composites that will affect a bio-molecular pathway. Established in 2004 as a stand-alone core, the lab has screened tens of millions of compounds for Northwestern investigators, providing insight into the biology of several diseases including cancer and Parkinson’s disease.

“We have state-of-the-art robotic equipment that can take thousands of molecules and screen one target to see whether those unique molecules do anything to that target,” said Karl Scheidt, PhD, Dow Company Research Professor of chemistry and CMIDD co-director. “The process combines sheer force with a deep understanding of biology, so having the HTAL be part of our suite of cores is extremely useful.”

ChemCore exists to aid investigators further down the pipeline by providing medicinal and synthetic chemistry, molecular modeling, and compound purification services.

“Our center started out as a concept to make knowledge and resources available on both campuses and has since grown to be a much larger vision,” Scheidt said. “‘Bench to bedside’ is an often quoted and great goal, but between those two words is a 10-year odyssey with potentially great payoff for society, or great failure for investigators. It’s our ability to fuel the process with excellent collaborations, deep and broad knowledge, and dedication to the University's commitment to biomedical research that makes this work.”

Not surprisingly, Feinberg faculty have been the primary collaborators of CMIDD, with members from the Robert R. McCormick School of Engineering and Applied Science and Weinberg College of Arts and Sciences also frequenting the center.

“As physicians, our job is to take care of patient diseases, and therapeutics are a mainstay. Yet, there are many diseases for which we just don’t have effective therapy,” said Bergan, pointing out that 50 percent of cancer patients still die. “Finding and discovering new drugs is one of the hardest things to do, period. But if you design a new medicine, it can literally change a life.”

Working to cultivate novel kinase inhibitors for use as therapy for a rare form of leukemia, John Crispino, PhD, Robert I. Lurie, MD and Lora S. Lurie
Faculty Profile: Karl Bilimoria, MD  
Director, Surgical Outcomes and Quality Improvement Center and  
Assistant Professor, Surgical Oncology

Dedicated to improving the quality and effectiveness of care provided to surgical and oncology patients, Karl Bilimoria, MD, MS’08, GME’10, assistant professor of surgery-surgical oncology, received the National Comprehensive Cancer Network (NCCN) Young Investigator Award and an American Cancer Society (ACS) grant in June. He will use the two-year NCCN grant to study the quality of care delivered to melanoma and breast cancer patients, and the ACS grant will be used to compare hospitals on the quality of cancer surgery provided in a collaboration of 51 NCI-designated cancer centers started by Bilimoria.

As director of the Surgical Outcomes and Quality Improvement Center, Bilimoria focuses on examining the quality of care delivered across the United States to develop strategies to improve healthcare quality. He is the medical director for surgical quality and collaborates with Northwestern Memorial Hospital on numerous practical quality improvement initiatives. He is also a faculty scholar at the American College of Surgeons, where much of his research has an immediate national impact.

He earned his medical degree in 2003 from Indiana University and received his master’s degree in clinical investigation in 2008 from Northwestern University. Bilimoria completed his residency in general surgery at Northwestern McGaw and his fellowship at the MD Anderson Cancer Center in surgical oncology.

Q&A

What are your research interests?

My research focuses on quality improvement strategies and policy evaluations related to quality initiatives.

Our quality improvement research works toward developing better ways to provide hospitals with comparative data to spur internal hospital quality improvement efforts. We also examine how to provide patients better comparative data through public reporting, which can assist them in selecting the best hospital for their surgical care. Our policy evaluations examine the effect of various structural, accreditation, and legislative efforts, such as public reporting and value-based purchasing, on quality of care in surgery and oncology.

What is the ultimate goal of your work?

I would like to facilitate providing hospitals with robust, accurate, and actionable data to allow targeted quality improvement efforts. For example, if we provide information to a hospital whereby they identify that they are an outlier for wound infections after colorectal surgery compared to other hospitals in the country, then that hospital can focus their efforts to improve in that specific area. Moreover, we would like to show that providing hospitals with these data does actually improve quality of care in a meaningful and sustainable way.

With respect to our policy evaluations, we hope to inform these debates with evidence to spur and encourage initiatives which actually do result in better healthcare quality.

What types of collaborations are you engaged in across campus?

We have a diverse group of collaborators, including researchers in the Center for Healthcare Studies, the Department of Medical Social Sciences, the Robert H. Lurie Comprehensive Cancer Center, the VA Center for Complex and Chronic Care, and at the American College of Surgeons. We also collaborate with the quality and process improvement teams at Northwestern Memorial Hospital. We have some exciting new collaborations with payers that will undoubtedly keep us busy.

How is your research funded?

Our research is funded by the Agency for Healthcare Research and Quality, the NIH, the American Cancer Society, the National Comprehensive Cancer Network, the American College of Surgeons, the DeBoer Family Sarcoma Foundation, and the Robert H. Lurie Comprehensive Cancer Center.

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

We have a great team that is growing quickly. Our group is comprised of surgeons, health services researchers, statisticians, analysts, a programmer, a program manager, a program assistant, and a grants administrator. Our collaborators offer a rich and diverse group of experts to augment the expertise within our group.

Continued on pg. 4
Staff Profile: Marissa Michaels
Laboratory Manager, Feinberg Cardiovascular Research Institute

Where were you originally from?
I was born in Highland Park, Ill. We moved to Palatine and then to Coral Springs, Fla., when I was four. I went to high school in Ft. Lauderdale, Fla., at Cardinal Gibbons High School.

What is your educational background?
For college, I returned to Chicago to attend Loyola University. I have a Bachelor of Science degree in biology with a theology minor and a Master of Science degree in molecular genetics.

Tell us about your professional background.
I started working at Northwestern after graduate school. I answered an ad in the Chicago Tribune for a research technologist II position and in July 1996 began in a rheumatology lab, where I spent nine-and-a-half years studying lupus. In October 2005, I moved to endocrinology, where I studied Pendred syndrome. In September 2010, I joined the lab of Douglas Vaughan, MD, as lab manager in the Department of Medicine for Feinberg. The lab is also affiliated with the Feinberg Cardiovascular Research Institute, and the focus is cardiovascular disease and, primarily, the mammalian plasminogen activator system and the role this system plays in cardiovascular disease.

What, if any, professional activities do you take part in?
I participated as an active member of the Northwestern University Staff Relations Committee from 2007 to 2012 and have been a member of the Northwestern University Institutional Biosafety Committee from 2009 to present.

What is your favorite part of the job?
Each day brings new challenges and rewarding experiences. It is a very diverse group of researchers, technicians, postdocs, fellows, and students working together toward common goals, and it is very challenging keeping things running smoothly. When we have a positive discovery and are able to publish the results, my job is very rewarding.

What do you like to do in your spare time?
In my spare time, I take long walks and agility classes with my very active rescue Dachshund, Toby. I also volunteer at Emily Oaks Nature Center in Skokie, Ill., where I help with the wildflower gardens, work on restoration of the grounds, and help out at all their fundraising events. I am very active in my parish, St. Mary, in Evanston, and am a member of the traditional and contemporary choirs, a cantor, art and environment committee member, and minister of the Eucharist.

Anything else we should know about you?
I love the outdoors, as I love to canoe and hike. My annual trips to the Boundary Waters Canoe Area Wilderness of upper Minnesota are something I always look forward to.

► Connect with Marissa on LinkedIn

Bilimoria Q&A, continued from pg. 3

Where have you recently published papers?
We have recently published in Medical Care, Health Services Research, the Journal of Clinical Oncology, Journal of the National Cancer Institute, Cancer, Annals of Surgery, Annals of Surgical Oncology, Archives of Surgery, and the Journal of the American College of Surgeons.

Which honors are you most proud of and why?
We were excited to receive this most recent grant from AHRQ as it is a major area of interest for our team and demonstrates a powerful collaboration between the Surgical Outcomes and Quality Improvement Center (SOQIC), the Center for Healthcare Studies, and the American College of Surgeons.

The grant focuses on trying to improve public reporting so it is more patient-centered and useful for patients when they are trying to select the best hospital for surgery.
Student Q&A: Benjamin Haley
Driskill Graduate Program in the Life Sciences

Where are you originally from?
I’m originally from Downers Grove, Ill. I’ve lived in Chicago for some time.

What is your educational background?
I did my undergraduate degree in honors biology at the University of Illinois in Champaign-Urbana.

What are your research interests?
Broadly, I want to use statistics to help people.

My thesis project is focused on the danger of radiation exposure. Radiation protection agencies estimate the risk of ionizing radiation exposure from studies of atomic bomb survivors. But atomic bomb survivors were exposed to one high-dose and high-dose rate exposure, while populations today are exposed to low-dose and low-dose rate exposures. The risk seen in atomic bomb survivors is divided by the dose and dose-rate effectiveness factor (DDREF) to estimate the risk of exposures at lower doses and dose rates. I am revisiting this estimate of DDREF using historic animal studies.

I also volunteer with a lab at Stanford called PERTS. We work on social psychology interventions that help students perform better in school. Many kids hold the debilitating (and wrong-headed) attitude that intelligence is something you are born with. We create online exercises that help students understand that the brain is like a muscle: the more it is worked, the stronger it grows. We use randomized controlled trials to measure the efficacy of these exercises. Amazingly, (to me) they seem to work. Low achieving students in our experimental groups score 0.2 GPA points higher, on average, than corresponding control students. We recently launched a study at the Khan Academy, which you can see if you visit the website. Students in this study finish two percent more exercises when they see our messages.

What has been your best experience at Feinberg?
The best thing about Feinberg has been flexibility. In my rotations, I was able to work on a remote control robot that performs crystallography at Argonne, and to analyze electronic medical records from patients at Northwestern Memorial Hospital.

Now, I have a lot of freedom to determine my thesis project, study what I want, and spend my time in the way I see fit. It’s liberating and productive.

How would you describe the faculty at Feinberg?
I’ve had some amazing experiences. Richard Miller, PhD, and Philip Hockberger, PhD, teach a great class called “Science and Society.” Each class is a roundtable discussion about the biggest achievements in science (relativity, the creation of the Royal Society, cloning, etc.) and how these have impacted society. It is one of my top five courses of all time.

What do you do in your free time?
I try to do lots, I suppose. I love taking online courses through coursera and udacity. My fiancé and I just started a course sponsored by Doris Buffet called ‘learning by giving’ where you study effective charitable giving. The class project is to give away $10,000. I’m an avid ice cream maker; saffron has been my favorite flavor so far. I love swimming, and I intend to swim to a ship wreck in Lake Michigan in a couple of weeks. I also enjoy attending the many music festivals Chicago has to offer.

► Connect with Benjamin on LinkedIn

AAMC Research Report

To build on this report, AAMC formed two expert panels comprised of key research leaders. The panels will convene later this year to develop recommendations regarding new and emerging areas of research and health disparities research.

More information, including a related webinar, is available on the AAMC’s web site.
Paul Bryce, PhD
Associate Professor of Medicine- Allergy-Immunology and Microbiology-Immunology

Project title: Regulation of Allergic Inflammation by Histamine

Sponsor: National Institute of Allergy and Infectious Diseases

This award is a renewal of Bryce’s R01 grant that focused on how mast cells—important immune cells that reside in our peripheral tissues—can orchestrate the development of inflammation. The team’s work during the first five years showed how these cells contribute to lung injury and to allergy—particularly focused on food allergy responses. An important finding was that histamine, one of the key mediators produced by mast cells, was necessary for allowing allergic inflammation to proceed. Rather than actually stimulating responses, Bryce demonstrated that the type 2 histamine receptor (H2R) acts as a modifier of how cells respond to Interleukin 4 (IL-4), which is a critical cytokine in driving allergic responses, including production of allergen-specific IgE antibodies. In the absence of H2R or upon blocking it, IL-4 failed to cause these pathogenic responses while some other responses persisted. It was this observation that formed the key basis of the renewal direction.

The current understanding of how cytokines work has an important unanswered issue: there are simply too few receptors and downstream signals from these receptors to explain all of the homeostatic and pathogenic effects they exert.

One theory the team proposes which might explain the H2R and IL-4 data is that "modify" signals can switch the nature of the response such that, rather than a simple "off-on" system, there are two "on" states. In this proposal, they hypothesize that signals that activate the mast cell to release its histamine, such as infection or allergens, switch the IL-4 response from good (homeostasis) to bad (inflammation), and that this is working through H2R.

The grant will look at this concept in animal models of allergy, at the molecular level using in vitro culture systems, as well as in patients with a disease known as Eosinophilic Esophagitis.

Bryce and his team have been studying this food allergy-associated disease in collaboration with Nirmala Gonsalves, MD, in the Division of Gastroenterology. While the connection is thought to be driven by these allergic cytokines, the team previously reported that mast cells and their products, including histamine, were highly up-regulated also.

Ultimately, Bryce believes targeting of these "modifier" signals may be an attractive way to shut off pathogenic responses without losing the homeostatic functions many immune signals provide. In the case of H2R, drugs are already available and in clinical use, and thus any findings from these studies may have relatively straightforward translational potential.

More sponsored research, pg. 7

New Clinical Research Resource

Lewis Smith, MD, professor of medicine at Feinberg and associate vice president for research at Northwestern University, recently announced the opening of the Center for Clinical Research (CCR), a program of Northwestern University's Clinical and Translational Sciences Institute (NUCATS), as part of a major commitment to the clinical research enterprise.

The FSM Researcher will include a feature story in coming months about the new resource. In the meantime, those involved with clinical research are encouraged to read Smith's "Director’s Message" to friends and colleagues of the NUCATS community to learn about the center's goals, services, and resources.

To contact the Center for Clinical Research directly, call CCR Navigation Services at 312-503-9999.
Sponsored Research

Jay Gottfried, MD, PhD
Associate Professor in Ken and Ruth Davee Department of Neurology and Weinberg College of Arts and Sciences

Project title: Spatiotemporal Mechanisms of Olfactory Processing in the Human Brain

Sponsor: National Institute on Deafness and Other Communication Disorders

It is increasingly clear that olfactory perception is impaired in a wide variety of neurological and neuropsychiatric disorders. However, this growing clinical appreciation for the human sense of smell is offset by a poor scientific understanding at the physiological level. Indeed, much basic knowledge about the human olfactory system is inferred from studies in rodents and insects, but whether the cortical computations established in animals are relevant for humans is largely unknown.

The major aim of this research project is to uncover the spatiotemporal mechanisms of odor processing in the human olfactory system. In collaboration with the Comprehensive Epilepsy Center and Functional Neurosurgery teams at Northwestern University, Gottfried’s team will record odor-evoked patterns of electroencephalographic (EEG) activity directly from the human brain in patients with medically intractable seizures. The highly accurate placement of high-density invasive electrodes around the medial temporal and orbital frontal lobes during standard surgical exploration—without any added risk to the patients—offers a unique window into the functional anatomy of the olfactory system with unparalleled temporal and spatial resolution. Studies are designed to compare odor-evoked oscillations in different brain regions, including the olfactory bulb, olfactory (piriform) cortex, and orbitofrontal cortex, and to understand how these different brain regions interact to support olfactory categorical perception and coding.

Work proposed here will yield a more comprehensive basic research understanding of human olfaction, particularly with regard to its temporal dynamics, and will provide a direct link to non-human animal studies. From a clinical translational perspective, this project may help in diagnosis and prediction of functional outcome in epilepsy patients, and open up new avenues for monitoring disease onset and progression in other neurological disorders involving the sense of smell.

New Lab Volunteer and Intern Process

The Northwestern University Office of Human Resources recently reviewed and updated its volunteer and intern process.

Moving forward, the University will make a distinction between volunteers and interns, and will be reviewing proposed arrangements using two updated sets of legal criteria that can be accessed online.

These differences include:

- Interns undergo training similar to that which would be given in a vocational school or receive an academic credit for the training
- Interns do not displace regular employees, but work under close supervision
- Employers do not derive immediate advantages from the activities of the intern
- Volunteers are not full-time employees
- Volunteer services are offered freely without pressure or coercion
- Volunteer services are of the kind typically associated with volunteer work

If the volunteer or intern is a minor, there are additional considerations for minors that the Office of Human Resources will need to evaluate.

Importantly, labs must notify Human Resources prior to any volunteer or intern start date to ensure the individual meets the requirements and qualifies as either a volunteer or an intern.

Human Resources requests notification at least two weeks prior to the individual’s planned start date to allow sufficient time for review of the proposed arrangement.

Volunteers and interns are required to successfully complete a background check prior to starting in the department (if at least 18 years of age), in addition to several other requirements.

Information and tools regarding this new process can be found on the Office of Human Resources web site, including a step-by-step process guide and form for requesting a volunteer or intern.

Feinberg faculty and staff are encouraged to email intern-volunteer@northwestern.edu or call 312-503-1584 with questions.
High Impact Factor Research: May and June 2013


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

Jing Jin, MD, PhD, joins as assistant professor in medicine- nephrology.

Jin was previously a post-doctoral fellow at the Samuel Lunenfeld Research Institute in Toronto, Ontario. He received his doctorate degree from the University of Toronto. Jin received his medical degree from Peking University in China, and also completed a clinical residency at Cardiovascular Institute & Fuwai Hospital, Chinese Academy of Medical Science, Beijing.

Jin studies aspects of angiogenesis involving mechanisms of protein-protein, protein-matrix, and protein-cell interactions. His long-term goal is to investigate cell surface binding potentials of anti-angiogenic polypeptides using proteomic tools. He holds one U.S. patent and has served as author or co-author on more than 20 articles in peer reviewed journals.

Sheetal Kircher, MD, joins as assistant professor in medicine- hematology/oncology where she focuses clinically on gastrointestinal malignancies.

Kircher was previously a clinical lecturer at the University of Michigan Hospitals and Health Center and the VA Ann Arbor Healthcare System in Ann Arbor, Mich. She earned her medical degree from Rush Medical College in Chicago, III., and completed an internal medicine internship and residency at the University of Chicago, then a medical oncology fellowship at Northwestern University Feinberg School of Medicine. Most recently, she completed a masters degree in health outcomes at the University of Michigan.

Her research interests focus on improving the quality of cancer care and better understanding trends in use and expenditure of services and drugs. She is also interested in evaluation of cancer-related health policies.

NIH News

NIH deputy director Sally Rockey, PhD, provided an overview of NIH’s system of percentiling.

Says Rockey, "NIH uses percentile calculations to improve our ability to compare applications across different application cycles and across different study sections. Percentiling allows NIH institutes to compare applications even when different study sections have different scoring behaviors."

The entire post is available on NIH’s RockTalk blog.

NIH recently posted a notice encouraging institutions to develop individual development plans for graduate students and postdoctoral researchers, as recommended by the recent ACD Working Group on the Biomedical Workforce. NIH is not making plan development mandatory, but also is encouraging them for graduate students.
Funding Opportunities

Prostate Cancer Research Program (PCRP): Prostate Cancer Pathology Resource Network Award

More information

Sponsors: United States Department of Defense, Department of the Army, U.S. Army Medical Research and Materiel Command, Office of Congressionally Directed Medical Research Programs

Submission Deadline: September 18 pre-application (req.)

Upper Amount: $9 million

Synopsis: This award is intended to provide infrastructure support for the development and maintenance of a prostate cancer biorepository through a collaborative network of multiple institutions that will facilitate the collection, processing, annotation, storage, and distribution of high-quality human prostate cancer biospecimens. Major emphasis must be placed on the acquisition and distribution of specimens in limited supply, and applications should address one of these PCRP areas: biomarker development, genetics, imaging, mechanisms of resistance, survivorship and palliative care, therapy, tumor and microenvironment biology. PIs must be at or above assistant professor (or equivalent).

Advanced Neural Prosthetics Research and Development (U01)

More information

Sponsor: United States Department of Health and Human Services, National Institutes of Health

Submission Deadline: October 5

Upper Amount: $5 million

Synopsis: The purpose of this award is to encourage applications to pursue translational and pilot clinical studies for neural prosthetics. The program will utilize the cooperative agreement mechanism to enable support for milestone-driven projects for the development and demonstration of clinically-useful neural prosthetic devices. Activities supported in this program include implementation of clinical prototype devices, preclinical safety and efficacy testing, design verification and validation activities, pursuit of regulatory approval for clinical study, and proof-of-concept or pilot clinical studies.

Featured Events

8.13 Myron L. & Muriel S. Bender Distinguished Summer Lectures in Organic Chemistry

"Hydrogen-Bonded Supramolecular Nanotubes and Spheres," presented by Jeremy Sanders, Department of Chemistry, University of Cambridge.

Date: Tuesday, August 13, 11 a.m. to noon

Location: Technological Pavilion, LR5
2145 Sheridan Road (Evanston campus)

Contact: mobuhanich@northwestern.edu
More information

8.28 Emergency Medicine Grand Rounds

Guest lecturer: Jason Haukoos, MD, MSc, research director, Emergency Medicine, at the University of Colorado.

Date: Wednesday, August 28, 11 a.m. to Noon

Location: Northwestern Memorial Hospital Feinberg Pavilion, Pritzker Auditorium
251 E. Huron St. (Chicago campus)

Contact: jill-craig@northwestern.edu
More information

9.9 2013 Oncofertility Conference

"Cancer and Fertility Around the Globe," includes poster session and keynote by Samuel Kim, MD, Obstetrics and Gynecology, University of Kansas Medical Center.

Date: September 9 and 10, all day

Location: Prentice Women's Hospital, 3rd Fl. L Conference Room South
250 E. Superior St. (Chicago campus)

Contact: a-krausfeldt@northwestern.edu
More information

9.13 Pediatric Grand Rounds

"The Golden Anniversary of Newborn Screening: Lessons Learned and Future Evolution, as Illustrated by Cystic Fibrosis," presented by Phillip M. Farrell, MD, PhD, Pediatrics and Population Health Sciences, University of Wisconsin.

Date: Friday, August 13, 8 to 9 a.m.

Location: Ann & Robert H. Lurie Children's Hospital of Chicago, 11th Floor Conf. Center, Rooms 11-152 & 11-160
225 E. Chicago Ave. (Chicago campus)

Contact: d-marshall4@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.