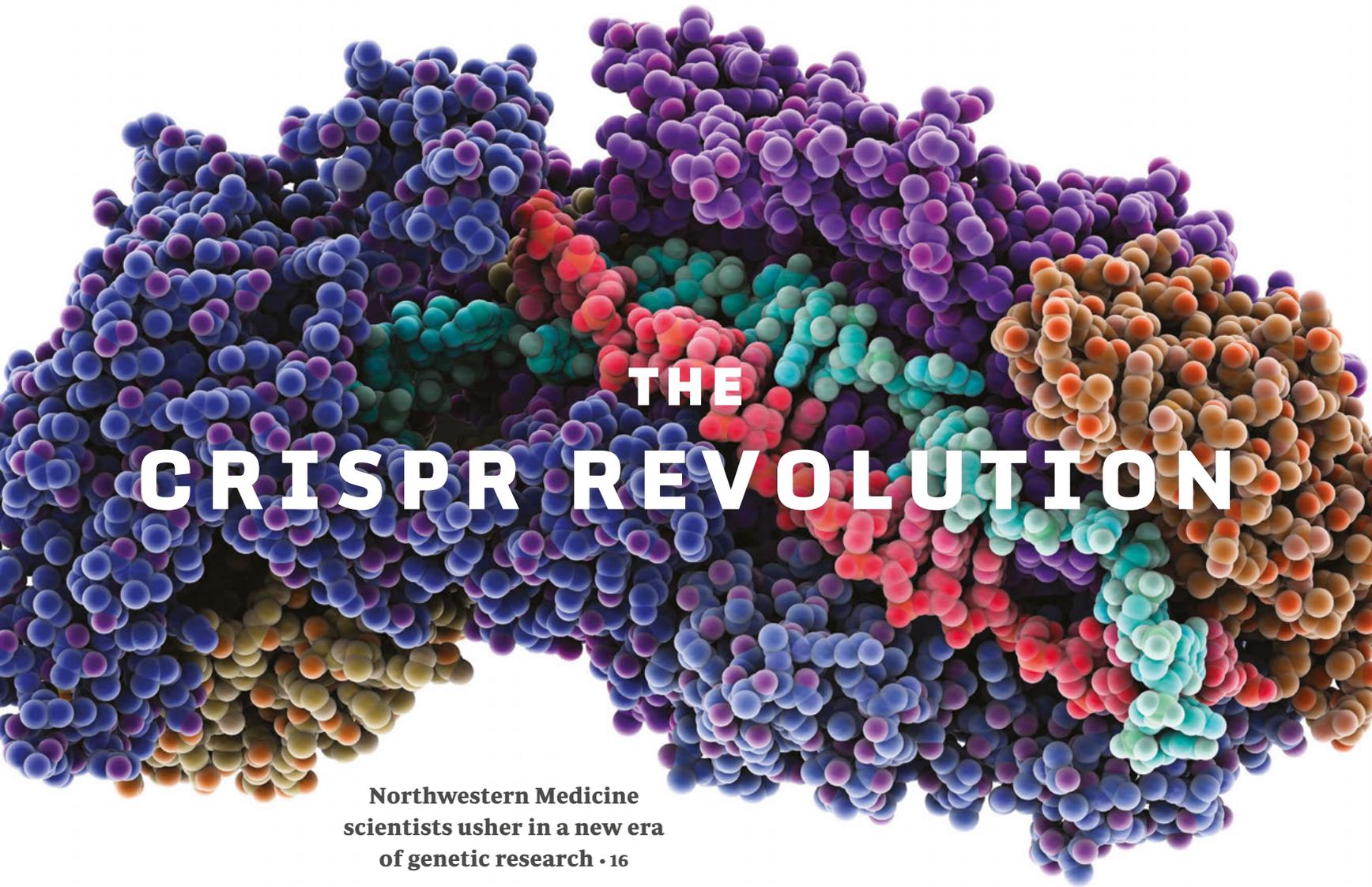


Northwestern Medicine

WINTER 2018



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A Lighter Side of Medical School

JAMMING AT IN VIVO

John Flaherty, MD, professor of Medicine in the Division of Infectious Diseases, jams with second-year medical student Nick Volpe in a performance by "The Hypochondriacs" during the 39th annual production of In Vivo, Feinberg's popular sketch comedy and variety show.

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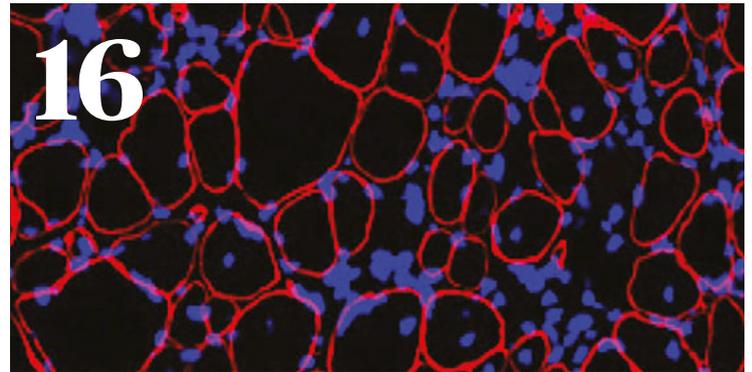
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A REMARKABLE YEAR

Reflecting on the medical school's accomplishments in 2017.



THE CRISPR REVOLUTION

Northwestern Medicine scientists usher in a new era of genetic research.



ONCOLOGY CLOSE-UP

Discover a program and a leader putting the Lurie Cancer Center at the forefront of its field.



FULL SPECTRUM OF GYNECOLOGIC CARE

New clinical programs provide collaborative, cutting-edge care for women of all ages.



PRECISION PATHOLOGIST

Daniel Brat is spearheading transformations in the field of pathology.

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ON THE COVER
 CRISPR-Cas RNA silencing complex. Computer model shows a max protein (green) bound to a strand of DNA (pink). Max, a member of the basic helix-loop-helix leucine zipper family of transcription factors, is involved in cell proliferation, differentiation and apoptosis. Transcription factors are proteins that bind to specific sequences of DNA and control the transcription of genetic information from DNA to RNA. (Laguna Design/Science Source)

Looking Forward in 2018



Eric G. Neilson, MD

Dean M. Harrison

EVERY TREATMENT EVER OFFERED TO A PATIENT was once an experiment in a lab, fueled by years of scientific effort. As we reflect on our successes in 2017 and plan for what is to come in 2018, it's important to acknowledge our commitment to developing the treatments that will become tomorrow's cures and to providing the most advanced healthcare to our patients. This reminds us of our purpose as we close one year and begin anew.

At Feinberg, we have made great strides to deliver on the promise of our mission to improve human health through education and discovery. Our students and trainees arrived on campus this year with extraordinary backgrounds (the new MD Class of 2021, for example, had median GPA and MCAT scores in the 98th percentile), and our graduates left with even more ambition and passion than when they came. These achievements are thanks to the exceptional faculty mentors in our educational programs and our innovative curriculum that emphasize flipped classrooms, team-based learning exercises, simulation, patient communication and student research. We are more confident than ever that our graduates are prepared to reshape the field of medicine.

Our research enterprise, too, continues to reach new heights. In the last year, our scientists published 238 papers in high-profile journals and funding grew more than 6 percent, confirming the prestige and impact our investigators have in their fields.

Construction of the Louis A. Simpson and Kimberly K. Querrey Biomedical Research Center is on track and will soon provide the space to grow our research enterprise even more.

In this issue of *Northwestern Medicine* magazine, we highlight many of the ways we are solidifying our place in emerging research areas: Our new Simpson Querrey Center for Epigenetics will investigate how environmental conditions impact the human genome. Our OncoSET program combines oncology with genomic sequencing to offer cutting-edge cancer care personalized to individual patients, while our new chair of Pathology leads national efforts to incorporate molecular findings into brain tumor diagnoses. And our cover story describes how many of Feinberg's laboratories are using innovative CRISPR-Cas9 gene editing techniques to better understand human disease and improve therapies.

The health system also enjoyed another successful year: Northwestern Memorial Hospital was ranked the top hospital in Chicago and Illinois for the sixth straight year and No. 13 nationally by *U.S. News & World Report*. We made improvements in physician and staff engagement and continued to report strong financial performance. We expanded the Bluhm Cardiovascular Institute to two Northwestern Medicine hospitals (bringing the total to four hospital locations), opened two new gynecology programs at Northwestern Memorial Hospital and expanded the Advanced Lung Disease Clinic to the northern suburbs. We also introduced the first combined MRI-PET machine to Chicago and began performing innovative new procedures, including implanting a novel device to manage advanced heart failure and another to give men with enlarged prostates a minimally invasive treatment option.

Looking forward, this spring we will be activating our system-wide electronic health record and opening the new Northwestern Medicine Lake Forest Hospital. These efforts are more examples

98th percentile

CLASS OF 2021'S MEDIAN GPA AND MCAT SCORES

238

PAPERS BY NORTHWESTERN MEDICINE SCIENTISTS PUBLISHED IN HIGH-PROFILE JOURNALS

6%

INCREASE IN RESEARCH FUNDING

#1 and #13

NORTHWESTERN MEMORIAL HOSPITAL RANKING IN CHICAGO AND ILLINOIS (#1) AND IN THE COUNTRY (#13)

of our *Patients First* mission and our relentless drive to be better.

It is worth taking stock of the remarkable things we have accomplished this past year — it inspires us to take on new challenges, feeds future discovery and forges stronger connections with our students, patients, mentees and collaborators. Our best wishes to all in the new year!

With warm regards,

Eric G. Neilson, MD
Vice President for Medical Affairs
Lewis Landsberg Dean

Dean M. Harrison
President and CEO
Northwestern Memorial Healthcare

ON CAMPUS

New Epigenetics Center to Study Role of Environment on Genes

\$10 MILLION GIFT CREATES SIMPSON QUERREY CENTER FOR EPIGENETICS

A new \$10 million gift from University trustees and supporters Louis A. Simpson and Kimberly K. Querrey will create a center at Feinberg to study the effects of environment on the activation and expression of genes.

The new Simpson Querrey Center for Epigenetics will investigate how environmental factors such as emotional experiences, chemical exposure, obesity, exercise, diet and drug therapies can modify genes packaged in human chromatin, causing them to become

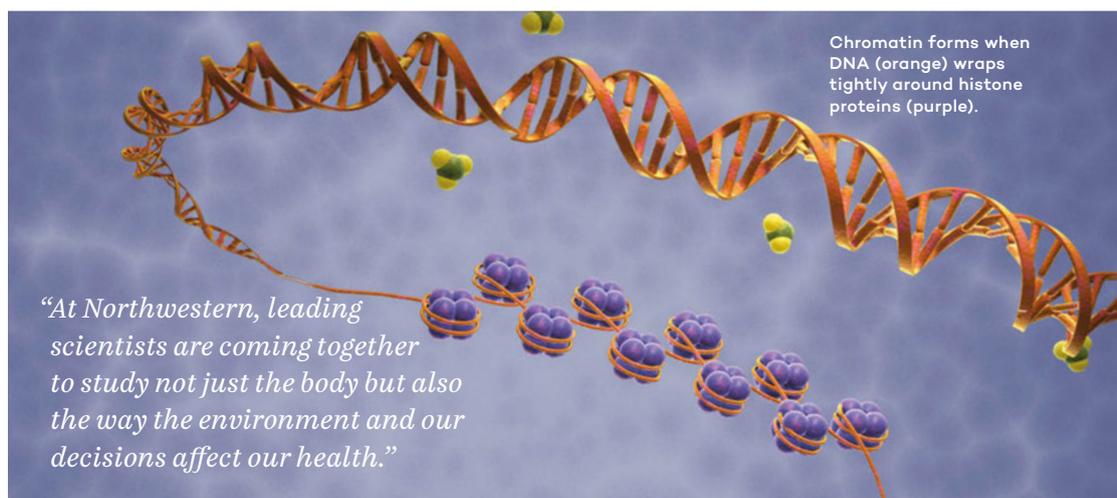
KEY DEFINITIONS

Epigenetics: the study of heritable changes caused by modification of gene expression rather than alteration of the underlying DNA sequence that makes up genes

Chromatin: a complex of DNA and proteins that packages and protects DNA and controls gene expression and DNA replication

more or less receptive to new biochemical signals. Epigenetic modifications of chromatin can have a direct effect on the regulation of gene expression. Some of this regulation is good, and some of it causes disease.

The center brings together experts in biochemistry, molecular genetics, computational



Chromatin forms when DNA (orange) wraps tightly around histone proteins (purple).

“At Northwestern, leading scientists are coming together to study not just the body but also the way the environment and our decisions affect our health.”

biology, fundamental biology, epidemiology and clinical medicine to develop foundational insights about how environmental conditions impact the human genome using sophisticated molecular, biochemical and computational methods.

“Epigenetic-driven insights are proving fundamental to a myriad of diseases including cancer, heart, immunologic and neurological conditions,” said Eric G. Neilson, MD, vice president for Medical Affairs and Lewis Landsberg Dean. “Understanding the details of how individual genes, groups of genes and environmental factors work together to determine the human condition is at the forefront of medicine today.”

The center will be led by Ali Shilatifard, PhD, the Robert Francis Furchgott Professor of Biochemistry and Pediatrics and chair of Biochemistry and Molecular Genetics. Shilatifard’s work focuses on understanding the intricate chromatin mechanisms that regulate gene expression.

This year, Shilatifard’s laboratory and his collaborators published several groundbreaking discoveries reporting the development of epigenetic targeted therapeutics for childhood leukemia, childhood brain cancer and adult triple negative breast cancer. One study on childhood brain tumors led to a phase I clinical trial planned for this year at the Ann & Robert H. Lurie Children’s Hospital of Chicago.

“Solving the world’s biggest problems requires creativity and collaboration,” Querrey said.

“At Northwestern, leading scientists are coming together to study not just the body but also the way the environment and our decisions affect our health. Lou and I are thrilled to be a part of this groundbreaking work.”

UPDATE

The generous new gift from Simpson and Querrey brings their total giving to Northwestern to \$164 million. See page 34 for a full update on **We Will. The Campaign for Northwestern.**



The mummy was prepared 1,900 years ago in Egypt and excavated in 1911. A recent CT scan confirmed she was a 5-year-old girl.

Exploring a Mummy's Secrets

Scientists peered inside an ancient mummy using CT scans and synchrotron X-rays to learn about bone strength over time.

WRITTEN BY *Will Doss*

USING THE BRIGHTEST X-RAY SOURCE IN THE WESTERN HEMISPHERE, Northwestern Medicine scientists directed a narrow beam of high-energy X-rays through an ancient mummy, aiming to reveal secrets about ancient Egyptian bone nanostructure that could help modern medicine better predict who might be at risk of fracture.

Led by Stuart Stock, PhD, research professor of Cell and Molecular Biology, the team used the Advanced Photon Source at Argonne National Laboratory this November to explore the structure of the mineral constituents of the mummy's bones without disturbing the mummy's wrappings.

The Roman-Egyptian mummy resides at the Garrett-Evangelical Theological Seminary on Northwestern's Evanston campus. A curator at Northwestern's Block Museum of Art stumbled upon it while investigating materials for an exhibit this winter.

Wanting to discover what was inside without disturbing the delicate portrait and wrappings, the curators contacted Stock to arrange a CT scan at Northwestern Memorial Hospital. Stock agreed to perform the scan, but wanted to go further: take the mummy to Argonne National Laboratory to analyze bone nanostructure using synchrotron X-ray diffraction.

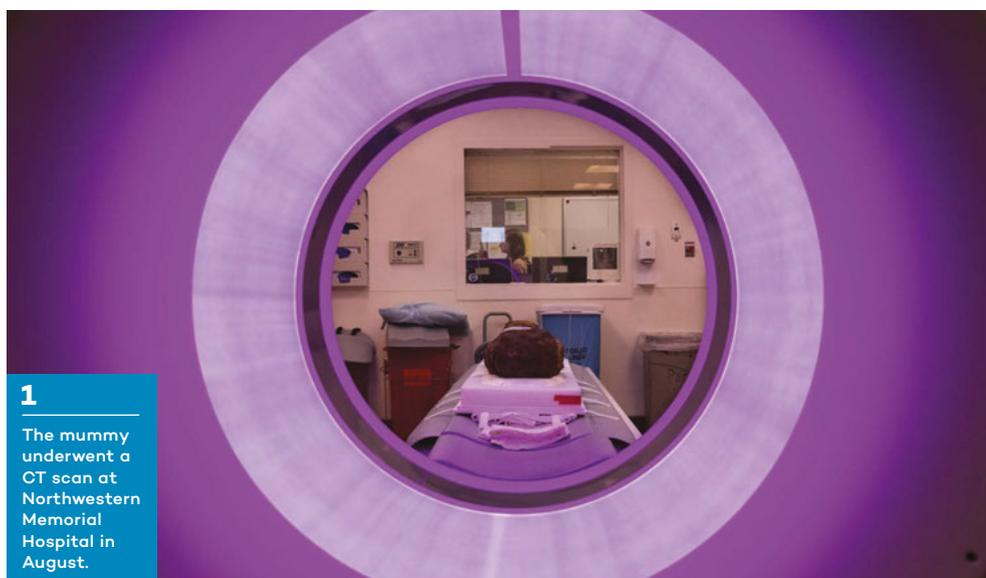
Bone contains a high density of nanocrystals and the periodic arrangement of atoms

within these nanocrystals scatter X-rays in different directions. The angles at which the X-rays diffract and the intensities of the different diffracted beams reveal information about the object's structure, according to Stock.

"If you know the angles and relative intensities of these diffracted beams, then you can identify what material it is — it's like a fingerprint," Stock said. "As far as I know, no one has tried to non-invasively interrogate what's inside an object like this."

Stock was most interested in bone competence, a measure of bone strength which becomes critical in osteoporosis.

The most significant determinant of bone competence is mineral density — the more



1

The mummy underwent a CT scan at Northwestern Memorial Hospital in August.

“WE’RE BASICALLY ABLE TO GO BACK TO AN EXCAVATION THAT HAPPENED MORE THAN 100 YEARS AGO AND RECONSTRUCT IT WITH OUR CONTEMPORARY ANALYSIS TECHNIQUES.”

mineral you have in your bones, the more they resist fracture. However, some older individuals who have fractures also have bones with high mineral density. According to Stock, some of this unexpected fracture risk is explained by poorly structured trabecular bone — the porous bone present at the ends of long bones — but that does not account for the whole discrepancy. Instead, it may be that the quality of the bone tissue varies.

“AS FAR AS I KNOW, NO ONE HAS TRIED TO NON-INVASIVELY INTERROGATE WHAT’S INSIDE AN OBJECT LIKE THIS.”

“There are epidemiological studies that say peak muscle mass and bone mass are protective through life, particularly for women,” Stock said. “I wanted to compare populations who had an active lifestyle with our more

modern sedentary populations — is there a difference in bone quality?”

Comparing the mineral nanostructure of the mummy’s bones with that of the bones of modern-day humans may quantify the benefits of an active lifestyle, improving clinicians’ ability to predict who is at risk for a fracture and enhancing preventative care.

“Right now in osteoporosis, we can look at bone density and trabecular bone structure and maybe predict fracture risk correctly 80 percent of the time,” Stock said. “We need to improve our predictive ability to around 95 percent, so we’ve got to track down additional factors.”

In addition to bone composition, Stock and colleagues will use X-ray diffraction patterns to identify other objects within the mummy’s wrapping, matching the patterns measured at Argonne with the patterns of other materials such as gold or rock.

“We have confirmed that the shards in the brain cavity are likely solidified pitch, not a crystalline material,” Stock said. “We are also investigating a scarab-shaped object, her teeth and what look like wires near the mummy’s head and feet.”

The findings from the synchrotron experiment, CT scan and other analyses will help investigators and historians better understand the life and death of this Roman mummy, according to Marc Walton, research professor of materials science and engineering at the McCormick School of Engineering.

“We’re basically able to go back to an excavation that happened more than 100 years ago and reconstruct it with our contemporary analysis techniques,” Walton said. “All the information we find will help us enrich the entire historic context of this young girl mummy and the Roman period in Egypt.”

2

In November, the mummy traveled to Argonne National Laboratory for a synchrotron X-ray experiment.



3

The angles and relative intensities of the diffracted beams revealed information about the body’s structure.

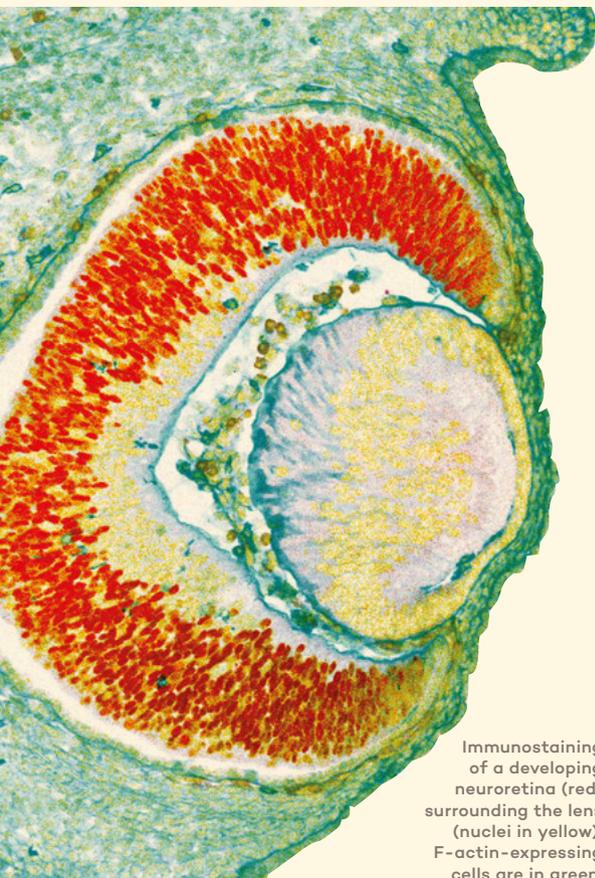


4

Scientists will study the mummy’s bone composition and identify other objects in her wrapping.



RESEARCH BRIEFS



Immunostaining of a developing neuroretina (red) surrounding the lens (nuclei in yellow). F-actin-expressing cells are in green.

DISEASE DISCOVERIES

STEM CELLS LEAD TO BETTER UNDERSTANDING OF RETINAL DEVELOPMENT



Northwestern Medicine scientists used embryonic stem cells and induced pluripotent stem cells to generate eye organoids that mimic early eye development, creating a tool that allowed them to characterize molecular events that regulate the formation of the complex organ. The findings were published in *Cell Reports*.

The scientists focused on the neuroretina, a collection of eye cells that help convert light into neural signals, and identified the gene *Rspondin-2* as a critical player in mammalian neuroretina differentiation.

The authors found that during early development, when the eye is initially forming and is still just an outgrowth of neural tissue, the activity of the transcription factor *Six3* is

required to repress *Rspondin-2* from the anterior part of the head where the eyes are eventually going to form.

“The prospect of using stem cell-based therapies to treat different types of retinal diseases is becoming a real possibility; therefore, having a better understanding of the cellular and molecular processes controlling eye morphogenesis and neuroretina differentiation is critical,” said principal investigator Guillermo Oliver, PhD, the Thomas D. Spies Professor of Lymphatic Metabolism. Nozomu Takata, PhD, a postdoctoral fellow in Oliver’s lab, was the first author.

The study also showed that stem cells can accurately recreate live organs in lab-grown models, opening up possibilities for future research.

“Our results further validate the organoid culture system as a reliable and fast alternative to identify and evaluate genes involved in eye morphogenesis and neuroretina differentiation *in vivo*,” Oliver said.

This work was supported by the National Eye Institute grant EY12162 and a Fellowship for Research Abroad from the Uehara Memorial Foundation.

CLINICAL BREAKTHROUGHS

Synthetic Cannabis-like Drug Reduces Sleep Apnea



A synthetic cannabis-like drug in a pill was safe and effective in treating obstructive sleep apnea in the first large multi-site study of a drug for apnea funded by the National Institutes of Health.

There is currently no drug treatment for sleep apnea, a sleep breathing disorder affecting about 30 million individuals in the United States. Untreated apnea raises the risk of heart disease, diabetes, sleepiness, cognitive impairment and a motor vehicle accident.

Participants in the Northwestern Medicine and University of Illinois at Chicago trial had reduced apnea and decreased subjective sleepiness, according to the study, published in the journal *SLEEP*.

The common treatment for sleep apnea is a CPAP (Continuous Positive Airway Pressure) device that delivers air to prevent collapse of the airway and breathing pauses. But adherence to the device can be challenging for many patients, some who simply stop using it.

Investigators looked at the effect of dronabinol, a synthetic version of the molecule Delta-9 THC (tetrahydrocannabinol), which is in cannabis, on sleep apnea. The phase 2 trial, with 73 patients over six weeks, was the largest and longest randomized, controlled trial to test a drug treatment for sleep apnea.

Dronabinol targets the brain rather than the physical problem of collapsing airways. This reflects the new belief that sleep apnea is not just a physical problem but may be caused

by multiple factors, such as poor regulation of the upper airway muscles by the brain, said co-lead author Phyllis Zee, MD, PhD, the Benjamin and Virginia T. Boshes Professor of Neurology and director of the Northwestern Medicine Sleep Disorders Center.

“The CPAP device targets the physical problem but not the cause,” Zee said. “The drug targets the brain and nerves that regulate the upper airway muscles. It alters the neurotransmitters from the brain that communicate with the muscles. Better understanding of this will help us develop more effective and personalized treatments for sleep apnea.”

This research was supported by grant U01-HL112856 from the National Heart, Lung, and Blood Institute.

MEDICAL EDUCATION

Comparing Physical Exam Education at U.S. Medical Schools



The resources used to teach the physical exam to pre-clerkship medical students vary widely across U.S. medical schools, according to a study published in *Academic Medicine*.

Teaching the physical exam is generally labor-intensive and requires significant human resources, including faculty, as well as standardized and actual patients, noted Toshiko Uchida, MD, Feinberg's director of Clinical Skills Education and first author of the study. As such, there have been concerns that some medical schools may be providing inadequate physical exam training.

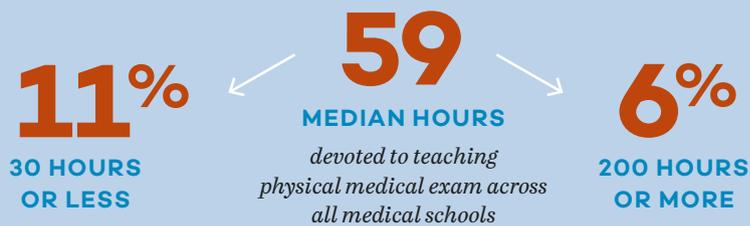
In the study, investigators aimed to understand the various resources and

pedagogical approaches that U.S. medical schools employ to teach the physical exam to pre-clerkship students.

The Directors of Clinical Skills Courses, a professional organization of clinical skills educators, administered a 49-question survey to all 141 medical schools accredited by the Liaison Committee on Medical Education.

"Some schools likely don't devote enough time or resources to teaching the physical exam in the pre-clerkship years," Uchida said. "There is also a great need for further research to determine how much time is enough to learn the physical exam, and how best we can deploy our resources so that students begin to master physical exam techniques."

Resources and Approaches Study Results



OF THE TIME SPENT TEACHING THE PHYSICAL EXAM



PRACTICE TIME SPENT WITH ACTUAL PATIENTS



SCIENTIFIC ADVANCES

SUICIDE MOLECULES KILL ANY CANCER CELL



Small RNA molecules originally developed as a tool to study gene function trigger a mechanism hidden in every cell that

forces the cell to commit suicide, reports a Northwestern Medicine study. The RNA suicide molecules can potentially be developed into a novel form of cancer therapy, the study authors said.

Cancer cells treated with the RNA molecules never become resistant to them because they simultaneously eliminate multiple genes that cancer cells need for survival.

"It's like committing suicide by stabbing yourself, shooting yourself and jumping off a building all at the same time," said senior study author Marcus Peter, PhD, the Tom D. Spies Professor of Cancer Metabolism.

The inability of cancer cells to develop resistance to the molecules is a first, Peter said. He and his team discovered sequences in the human genome that when converted into small double-stranded RNA molecules trigger what they believe to be an ancient kill switch in cells to prevent cancer. He has been searching for the phantom molecules with this activity for eight years.

"We think this is how multicellular organisms eliminated cancer before the development of the adaptive immune system, which is about 500 million years old," he said. "It could be a fail-safe that forces rogue cells to commit suicide. We believe it is active in every cell protecting us from cancer."

This study, which was published in the journal *eLife*, and two other Northwestern studies in *Oncotarget* and *Cell Cycle* by the Peter group, describe the discovery of the assassin molecules present in multiple human genes and their powerful effect on cancer in mice.

This research was funded by grants T32CA070085, T32CA009560, R50CA211271 and R35CA197450 from the National Cancer Institute.

MEDIA SPOTLIGHT

The New York Times

Amish Mutation Protects Against Diabetes and May Extend Life

Amish people living in a rural part of Indiana have a rare genetic mutation that protects them from Type 2 diabetes and appears to significantly extend their life spans, according to a new study published in *Science Advances*. The mutation affects a mysterious protein called plasminogen activator inhibitor-1, or PAI-1, that is known primarily for its role in promoting blood clotting.

Douglas Vaughan, MD, chair of Medicine, took a team of 40 investigators to Berne, Indiana, set up testing stations in a recreation center, and spent two days doing extensive tests on 177 members of the community, many of whom arrived by horse and buggy. “Some of the young men we collected blood from



fainted because they had never had a needle stick in their life,” said Vaughan. What he and his colleagues discovered was striking. Amish carriers of the mutation live on average to age 85, about 10 years longer than their peers. Among the Amish who did not have the mutation, the rate of Type 2 diabetes was 7 percent. But for carriers of the mutation, the rate was zero, despite leading the same lifestyle and consuming similar diets.



photo courtesy of Novocure

abc NEWS

Electric Fields Therapy Shows Promise for Brain Cancer Patients

“My patients have been going skiing,” said Roger Stupp, MD, chief of Neuro-oncology in the Department of Neurology and lead author of a study published in *JAMA* that tested a home-based electrical field treatment known

as tumor-treating fields to help patients with glioblastoma. The treatment, for most, is surprisingly manageable. Doctors place four electrodes on a patient’s shaved scalp, where they’re worn for most of the day. The electrodes create low-intensity electrical fields within the brain that kill dividing cells. “I have a patient who I met here in Chicago who has gone on a safari in Africa twice now,” Stupp said.

REUTERS

Obesity, Poverty Help Explain Higher Diabetes Risk for U.S. Blacks



Even though black adults are more likely to develop diabetes than white adults, the increased risk is largely due to obesity and

other risk factors that may be possible to change, a U.S. study published in *JAMA* suggests. “To eliminate the higher rate of diabetes, everybody needs to have access to healthy foods, safe spaces for physical activity and equal economic opportunity to have enough money to afford these things and live in communities that offer this,” said lead author Michael Bancks, PhD, a postdoctoral fellow in Preventive Medicine at Feinberg.

FACULTY AWARDS & HONORS



Mary McDermott, MD, '92 GME, the Jeremiah Stamler Professor of Medicine in the Division of General Internal Medicine and Geriatrics and of Preventive Medicine, was named a Distinguished Scientist by the American Heart Association. The award honors prominent scientists and clinicians who have made significant contributions to the understanding of cardiovascular disease and stroke. McDermott has dedicated her research to lower extremity peripheral artery disease (PAD); her many accomplishments include demonstrating that supervised treadmill exercise improves walking ability among people with PAD, even when they are asymptomatic or have atypical leg symptoms.

McDermott will also lead a new research network center sponsored

by the AHA focused on calf muscle pathology and disability in PAD. 📍 1

Laimonis Laimins, PhD, the Guy and Anne Youmans Professor and chair of Microbiology-Immunology, and **Richard J. Miller, PhD**, the Alfred Newton Richards Professor of Pharmacology, were named Fellows of the American Association for the Advancement of Science. Laimins was recognized for his contributions to the field of viral oncology, particularly for his studies on the differentiation-dependent life cycle of human papillomaviruses. Miller was recognized for his contributions to neuroscience and neuropharmacology, particularly in elucidating the role ion channels and receptors play in synaptic communication in health and disease. 📍 2, 3

Firas Wehbe, MD, PhD, assistant professor of Preventive Medicine in the Division of Health and Biomedical Informatics, has been appointed Northwestern Medicine's inaugural chief research informatics officer. 📍 4

Patricia Garcia, MD, MPH, '91 GME, professor of Medical Education and Obstetrics and Gynecology in the Division of Maternal-Fetal Medicine, was named associate dean for curriculum. 📍 5

Alexis Thompson, MD, MPH, professor of Pediatrics in the Division of Hematology, Oncology, and Stem Cell Transplantation, has been named president of the American Society of Hematology. 📍 6

Richard D'Aquila, MD, the Howard Taylor Ricketts, MD, Professor of Medicine in the Division of Infectious Diseases,

and Phil Hockberger, PhD, associate professor of Physiology, were named associate vice presidents to Northwestern University's Office for Research.

June McKoy MD, JD, MBA, was chosen to join the National Commission on Orthotic and Prosthetic Education (NCOPE) board of directors. The NCOPE is responsible for setting education standards of all professionals in the field of orthotics/prosthetics. 📍 7

Emily Rogalski, '07 PhD, was named one of Crain's Chicago Business's "40 Under 40." She was recognized as a disruptor who is "upsetting the status quo" through her groundbreaking work with SuperAgers.

William Gradishar, MD, the Betsy Bramsen Professorship of Breast Oncology and interim chief of Hematology and Oncology in the

Department of Medicine, was among the top 27 breast oncologists in the country based on data from Grand Rounds, a company that uses a machine learning algorithm to analyze publicly available and proprietary data about physicians, as reported by *Forbes*.

Donald Lloyd-Jones, MD, senior associate dean for Clinical and Translational Research and chair of Preventive Medicine, was among the top 27 cardiologists.

Amy Paller, MD, the Walter J. Hamlin Professor and chair of Dermatology, was selected by her colleagues in the Women's Dermatologic Society to receive the 2018 Wilma Bergfeld, MD Visionary & Leadership Award.

Peter Penzes, PhD, the Ruth and Evelyn Dunbar Professor of Psychiatry and Behavioral Sciences, was named director of Feinberg's newly

announced Center for Autism and Neurodevelopment. The center's mission is to catalyze scientific collaborations to better understand the biological bases of autism and related neurodevelopmental disorders and to translate those findings into new treatments.

H. William Schnaper, MD, the Irene Heinz Given and John LaPorte Given Research Professor of Pediatrics in the Division of Kidney Diseases, received the 2018 American Society of Pediatric Nephrology Founders' Award, which recognizes individuals who have made a unique and lasting contribution to the field of pediatric nephrology. scientific collaborations to better understand the biological bases of autism and related neurodevelopmental disorders and to translate those findings into new treatments.



REFLECTING ON OUR

ACCOMPLISHMENTS IN 2017

A REMARKABLE YEAR

Record-breaking research activity.

A curriculum that better prepares students for clerkships.

A new skyscraper takes shape on campus.

Read on for some of the top news from the Feinberg School of Medicine in 2017. >>

HIGH-IMPACT RESEARCH

[A sampling of the breakthrough findings published by Feinberg-led research teams in the previous year.](#)

Surgical residents across the country have grown accustomed to **flexible duty hour requirements**, without rules on maximum shift lengths and time off between shifts, which were previously shown to be safe for patients and better for resident education. (*New England Journal of Medicine*)

Simple behavioral interventions can effectively curb **inappropriate antibiotic prescribing**, if adopted for the long term. (*Journal of the American Medical Association*)



RESEARCH »

Feinberg's Funding Surpasses \$471 Million

Sponsored research awards secured by principal investigators at the medical school grew to \$471.7 million last fiscal year, a 6 percent increase over the previous year.

"Feinberg's remarkable research growth continued last year, despite overall National Institutes of Health funding staying flat for medical schools as a whole," said Rex Chisholm, PhD, vice dean for scientific affairs and graduate education.

"We're proud to say that last year's funding covered a wide variety of disease-based science and cross-cutting biomedical themes," he added. "Our strengths in leveraging big data, reducing health disparities and fundamental science have translated to new techniques and clinical questions that we're just now beginning to explore."

\$471.7
MILLION

The medical school's sponsored research awards totaled \$471.7 million in 2017.

72
PERCENT

Feinberg generated 72% of all research dollars at Northwestern University.

+6
PERCENT

Sponsored research awards were up six percent in 2017 from 2016.

Groundbreaking Molecular Discoveries



The lab of Ali Shilatifard, PhD, the Robert Francis Furchgott Professor of Biochemistry and Pediatrics and chair of Biochemistry and Molecular Genetics, had a

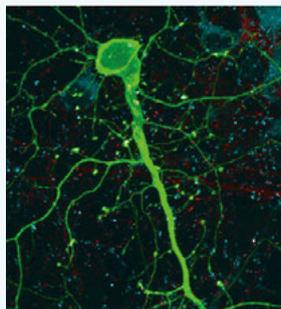
prolific year, publishing papers in journals including *Science*, *Nature Medicine*, *Cell* and *Genes and Development*.

Among the discoveries, the team identified the genetic driver of mixed lineage leukemia and a targeted molecular therapy that halts the proliferation of leukemic cells. The scientists also found a molecule that stops the growth of aggressive pediatric brain tumor diffuse intrinsic pontine glioma, and they learned that targeting the SET1B protein in the cytoplasm of cells may be able to treat triple-negative breast cancer. Other findings elaborated on scientists' understanding of gene expression and embryonic stem cell development.

"This work could not have been done anywhere in the world except Northwestern Medicine, because of all the scientists and physicians who have been recruited here during the past five years and how they work together to link basic scientific research to the clinic." – Ali Shilatifard

Shilatifard will lead Feinberg's new Simpson Querrey Center for Epigenetics (read more on page 3).

→ A new method of analyzing non-coding regions of DNA in neurons may pinpoint which genetic variants are most important to the development of **schizophrenia** and related disorders. (*Cell Stem Cell*)



→ Normal agers lose volume in the cortex, which contains neurons, twice as fast as **SuperAgers**, a rare group of older people whose memories are as sharp as those decades younger. (*Journal of the American Medical Association*)



NORMAL AGERS
lose volume in the cortex as they age



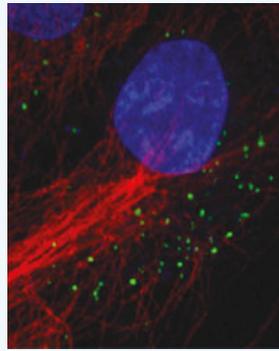
SUPERAGERS
lose volume in the cortex at 1/2 the rate of normal agers

→ A promising bioactive nanomaterial has the potential to stimulate **bone regeneration** and improve quality of life for surgical patients and lead to less-invasive procedures. (*Nature Nanotechnology*)

HIGH-IMPACT RESEARCH *con't*

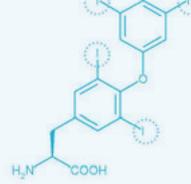
The neuronal degeneration in patients with **Parkinson's disease** was linked to a toxic cascade beginning with an accumulation of oxidized dopamine and the protein alpha-synuclein, providing a possible therapeutic pathway. (*Science*)

Inhibiting the process of autophagy — a natural process of cell destruction that also plays a protective role under stress conditions — may enhance the effects of radiation therapy for **glioblastoma**. (*Cancer Cell*)



The **human immunodeficiency virus** uses proteins called diaphanous-related formins to hijack the cytoskeleton of healthy cells. (*Proceedings of the National Academy of Sciences*)

Two commonly used drugs, thyroxine and metformin, erased the learning and memory deficits in rat pups caused by **fetal alcohol exposure** when the drugs were given after birth, potentially identifying a treatment for the disorder. (*Molecular Psychiatry*)



ACADEMICS »

Number of New Students by Program

161

Doctor of Medicine Program

30

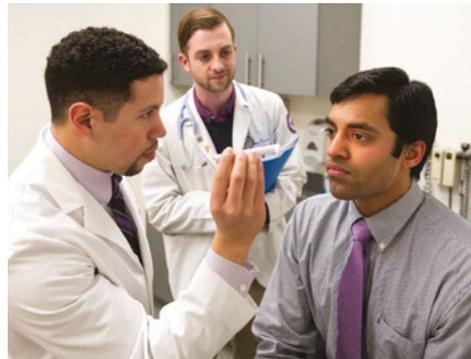
Driskill Graduate Program in the Life Sciences

New MD Curriculum Assessed

Last fall, Northwestern Medicine faculty described the medical school's comprehensive curriculum redesign, rolled out in 2012 with the graduating class of 2016, and reported early outcomes on student achievement, confidence and engagement in a paper published in *Academic Medicine*.

Students' U.S. Medical Licensing Examination Step 1 and Step 2 scores stayed stable between the old and new curriculums, while student surveys demonstrated that those in the current curriculum felt significantly better prepared in clinical skills before entering clerkships compared to those who went through the former curriculum. Further, students reported greater confidence in their professional development.

"We have significantly more clinical immersion now, and our students tell us that as a result, when they see patients they understand the importance of basic science content that might have

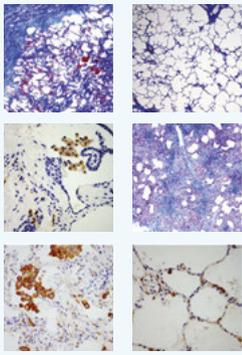


"We have significantly more clinical immersion now. [Students] see they are making a meaningful difference in patients' lives, and that's invigorating."

otherwise seemed dry," explained Heather Heiman, MD, leader of the curriculum's clinical medicine element. "[Students] see they are making a meaningful difference in patients' lives, and that's invigorating."

RECORD-BREAKING RESEARCH DAY →

More than 400 abstracts showcased the diversity of innovative research taking place at Feinberg. The 13th Annual Lewis Landsberg Research Day last spring included projects on basic science research, clinical research, public health and social sciences research, and education research. Winners of the poster competition focused on areas of research spanning from myofilament components in arrhythmia and dilated cardiomyopathy to longitudinal studies of primary care clerkships and patient outcomes.



←
A unique population of immune cells called monocyte-derived alveolar macrophages plays a key role in the development of **pulmonary fibrosis**; targeting such cells could lead to new treatments for the disease. (*The Journal of Experimental Medicine*)



Kaylin McMahon, '17 PhD (L) and Doug Wilcox, '16 PhD (R)

Celebrating PhD Students

In 2017, Feinberg welcomed 30 new PhD students from as far away as Puerto Rico, Russia and India to the Walter S. and Lucienne Driskill Graduate Program (DPG) in Life Sciences. During the sixth annual Driskill Day last fall, DGP students and faculty received awards for their innovative research and mentorship. Among them, Kaylin McMahon, '17 PhD, was recognized for her work developing bioinspired delivery vehicles for nucleic acid therapies for cancer, while Doug Wilcox, '16 PhD, an MD/PhD student in the Medical Scientist Training Program, received an award for his research on the age-dependent mechanisms of pathogenesis in herpes simplex virus encephalitis.

20

Northwestern University Interdepartmental Neuroscience Program

15

Medical Scientist Training Program

4

Clinical Psychology PhD Program

3

Health Sciences Integrated PhD Program

1

Doctor of Physical Therapy/PhD Engineering Program



CAMPUS »

Early 2017



Late 2017

Simpson Querrey Biomedical Research Center Nears Completion

“This building is a blend of a new construction and stacking on the Robert H. Lurie Medical Research Center. Each floor will be connected to the Lurie facility, and it will be wrapped with a full plaza featuring green space on the outside. The building will also have a sky bridge that connects to the Ward Building.”

— Chris Jones, senior superintendent at Power Construction, general contractor of the project

Over the course of 2017, the Louis A. Simpson and Kimberly K. Querrey Biomedical Research Center progressed from an extensive underground construction project to a 300-foot tall, 14-story structure.

In June, the Northwestern community gathered to celebrate as a ceremonial steel beam was set in place atop the Simpson Querrey Biomedical Research Center. The ceremony marked a major milestone in the construction of the 600,000-square-foot building, which will significantly expand the medical school’s research enterprise.

In October, two years after the university broke ground on the building, extensive mechanical, electrical, duct and piping work was taking place behind the exterior of the building by more than 200 skilled trades workers onsite.

Over the next year, the team will finish installing windows on the outside of the building and begin connecting a bridge to the Ward Building. The outdoor plaza work will also start to take shape and the interior work on the lab floors will become a main focus.



Sketches from the plans for the new building, designed by architecture firm Perkins+Will.

HONORS »

Medical School and Hospital Affiliates Rank High



In 2017, Feinberg maintained its standing among the best research-oriented medical schools in the country, placing 17th in the latest *U.S. News & World Report* rankings. Meanwhile, the company recognized three Northwestern



Medicine hospitals in its 2017-18 rankings of America's Best Hospitals. The Shirley Ryan AbilityLab once again earned the top spot among rehabilitation hospitals in the country, and Lurie Children's ranked first among children's hospitals in Illinois.

1



2



3



4



FACULTY RECOGNIZED WITH PRESTIGIOUS AWARDS

Many Feinberg faculty were recognized nationally by their peers as leaders in their fields.

Among them, **Donald Lloyd-Jones, MD, ScM** (1), senior associate dean for clinical and translational research and chair of Preventive Medicine, who was named Physician of the Year by the American Heart Association and a member of the Association of American Physicians.

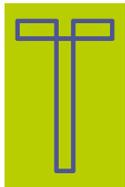
Karl Bilimoria, MD, '08 MS, '10 GME (2), director of the Northwestern Surgical Outcomes and Quality Improvement Center and the John Benjamin Murphy Professor of Surgery and Medical Social Sciences, and **Sarki Abdulkadir, MD, PhD** (3), the John T. Grayhack, MD, Professor of Urological Research and professor of Pathology, joined the American Society for Clinical Investigation.

Melissa Simon, MD (4), the George H. Gardner Professor of Clinical Gynecology, was appointed to the U.S. Preventive Services Task Force to make evidence-based recommendations for preventive screenings, counseling services and medications. ■

THE CRISPR REVOLUTION

Northwestern Medicine scientists usher in a new era of genetic research.

Written by Will Doss



he McNally lab members were shocked.

For the first time, they had used a new gene editing technique that promised to transform how scientists investigated the human genome. Prior to that day in late 2014, editing genes in mammalian cells had been a time-consuming process — sometimes requiring screening hundreds of clones to find one with altered DNA — and it often ended in failure. But then, Eugene Wyatt, PhD, a postdoctoral fellow in the lab, generated a cellular model of genetic disease in human embryonic kidney cells faster than ever before by harnessing a specialized region of DNA called CRISPR.

“More than 80 percent of the clones showed evidence of editing,” says Elizabeth McNally, MD, PhD, the Elizabeth J. Ward Professor of Genetic Medicine and director of Feinberg’s Center for Genetic Medicine. “This was truly revolutionary — older methods only worked in very specific cells and relied on waiting for a cell’s natural machinery to edit genes. With CRISPR, that machinery could be directly introduced into the cells, dramatically improving efficiency.”

Tasks such as creating a mouse model of disease, which previously took about

three years, now would take just four to six months, allowing scientists around the world to more quickly understand mechanisms of disease and more efficiently translate those discoveries from bench to bedside. At Feinberg, CRISPR gene editing is being used today in many settings, including to isolate mutations that cause neurological diseases and to run large-scale genetic screens to understand how individual genes can damage — or protect — cells.

Northwestern Medicine scientists are quick to point out that CRISPR-Cas9 is not just a laboratory tool; it also has tremendous potential for use in patients, though there are still unresolved ethical and regulatory issues to think through before editing live human genomes. But its first experimental use in patients is closer than most realize, according to McNally.

“If you had asked me last year, I would’ve told you it will be ten years before somebody injects a patient with a genome-editing virus,” McNally says. “Now I think it’s about two or three years away.”

That prediction underlines the head-spinning pace at which CRISPR technology is changing genetics. The first peer-reviewed papers showing successful gene editing in mammals were published just five years ago.

CRISPR AT FEINBERG

Using CRISPR to edit the genomes of human cells or model organisms has become a staple of research activities at Feinberg — especially when combined with induced pluripotent stem cells (IPSCs).

Scientists can harvest adult cells from a human subject, turn those into stem cells and direct the resulting IPSCs to develop into a specific type of tissue, such as cardiac cells, neurons or skeletal muscle tissue. This technique helps investigators identify cellular mechanisms of disease and can be combined with CRISPR to isolate disease-causing mutations.

For example, stem cells can be created using genetic material from patients with amyotrophic lateral sclerosis (ALS), and those cells differentiated into motor neurons. Investigators can compare those neurons to neurons from healthy individuals, looking for genetic mutations in the diseased model. If they find a suspicious mutation, they can use CRISPR to reverse the genetic mutation, creating a stem cell line identical to the patients’ cells, but without the mutation — this is called an isogenic control line. ⇒



☞ If you had asked me last year, I would've told you it will be ten years before somebody injects a patient with a genome-editing virus. Now I think it's about two or three years away. ☞

⇒ How CRISPR Works ⇒

Just as CRISPR was transforming what scientists can do with cells, it equally changed the landscape for genetically engineering mice to model human diseases. The diagram at right illustrates how the CRISPR-Cas9 gene editing complex works. A sequence of RNA (green) programmed to find a specific segment of DNA (blue) is inserted into a cell along with the Cas9 enzyme (purple). Once the RNA finds the matching DNA, Cas9 cuts it. In that space, a fragment of donor DNA containing new genetic information (red) can be inserted.

“This allows us to test whether a phenotype or defect in a motor neuron is caused by that particular mutation,” says Evangelos Kiskinis, PhD, assistant professor of Neurology. “If the defect goes away, we’ve established the mutation is necessary for the defect.”

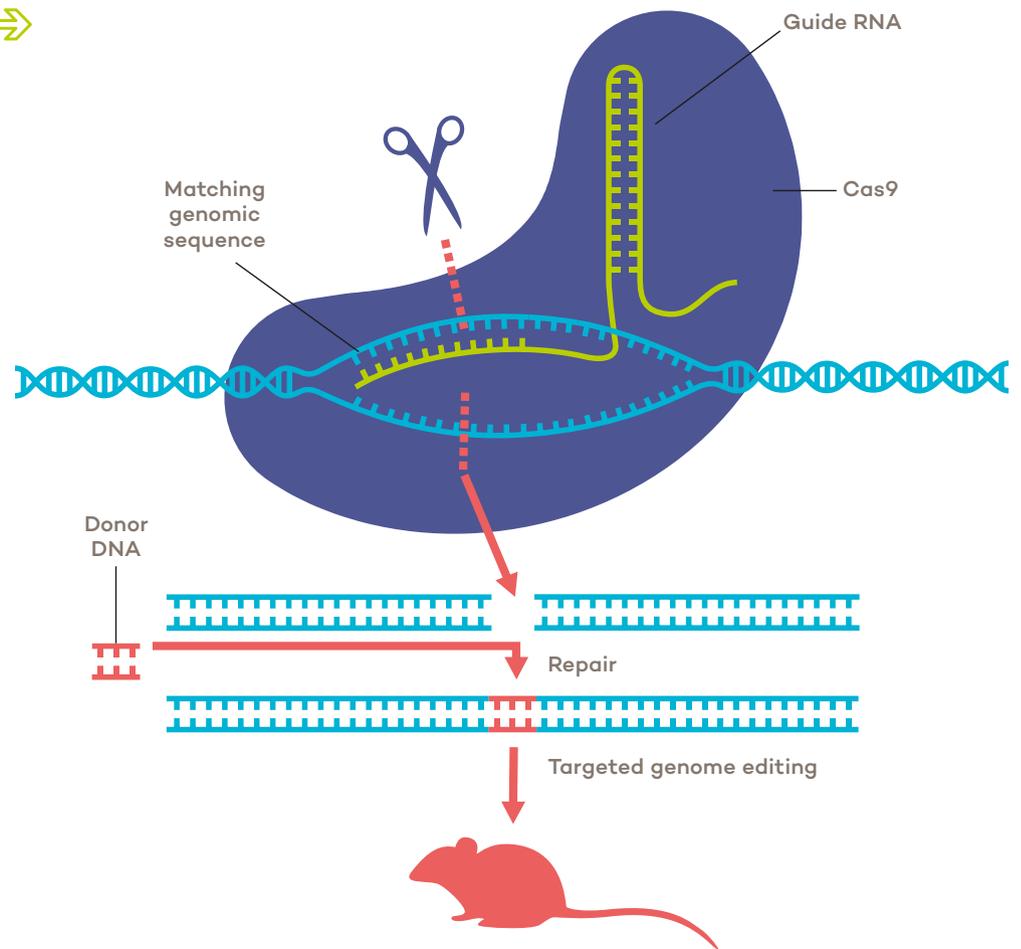
Kiskinis also uses CRISPR to do the opposite experiment. He takes a healthy stem cell line, introduces the mutation using CRISPR and asks if that change is sufficient enough to induce the same phenotype.

This method becomes even more important when looking at diseases caused by a combination of genes, such as epilepsy. Kiskinis and his colleagues have introduced a known epilepsy-causing gene variant into a variety of stem cell lines derived from healthy individuals. They’re looking for insights into the impact of an individual’s broader genetic background and why certain people develop epilepsy and others don’t.

“This is the first time we are able to do this in human cells,” Kiskinis says. “Before, it was technically possible, but extremely challenging; it would take a very long time.”

Another application of CRISPR is in large-scale genetic screens, a fast and simple way to investigate the effects of individual genes in cells. Navdeep Chandel, PhD, the David W. Cugell, MD, Professor of Medicine, used this method to narrow down which genes made a person vulnerable to Parkinson’s disease after repeated exposure to an herbicide called paraquat.

Epidemiological studies indicate that farmers exposed to paraquat have a higher risk of Parkinson’s disease. A major cause of



Parkinson’s disease is a loss of function in dopamine neurons, which are known to be vulnerable to oxidative stress.

“Paraquat generates a lot of oxidants. Naturally those dopamine neurons will be the most susceptible to damage from the pesticide,” says Chandel.

His team conducted a CRISPR positive-selection screen, creating thousands of cells with one individual gene turned off.

They then exposed the cells to paraquat — the majority of them died, but not all. Certain cells with knocked-out genes were resistant to paraquat, suggesting those genes may be responsible for the toxicity. One gene in particular, called POR, was pinpointed as the main source of damage-causing oxidation, according to Chandel.

Investigating oxidant stress could pay dividends in the future, including in the development of drugs designed to generate oxidative stress in cancer cells, killing them while leaving healthy cells alone. While some drugs currently exist, not enough is known about their pathways to create a functioning

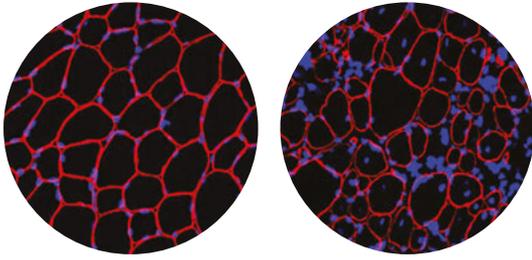
compound, says Chandel, a member of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University.

“The biology of oxidative stress is still a mystery,” he says. “CRISPR positive-selection screens could be a way to figure it out.”

UNANSWERED QUESTIONS

While there’s little legal or ethical debate around using CRISPR with cultured cells or non-embryonic stem cells, using the tool to edit the genome of living humans — especially in a manner where changes would be inherited by children — is still uncharted territory. Scientists in China reported using CRISPR to edit a gene responsible for a deadly blood disorder in non-viable embryos, but few embryos survived and it set the international scientific community off into a fiery debate.

However, it’s no longer a question of *if*, but rather a question of when CRISPR-like technology will be used in humans, according to Raj Awatramani, PhD, associate professor of Neurology in the Division of Movement Disorders.



Human induced pluripotent stem cells that have been gene edited with CRISPR from the lab of Elizabeth McNally, MD, PhD.

“Society doesn’t keep pace with the science,” says Awatramani, who uses CRISPR to create model neurons vulnerable to Parkinson’s disease. “We need to have new ethical guidelines to deal with genome editing in humans. Right now, it’s gray, gray and grayer.”

Several companies are racing to be the first to use CRISPR in living humans, usually to treat serious chronic diseases such as HIV/AIDS or Duchenne muscular dystrophy, according to McNally. For Duchenne, the proposed treatments would involve injecting a patient — probably a young child — with a virus containing CRISPR material. Early models show that even if uptake only occurs in some cells, symptoms are relieved because the corrected cells tend to compensate for the diseased cells.

“It’s nerve-racking when we’re talking about children,” says McNally, who testified about the importance of using this method to treat genetic disease to the U.S. House of Representatives Committee on Science, Space and Technology in 2015. “Diseases like Duchenne muscular dystrophy are so difficult for patients and their families that it could be argued trying the therapy is the right thing to do, as long as it’s reasonably safe.”

Regardless of its future as a therapeutic tool, CRISPR has entrenched itself as a central mechanism for genetics research, in an astonishingly short period of time. Combined with the adaptability of iPSC, the technologies have irrevocably changed genetics for the better.

“There’s no question, when people look back 100 years from now, they’ll find it hard to believe all of this was discovered at the same time,” McNally says. “This is truly a revolutionary time for genetics.” ■

Local Beginnings

First discovered by Francisco Mojica in Spain in 1993, CRISPR is made up of short, repeated sequences of DNA and non-coding spacer DNA. Its purpose confounded investigators. But by 2003, Mojica had identified thousands of sequences of genetic code in CRISPR that matched snippets of bacterial and viral genomes. He hypothesized that CRISPR was part of an adaptive immune system that copies sequences from invading microbes to ward off viral infections of bacteria. Scientists around the world recognized CRISPR’s potential as an experimental tool and set out to investigate it further.

Northwestern University was the setting of important research establishing the basic science behind CRISPR. In 2008, Luciano Marraffini, PhD, a postdoctoral fellow in the lab of Erik Sontheimer, PhD, then an associate professor of Biochemistry, Molecular Biology and Cell Biology at Northwestern’s Weinberg College of Arts and Sciences, became the first to empirically prove CRISPR destroys plasmid or virus DNA molecules directly and to suggest that it can be programmed to target any DNA. They published their findings in a landmark paper in *Science*.

“Our work was a breakthrough in the understanding of CRISPR, since it explained how it works at the molecular level,” says Marraffini.

Sontheimer adds, “Most important of all, we were the first to recognize and explicitly articulate the possibility that CRISPR could be repurposed for genomic engineering.”

The pair filed a patent declaring CRISPR could be used to manipulate the genomes of complex organisms, but the patent was denied, citing lack of experimental demonstration.

By then, other investigators had linked the CRISPR system with Cas9, an enzyme that modifies DNA, and begun to harness the whole complex for genome editing. The final breakthrough happened in January 2013, when five groups from around the world published independent studies within three weeks showing the system could be programmed to target specific points of DNA in mammalian cells. Among them were scientists from the Massachusetts Institute of Technology, who collaborated with Marraffini, then at The Rockefeller University, to publish a paper in *Science* demonstrating that the CRISPR sequence can be transcribed into short RNA sequences that drag Cas9 to a specific locus and cut the DNA, turning the targeted gene off.

This discovery rocked the field of genetics: Just nine months after the initial *Science* publication, an additional 1,500 articles on the CRISPR-Cas9 complex had been published, refining and improving the tool. This was made possible by the decision to make CRISPR reagents readily available online with instructions to help scientists design the right experimental tools, says McNally.



We were the first to recognize and explicitly articulate the possibility that CRISPR could be repurposed for genomic engineering.



Oncology

Discover a program and a leader putting the Lurie Cancer Center at the forefront of its field.

CURATED CANCER CARE

Physicians and scientists in OncoSET are teaming up to help pioneer precision oncology.

Until recently, treatment for patients with cancer generally followed a broad-brush, one-size-fits-all approach. Today, it is recognized that each cancer — just like each patient — is unique.

Armed with the understanding that distinct genetic mutations and abnormalities are at the root of every patient's cancer, physicians and scientists now aim to usher in an era where treatment is truly tailored to the individual. The hope is that providing therapies targeted to the specific genetic drivers of cancer will reduce the toxic side effects seen in less precise treatments and offer patients improved outcomes overall.

Such is the case with Chuck Maniscalco. In the fall of 2016, Maniscalco, a retired Chicago business executive in his 60s, was diagnosed with Stage IV lung cancer — a disease his mother and younger sister both died of years earlier.

In the past, his treatment options would typically have been limited to standard chemotherapy. But after receiving genetic testing at the Robert H. Lurie Comprehensive Cancer Center of Northwestern University, Maniscalco learned he had a mutation in the epidermal growth factor receptor (EGFR), which can fuel cancer growth. As a result, he was a candidate for Tarceva (erlotinib), an oral medication that specifically targets the activity of the EGFR protein.

“I am the beneficiary of research, pure and simple. By all rights, I shouldn't be alive, much less up and at it every day,” says Maniscalco, a year and a half after his diagnosis. “The team of people who are caring for me at the Lurie Cancer Center are fabulous, but it is the research that led to targeted treatments that is the key to my life.”

This is the potential of precision oncology, and the premise of OncoSET, the flagship clinical and research program at the Lurie Cancer Center. First launched in 2015, OncoSET is the Lurie Cancer Center's entry into the emerging movement of precision medicine. Through an innovative three-step process — Sequence, Evaluate, Treat — the clinic couples oncology with genomic sequencing to offer cutting-edge cancer care personalized to each patient.

“This is really the most advanced form of oncology,” says Amir Behdad, MD, assistant professor of Pathology, director of Cancer Molecular Diagnostics and co-director of OncoSET's Molecular Tumor Board. “If we can attack only a target that's unique to a patient's tumor cells — as opposed to globally attacking the body with chemotherapy — that's a really attractive option.”

This strategy, Behdad notes, has only recently become possible thanks to advances in genetic technology. Next-generation sequencing has now enabled scientists to obtain a robust understanding of the genetic profile of tumors, which had previously represented a significant challenge. With more knowledge of the molecular makeup of tumors, therapies designed



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CHUCK MANISCALCO
Lung cancer survivor

The OncoSET Process

Through an innovative three-step process, the Lurie Cancer Center's flagship clinical and research program offers cutting-edge cancer care personalized to each patient.



Close-up



Top left and bottom right: Lurie Cancer Center members look for circulating tumor cells isolated from liquid biopsies; they hope to find mutations in the cells that will inform diagnosis and treatment for specific cancer patients. Top right: Massimo Cristofanilli, MD, director of OncoSET. Bottom left: Cancer leaders at the inaugural OncoSET Symposium last spring.

to target specific tumor markers have since followed.

“We created OncoSET because science and technology are driving big changes in the way we treat cancer, and as the leading cancer center in Chicago, we thought we should offer precision medicine to our patients first,” says Leonidas Platanius, MD, PhD, director of the Lurie Cancer Center. “I believe very strongly that this is the way medicine will be practiced 10 years from now.”

A CLINICAL PROGRAM, INFORMING TOMORROW'S CURES

In addition to helping individual patients, there's another, broader, benefit to the OncoSET model: By collecting and analyzing

extensive genomic data, OncoSET informs ongoing discovery of targeted cancer drugs and helps advance pre-clinical research at Feinberg and around the world.

“There were a couple of major goals we wanted to accomplish very quickly,” says Massimo Cristofanilli, MD, director of OncoSET and associate director for Translational Research at the Lurie Cancer Center. “One, of course, was to be more precise in treatment planning for patients and establish the clinical service. But at the same time, we also wanted to advance translation and feed our research purpose.”

The OncoSET process begins with a simple blood draw from a patient for a liquid biopsy (in some cases, a traditional tissue biopsy is available as well). Through

collaborations with commercial partners for genetic testing, OncoSET leverages next-generation genomic sequencing to pinpoint changes in specific genes and produce a comprehensive profile of a patient's tumors. (OncoSET is currently focused on analyzing solid tumors, but will soon also evaluate hematologic malignancies, such as lymphoma and leukemia.)

“We've created the first clinic in Chicago — and one of only a few in the country — where it doesn't matter where the tumor is located. What matters now is the composition of the tumor and the patient's genomic analysis,” explains Platanius, who is also the Jesse, Sara, Andrew, Abigail, Benjamin and Elizabeth Lurie Professor of Oncology. →

Every week, OncoSET's Molecular Tumor Board gathers to analyze the sequencing results of individual patients, one by one.

During this evaluation stage, it's all hands on deck: The multidisciplinary team, co-directed by Cristofanilli and Behdad, is made up of medical, surgical and radiation oncologists, along with pathologists, molecular scientists, pharmacologists, radiologists, genetic counselors, bioinformaticians and other experts across a range of specialties.

Informed by the tumor's unique profile, the team devises an optimal treatment plan for each patient. That treatment, based on the molecularly defined targets, might include an available drug or enrollment in an early-stage clinical trial being conducted at Northwestern.

Since its inception, the Molecular Tumor Board has evaluated the genetic profiles of hundreds of patients, many of whom had advanced stage cancer or cancer that was unresponsive to standard treatment. Not only has the model made a real difference in individual patient outcomes, but with basic scientists at the table, new insights gleaned through the clinic may eventually serve as the building blocks of tomorrow's targeted cures.

"After doing these gene profiles and analyses of patients, we can bring all that information back to the lab," Platanius explains. "We can try to better understand some of the abnormalities we detect — we still don't know the importance of many — conduct more studies, develop new drugs and, eventually, bring them back to the clinic."

PIONEERING A FUTURE OF PRECISION ONCOLOGY

OncoSET has also emerged as a national leader in advocating for a precision medicine approach to cancer care and research.

"One important focus for this program is educating physicians on the value of this model," says Cristofanilli, also a professor of Medicine in the Division of Hematology and Oncology. "We want to be on the forefront in demonstrating its utility."

With that mission in mind, OncoSET hosted its inaugural symposium last spring, sharing significant advances in precision oncology with healthcare professionals from across the country and discussing strategies for translating new discoveries into clinical practice. The Second Annual Lurie Cancer Center OncoSET Symposium: Practical Applications of Precision Medicine will be held May 17, 2018.

In OncoSET, patients are also enrolled in a prospective registry study — now totaling more than 400 entries — which provides a rich database for basic scientists investigating particular mutations. The team is actively working on developing retrospective analyses of treatment outcomes.

"We coordinate our data with other institutions all over the country. Eventually, after enough information has accumulated, there will be a tipping point — really a drastic change — in the way we practice oncology," says Platanius, also a professor of Medicine in the Division of Hematology and Oncology, and of Biochemistry and Molecular Genetics.

This new approach to oncology is still at an experimental stage, of course, and the OncoSET team notes that as science and technology in

this area rapidly evolve, so will the process of providing precision cancer care. The program is currently centered on genomics and molecular diagnostics, but in the future new tools like epigenetic analysis, proteomic analysis and metabolomics may also help match patients with the individualized treatment plan that might benefit them most.

"The more we understand in science, the more we will be bringing it back to OncoSET to optimize our analysis," Platanius adds. "We think this is the future, and we are moving fast." ■

"Eventually, after enough information has accumulated, there will be a tipping point — really a drastic change — in the way we practice oncology."

LEONIDAS PLATANIAS, MD, PHD
Director of the
Lurie Cancer Center

To refer a patient or request a consultation, email OncoSET@northwestern.edu or call 312-472-1234.

A DOCTOR AT HEART

Deputy Director Maha Hussain oversees clinical research, but never forgets her primary goal: having an impact on patients.

There's an old Iraqi proverb that has stuck with Maha Hussain, MD, since she left her native country: "You can't clap with one hand."

For Hussain, deputy director of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University, it's an idea at the core of her approach to personal and professional success.

"It takes a team," Hussain says. "Throughout my career, I have been successful in part because of collaboration with other people — whether it was colleagues I worked with or the support of my husband and family."

Hussain, who joined Northwestern in September 2016, is an internationally recognized authority on clinical research and a leading expert in genitourinary oncology, especially prostate and bladder cancer. She is also an active clinical investigator focused on novel therapeutics and a practicing oncologist at Northwestern.

"In some ways, I wear many hats. But deep down, I'm a doctor at heart," says Hussain, also the Genevieve E. Teuton Professor of Medicine in the Division of Hematology and Oncology. "I didn't get into this just to sit in an office all day. Everything I do, even while in an administrative job, needs to have a direct or indirect impact on patients."

As part of that mission, some of Hussain's chief responsibilities at the Lurie Cancer Center are enhancing clinical trial infrastructure, expanding clinical trial protocols, facilitating scientific translation and forging partnerships that grow clinical research opportunities for cancer patients.

"At Northwestern, we all provide exceptional care. But I always say that exceptional care will never be good enough if we don't have a cure or impactful



“There is an incredible willingness here to work together to impact patient outcomes through science, research, mentorship and excellence in medical care.”

MAHA HUSSAIN, MD
Deputy Director of the
Lurie Cancer Center

in the mid-1980s. It was an exciting era, she says, with many discoveries, clinical trials and investments being made in research. Cures were becoming possible, such as in testicular cancer, and cancer was no longer automatically “a death sentence.” But while caring for patients in a local VA hospital, Hussain was also deeply discouraged by the lack of progress in prostate cancer.

“It was just so awful to see men coming in with horrible disease, and you had really hardly anything to do for them,” Hussain says. “To me, it was a turning moment — I realized this is an area where there’s a clear need for impact. And I felt an urgent need to contribute.”

A FULL CAREER

In her career since then, Hussain’s research and leadership have helped improve standards of care for metastatic hormone-sensitive and castration-resistant prostate cancer. She has authored close to 250 scientific publications and book chapters and taken leadership roles in a variety of national oncology committees. Amidst that work, she has continued to care for patients as a clinician and serve as a teacher and mentor. She has also put a priority on outside interests — her family, including a son and daughter, and hobbies such as travel, reading, photography, cooking and a robust social life.

After her time at Wayne State, Hussain was recruited to the University of Michigan, where she spent almost 14 years in top scientific and leadership positions before joining Northwestern.

“I was ready to take on the adventure of working with a new team, with the wonderful brain trust at Northwestern, in order to develop the best possible clinical research for our patients,” Hussain says. “There is an incredible willingness here to work together to impact patient outcomes through science, research, mentorship and excellence in medical care.” ■

treatments for our patients,” Hussain says. “That’s why my passion is research. Research is what will cure cancer.”

FROM BAGHDAD TO DETROIT

As far back as she can remember, Hussain has always wanted to become a physician. Growing up in Baghdad, her family encouraged her to pursue her goals. “I never thought that because I was a woman I shouldn’t be a doctor,” she says. “It was a very open culture, where education and performance was the great equalizer.”

After graduating from the prestigious Baghdad University College of Medicine in 1980,

Hussain and her husband, also a physician, left to pursue their residency training abroad, just as the Iraq-Iran war was breaking out. After three years in England, they landed in Detroit, where a few of Hussain’s family members had already immigrated.

The couple planned to return to Iraq after completing their training. “But there was one war there after another, and we elected to stay,” Hussain says. “It was the best decision we have ever made. Baghdad is our motherland, but the U.S. is our home.”

Hussain was first drawn to oncology during her residency at Wayne State University

Journey to Northwestern Medicine

Hussain’s arrival at Northwestern Medicine spanned three countries and two universities.







FULL SPECTRUM

OF GYNECOLOGIC CARE



New clinical programs provide collaborative, cutting-edge care for women of all ages.



“I AM A VERY HAPPY PATIENT,” says Umang Singh of Lake Forest, Illinois.

In summer 2003, after trying to start a family with no luck and seeing several doctors, Singh, then in her 30s, sought help from Magdy Milad, MD, MS, chief of Gynecology and Gynecologic Surgery at Northwestern Memorial Hospital. He found the cause of her infertility: advanced endometriosis. After undergoing small-incision laparoscopic surgery, Singh became pregnant five months later.

Fast forward 13 years. In summer 2016, Singh, now a

mother of three, began experiencing heavy uterine bleeding to the point of developing anemia. Her endometriosis had seemingly “returned with a vengeance.” She was told by a gynecologist that a radical hysterectomy and early menopause were in her immediate future, but didn’t believe that was her best option. Neither did Milad. That November, he performed a minimally invasive procedure that quickly alleviated Singh’s problem.

From puberty to menopause, women like Singh keep their reproductive systems

healthy with annual checkups and general gynecologic care from their regular gynecologists and primary care physicians. But when routine care becomes something more challenging, obtaining specialized gynecological expertise for complex conditions can frequently result in a disjointed endeavor for patients and physicians alike. Many women must seek answers to their “female” problems on their own, going from one specialist referral to another to find care that best addresses their needs — *until now.* »

In July, Northwestern Medicine launched the Center for Comprehensive Gynecology (CCG) at Northwestern Memorial Hospital, with Milad as its medical director. Featuring a one-of-a-kind multidisciplinary approach, the new center offers women a unique one-stop shop for highly specialized care for complex gynecological disorders and diseases. Housed in the Northwestern Medicine Lavin Family Pavilion, the center integrates the expertise of minimally invasive gynecologic surgeons, interventional radiologists, psychiatrists, physical therapists, psychologists and others. All working together as a team in one place and space, these experts deliver collaborative leading-edge care that is patient-centered rather than procedure-focused.

“Our mission is to treat women across the spectrum of their lives with leading-edge technology and the latest therapies,” says Serdar Bulun, MD, the chair and John J. Sciarra Professor of Obstetrics and Gynecology. “Our approach is agnostic across the specialties. It’s not a matter of medical therapy versus surgery versus an interventional radiology procedure. Our goal is to provide the best treatment and follow-up for each and every patient.”

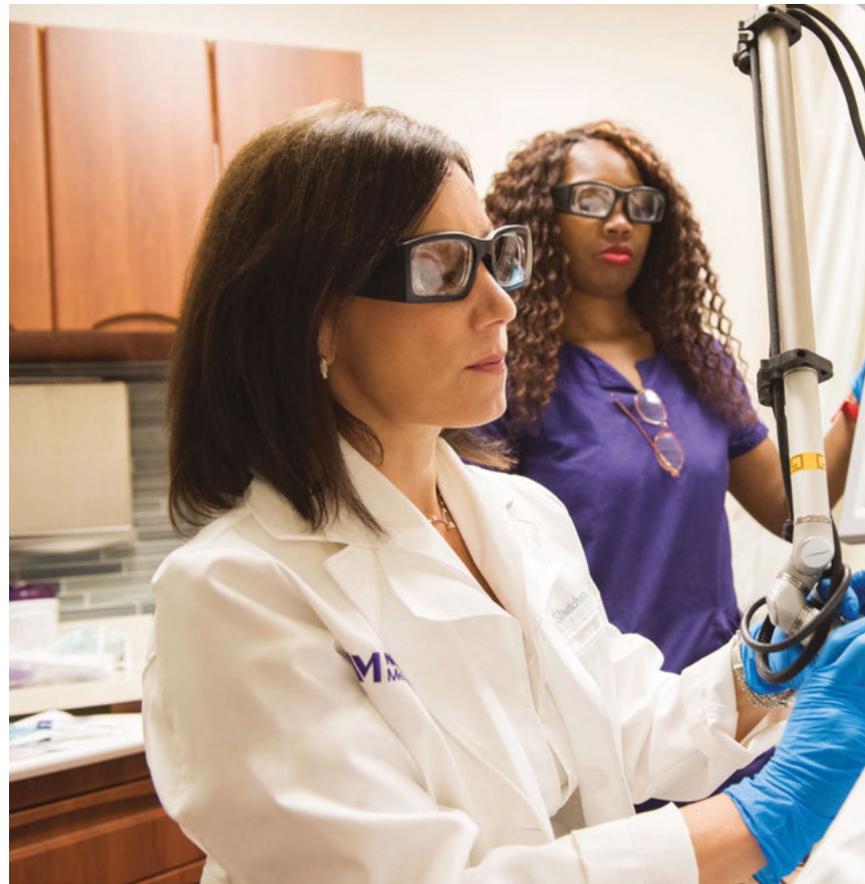
UN-COMPLICATING THE COMPLEX

Every day, experienced physicians care for women with fibroids, endometriosis, ovarian cysts, uterine abnormalities

or tubal disease. While all very common problems of the female reproductive system, they can sometimes become, well, complicated.

“We provide highly integrated specialized care that frequently goes beyond the purview of the general obstetrician/gynecologist,” explains Milad, who is also the Albert B. Gerbie, MD, Professor of Obstetrics and Gynecology and chief of Minimally Invasive Gynecologic Surgery at Feinberg. “Many women with fibroids or in menopause, for example, receive wonderful care from their regular doctors. But if a woman has fibroids so large they are affecting fertility or severe menopausal symptoms that are disrupting their lives, we can help.”

The collaborative approach of the CCG is a particularly distinguishing feature, especially in the case of fibroid treatment. Noncancerous uterine tumors, fibroids can cause a host of symptoms from heavy menstrual bleeding to pelvic pressure and pain. Treatment strategies range from gynecologic surgery (open and minimally invasive) to remove them and/or the uterus, to minimally-invasive interventional radiology procedures such as uterine fibroid embolization (UFE) to shrink them. The options, though, are provided by different physicians: the former, gynecologists and the latter, interventional radiologists. Typically, the two specialty areas work in separate silos, forcing patients to do the legwork. Northwestern Medicine’s CCG may be the first to unite



“Our mission is to treat women across the spectrum of their lives with leading-edge technology and the latest therapies.”

interventional radiologists and gynecologists in one location to jointly see patients.

“It’s unheard of,” says Milad of this rare partnership. “Working physically side by side allows us to offer patients the best treatment strategy for their particular situation and provide thorough follow-up as a team.”

UFE has only been available in the United States since the mid-1990s. One of the early pioneers in the relatively young field, Northwestern Medicine’s interventional radiology team is a national leader in this innovative, nonsurgical alternative to hysterectomy.



Lauren Streicher, MD, '83 GME, medical director of the Center for Sexual Medicine and Menopause works with state-of-the-art technology, including a medical CO2 laser that stimulates vulvar and vaginal tissue to restore lubrication and elasticity.



SEXUAL HEALTH REVOLUTION

Embarrassment prevents many women from bringing up difficulties with sex — from lack of desire to painful intercourse — with their doctors. Yet an estimated 40 percent of women of all ages have physical, medical, hormonal or emotional issues that can interfere with intercourse and intimacy.

“Sexual medicine as well as menopause are two unmet elements of women’s health that often go unaddressed either because the patient is reluctant to discuss symptoms with their physician or the patient and/or

their doctor doesn’t know there are clinical experts with solutions to their problems,” says Lauren Streicher, MD, '83 GME, medical director of a recently established Northwestern Medicine clinical center focused on filling this void in the care of women.

In October, the new Center for Sexual Medicine and Menopause (CSMM) opened its doors. Sharing space and staff with the CCG, the CSMM brings together a multidisciplinary team of physicians, advanced practice nurses, certified sex therapists and pelvic floor physical therapists. Comprised of three major areas of expertise, the center offers clinical programs in sexual medicine, menopause and vulvovaginal disorders. In addition to providing a broad array of both hormonal and non-hormonal treatment options, the clinic also features state-of-the-art technology such as the Mona Lisa Touch, a medical CO2 laser that stimulates vulvar and vaginal tissue to restore lubrication and elasticity.

Many major academic medical centers provide some level of sexual medicine or menopause services, especially for patients with specific illnesses like cancer. The CSMM not only addresses the impact of other illness, such as diabetes and heart disease, but also utilizes a collaborative approach that sets it apart.

“Sexual health and hormonal issues touch almost every medical specialty,” says Streicher, an clinical associate professor of Obstetrics and Gynecology. “Unlike other programs that make the diagnosis and then



“Unlike other programs that make the diagnosis and then refer patients out to other specialists, we bring experts to the center to see our patients.”



refer patients out to other specialists, we bring experts from dermatology, urogynecology and other disciplines to the center to see our patients.”

Along with clinical care, the CCG and CSMM provide fertile ground at Northwestern Medicine for research and medical training efforts focused on complex gynecologic problems. In obstetrics and gynecology, fellowships in minimally invasive gynecologic surgery are among the most competitive in the discipline across the country. For every one position, there are more than 60 applicants. Says Milad, “There’s a tremendous need for training gynecologists in complex surgical procedures.”

At the CSMM, opportunities will also abound for further educating not only physicians in training and those currently practicing, but also patients themselves, according to Streicher.

“Problems with sexual intercourse and intimacy and even non-sexual hormonal issues are somewhat taboo topics in the doctor-patient relationship,” she says. “Increasing awareness will help to start the conversation among women and let them know that help is readily available, and they don’t have to just accept their situations for the rest of their lives.” ■

1: The Center for Comprehensive Gynecology (CCG) team, from left to right: Susan Tsai, MD, Angela Chaudhari, MD, Magdy Milad, MD, MS, and Patricia Handler, MSN.

2: Milad, medical director of the CCG, is chief of Gynecology and Gynecologic Surgery at Northwestern Memorial Hospital.

3: The two centers share space and staff in the Northwestern Memorial Lavin Family Pavilion.

Though pathologists usually work behind the scenes in laboratories, rather than face-to-face with patients, their role in clinical care is crucial.

“It’s estimated that about three-fourths of the data in the electronic medical record is laboratory data and at least two-thirds of clinical decisions are influenced by laboratory results,” says Daniel Brat, MD, PhD, Feinberg’s new chair of Pathology.

Pathology is also a field that’s rapidly evolving, in parallel with advances in precision medicine and a trend toward sub-specialization. Brat, a neuropathologist who has spent nearly two decades studying diffuse gliomas, is spearheading this evolution within the arena of brain tumor diagnostics while straddling

the tumors into three distinct subtypes associated with a tumor’s behavior and prognosis. These results, published in the *New England Journal of Medicine*, suggested that genetic status is a more accurate and consistent indicator of a tumor’s classification than the relatively subjective process of histologic evaluation.

“That study, among others, started a transformation that has been critical in our field,” Brat says. “We are now incorporating molecular findings into our primary diagnoses — making them definitional, rather than an association. That was a big step for us.”

In 2016, the World Health Organization (WHO) updated its international reference guide for classifying central nervous system tumors, outlining for the first

Written by Nora Dunne
Photography by Teresa Crawford

PRECISION PATHOLOGIST

the line between scientific investigation and the practice of medicine.

“As the stewards of biospecimens, as well as the laboratory results and basic science findings that are derived from them, pathologists are in a prime position to advance understanding of human disease over the long term, while also supporting clinical care on a daily basis,” Brat says.

FROM HISTOLOGY TO GENOMIC ANALYSIS

For more than a century, pathologists have diagnosed most diseases by looking at tissue samples under a microscope. By assessing the appearance and behavior of brain tumor cells, neuropathologists have classified and graded gliomas to help clinicians determine the best treatment plans for their patients. In 2015, Brat led a study conducted by a team of more than 300 scientists from 44 institutions worldwide challenging that status quo.

The investigators, part of the Cancer Genome Atlas Research Network, analyzed the genetic makeup of samples from 293 adults with a lower-grade glioma, a broad and clinically unpredictable class of brain tumor. Looking at molecular markers like mutations and gene deletions, the scientists were able to divide

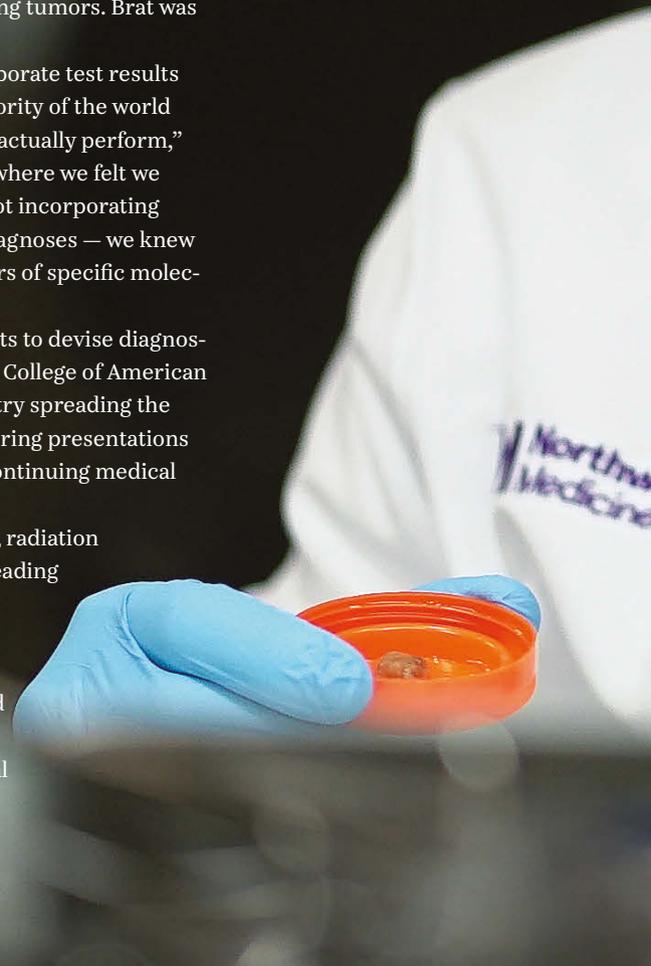
time molecular parameters for defining tumors. Brat was a heavily involved co-author.

“The WHO doesn’t want to incorporate test results into their diagnoses that the vast majority of the world doesn’t have the tools or expertise to actually perform,” he says. “However, it got to the point where we felt we were doing patients a disservice by not incorporating molecular alterations into primary diagnoses — we knew too much about the different behaviors of specific molecular subtypes of brain tumors.”

Brat is now leading national efforts to devise diagnostic and testing guidelines through the College of American Pathologists. He also travels the country spreading the word about these new findings, delivering presentations to hospital leadership and teaching continuing medical education courses to practitioners.

“Pathologists, neuro-oncologists, radiation oncologists and neurosurgeons are reading scientific papers and seeing reams of molecular profiles on hundreds of brain tumor patients with tens of thousands of markers being clustered by computer algorithms,” he says.

“They need guidance on what practical clinical tests to perform to make these diagnoses.” »





Daniel Brat is spearheading transformations in the field of pathology.

Dr. J. Brat, MD,
Pathology

Classifying brain tumors is a theme that has marked Brat's career since his early days as a fellow, when he first described a rare tumor now known as chordoid glioma. Over time it was accepted as a new entity by the WHO and found to have a specific genetic signature.

"It's been extremely satisfying seeing my findings get implemented broadly and improving clinical care worldwide. The whole process is eye-opening and a bit addictive," he admits.

That thirst for discovery has made Brat an expert in his field.

"Dr. Brat is a recognized leader, both nationally and internationally," says C. David James, PhD, professor of Neurological Surgery and a collaborator of Brat's. "His research is at the forefront of the individualized medicine movement for tailoring cancer treatments to the unique characteristics of individual tumors."

Brat earned his medical degree and a PhD in biomedical sciences from Mayo Medical School in 1994 and then completed his residency and a fellowship at Johns Hopkins Hospital. After training, he accepted a faculty position at Emory School of Medicine, where he remained for 17 years until joining Feinberg last September.

"Northwestern is a phenomenal institution, and I thought the pathology department, with the right resources and leadership, could become one of the nation's best," he says. "In addition, the brain tumor group here has had a really exceptional rise, both in the Chicago area and nationally, and I was thrilled to become a part of that."

Though he was born in Detroit, and grew up in Minneapolis, Brat was also drawn to Northwestern and Chicago for personal reasons: His father, Paul Brat, '63 MD, earned his medical degree here, and his mother currently lives in the city's suburbs.

leader, Brat plans to grow the department's residency program, add four new fellowships — in gynecologic pathology, molecular pathology, transfusion medicine and microbiology — and continue recruiting and developing the faculty.

"Our faculty is extremely dedicated and talented. I'd like to shine a light on their successes, so they are more visible nationally and internationally," he says.

Brat is also a strong proponent of the experimental side of pathology. The department has a collection of investigators focused primarily on mechanisms of inflammation, epithelial biology and cancer. In his own National Institutes of Health-funded basic science lab, Brat investigates the mechanisms that cause diffuse gliomas to progress.

"The next stage after characterizing genetic alterations of cancer is to understand how these influence biological behavior, so that we can devise better treatments," he says. "Right now, a clinical study that demonstrates a two- or three-month increase in life expectancy for a patient with glioblastoma will get published in a very high profile journal. Big picture, that's still a dismal prognosis. We've got a lot more work to do."

In one project, his team is exploring how necrosis (cell death) and hypoxia (low oxygen) trigger rapid progression of glioma. In another, Brat's lab uses drosophila (fruit flies) — a simplified genetic model — to study a gene that leads to brain tumor growth when deleted. Ironically, that gene is called "brain tumor," or "BRAT" for short.

For fun outside of work, Brat watches his favorite sports teams — picking up more every time he moves — goes to movies and plays, and listens to classical music.

"But right now, I live four blocks away from work, which is a little bit dangerous, because I do love my job," he says. "Pathologists really enjoy what they do, from providing expert diagnoses, to long days in the lab, to teaching the next generation of pathologists." +

THE MANY SIDES OF PATHOLOGY

Broadly, the practice of pathology can be split into two branches: **Anatomic pathologists** examine biopsy and surgical resection

specimens and make diagnoses based on what they see under the microscope in tandem with immunohistochemistry, molecular analysis and other tests. Meanwhile, **clinical pathologists** manage the laboratories that provide test results that help guide patient care. There are also many

subspecialties within these branches, based on the kinds of samples or diseases examined.

"There's been an explosion of information about disease that didn't exist 30 years ago," Brat says. "With cancer, for instance, it would be very difficult to be a generalist today with expertise in breast cancer, leukemia and lymphoma and brain tumor sub-classifications. It's just too much information for a single mortal to carry."

Feinberg's Department of Pathology currently consists of 14 specialties, six main areas of research and nearly 100 faculty. As their

"The next stage after characterizing genetic alterations of cancer is to understand how these influence biological behavior, so that we can devise better treatments."



1: Cheryl Olson, laboratory manager, and Subhas Mukherjee, PhD, research assistant professor of Pathology, with Brat in his lab. | 2: Samples of brain tumor tissue in the "gross room" at Northwestern Memorial Hospital. | 3: Qinwen Mao, MD, PhD, associate professor of Pathology, and Alexa Derayunan, surgical pathology technologist, examine the samples with Brat to make a diagnosis.

Alumni showed off their pride for Feinberg at tailgates and a board member reception last fall.

'CATSMD' Ideals

A letter from Jim Kelly, '73 MD

In my initial talk with our Medical Alumni Association Board (MAAB) last spring, I expanded the acronym "MCATS" penned by Bruce Scharschmidt, '70 MD, former president of the MAAB, to "CATSMD." Here I will explain the meaning of this new acronym.

C CULTURE We want the MAAB to encourage a culture of commitment and giving back to Feinberg students, graduates and GMEs. Each of us can give back in our own way: some by being home sponsors through our HOST program for fourth-year students, some by serving on the board, others by contributing to the Nathan Smith Davis Society or mentoring medical students and HPMEs about the journey ahead.

A ALIGNMENT To be successful, our board policies need to align with the priorities of the Feinberg administration and you, our alumni constituents. We expanded our Women in Medicine program with a tea and panel discussion at Alumni Weekend last year and will continue that program this year. We also started an MDs in Business seminar series with a successful inaugural event this fall. Aligning in this way, we amplify the MAAB's message with help from our full-time support staff.

T TALENT In 2016, the MAAB recognized that we needed greater diversity on our board with respect to ethnic background, age and geography. We also needed a mechanism in place to have current Feinberg student leaders on the MAAB. Both of these priorities have been accomplished. We recruited 20 new MAAB members over the past two years and upgraded the geography, diversity and age of the board simultaneously. We also worked with the Student Senate to make their president a member of the MAAB. We like where we are in early 2018, but we have the mechanisms in place to adopt and change if we need to.

S SUPPORT We help our students by encouraging scholarship support from individual classes as well as contributions from individuals and families. We have united around the concept of a tuition-free medical school. With the

average debt of a Feinberg medical school graduate being \$169,000, we've never been more aware of the need to support our Feinberg students.

M MATTERS Northwestern and Feinberg should matter to all of us. While clearly the trajectory of the medical school is on the rise locally and nationally, Feinberg graduates should share some personal responsibility to help catalyze change and positively affect this moment in medicine. We encourage participation and being a part of the evolving change going on in medicine today.

D DEDICATION We provide programming, services and opportunities dedicated to the ideals of Feinberg, professionalism and impacting the medical school through scholarship, life-long learning and giving back to the institution that links us all.

So many in our alumni base already work hard to move the "CATSMD" goals forward. Thank you for your hard work and generosity! Together we're making a real difference at our medical school.





Ora Hirsch Pescovitz, '79 MD

Setting the FOUNDATION

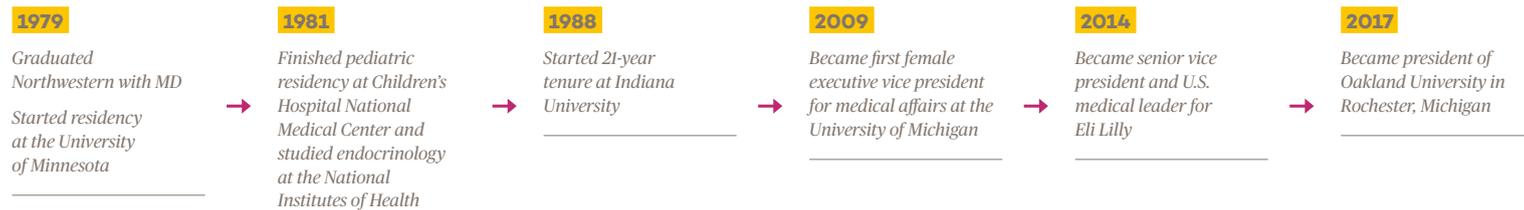
WRITTEN BY *Amber Bemis*

Ora Hirsch Pescovitz, '79 MD, credits her academic career at Northwestern University for laying the groundwork for her multifaceted career, including in her latest position as president of Oakland University in Rochester, Michigan.

"I acquired many important skills during medical school — I became a more careful listener, more passionate and compassionate and more attentive to scientific data — all imperative throughout my entire medical career and now in my new role," Pescovitz says.

Along with playing a critical role in her career, Northwestern is the setting of many fond memories throughout Pescovitz's life. She met her late husband, Mark Pescovitz, '78 MD, on the first day of orientation week; she drank her very first cup of coffee during an overnight shift as a medical student worker at the *Chicago Tribune*; and she has watched her daughter Naomi Pescovitz, '09 in journalism, her brother →

PESCOVITZ'S CAREER EVOLUTION



Emmet Hirsch, '88 MD, '92 GME, sister-in-law Arica Hirsch, '91 MD, '92 GME, and other family members graduate from Northwestern. Needless to say, Pescovitz has a lot of Northwestern pride.

Pescovitz began her academic career at Northwestern in the Honors Program in Medical Education (HPME), a cohort-style program where undergraduates complete a bachelor's and medical degree in six years.

"I loved being in the HPME," she says. "Our class had a very collaborative spirit. We all thought about the well-being of our patients but also the well-being of each other, and many of us are still close even 40 years later."

In 1974, the HPME was considered progressive for the number of women who were a part of the program. Of the 60 students enrolled, 12 were women.

"Some of my lifelong passions and leadership roles started in medical school. I was encouraged by faculty Arthur Veis and Jack Snarr to get involved in student activities such as the Organization of Student Representatives — this really sparked my love for university administration and played an enormous role in my student life and my long-term career," Pescovitz says.

After medical school, she and Mark married and both accepted residency positions at the University of Minnesota. Two years later they moved to Washington D.C., where she finished her pediatric residency at the Children's Hospital National Medical Center and then went on to study endocrinology at the National Institutes for Health.

Following their time in Washington, D.C., the couple settled at Indiana University where she worked as an associate professor of pediatrics and he as a transplant surgeon.

During her 21-year tenure at Indiana, Pescovitz rose through the ranks and held many leadership roles including executive

associate dean for research affairs, president and CEO of Riley Hospital for Children and interim vice president for research adminis-



tration. She is also an accomplished investigator. Her work focuses on the physiologic and molecular mechanisms responsible for puberty and growth disorders,

with an emphasis on developing novel therapies for these conditions.

Although she has published more than 190 research publications, she describes the moments in her career where she brought people together to collaborate as her proudest accomplishments.

"While I was the dean of research, I was the PI on a \$155 million grant called the Indiana Genomics Initiative — this was the largest grant the university had ever received — and it was my job to organize the faculty who would be conducting the work," Pescovitz says. "This is what I am best at: inspiring others to do their finest work and bringing them together. I think this stems from my time at Northwestern where I saw collaboration succeed for the common good."

In 2009, she was recruited as the first female executive vice president for medical affairs at the University of Michigan, where she was in charge of collaboration and activities between the academic health system's hospitals and health centers and its medical school. There she managed three hospitals, more than 120 health centers and clinics and the University of Michigan Medical School, and oversaw \$3.3 billion in revenue and \$490 million in research funding.

During the winter of 2010, Pescovitz's husband Mark was killed in a tragic car accident.

"When this happened I had to think hard about how I wanted to spend the rest of my career," she says.

"Our class had a very collaborative spirit. We all thought about the well-being of our patients but also the well-being of each other, and many of us are still close even 40 years later."

After finishing her contract at Michigan in 2014, Pescovitz took a short sabbatical before being recruited to work at pharmaceutical company Eli Lilly in Indianapolis as the senior vice president and U.S. medical leader. There



she focused on learning about the process of drug discovery.

Knowing that her heart was in academia, in July 2017 Pescovitz accepted a position at Oakland University, where she plans to focus on increasing research and the University's strategic growth plan.

As president, she plans to follow the lifelong leadership principles she calls her "8 Cs," many of which she says stem from ideas formed at Northwestern.

"My vision is to unlock the potential of individuals and leave a lasting impact through the transformative power of education and research," she says.

PRESIDENTIAL PRINCIPLES (THE 8 Cs)

Moral compass
Compassion
Courage
Contribution
Commitment
Communication
Collaboration
Creativity

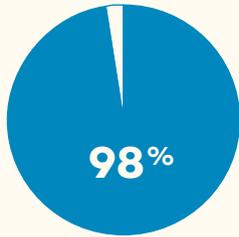
Resources are still needed to create a tuition-free medical school, endow the efforts of our talented faculty, and support our innovative research and teaching programs.

Campaign Update

The generosity of thousands of alumni, faculty and friends is helping us impact the health of humankind.

CAMPAIGN FOR NORTHWESTERN MEDICINE

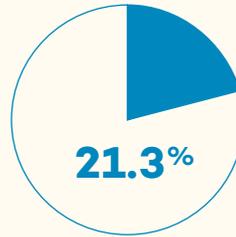
\$1.72 billion



\$1.72 billion raised of \$1.75 billion goal

SCHOLARSHIPS

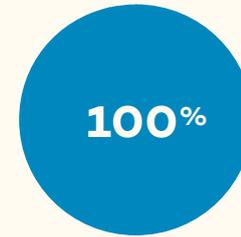
\$170 million



of \$800 million goal raised for a tuition-free medical school

FACULTY CAMPAIGN

\$3 million



of Feinberg department chairs contributed

CAMPAIGN PRIORITIES

With the partnership of new and longtime benefactors, we are raising crucial funds to:

- Build out ten core institutes that bring together patient care, research, education, community service and advocacy
- Build the new Louis A. Simpson and Kimberly K. Querrey Biomedical Research Center
- Construct a centerpiece hospital and medical office facilities at Northwestern Medicine Lake Forest Hospital
- Create endowed professorships that accelerate the efforts of our most accomplished and promising faculty physicians and scientists
- Establish endowed and expendable innovation grants for breakthrough research
- Create scholarships for our exceptional medical, PhD and physical therapy students, and nurses
- Establish fellowships to support our best and brightest trainees



The cost of medical school and living in Chicago are honestly tremendous.

With Dr. Betty Hahneman's generous support and that of so many other scholarship donors, my fellow students and I can take out less loans and, thus, have more options after graduation. Having less debt will make it easier to focus on my passion for service rather than the pursuit of financial gain. After medical school, I hope to work as a clinician while working on health policy, perhaps in research or implementation. I also will continue to advocate for patients and those who cannot even afford to be patients.



Robert Tessier, Class of 2021
Betty M. Hahneman, MD, MPH, Scholar

67

new scholarships created during *We Will. The Campaign for Northwestern Medicine*



Northwestern has helped shape my life and career as an academic physician.

I am a proud faculty member and alumnus, and I'm happy to support this fundraising effort, both as a donor and advocate, because I know that the funds we provide will support breakthrough medical education and ultimately improve patient care and change people's lives for the better.



Neil Stone, '68 MD, '74, '75 GME
Robert Bonow, MD, Professor of Medicine

795

faculty members made a gift of any amount to Feinberg

153

different funds supported

*All numbers as of December 31, 2017.

PROGRESS NOTES

*We'd love to hear from you!
Please share your recent
news, accomplishments and
important milestones with us.*



Send your updates and high-resolution photos to medcommunications@northwestern.edu.

We will publish them in an upcoming issue of the magazine.

1950s

Ruth Benson, '55 BSN, writes, "I graduated with a BS in Nursing in 1955. I have been living in Fairbanks, Alaska, since 1960 and retired from a position as a contract nurse practitioner in family planning at the Fairbanks Regional Health Center in 1992. Before that, I had been a nurse practitioner in college health at the University of Alaska Fairbanks. Most of my university work took place at St. Olaf College in Northfield, Minnesota, for the three years before I enrolled at Evanston Hospital in 1952. It all seems extremely remote now!"

1960s

Michael L. Friedman, '67 MD, shared memories from the Chicago Maternity Center after reading about a novel set there written by David Kerns, '68 MD. Friedman writes, "We spent two weeks going into the West Side neighborhoods of Chicago to deliver babies under the most primitive conditions — often without any electric lights. I can remember it as though it was yesterday.

We went in pairs with a nurse, and each of us wore our short, white medical school jacket and carried our black doctor bag. We also carried red rubber gloves, which had to be boiled and dried off to be sterile. At night, we went with a police escort.

To this day, I still have my Maxwell Street Dispensary diploma from the Chicago Maternity Center hanging on the wall of my office. I am still working as an OB-GYN for UCLA Health in Torrance, California." 📷 1

Charles F. Koopmann Jr., '69 MD, was presented with the Bicentennial Faculty Governance Lifetime Achievement Award at the University of Michigan. Now retired from the university, Koopman led the pediatric division of the Department of Otolaryngology and also served on the advisory board for intercollegiate athletics.

1970s

James (Jim) E. Bourdeau, '73 PhD, '74 MD, received the Albert Nelson Marquis Lifetime Achievement Award from Marquis Who's Who. Following a career that encompassed basic research in renal physiology, clinical practice in nephrology and kidney transplantation, and service on the American Board of Internal Medicine's Test-Writing Committee in the subspecialty of nephrology, Bourdeau has retired in Satellite Beach, Florida, while spending as much time as he can find in Quebec City, Canada.

David Green, MD, '74 PhD, professor emeritus of Medicine in the Division of Hematology and Oncology at Feinberg, was recently selected to receive the "Walk in Our Shoes" Award from the Bleeding Disorders Alliance of Illinois.

1980s

Richard B. Lanman, '81 MD, a biotechnology entrepreneur, was named to the board of directors for BIOLASE, Inc., a dental laser company.

Boris Lushniak '83 MD, MPH, was recognized by the American Medical Association (AMA) with a Distinguished Service Award for his contributions to the field of public health. Lushniak played an active role in government



"TO THIS DAY, I STILL HAVE MY MAXWELL STREET DISPENSARY DIPLOMA FROM THE CHICAGO MATERNITY CENTER HANGING ON THE WALL OF MY OFFICE." —MICHAEL L. FRIEDMAN, '67 MD

service for nearly 30 years, having served as U.S. Surgeon General (Acting) from July 2013 to December 2014. He was also Deputy Surgeon General from 2010 to 2013 and from 2014 to 2015, as well as assistant commissioner for counterterrorism policy for the U.S. Food and Drug Administration from 2004 to 2010. AMA



Chair-Elect Jack Resneck, Jr., MD, recognized Lushniak for his leadership in several disaster responses, including his role commanding the only U. S. Government hospital in Liberia treating Ebola patients during the Ebola crisis in 2015. In January 2017, Lushniak became dean of the University of Maryland School of Public Health. [📷 2](#)

Janet Prokop Pregler, '88 MD, received for the second time in her career the “Women of the Year” award from the Los Angeles County Board of Supervisors and The Los Angeles County Commission for Women.

Pregler is a nationally recognized educator and advocate in woman's health. Director of the Iris Cantor-UCLA Women's Health Center and a professor of Clinical Medicine at UCLA she is co-editor of the textbook “Women's Health: Principles and Clinical Practice.” She has developed educational programs on women's health for the American College of Physicians, Centers for Disease Control and Prevention, National Heart, Lung, and Blood Institute, and the Department of Health and Human Services Office on Women's Health.

Her husband *Johnathan Pregler, '88 MD*, is a professor of Anesthesiology and director of Operative Services at UCLA. He is past-president of the California Society of Anesthesiologists and active nationally with the American Society of Anesthesiologists as its representative on the Centers for



“THIS PIVOT AND SWING DANCE BETWEEN CAPILLARY CELL OUTER MEMBRANES AND MITOCHONDRIA PRODUCES POWERFUL FEEDBACK LOOPS THAT INCLUDE INTERSTITIAL SPACE MESENCHYMAL CELLS AND THE END ORGAN ITSELF.”

-ROBERT BUCKINGHAM, MD, '79 GME

Medicare & Medicaid Services Panel on Hospital Outpatient Payment. The Preglers have three children, one currently a freshman at Northwestern University. They look forward to the upcoming alumni reunion and reuniting with classmates and friends.

1990s

Malcolm M. Bilimoria, '91 MD, '98 GME, a surgical oncologist at Northwest Community Hospital in Arlington Heights, Illinois, completed a 19,341-foot scale of Mount Kilimanjaro in October with his patient Ken Brown, a survivor of adenocarcinoma of the pancreas. [📷 3, 4](#)



Michael H. Goldstein, '93 MD, MBA, was appointed as chief medical officer for Ocular Therapeutix, a biopharmaceutical company focused on developing therapies for eye diseases and conditions.

Raymond “Ramiro” Sanchez, '94 MD, was presented with the Albert Nelson Marquis Lifetime Achievement Award. He is a trained psychiatrist who is senior vice president of global clinical development at Otsuka Pharmaceutical Development and Commercialization in Princeton, New Jersey.

Sheila Gujrathi, '96 MD, was appointed to the board of directors and named as a strategic advisor for TP Therapeutics, Inc., a privately held, clinical-stage biopharmaceutical company focusing on addressing oncology drug resistance.

2000s

Eugene Lin, '07 MD, medical director of the Mercy Life Flight Network Mobile Stroke Unit and director of the annual Mercy Health Stroke Symposium, received a 2017 “20 Under 4” Leadership Recognition Award. The award recognizes individuals in northwest Ohio and southeast Michigan under the age of 40 who have distinguished themselves in their career and/or community.

2010s

Frank A. Clark, '10 MD, has been appointed to the Dean's Council on Advancement for the Virginia Tech Carilion School of Medicine. The council is a committee of volunteers created to advance the stature of the medical school by providing guidance, assistance, advocacy and philanthropic investment in support of the school's strategic objectives.

Samaa Kemal, '17 MD, '17 MPH, presented her culminating experience research paper at the 2017 22nd Annual Injury Free Coalition for Kids conference on December 1-3. Kemal's presentation was awarded best research paper distinction.

Kemal's study evaluated trends and risk factors over time for self-reported gun carrying among freshman and sophomore public school students in Chicago, New York City and Los Angeles using 2007-2013 Youth Behavioral

Risk Factor data. Students reported exposure to violence and related stressors including fighting, perceptions of safety and other high-risk behaviors. The study found a much higher self-reported rate of gun carrying and a higher burden of violence exposure among Chicago respondents across all study waves. These data predate the recent (2016) surge in Chicago shootings and homicides, yet the higher rate of gun carrying in Chicago may reflect easier access to firearms as well as more intensive segregation, poverty and hopelessness than what was experienced by youth in other cities. The paper will be published in an upcoming issue of *Injury Epidemiology*.

GME

Robert Buckingham, MD, '79 GME, published his second book on chronic inflammation called "Rejuvenation!: How the Capillary-Cell

Dance Blocks Aging while Decreasing Pain and Fatigue" (July 2017, iUniverse), two years after his first book "Hazing Aging."

He writes, 'Rejuvenation!' dives into the mechanics of how capillary cells actually support two organ systems, as they go about their business of sanitizing the interstitial space and supporting the end organ. They accomplish this task with a dynamic and complex outer membrane receptor system that has a major feedback loop relationship with their mitochondria. As they increase their permeability, mitochondria shift combustion to energy to support active transport of immune arsenal into the interstitial space. When outer membranes decrease immune arsenal trafficking, they cause mitochondria to shift combustion to nitric oxide, which chain reacts a causes a completely different set of capillary cell operations.

This pivot and swing dance between capillary cell outer membranes and mitochondria produces powerful feedback loops that include interstitial space mesenchymal cells and the



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end organ itself. Chronic inflammation within interstitial space disrupts these feedback loops by cannibalizing the capillary cell from the inside out by employing a combination of vascular inflammatory free radicals and the body's own immune arsenal.”

Henry J. Przybylo, MD, '85 GME, published “Counting Backwards: A Doctor’s Notes on Anesthesia,” a book that chronicles his career and thoughts about the specialty during his long career at Northwestern. Przybylo is an associate professor of Anesthesiology at Feinberg and a pediatric anesthesiologist at Ann & Robert H. Lurie Children’s Hospital of Chicago.

Julian Schink, MD, '86 GME, joined Cancer Treatment Centers of America (CTCA) as chief of Gynecologic Oncology. He will also serve as medical director of Gynecologic Oncology and Medical Oncology at the CTCA at Midwestern Regional Medical Center in Zion, Illinois. Schink brings more than 30 years of oncology experience to the organization, specializing in surgery, chemotherapy, hormone therapy and targeted therapy treatments for patients with gynecologic cancers. Schink will oversee the national Gynecologic Oncology Program at CTCA, serving patients in the treatment of cervical, ovarian, uterine, and vaginal and vulvar cancers, as well as gestational trophoblastic diseases. 📷 5

Susan Cohn, MD, '87 GME, was named to the board of directors for St. Baldrick’s Foundation.

She is the dean for clinical research at the University of Chicago Medicine and Biological Sciences and a professor of Pediatrics and section chief of Hematology/Oncology in the Department of Pediatrics.

ERIC MIZUNO, MD, '92 GME, HITCHED A RIDE ON A PRIVATE PLANE AND LANDED AT A CLOSED AIRPORT IN PUERTO RICO TO PROVIDE MEDICAL EXPERTISE AND MEDICATION JUST TWO WEEKS AFTER HURRICANE MARIA RAVAGED THE ISLAND IN SEPTEMBER.

E. Dale Abel, MD, PhD, '92 GME, was elected president-elect of the Endocrine Society. His term will commence March 20, 2018, and his presidential term will begin on March 20, 2019, for one year. Abel is the Francois M. Abboud Chair in Internal Medicine at the University of Iowa Carver College of Medicine. 📷 6

Eric Mizuno, MD, '92 GME, hitched a ride on a private plane and landed at a closed airport

in Puerto Rico to provide medical expertise and medication just two weeks after Hurricane Maria ravaged the island in September. Mizuno’s private practice, OMNI Healthcare, serves a large Puerto Rican patient population in Chicago’s Humboldt Park, so he immediately felt called to respond to the overwhelming needs of the island’s residents. Mizuno is also a clinical assistant professor of Medicine in the Division of General Internal Medicine and Geriatrics at Feinberg. 📷 7

Richard Lawrence Makowiec, MD, '99 GME, joined Franciscan Physician Network Orthopedic Specialists, which is based in Indianapolis.

Laure DeMattia, MD, '03 GME, joined Norman Regional Health System, which is based in Oklahoma. DeMattia specializes in medical weight loss. 📷 8

Melina Kibbe, MD, '03 GME, received the prestigious Dr. Rodman L. Sheen and Thomas G. Sheen Award at the annual meeting of the New Jersey Chapter of the American College of Surgeons, held December 2, 2017, in Iselin, New Jersey. The Sheen Award is presented each year to honor individuals who have made outstanding contributions to the medical profession. Kibbe inspired attendees with her presentation of “When Mice are Men: Sex Bias in Surgical Research” during the meeting.

Kibbe was elected as a member of the National Academy of Medicine on October 14,

In Memoriam

Northwestern Medicine expresses its condolences to the families and friends of the following alumni (listed in order of their graduation year) and faculty who have recently passed away. All dates are in 2017.

ALUMNI

Sam A. Marascalco, '43 DDS
Tucson, Arizona
FEBRUARY 1

Gerald O. McDonald, '47 MD, '48 GME
Great Falls, Virginia
OCTOBER 12

Robert W. Denton, '47 MD
Bishop, California
OCTOBER 28

George R. Clutts, '48 MD
Greensboro, North Carolina
SEPTEMBER 13

Mary M. Stoskopf, '49 MS
Overland Park, Kansas
NOVEMBER 4

Charles H. Boggs Jr., '50 MD, '56 GME
Roanoke, Virginia
OCTOBER 8

E. Eliot Benezra, '50 MD
Oak Brook, Illinois
OCTOBER 2

Charles Boggs Jr. '50 MD, '56 GME
Roanoke, Virginia
OCTOBER 8

Margaret P. Steinam, '52 MD, '54, '56 GME
Mequon, Wisconsin
NOVEMBER 20

David Paul Cooney, '54 MD
Stanford, California
SEPTEMBER 27

William R. Vogler, Jr., '54 MD
Decatur, Georgia
DECEMBER 2

Maurice K. Roskelley, '56 MD
Salt Lake City, Utah
SEPTEMBER 23

Dale R. Hines, '57 MD
Dayton, Ohio
SEPTEMBER 19

Stanley M. Englander, '59 MD
Rockland, Maine
OCTOBER 19

Pacita Manalo Estrella, '63 MD
Reno, Nevada
OCTOBER 20

Emmett J. Sharkey, '65 MD
San Diego, California
OCTOBER 8

Edward M. Katz, MD, '65, '66 GME
Menlo Park, California
SEPTEMBER 24

Norman K. Wood, '66 MSD, '68 PhD
Perth, Ontario, Canada
OCTOBER 21

Winston D. Crabb, '67 MD
Rio Rancho, New Mexico
SEPTEMBER 30

Michael W. Witwer, '67 MD, '73 GME
Santa Rosa, California
SEPTEMBER 25

Robert Scott Zeiders, MD, '67 MD
Savoy, Illinois
NOVEMBER 24

Robert G. Cook, MD, '78 GME
Kenosha, Wisconsin
SEPTEMBER 23

Susan M. Haack, MD, '88 GME
Anthem, Arizona
DECEMBER 30

Thomas J. Mango, '89 MD
Granger, Indiana
OCTOBER 3

Danielle Alana Peress, MD, '16 GME
New York, New York
NOVEMBER 26



2017. Election to the Academy is considered one of the highest honors in the fields of health and medicine and recognizes individuals who have demonstrated outstanding professional achievement and commitment to service.

9, 10

Richard Zorowitz, MD, '09 GME, was named a 2017 Top Doctor in Washington, D.C. He is a physical medicine and rehabilitation physician with the MedStar National Rehabilitation Network.

Hala Yamout, MD, '13 GME, received the 2017 St. Louis Veteran Affairs (VA) Medical Staff Recognition Award. Yamout is a staff physician in the Department of Nephrology at the St. Louis VA.

DPT

Patrick Blair, '90 BSPT, joined Olympic Physical Therapy as a physical therapist. Blair has 27 years of outpatient orthopedic experience working in the south suburbs of Chicago. His area of clinical interest is hand and upper extremity rehabilitation.

MARK ONE OR MORE BOXES

A young alumnus debates the utility of clustering patients into demographic categories.

The 80-year-old woman came to my ER with lower abdominal pain. I started thinking through my differential: diverticulitis, urinary tract infection, maybe appendicitis. Her labs came back showing nothing. During a second round of questions, she mentioned a new boyfriend at the nursing home. It turned out that my frisky octogenarian had a case of chlamydia.

We categorize people in medicine all the time. Young, old, black, white, female, male,

THESE BOXES AND I HAVE A bipolar relationship. I find boxes complicated because they are frustratingly inexact and reductionist but still point out significant societal trends to address.

this, that. Every demographic survey has a slew of boxes that tries to compartmentalize us as people. These boxes and I have a bipolar relationship. I find boxes complicated because they are

frustratingly inexact and reductionist but still point out significant societal trends to address.

The analytical side of me contests the boxes. What should be an orderly and intuitive grouping generally ends up a messy hodgepodge of categories forming an impossible Venn diagram.

Consider the U.S. government's five minimum categories for collecting data on race: American Indian or Alaska native, Asian, black or African American, Native Hawaiian or other Pacific Islander, and white — the race boxes are a mix of skin tone, people group and geographic region. What about my Russian friends? Do they pick Asian to match geography or white to match skin color? Or friends from Algeria or Pakistan, both of whom the government unceremoniously dumps into the white category.

The category of Pacific Islander includes less than 2 million people globally, while the category Asian includes 4.5 billion and would lump together the experiences of Chinese and Indian Americans. If someone orders Asian food, they would be surprised if they got dosas and tandoori chicken, which means that Grubhub somehow outpaces many electronic health records at differentiating people groups. Boxes reduce individuals to often ill-fitting categories that may not reflect their experience.

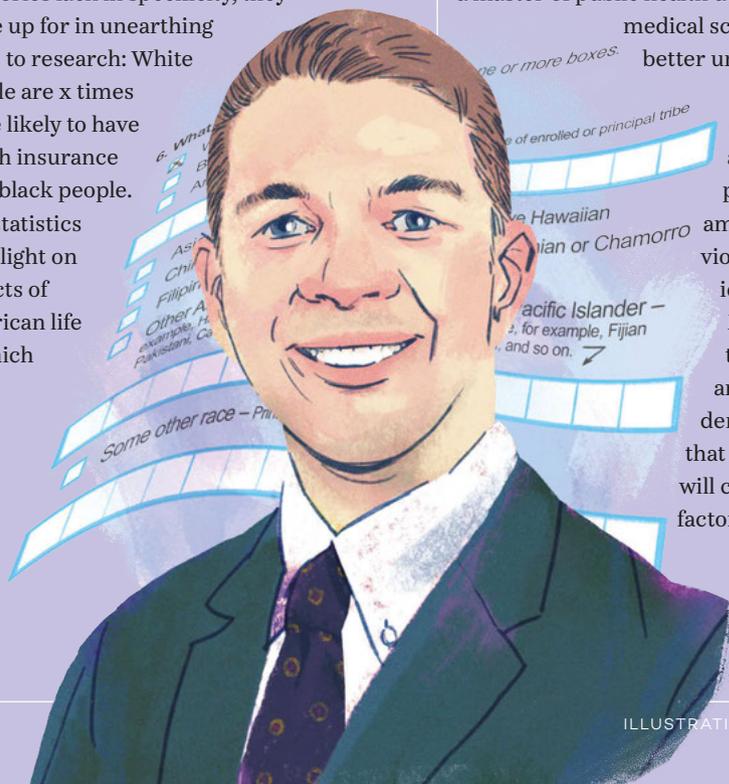
Boxes perform better in revealing trends of inequality in populations, where large sample sizes average out disparate individual experiences. The ignoble groupings have a brutal simplicity, yet still manage to reveal large disparities. What the roughhewn categories lack in specificity, they make up for in unearthing areas to research: White people are x times more likely to have health insurance than black people. The statistics shed light on aspects of American life in which

certain groups have unequal outcomes. As physicians, we must both be cognizant of these patterns and seek to eliminate them.

As a physician, I use demographic information daily to risk stratify patients while taking their history. There are many determinants of health, and understanding the risk ratios associated with certain population groups helps to steer my workups. That being said, individuals are unique. I anchored on my 80-year-old's likely diagnoses differently because we less frequently associate sexually transmitted infections with the elderly. It is crucial to remember that our patients may come from anywhere on the bell curve.

At a population level, knowledge of disparities between groups helps me advocate to eliminate those differences. I chose to pursue a master of public health degree during

medical school so that I could better understand the disparate epidemiology of disease and address it through policy, especially among victims of gun violence and the residentially displaced. My hope is that through advocacy and hard work, the demographic boxes that our patients check will cease being risk factors for disease.





1583-present

Artifacts from Special Collections

RARE BOOKS

Feinberg's Galter Health Sciences Library and Learning Center houses thousands of rare, unique and historical materials within its Special Collections Department. The collections include medical and dental works from European and American sources, spanning the 15th through the 20th centuries, with strengths in anatomy, pathology, obstetrics and gynecology, and urology, among other areas. The department also

houses medical and dental artifacts, manuscripts, institutional and personal archives and more.

Pictured above: The top nine images posted to the Special Collections' Instagram account ([galter_special_collections](#)) in 2017. Among these pages are a municipal report on all the deaths reported in London in the year 1665, including "French Pox" and "Kings Evil" (third row, third column), and a 17th century medical book that attempts to classify deformities and congenital abnormalities, including those that afflict fantastical creatures (third row, second column).

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