Northwestern Neternet

Tracine Back

Northwestern scientists get to the genetic roots of epilepsy to tackle this life-altering disorder. p. 14

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Dressed for Success

First-year medical students donned their white coats for the first time at Founders' Day on August 5. The annual celebration welcomes a new class of medical students to campus, honors Feinberg's founders, and marks the official start of the academic year.

Northwestern Medicine magazine is published quarterly for alumni and friends of Northwestern University Feinberg School of Medicine, Northwestern Memorial HealthCare, and the McGaw Medical Center of Northwestern University.

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Fall 2022

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TRACING BACK

Northwestern scientists are working to understand the genetic etiology of epilepsy to develop more effective, if not curative, therapies.



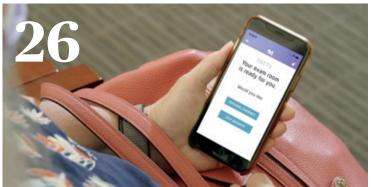
UNLOCKING THE MYSTERIES OF THE HUMAN BRAIN

The new chair of the Department of Psychiatry and Behavioral Sciences, Sachin Patel, MD, PhD, brings a unique blend of clinical psychiatry practice and neuroscience research.



NEXT-LEVEL WEARABLE TECH

Wearable tech has reached new heights as Northwestern scientists continue to push the limits on how medical devices can be integrated on and within our bodies.



THE CLINIC OF THE FUTURE

Northwestern Medicine is launching a new digital platform to ensure better care and more face time with patients.

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LEADERSHIP

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ON THE COVER

Evidence is increasing that the causes of epilepsy are rooted in the genetics of brain development. This computer-generated image depicts a DNA molecule wrapped around a human brain. Science Photo Library.

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LEADERSHIP

The Things That Matter



HE 80/20 RULE SAYS ONLY A FEW THINGS WILL MATTER. BIOMEDICAL SCIENCE IS ONE

of them. That is why our commitment to discovery remains earnest. But commitment alone does not ensure results. Our goals require dedicated vision and investment, and we have been immensely fortunate to benefit from superb research faculty and donors who have provided that and more.

A combination of awards and generous contributions from forwardthinking philanthropists have led to Feinberg principal investigators securing \$650 million in research funding during the 2021-22 fiscal year — the largest amount in the school's history. The medical school provides 70 percent of Northwestern University's total research funding dollars.

Not long before this issue of Northwestern Medicine went to print, we announced a new \$100 million gift to Feinberg from Kimberly K. Querrey ('22, '23 P) and the Louis Simpson Trust that will significantly expand the university's biomedical research enterprise (read about the key projects these funds will set in motion on page 3). Over the years, gifts from Querrey and Louis A. Simpson '58 ('96 P) have focused on initiatives that propel academic excellence, spur innovation, enable transformative research, and most importantly, help people.

Another generous gift, from the Patrick G. '59, '09 H ('97, '00 P) and Shirley W. Ryan '61, '19 H ('97, '00 P) Family, has endowed the Ryan Family Center for Global Primary Care within the Robert J. Havey, MD Institute for Global Health, helping to advance the institute's mission to improve human health for a better world as well as launching the Patrick and Shirley Ryan Institute for Neurodevelopment to bring an astonishing new level of understanding to how cognition and memory develop in alignment with the National Institutes of Health (NIH) Brain Research Through Advancing Innovative Neurotechnologies (BRAIN) Initiative.

We are honored to be the recipients of such wonderful support.

Just as critical to our work is funding from the NIH, and I am delighted to report that this fiscal year, we saw a nearly seven percent increase in NIH grants over the previous period — overall, \$448 million was awarded to our investigators to accelerate the pace of scientific progress.

This includes essential ongoing support for established entities, such as Northwestern University Clinical and Translational Science (NUCATS) Institute and the Robert H. Lurie Comprehensive Cancer Center, as well as new grants that allow us to further explore areas of medicine that need examining.

One such novel project is a sevenyear grant to study a "pill-in-pocket" strategy to prevent stroke in patients with atrial fibrillation, the most common heart rhythm disorder in adults, awarded to Rod Passman, MD, director of the Center for Arrhythmia Research and the Jules J. Reingold Professor of Electrophysiology (read more on page 19).

Another transformative NIH grant, totaling \$16 million over five years and designed to address the dearth of underrepresented minorities in the life sciences, will fund the hiring of 15 new tenure-track faculty at Northwestern. The initiative, called Northwestern University Recruitment to Transform Under-Representation and achieve Equity (NURTURE), will also ensure the success of faculty members from underrepresented populations (read more on page 4).

One of the most gratifying aspects of working in the life sciences is witnessing the discoveries that come to fruition in the years after funding has been granted. Several years ago, Northwestern was awarded a \$12 million, five-year NIH grant to launch a center dedicated to advancing the genetic understanding of epilepsy. Four years in, center director Alfred George, Jr., MD, chair and Alfred Newton Richards Professor of Pharmacology, and his colleagues have made amazing strides in this area (read more on page 14).

Tackling the complex scientific questions of today not only requires increasing amounts of fuel for our investigators, but also demands a remarkable amount of commitment, time, and energy. More than 6,000 clinical trials and research studies were conducted at Feinberg in the last academic year, and 50 patents and nine new start-ups were established. I am tremendously proud of this effort to improve the health of people.

All of these efforts ladder up to the promise of discovery. Discovery is the lifeblood of our identity as a high-performing, research-driven health system. And discovery is only possible with investment. In this regard, we are fortunate to find ourselves at an extraordinary place. Yet, we have much more to do. Together, we will stay laser-focused on the things that matter.

With warm regards,

Eric G. Neilson, MD

Vice President for Medical Affairs Lewis Landsberg Dean

PULSE

Kimberly Querrey, Louis Simpson Trust Give \$100 Million to Feinberg

orthwestern University Trustee Kimberly K. Querrey ('22, '23 P) and the Louis Simpson Trust have made a new \$100 million gift to the Feinberg School of Medicine to significantly expand the University's biomedical research enterprise. Part of a transformational \$121 million gift to Northwestern University, the gift will advance scientific discovery at Feinberg and reinforce the university's position as a global research powerhouse.

"Kimberly is a visionary philanthropist who cares deeply about groundbreaking science and biomedical research," said Eric G. Neilson, MD, vice president for medical affairs and Lewis Landsberg Dean. "This generous gift will enable us to advance our research mission innovatively and imaginatively to transform human health by accelerating the pace of discovery for the benefit of clinical medicine."

The gift will support several new initiatives at Feinberg: \$64 million will support the construction of a 19-level tower with 15 lab floors, expanding the Louis A. Simpson and Kimberly K. Querrey Biomedical Research



Center and making it the largest academic biomedical research facility in the world. The gift will also provide \$25 million to create and endow the Simpson Querrey Lung Institute for Translational Science, which will be directed

"This generous gift will enable us to advance our research mission innovatively and imaginatively to transform human health."

Eric G. Neilson, MD

by GR Scott Budinger, MD, the Ernest S. Bazley Professor of Airway Diseases and chief of Pulmonary and Critical Care in the Department of Medicine. The institute will advance new basic discoveries in pulmonary medicine for the benefit of patients.

Another \$10 million will create and endow the new Simpson Querrey Center for Neurovascular Sciences, which will be directed by Farzaneh Sorond, MD, PhD, vice dean of Faculty Affairs and the Dean Richard H. Young and Ellen Stearns Young Professor and chief of Stroke and Vascular Neurology in the Ken and Ruth Davee Department of Neurology. The center will advance new ideas related to neurovascular diseases across medical disciplines.

Finally, \$1 million will support the Kimberly Prize in Biochemistry and Molecular Genetics, which Querrey established in 2022 in honor of Simpson. Jennifer Doudna, PhD, was recently named the inaugural winner (see sidebar).

CRISPR PIONEER RECEIVES INAUGURAL KIMBERLY PRIZE

RISPR pioneer and Nobel Laureate Jennifer Doudna, PhD, has received the inaugural \$250,000 Kimberly Prize. Doudna was selected for her fundamental biochemical studies providing molecular insight into the function of CRISPR/ Cas9 systems as tools for genome editing and the application of her work to biology and medicine.

The new award, given by Kimberly Querrey in honor of her late husband, Louis Simpson, is the largest biochemistry award offered in the U.S. It will be awarded annually to a scientist who has made outstanding biochemical research contributions to the molecular basis of life with a direct demonstrated link of their discovery into the clinic. The prize is given by the Simspon Querrey Institute for Epigenetics, directed by Ali Shilatifard, PhD, the Robert Francis Furchgott Professor and chair of Biochemistry

and Molecular Genetics, and administered by Feinberg. Doudna will deliver her lecture at Northwestern this spring.

Northwestern Receives \$16 Million Grant to Support Faculty Recruitment and Equity

transformative grant totaling \$16 million over five years awarded to Northwestern by the National Institutes of Health (NIH) aims to increase full participation of underrepresented groups in the life sciences at Northwestern by funding the cluster hiring of new faculty in the areas of cancer, cardiovascular, and brain and behavioral sciences.

The five-year grant, along with support from Northwestern, will allow the university to hire 15 new tenure-track faculty and will deploy innovative strategies to ensure the success of faculty members from historically underrepresented populations. The funding is designed to address the dearth of underrepresented minorities in the life sciences. The initiative aligns with Northwestern's values, which emphasize the benefits of diversity, equity, and inclusion. This overarching initiative, called the Northwestern University Recruitment to Transform Under-Representation and achieve Equity (NURTURE), program is one of only 11 such awards to date in the country. "This grant is an amazing dream come true. I have traversed the entire academe over 17 years here at Northwestern and am excited for the opportunity to lead substantive change in the institution with how we recruit, hire, onboard, support, and retain diverse faculty," said Melissa Simon, MD, MPH, the George H. Gardner, MD, Professor of Clinical Gynecology, director of the Center for Health Equity Transformation and associate director of community outreach and engagement for the Robert H. Lurie Comprehensive Cancer Center of Northwestern University, and the primary investigator and project leader for the grant.

Along with Simon, co-primary investigators on the NURTURE project will be: Eric Perreault, PhD, associate dean for research, professor of Biomedical Engineering in the McCormick School of Engineering and professor of Physical Medicine and Rehabilitation; and Clyde Yancy, MD, MSc, vice dean for Diversity and Inclusion and chief and Magerstadt Professor of Cardiology in the Department of Medicine.



"I have traversed the entire academe over 17 years here at Northwestern and am excited for the opportunity to lead substantive change in the institution with how we recruit, hire, onboard, support, and retain diverse faculty."

MELISSA SIMON, MD, MPH

GRANT TO INVESTIGATE IF APPLE WATCH CAN REDUCE RELIANCE ON BLOOD THINNERS

orthwestern and Johns Hopkins University have been awarded a multimillion-dollar grant from the National Heart, Lung, and Blood Institute to study a "pill-in-pocket" strategy to prevent stroke in patients with atrial fibrillation (AFib). The approximately \$37 million award will fund the seven-year trial, called the Rhythm Evaluation for AntiCoagulaTion (REACT-AF) trial. Rod Passman, MD, director of the Center for Arrhythmia Research and the Jules J. Reingold Professor of Electrophysiology in the Department of Medicine, will serve as principal investigator. Read more on page 19.





Research Day 2022 Celebrates Scientific Discovery

ore than 480 investigators, students, trainees, and faculty presented scientific posters and abstracts at Feinberg's 16th Annual Lewis Landsberg Research Day. This year's event saw a recordbreaking number of participants and presentations after a two-year hiatus due to the COVID-19 pandemic.

"Research Day 2022 is the largest and most energetic research event ever. This is a great start for the research enterprise for the new academic year," said Rex Chisholm, PhD, vice dean for Scientific Affairs and Graduate Education, the Adam and Richard T. Lind Professor of Medical Genetics, and a professor of Cell and Molecular Biology and of Surgery.

This year's keynote address was delivered by Joshua Denny, MD, MS, chief executive

officer of the National Institutes of Health's All of Us Research Program.

"As we thought about the All of Us Research Program, we really wanted to think about the different ways we could capture different streams of information, bringing them together, creating new kinds of datasets and tools and, importantly, increasing participant population to really help us learn about ways we could intervene on healthcare and make things better," Denny said.

Throughout the event, attendees browsed hundreds of scientific posters and spoke with investigators, including second-year medical student Thomasz Gruchala, who presented his research about the correlation between bed mobility and mortality in patients with glioma after inpatient rehabilitation. "The benefit of bed mobility is that anyone is able to measure it; there's no advanced clinical training that's needed," Gruchala said.

Another research project, led by Anna Marie Pacheco Young, MD, MPH, a secondyear resident in obstetrics and gynecology, found that a majority of pregnant women with substance use disorders who were admitted to a healthcare center were eligible for the HIV prevention medication pre-exposure prophylaxis, commonly known as PrEP. "We think that not only is this a call to providers to offer PrEP to women with substance use disorders during pregnancy, but also to be on high alert for women with a comorbid psychiatric illness," Young said.



NATHANS DELIVERS NEMMERS PRIZE KEYNOTE LECTURE

eremy Nathans, MD, PhD, an investigator of the Howard Hughes Medical Institute and a professor at Johns Hopkins University School of Medicine, and recipient of the 2022 Mechthild Esser Nemmers Prize in Medical Science, delivered a keynote lecture on the molecular mechanisms of visual systems on September 20. The Nemmers Prize in Medical Science is awarded by Northwestern to a physician-scientist whose body of research exhibits outstanding achievement in their discipline as demonstrated by works of lasting significance.

Two New Centers Launched

RYAN FAMILY CENTER FOR GLOBAL PRIMARY CARE



PULSE

Robert J. Havey, MD

A gift from the Patrick G. '59, '09 H ('97, '00 P) and Shirley W. Ryan '61, '19 H ('97, '00 P) Family will endow the Ryan Family Center for Global Primary Care within the Robert J. Havey, MD Institute for Global Health, which has a mission to improve health for a better world. The primary care center's focus is to collaborate with partner institutions in

international environments where critical healthcare is most needed. Northwestern will help identify opportunities for research and training, build capacity

for more primary care patients and, ultimately, improve health promotion, disease prevention, treatment, rehabilitation and palliative care. The gift is part of a transformational \$480 million gift from the Ryan Family to the University that was announced in September 2021.

"This wonderful gift from the Ryan Family enables Northwestern to expand our critically important work across the globe to improve lives and transform human health," said Eric G. Neilson, MD, Lewis Landsberg Dean and vice president for Medical Affairs at Feinberg. "It is support like this that accelerates the pace of discovery for some of society's most important health issues. We are very grateful for their commitment to the science in medicine."



CENTER FOR HUMAN IMMUNOBIOLOGY



Northwestern has established the Center for Human Immunobiology (CHI), with the goal of bringing together interdisciplinary scientists and clinicians to uncover the molecular mechanisms of the immune system and translating new discoveries into innovative cures for immune-regulated diseases.



The center will be directed by Stephanie Eisenbarth, MD, PhD, the incoming chief of the Division of Allergy and Immunology in the Department of Medicine and the Roy and Elaine Patterson Professor of Medicine.

Stephanie Eisenbarth, MD, PhD

"Understanding how the immune system fights new viruses, controls the growth of cancer, inappropriately responds to allergens, and targets the body's own tissues is critical to human health, and the interdisciplinary teams we plan to build will help us examine these questions through multiple lenses," said Eisenbarth, who previously served as the associate chair of research in the Department of Laboratory Medicine and co-director of the Program in Translational Biomedicine at Yale University.

The new center — which has been allocated 9,000 square feet of newly renovated lab space on the Chicago campus in the Tarry Building - will unite trainees, clinicians and immunologists spanning 28 departments at Feinberg to stimulate innovative new approaches to treat diseases caused or amplified by the immune system. The medical school has also allocated funds to recruit new scientists at the forefront of research in immunology to the faculty.

Novel Telehealth Strategy Will Treat Multiple Cancer Risk Behaviors

fter people are diagnosed with cancer, their health risk behaviors — smoking, overeating and lack of physical activity — affect the likelihood that they will not respond to treatment, that they will have side effects from treatment, and that they will get a new cancer. They also are more likely to get heart disease or diabetes.

A first-of-its-kind trial funded by the National Cancer Institute (NCI) will test whether a telehealth-based intervention that addresses all three behavioral risk factors at once can modify cancer patients' lifestyles to improve their outcomes. The trial will recruit 3,000 participants at 11 Northwestern Medicine hospitals.

Northwestern's Program for Scalable TELeheaLth Cancer CARe (STELLAR) is part of a new initiative that is funding four NCI Telehealth Cancer Research Centers of Excellence, and is supported by the Cancer Moonshot, a White House initiative first launched in 2016 and reignited by President Biden in 2022 to accelerate the rate of progress against cancer. Northwestern will receive \$5.5 million in funding over five years.

"These risk behaviors are the same for most chronic diseases, which is important because many cancer patients are more likely to die from cardiovascular diseases than from their cancer," said project leader Bonnie Spring, PhD, chief of Behavioral Medicine in the Department of Preventive Medicine, program co-lead for cancer prevention at the Robert H. Lurie Comprehensive Cancer Center of Northwestern University and director of the Center for Behavior and Health.

Spring's center has already developed evidence-based, technology-assisted telehealth interventions to separately treat obesity, smoking and lack of physical activity.

"Nothing like this exists," Spring said. "Over the years, we have developed separate treatments for these risk behaviors. Now we





"These risk behaviors are the same for most chronic diseases, which is important because many cancer patients are more likely to die from cardiovascular diseases than from their cancer." BONNIE SPRING, PHD

are putting them together. That's an efficiency. Ordinarily it would be burdensome and expensive to deliver a treatment for even one of these risk behaviors."

The project reduces the cost of treatment by training bachelor's-level 'health promotionists' to coach patients under the supervision of clinical health psychologists. Physicians and nurses don't have time to treat these behaviors, Spring said, and even if they did, the cost would be much higher.

Participants are coached remotely by telephone and trained to use an app that tracks their behaviors. The data are sent to their coach electronically.

"If they are not losing weight, the coach can see what is causing it," Spring said. "What high-calorie foods are they eating? Are they eating too late at night? Are they inactive? It's what makes the coaching very efficient and personalized."

PULSE

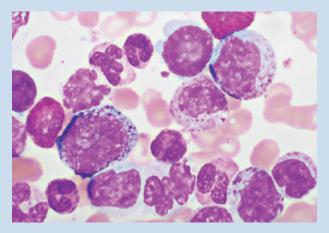
RESEARCH BRIEFS

DISEASE DISCOVERIES

EXPLORING NOVEL MECHANISMS AND THERAPEUTIC TARGETS FOR ACUTE MYELOID LEUKEMIA



Patients with acute myeloid leukemia (AML), the most common type of adult blood cancer, show large-scale genomic mutations and altered DNA folding patterns that could help identify potential therapeutic targets, according to a Northwestern Medicine study published in *Nature*. Feng Yue, PhD, the



Duane and Susan Burnham Professor of Molecular Medicine, was senior author of the study.

AML is caused when myeloid cells in bone marrow interfere with the production of other blood-producing cells. AML can present as different combinations of genomic mutations in different patients. These mutations disrupt proper cell functioning, including the organization of chromatin 3D structures that regulate cell replication and differentiation transcription.

Different subtypes of AML are driven by these distinct genomic mutations, which creates a roadblock for treatment — patients with different subtypes can respond differently to the same therapy.

"Therefore, it is crucial to understand how those subtype-defining mutations give rise to the leukemia cell phenotype through changing the chromatin 3D structure," said Yue, who is also a professor of Biochemistry and Molecular Genetics, of Pathology and director of the Center for Cancer Genomics at the Robert H. Lurie Comprehensive Cancer Center of Northwestern University.

CLINICAL BREAKTHROUGHS

Emerging Therapy for Relapsed Lymphoma



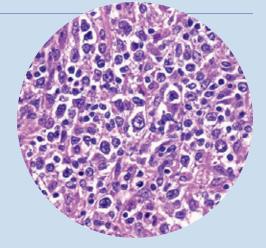
An emerging therapy showed promise in patients with relapsed B-cell lymphoma who are not good candidates for stem cell

transplants, according to a non-randomized phase II trial published in *The Lancet Oncology*. Leo Gordon, MD, the Abby and John Friend Professor of Oncology Research and professor of Medicine in the Division of Hematology and Oncology, was the senior author of the study.

Called chimeric antigen receptor therapy (CAR-T), the treatment genetically modifies patient T-cells into aggressive cancer killers. Clinicians collect T-cells from patients in a procedure called leukapheresis (which involves removing T-cells from the blood), then send the cells to a laboratory where new genes are inserted into those cells. The genes cause the T-cells to recognize and attack a target — in this case, a particular protein on lymphoma cells. This process of manufacturing the cells can take several weeks, and afterwards, the cells are infused back into the patient.

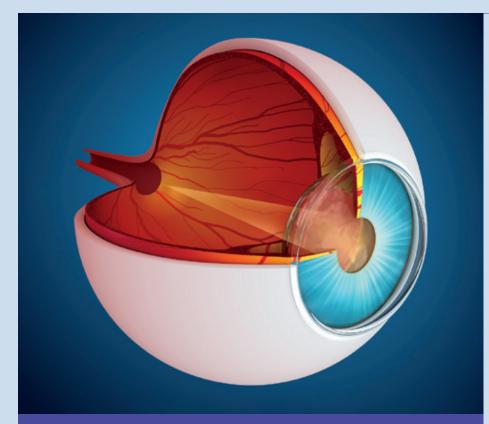
The results of the trial were promising, Gordon said, but there are additional questions to ask about CAR-T in patients with B-cell lymphoma. In the future, he wants to examine usage of CAR-T therapy earlier in disease.

"We see many high-risk patients where we don't expect a complete response from chemotherapy — can CAR-T be used here to produce better outcomes?" he asks. This study was funded by Juno Therapeutics, a Bristol-Myers Squibb company.



THE RESULTS OF THE TRIAL WERE PROMISING BUT THERE ARE ADDITIONAL QUESTIONS TO ASK.

This work was supported by National Institutes of Health grants R35GM124820, IR01HG009906, R01HG011207, U01CA200060 and R24DK106766, and National Cancer Institute grants R35 CA197594-01A1, R01 CA216421 and PS-OC U54 CA143869-05.



SCIENTIFIC ADVANCES

New Insights in Retinal Neurons



Northwestern Medicine investigators have identified a new type of retinal ganglion cell, the neurons in

the retina that encode the visual environment and transmit information back to the brain, according to a study published in *Neuron*.

The specific features of this cell, which is called a "bursty suppressedby-contrast" (bSbC) retinal ganglion cell (RGC), overturn a decades-old assumption about the relationship between the cells' inputs from photoreceptors and outputs to the brain, according to Gregory Schwartz, PhD, the Derrick T. Vail Professor of Ophthalmology and senior author of the study.

"The classic view was that these ganglion cells simply integrate their excitation and inhibition inputs, and that will tell you how the cell responds to visual stimulus," said Schwartz, who is also a professor of Neuroscience. "Our findings reveal that these cells have their own intrinsic computation, which has interesting implications for things like retinal prosthetics." There are more than 40 types of RGCs which transmit information about specific and complex characteristics of a visual scene, including motion, direction, orientation and color. For example, the "off sustained alpha" (OFFsA) RGC type has a baseline firing rate, but when light increases, the cell's signaling to the brain decreases and vice versa.

In the study, investigators compared the responses of OFFsA and bSbC ganglion cell types to different

THE SPECIFIC FEATURES OF THIS CELL OVERTURN A DECADES-OLD ASSUMPTION.

visual stimuli, recording the resulting signals that would be sent to the brain. The study authors discovered the bSbC

has a curious mechanism: The cell has a baseline rate of signaling towards the brain, but both increases and decreases in light result in decreased signaling, a one-way signaling pattern.

unding for this study was provided by National Institutes of Health rants F31 EV030737 and DP2 EV026770-01, Northwestern University epartment of Ophthalmology Derrik T. Vaii Endowed Chair Funds, and esearch to Prevent Blindness Challenae Career Development Award

DISEASE DISCOVERIES

INFLAMMATORY SIGNALING LINKED TO LEUKEMIA PROGRESSION



An inflammatory signaling protein called interleukin-6 (IL-6) has been linked to the progression of acute myeloid leukemia, representing

a potential target for future treatments of the disease, according to a recent Northwestern Medicine study published in the Journal of Clinical Investigation.

Myelodysplastic syndromes (MDS) are aging-related disorders in which the body produces blood cells ineffectively, which carries the risk of progression to acute myeloid leukemia. While the increased risk of leukemia from MDS has been well-established, the exact mechanisms behind the progression, especially in relationship to aging, have been poorly understood.

"We are surprised to find that IL-6, among many other inflammatory signaling proteins, plays an essential role in MDS to AML progression during aging," said Peng Ji, MD, PhD, '15 GME, professor of Pathology in the Divisions of Experimental Pathology and Hematopathology, the senior author of the study.

The study was supported by Department of Defense grant CA140119, National Institute of Diabetes and Digestive and Kidney Disease grant R01-DK124220, National Heart, Lung, and Bload Institute grants R01-HL148012 and R01-HL150729, and a Translational Bridge grant from the Robert H. Lurie Comprehensive Cancer Center of Northwestern University. The study was also partially supported by grants from the Global Research Award from American Society of Hematology, the Provincial Natural Science Foundation of Hunan No. 2021.JJ30163, the Changsha Municipal Natural Science Foundation No. kq2007053, and High-level Talent Research Startup Fund of Hunan University.



PULSE *Research Briefs*

SCIENTIFIC ADVANCES



INVESTIGATING THE ROLE OF DOPAMINE CIRCUITS IN HABIT FORMATION



Scientists have uncovered how dopamine connects subregions of the striatum essential for habit formation, according to a study

published in *Cell Reports*. These findings may change the overall understanding of how habits are formed — and could be broken.

"The circuits are going both ways, and so maybe that gives potential ideas of how to break a bad habit if there's a circuit allowing information flow to go the other way," said Talia Lerner, PhD, assistant professor of Neuroscience and senior author of the study.

The basal ganglia are a group of nuclei below the brain's cortex, which operate primarily in closed parallel loops. These loops, or circuits, originate from different regions of the dorsal striatum, including an associative circuit controlling goal-directed behaviors from the dorsomedial striatum and a somatosensory circuit controlling habit formation from the dorsolateral striatum. In addition to closed loops, it has long been hypothesized that there is an open "ascending spiral" loop that allows goal-directed behaviors to become habits. But the hypothesis has been difficult to test — until now, with the use of new transsynaptic and intersectional genetic tools.

"The exciting thing in this study is that we were able to use new tools to trace both forward circuits and backward circuits and really test if there are synaptic connections where we think they should be and if they work in the way we think they should," Lerner said.

This work was supported by a National Institutes of Health (NIH) K99/ROO Award (ROOMH109569) and a NIH-National Institute of Neurological Disorders and Stroke T32 Award (T32NSO41234).

CLINICAL BREAKTHROUGH

Bigger is Better for Genetic Tests That Check for Cardiomyopathy, Arrhythmias



When it comes to genetic testing for cardiomyopathy and heart arrhythmias, the bigger the test panel, the better, according to

a new study published in *JAMA Cardiology*. Elizabeth McNally, MD, PhD, the Elizabeth J. Ward Professor of Genetic Medicine and director of the Center for Genetic Medicine, was the corresponding author.

Currently, physicians typically use small gene tests, which are focused on finding specific types of cardiomyopathy (a disease of the heart muscle that makes it harder for the heart to pump blood to the rest of the body) or specific types of arrhythmias (an irregular heart rhythm). But in the new study, scientists found that using a large genetic panel that checks for many genes at the same time is more likely to identify whether a study participant has both cardiomyopathy and a heart arrhythmia. In fact, the combined testing approach in the study captured approximately 11 percent of patients who would have been missed if genetic testing had been restricted to a specific suspected disease subtype. This type of genetic diagnosis helps predict the course of illness for patients and, in some cases, also points to specific therapies.

"It turns out there is genetic crossover in which the same gene can be linked to both cardiomyopathy and arrhythmias, so ordering a larger test improves the odds of getting a result," McNally said. "For some of the genetic cardiomyopathy subtypes, patients can get arrhythmias much earlier in the course of disease, so we use device management more readily than we would in cases without these specific genetic diagnoses."

Funding for this study was provided by the American Heart Association, the National Institutes of Health (grant HL128075) and Invitae.



DISEASE DISCOVERIES

NEW THERAPEUTIC APPROACH COULD PREVENT INJURY TO FRAGILE TRANSPLANTED LUNGS



Northwestern Medicine scientists have discovered a potential therapeutic target in the donor lung that can

prevent primary graft dysfunction (PGD) in lung transplant recipients, according to findings published in the *Journal of Clinical Investigation*. GR Scott Budinger, MD, chief of Pulmonary and Critical Care in the Department of Medicine and the Ernest S. Bazley Professor of Airway Diseases, was senior author of the study.

In 2017, Northwestern scientists published a critical discovery about PGD: After transplant, blood immune cells called non-classical monocytes (NCMs) retained in the donor lung activate a pathway that attracts damaging neutrophils from the host into the newly transplanted lung.



Those findings suggested that targeting NCMs in donor lungs could potentially prevent the development of PGD.

With the current study, the team has taken the initial discovery a step further, finding the pathways that activate these cells after transplant. Even more importantly, they found that a protein on these cells, CD11b, can act as a molecular "brake" to reduce their activation.

A critical finding of this paper is that an activator of the CD11b braking system LA-1, administered only to the donor lung before transplant, markedly reduced the severity of transplant induced early lung injury, according to Budinger.

"This is important because treatment of the donor lung before transplant is possible using *ex vivo* perfusion or 'lung in a box' systems," he said. "Since the recipient never needs to receive the drug, this strategy is likely to reduce any side effects of the drug."

This study was supported by National Institutes of Health grants HL145478, HL147290, HL147575, U19A135964, P01AG049665, P01AG04966509S1, P01HL154998, R01HL147575, and Veterans Affairs grant I01CX001777.

SCIENTIFIC ADVANCES

Scientists Discover Novel Cellular Mechanisms Behind Transcription Elongation



Northwestern Medicine investigators have discovered novel mechanisms underlying a specific transcription factor

essential for elongation control, the process of synthesizing RNA from DNA, according to findings published in *Molecular Cell*. Yuki Aoi, PhD, a postdoctoral fellow in the Shilatifard laboratory, was lead author of the study.

"This is another superb molecular study by Dr. Yuki Aoi, who has been systematically dissecting transcription and transcription elongation control inside the cells using the outstanding methods he has developed," said Ali Shilatifard, PhD, the Robert Francis Furchgott Professor and chair of Biochemistry and Molecular Genetics, who was senior author of the study. Gene expression is regulated at the level of transcription elongation control, which is driven by the multiprotein complex called RNA polymerase II. During transcription elongation, RNA polymerase II travels along one strand of DNA and copies genetic information to a strand of RNA. When this process is upset, diseases such as cancer or neurological disorders can develop.

For RNA polymerase II to control transcription elongation, different transcription factors must bind to or dissociate from RNA polymerase II. But precisely how these transcription factors help RNA polymerase II regulate elongation inside the cells has remained elusive.

"This elongation state is very important for reading the genetic information in every single cell in our bodies, but its regulation inside the cells is extremely complex. So, we are trying to understand how RNA polymerase II regulates elongation inside the cell using cellular and molecular system that we have developed," said Aoi.

This work was supported by the JSPS Research Fellowship for Young Scientists, the Uehara Memorial Foundation Research Fellowship, National Cancer Institute Cancer Center Support Grant P30 CA06053, instrumentation award S100D025194 from the National Institutes of Health's Office of the Director, National Resource for Translational and Developmental Proteomics supported by P41 GM108569, and the National Cancer Institute grant R35CA197569

MEDIA SPOTLIGHT

The New York Times

Uterine Cancer Cases Are Rising. Here's What to Know.

Rates of uterine cancer have been increasing in the U.S., particularly for Black and Hispanic women. When we talk about uterine cancer, most of the time, we're talking about endometrial cancer, which starts in cells that form the lining of the uterus, said Emily Hinchcliff, MD, MPH, assistant professor of Obstetrics and Gynecology. The other, much rarer, type of uterine cancer is uterine sarcoma, which develops in the muscles supporting the uterus. Abnormal bleeding is the most common symptom of uterine cancer. For younger women, a change in bleeding pattern including bleeding between periods and heavy bleeding in general - can be a symptom of uterine cancer. Other early symptoms of uterine cancer include pelvic pain or pressure. Patients might experience bloating or changes in their bowel habits, which could look like constipation or diarrhea, Hinchcliff said.



USNews

Hypertension in Pregnancy is Getting More Common for Gen Z Women

Gen Zers and millennials are about twice as likely to develop high blood pressure during pregnancy than women from the baby boom generation were, a new study finds. This includes conditions such as preeclampsia and gestational hypertension. "While there are many reasons for the generational changes observed, we hypothesize that this is, in large part, due to the observed generational decline in heart health," said study co-author Sadiya

USNews

Common Lung Function Test Often Misses Emphysema in Black Patients

Spirometry, the most common test of lung function, is most likely not detecting signs of emphysema in some people with the lung ailment, a new study says. The test measures how much air you can breathe in and out of your lungs, as well as how easily and fast you can blow air out.

Lead investigator Gabrielle Liu, MD, an instructor of Medicine in the Division of Pulmonary and Critical Care, and her colleagues set out to see how well spirometry detects emphysema, a condition in which the air sacs of the lungs become damaged and enlarged. It is one of the conditions that comprise chronic obstructive pulmonary disease.

The study found Black men are at greater risk of suffering from undiagnosed emphysema,

since the way spirometry results are interpreted appears to "normalize" their bad lung function, according to Liu. She said the equations used to analyze spirometry results "incorporate race, and they basically normalize having a lower lung function if you're a Black adult compared to a white adult."

The researchers drew data from a heart and lung disease study that's been ongoing since 1985. They looked at nearly 2,700 participants who'd had both a spirometry test and a CT scan as part of the study. The investigators found that nearly 5 percent of people with normal spirometry results actually had signs of emphysema on their CT images. Based solely on spirometry, these patients would go undiagnosed. Khan, MD, assistant professor of Medicine in the Division of Cardiology and Preventive Medicine in the Division of Epidemiology. "High blood pressure during pregnancy is a leading cause of death for both mom and baby ... high blood pressure during pregnancy is associated with increased risk of heart failure and stroke in the mother and increased risk of the baby being born prematurely, being growth restricted, or dying," she said.

TODAY

Walking This Number of Steps Every Day Can Reduce Dementia

Walking 10,000 steps a day can cut the risk of dementia in half, and just 4,000 daily steps can reduce dementia risk by a quarter, a new study finds. "I think this research offers an important opportunity to explore how the number of steps and their intensity may play a role in the risk for dementia and in the health of our brains," said Emily Rogalski, PhD, the Ann Adelmann Perkins and John S. Perkins Professor of Alzheimer's Disease Prevention and associate director of the Mesulam Center for Cognitive Neurology and Alzheimer's Disease. But she points out that there will unlikely be a one-size-fits-all strategy for diminishing dementia risk and applying science will require a fit with individual needs.

FACULTY AWARDS & HONORS

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Herbert Meltzer,











Donald Lloyd Jones, MD, ScM, chair of the Department of **Preventive Medicine** and the Eileen M. Foell Professor of Preventive Medicine in the Division of Epidemiology, of Medicine in the Division of Cardiology, and of Pediatrics. received the American Heart Association's Distinguished National Leadership Award. 🔯 1

Steve Xu, MD, MSc,

assistant professor of Dermatology and of Pediatrics in the Division of Dermatology, and the Ruth K. Freinkel, MD, Professor, was named to MIT Technology Review's 2022 class of Innovators Under 35, an annual list recognizing the "brightest young minds working in technology today." Xu was lauded in the material science category for being part of a Northwestern team that created soft, flexible, skinsafe patches that can monitor a baby's vital signs wirelessly. 🙆 2

MD, professor of Psychiatry and Behavioral Science in the Division of General Psychiatry, of Neuroscience and of Pharmacology, received the Institute of Living's annual C. Charles Burlingame, MD, Award, presented annually to a "luminary in American and international psychiatry who has made significant contributions to

Mary McDermott,

the field." 🔯 3

MD, the Jeremiah Stamler Professor of Medicine in the Division of General Internal Medicine and of Preventive Medicine in the Division of Epidemiology, was awarded the 2022 PVD Distinguished Achievement Award by the American Heart Association's Council on Peripheral Vascular Disease (PVD). 10 4

Matthew DeBerge,

PhD, research assistant professor of Pathology, was awarded the BCVS Outstanding Early Career Investigator Award by the American Heart Association's Basic Cardiovascular Sciences (BCVS) Council. 10 5

Clyde W. Yancy, MD,

MSc, vice dean for Diversity and Inclusion, chief of Cardiology in the Department of Medicine and Magerstadt Professor of Medicine in the Division of Cardiology and of Medical Social Sciences, received the 2022 Gold Heart Award from the American Heart Association. 10 6

Josh Levitsky, MD,

'08 MS, professor of Medicine in the Division of Gastroenterology and Hepatology, of Medical Education, and of Surgery, has been selected as president-elect of the American Society of Transplantation (AST). Levitsky's term as president will begin in June 2023. With more than 4,000 members, the society is the largest transplant organization in North America and is a

recognized authority for research, advocacy, education and organ donation. **© 7**

Amy Paller, MD, chair of the Department of Dermatology and the Walter J. Hamlin Professor of Dermatology, and professor of Pediatrics in the Division of Dermatology was named recipient of the 2022 Tripartite Legacy Faculty Prize in Translational Science and Education. Feinberg presents this honor annually to a faculty member who has demonstrated excellence in research that emphasizes translational approaches, teaching, mentoring,

Talia N Lerner, PhD,

and leadership.

assistant professor of Neuroscience, has been awarded the Janett Rosenberg Trubatch Career Development Award by the Society for Neuroscience. The award recognizes originality and creativity in research and promotes success during academic transitions prior to tenure.

Yuan Luo, PhD, associate professor of Preventive Medicine in the Division of Health and Biomedical Informatics, of Pediatrics and in the McCormick School of Engineering, has been named vice chair of the Scientific Program Committee for the American Medical Informatics Association (AMIA) 2023 Informatics Summit taking place in March in Seattle.

Jen Brown, MPH.

lecturer of Preventive Medicine in the Division of Public Health Practice, and director of the Alliance for Research in Chicagoland Communities (ARCC), has been appointed co-chair of the Patient-Centered Outcomes Research Institute's (PCORI) Advisory Panel on Patient Engagement.

Sara Becker, PhD,

director of IPHAM's new Center for Dissemination and Implementation Science (CDIS), professor of Psychiatry and Behavioral Sciences and of Medical Social Sciences, and the Alice Hamilton Professor of Psychiatry, and Kelli Scott, PhD, assistant professor

of Medical Social Sciences and a member of CDIS, won the Society for Implementation Research Collaboration (SIRC) Award for Best Research-focused Symposium.

Dinee Simpson, MD,

vice chair for Faculty Development and Diversity in the Department of Surgery and assistant professor of Surgery in the Division of Organ Transplantation, was named an NYU Alumni Changemaker for developing Northwestern Medicine's African American Transplant Access Program.

MAGAZINE.NM.ORG 13



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Written by Cheryl SooHoo Photography by Gr8y Productions

Feinberg scientists get to the genetic roots of epilepsy to tackle this common and life-altering disorder.

pilepsy, with its unpredictable seizures, threatens the lives and quality of life for as many as one percent of the world's population. Misfiring brain neurons are the hallmark of the neurological disorder that occurs for myriad reasons — from head trauma to infection — with genetic mutations being another key driver. Only in recent years has genetic testing become the standard of care, accelerating research aimed at better understanding the genetic etiology of the disease to develop more effective, if not curative, therapies.

"The evidence continues to mount that the causes of epilepsy are rooted in the genetics of brain development," says Alfred L. George Jr., MD, the Alfred Newton Richards Professor and chair of Pharmacology and director of the interdisciplinary, multi-institutional Channelopathy-Associated Epilepsy Research Center, funded by the National Institutes of Health (NIH) Centers Without Walls initiative. "It seems likely that common forms of epilepsy occur because of genetic variation in many genes, whereas less common, yet often more severe, forms of the disease can be traced to mutations in single genes."

Northwestern Medicine is one of the few places in the country where a critical mass of investigators studies the genetic underpinnings of epilepsy in both children *and* adults. Collaborating with epileptologists caring for patients at Ann & Robert H. Lurie Children's Hospital of Chicago and Northwestern Memorial Hospital, Feinberg research teams have extraordinary access to the invaluable clinical information needed to translate new breakthrough therapies into 21st century care.

PINPOINTING EARLY-ONSET EPILEPSY GENES

When it comes to epilepsy, the gene KCNQ2 strikes early. A newborn who experiences an obviously unexplainable seizure within 48 hours of life has a better-than-average chance of having a KCNQ2 genetic mutation. Encoding a neuronal potassium channel, KCNQ2 controls electrical activity in the brain. KCNQ2 is one of the most frequently found genes associated with neonatal epilepsy. While seizures may resolve within the first year for some children who go on to develop normally, others have persistent seizures that can severely impact their cognition, communication, and physical function.

In 1998, two separate U.S. and European research teams simultaneously identified KCNQ2 and its connection to early-life monogenetic or single-gene causing epilepsies. Since that time, increased genetic testing uncovers more and more individuals with KCNQ2-related epilepsies. The significance of this gene did not escape the attention of George and key collaborators at Lurie Children's and elsewhere when establishing the Channelopathy-Associated Epilepsy Research Center in 2018. KCNQ2 was one of the first genes tackled by the center, which is supported by a five-year \$12 million grant from the National Institutes of Health that began the same year.

"Another important aspect of studying KCNQ2 was the existence of an FDA-approved drug called retigabine that boosts the activity of the ion channel encoded by this gene," George adds. "We studied a large number of KCNQ2 mutations to understand their functional >

FOCUS ON ADULTS WITH EPILEPSY

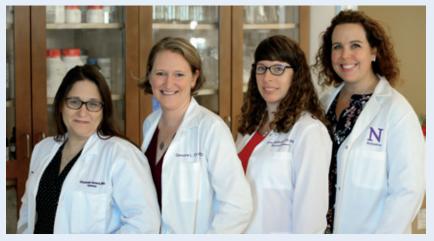
he past 20 years has seen an exponential growth in our understanding of the genetics of epilepsy. A decade ago, about five genes were known to cause the disorder. Today, hundreds of genes associated with epilepsy have been identified, offering a launching pad for developing new treatments not only for children, but also those who have grown up with or begun experiencing seizures sometime during adulthood.

While most epilepsy research has focused on children, little has been conducted on genetic causes in adult patients. In addition to pediatric epilepsy, Gemma Carvill, PhD, assistant professor of Neurology, of Pediatrics, and of Pharmacology, has carved out a unique niche by investigating genetic variants that can cause the disease in adults. To that end, she partners with Elizabeth Gerard, MD, associate professor of Neurology, in directing the Adult Epilepsy Genetics Translational Research Program at Northwestern Memorial Hospital – one of just a few programs of its kind in the country.

An NIH New Innovator Award recipient, Carvill received a \$1.5 million five-year grant in 2018 to support her work. In the area of adult epilepsy, some of the variants identified by the Carvill lab occur in genes of the mTOR pathway, which helps promote cell growth and proliferation. In the June issue of *Brain*, Carvill and colleagues described their discovery of a new method to determine whether individual genetic variants in the epilepsy-associated gene SZT2 cause a neurodevelopmental disorder.

SZT2 variants have been associated with early-onset epilepsy and developmental delays. The gene also plays a role in the mTORC1 signaling pathway. Classifying SZT2 variants as benign or pathogenic has been a challenge due to the large size of SZT2, which contains more than 3,400 amino acids. Using CRISPR-Cas9 genome editing and next-generation sequencing, the team developed a rapid assay to ultimately reclassify a recurrent variant as pathogenic and determine that it is also a founder variant prevalent in individuals of Ashkenazi Jewish ancestry. This finding has implications for including the variant in targeted prenatal testing panels and identifying individuals eligible for more tailored therapeutic approaches.

"While identifying the genetic cause of epilepsy is beneficial, the major impact of this work is when it informs clinical care or leads to precision therapies," says Carvill. "We are always working to take that next step and look for ways to capitalize on discoveries to understand epilepsy, find new treatments, and make a difference in the lives of patients and their families."



From left to right: Elizabeth Gerard, MD; Gemma Carvill, PhD; clinical research associate Irena Bellinski, RN, MPH; and senior genetic counselor Lisa Kinsley, MS, CGC. Photo by Teresa Crawford.

consequences, while also examining which ones were amenable to treatment with this drug."

KCNQ2 variants associated with early onset epilepsy number in the hundreds for this single gene. Many laboratories have limited capacity to study more than a handful of genetic mutations at a time, making progress painfully slow for families pleading for more effective therapies for their children. Fortunately, Feinberg's Department of Pharmacology houses an automated electrophysiology platform for high-throughput drug screening of ion channels - sophisticated equipment typically found in the pharmaceutical industry. In the February 2022 issue of JCI Insight, George and his team published their work using this technology to study the effect of retigabine on a record-breaking 80 variants of KCNQ2. This unprecedented large-scale evaluation revealed that not all KCNQ2 mutations respond the same way to retigabine and that may have implications for identifying which patients will most benefit from the drug and possibly other similarly acting drugs currently in development.

Other KCNQ2 discoveries at Northwestern have catalyzed new directions in developing novel therapies. In a study published in the February 2021 issue of *eLife*, Feinberg investigators for the first time characterized how a KCNQ2 variant affects human neuronal activity

in a "dish." The scientists used patient-derived neuron models originated in the laboratory of Evangelos Kiskinis, PhD, assistant professor of Neurology in the Division



Evangelos Kiskinis, PhD

of Neuromuscular Disease in the Ken and Ruth Davee Department of Neurology, to examine the impact of KCNQ2 mutations. The KCNQ2specific models exhibited electrophysiology activity — a burst-suppression activity model — similar to patterns seen in the electroencephalograms of children with KCNQ2 epilepsy.

This work further inspired Kiskinis, George, and other collaborators to develop customized therapeutic molecules to target KCNQ2. The team's gene therapy approach employs a modified RNA technology called antisense oligonucleotides (ASOs). The



Feinberg's Department of Pharmacology houses an automated electrophysiology platform for high throughput drug screening of ion channels — sophisticated equipment typically found in the pharmaceutical industry.

gene-modulating ability of ASOs offers a viable, more personalized option for treating uncommon diseases like genetic epilepsies. In recent years, RNA therapeutics have proven successful in treating spinal muscular atrophy — a rare neuromuscular disorder that was once universally fatal. Currently, no ASO therapeutic exists for treating pediatric epilepsy, but based on preliminary data from a proof of concept study completed last year, Feinberg investigators are hopeful.

"We demonstrated that we could use our patient-specific stem cell models to screen and validate customized ASO molecules to target specific KCNQ2 mutations," Kiskinis shares about the study's early findings. On the basis of these promising results, the team applied this summer for a three-year \$1.5 million external grant to further advance this innovative work.

"We hope that effective ASO therapies will



Epilepsy researcher and geneticist Jennifer Kearney, PhD, with George.

be able to treat seizures as well as associated comorbidities such as developmental delays," he adds.

Epilepsy researcher and geneticist Jennifer Kearney, PhD, associate professor of Pharmacology, develops animal models of childhood epilepsy for preclinical evaluation of drug compounds. While KCNQ2 remains an important gene of interest, there are many more epilepsy-linked genes under study at Northwestern. In 2014, Kearney's team was the first to describe KCNB1 as a new variant involved in the misfiring of neurons, leading to pediatric epileptic seizures. She is currently focusing on a sodium channel gene called SCN2A.

"SCN2A has a very interesting Goldilocks effect," she explains. "Mutations that enhance the gene's function lead to epilepsy and the ones that inhibit the gene's function result in disorders on the autism spectrum." Kearney is developing a mouse model to better understand the function of SCN2A variants and their impact on early-onset epilepsies.

"What's emerging is the idea that conventional drugs aren't the only therapeutic weapons at our disposal," George says. "I'm excited and optimistic about discovering new molecular and genetically-based therapeutic strategies, such as those using RNA, for treating disorders like epilepsy." أ

SURGICAL CARE FOR SEIZURES

bout one third of patients with epilepsy continue to have seizures despite taking multiple medications. But a significant renaissance in epilepsy surgery in the last decade



Joshua Rosenow, MD

has opened up the possibility of a surgical cure to many patients who were previously not considered surgical candidates, says Joshua Rosenow, MD, director of Functional Neurosurgery. Furthermore, many patients who would have had larger, more invasive procedures can now undergo smaller, minimally invasive procedures with shorter recovery times.

"We can place a small laser fiber directly into the seizure zone through a tiny opening in the skull and destroy it under real-time MRI guidance," explains Rosenow, who is also a professor of Neurosurgery, of Neurology and of Physical Medicine and Rehabilitation. In this scenario, patients typically only stay in the hospital one night and are back to full activity quickly.

In situations where the area of the brain causing seizures cannot be removed without causing disability, surgeons can now implant electrodes in the affected region. These electrodes are connected to a device mounted in the skull that continuously reads the electrical signals from that area. "We can teach the device to recognize the seizure patterns on the EEG, and the device can deliver stimulation in response to these patterns like a 'brain defibrillator,'" Rosenow says. He adds that recent improvements in vagus nerve stimulation devices mean that they can also sense a person's heart rate and deliver extra stimulation if the heart rate increases at the start of a seizure. Finally, not only can responsive neurostimulation therapy significantly reduce seizures, but investigators can acquire valuable insights about a patient's epilepsy from many hours of EEG recordings.

"We see this as the most exciting time for our specialty and look forward to continuing to help people with chronic neurologic conditions live better lives," Rosenow says.



NEXT-LEVEL WEARABLE TECH

Northwestern scientists are developing a wide array of sensing and therapeutic devices that can be easily integrated on and within our bodies.

Written by Emily Ayshford

sticker that diagnoses cystic fibrosis. A wireless sensor that monitors blood flow in the brain. A potentially game-changing implantable device that relieves pain on demand — without the use of drugs.

Each of these wearable and implantable technologies is a leap of innovation on its own, but it's only a fraction of what John Rogers, PhD, has achieved in the past two years.

With an engineer's mindset and input from clinicians and investigators across the medical spectrum at Feinberg, Rogers and his team take complex hospital-room apparatuses — clunky machines, sensors strung with wires — and collapse them into tiny flexible devices that can be placed wirefree on the skin. For implantable devices, they are also re-imagining how such devices can interact with vital organs as needed — whether to pace a heart or numb nerves — then dissolve harmlessly once their job is finished.

As the Louis Simpson and Kimberly Querrey Professor of Materials Science and Engineering, Biomedical Engineering and Neurological Surgery, Rogers has been innovating and refining these sorts of devices for years, ever since he developed the first-ever stretchable transistor in 2006. When he arrived at Northwestern from the University of Illinois Urbana-Champaign in 2016, he was already famous for his innovations in the field but wanted his group "more intimately embedded in a robust, broad medical community," he says.

HELPING THE MOST VULNERABLE PATIENTS: SOFT SENSORS

Rogers's wearable sensors have flipped the idea of planar, rigid electronics that dominate medical technology. His team's devices are soft, stretchy, and flexible, adhering gently to the skin and moving easily with the body.

In 2019, his team developed these soft sensors to monitor babies in the neonatal intensive care unit, measuring their vital signs without the need for wires. Developed in collaboration with Amy Paller, MD, the chair and Walter J. Hamlin Professor of Dermatology and other collaborators at Ann & Robert H. Lurie Children's Hospital of Chicago, the sensors were a breakthrough for premature babies and their parents, who often dealt with tangles of wires that prevented cuddling and physical bonding. The study was published in the journal *Science*.

"If you consider what patient population would be most positively impacted by a soft, wireless medical technology, you think about vulnerable patients, where premature babies come in at the top of the list," Rogers says. "As a result, we prioritized efforts to gear our technology around the needs of those patients, given the profound potential benefits."

That sort of motivation has continued to push innovation in his lab. More recently, the team developed a novel wireless device about the size of a Band-Aid that improves realtime monitoring of blood flow and oxygenation in the brain for neonatal and pediatric patients. This sort of monitoring helps ensure proper neurodevelopment, especially for those in intensive care units who require constant care and observation. The work was published in *Proceedings of the National Academy of Sciences (PNAS)*.

They've also developed new ways to test newborns for potential diseases. All newborns are screened for cystic fibrosis, the most-common life-shortening genetic disease. Currently, the screening involves blood through a heel prick, and if that screen is abnormal, pediatricians order a sweat test. During the sweat test, the baby must wear a hard, wrist-strapped device for up to 30 minutes to collect sweat, separately analyzed using a benchtop apparatus, all conducted by trained medical personnel. ►



Using Wearables to Change AFib Treatment Guidelines

arly in his career, cardiac electro physiologist Rod Passman, MD, had a patient with an abnormal heartbeat — a condition called atrial fibrillation (AFib) — that was well controlled with medications. Guidelines then (and now) say that patients with AFib should be on blood thinners continuously because they are at increased risk for stroke, regardless of how much time patients spend in AFib.

But in this case, the patient suffered from an intracranial bleed — worsened by the blood thinner. The bleed caused lasting physical and mental damage. "It ruined his life," says Passman, director of the Center for Arrhythmia Research and the Jules J. Reingold Professor of Electrophysiology in the Department of Medicine. "It was a disaster from everyone's perspective."

Passman considered whether everyone who had abnormal heart rhythms needed to be on such medication, especially when newer blood thinners were put on the market that only took an hour or two to thin the blood and technologies that could continuously and remotely monitor the heart were becoming available.

Through a \$10,000 philanthropic gift from a donor, Passman was able to work with a company that developed an implantable cardiac monitor to develop a pilot study which was published in *Journal of Cardiac Electrophysiology*. The idea was to only put patients on blood thinners for a few weeks only in response to a prolonged episode of AFib. And while the pilot study showed the concept was feasible, the chip itself was expensive and therefore not scalable to the tens of millions of people around the world who suffer from this disorder.

When wearable devices like the Apple Watch came to the market, Passman saw a chance to monitor heart rhythms in a wider range of patients and create a new era of personalized medicine for stroke prevention. While it is estimated that between 2.5 and 5 million Americans are living with AFib today, that number is estimated to grow to 12.1 million by 2030.

Now, Northwestern and Johns Hopkins University have been awarded a \$37 million grant from the National Heart, Lung, and Blood Institute to fund a seven-year trial, called the Rhythm Evaluation for AntiCoagulaTion (REACT-AF) trial that will incorporate the use of an app on Apple Watch to monitor AFib to attempt to reduce patients' continuous and lifelong reliance on blood-thinning medication.

In the trial, patients will wear an Apple Watch, which can monitor heart activity and notify patients when they're entering an episode. When notified, patients will take blood-thinning



medication for a few weeks during the highrisk window for stroke and can discontinue if they do not have another episode. The trial will begin enrolling patients in the spring of 2023. Partnering institutions include Johns Hopkins, Stanford University, and University of California at San Francisco.

Passman hopes that if the study shows this strategy is safe, it will change the way the condition is managed. "To have a tragic patient experience and use that to develop a pilot study and ultimately take the idea to clinical trial has been an amazingly rewarding experience," Passman says. "As clinicians, we see gaps in treatment every day. This shows there is always room in medicine for questioning and challenging the dogma." 66

We are aiming not only to reproduce the measurements that form the standard of care today, but also to pioneer new classes of sensors, all under the umbrella of advanced techniques in data analytics.

- John Rogers, PhD

Rogers and his collaborators, including Susanna McColley, MD, professor of Pediatrics in the Division of Pulmonary and Sleep Medicine, a cystic fibrosis expert, and a Lurie Children's and Northwestern Medicine pediatric pulmonologist, developed a novel skin-mounted sticker that captures sweat in microfluidic channels that pass to microscale reservoirs that change color to provide an accurate, easy-to-read diagnosis of cystic fibrosis within minutes. Unlike standard testing protocols, the sticker is easy to use, comfortable on the skin and low in cost, suitable for testing in remote or resource constrained areas of the world. The study was published in *Science Translational Medicine*.

Funding from the Gates Foundation led the researchers to also consider the entire maternal-fetal cycle, and soon the team had tackled the cumbersome fetal-monitoring belts that pregnant women must wear in the hospital and during labor. With Rogers's system, pregnant women wear three small, soft, flexible wireless sensors that measure the mother's and baby's vital signs simultaneously, as well as provide new data, including information about the mother's physical movements and laboring positions, that is not collected with current technology. The sensors were developed with Rogers's frequent collaborator Shuai "Steve" Xu, MD, MSc, the Ruth K. Freinkel, MD, Professor and assistant professor of Dermatology and of Pediatrics in the Division Dermatology. The work, which was published in the Proceedings of the National Academy of Sciences, included data not only from Prentice Women's Hospital but also from nearly 500 women throughout the intrapartum period in health clinics in Zambia, demonstrating the ability to operate cost-effectively in environments with limited hospital infrastructure. Xu and Rogers also collaborated





Skin-mounted and implanted devices monitor body temperature, oxygen levels, respiration, muscle tone, physical activity, and the heart's electrical activity.

on a wearable sensor that tracks children's suffering with eczema, and adults with itch symptoms, publishing the study in *Science Advances*.

The possibilities with these wearable sensors are seemingly endless. "Now that we have a foothold in this area, we're developing other kinds of sensors we can drop into these same basic soft, wireless platforms," he says. "We are aiming not only to reproduce the measurements that form the standard of care today, but also to pioneer new classes of sensors, all under the umbrella of advanced techniques in data analytics. There's a tremendous amount of opportunity in that direction."

A TEMPORARY, DISSOLVING PACEMAKER

As Rogers and his team had conversations with Feinberg investigators, they began to understand various clinical uses of devices that are implanted into the body to perform a temporary function that addresses a transient patient need, and then are surgically extracted. Cardiac surgeons, for example, asked if his team could develop an alternative to the wired, temporary pacemakers used with patients during recovery following certain types of cardiac surgeries.

The idea for a wireless, bioresorbable electronics technology had intrigued his team for years. In fact, some years ago they developed a collection of materials and



manufacturing techniques for integrated circuits that can dissolve in water, in the context of a Defense Advanced Research Projects Agency funded project in transient electronics for military purposes. They were interested in possibilities for adapting that technology for patient care. In 2022, they introduced an implantable, wireless pacemaker that is integrated into a coordinated network of four soft, flexible, wireless, wearable sensors and control units placed around the upper body. The work was published in *Science*.

This wireless network of skin-mounted and implanted devices, developed in a collaboration with Rishi Arora, MD, professor, and Anna Pfenniger, MD, PhD, assistant professor, of Medicine in the Division of Cardiology, and Bradley Knight, MD, the Chester C. and Deborah M. Cooley Distinguished Professor of Cardiology, monitors body temperature, oxygen levels, respiration, muscle tone, physical activity, and the heart's electrical activity.

The system then uses algorithms to analyze this combined activity in order to autonomously detect abnormal cardiac rhythms and decide when to pace the heart and at what rate. All this information is streamed to a smartphone or tablet, so physicians can remotely monitor their patients.

"Joining these two areas — wireless sensors on the skin and bioresorbable implants in the body — could potentially allow patients to be released from the hospital earlier following a cardiac surgery," Rogers says.

AN IMPLANTABLE DEVICE TO TREAT PAIN

Perhaps the most exciting of Rogers's recent work, published in *Science*, is a new dissolving implantable device that relieves pain on demand without drugs. The biocompatible, water-soluble device works by softly wrapping around nerves to deliver precise, targeted cooling, which numbs nerves and blocks pain signals to the brain.

An external pump enables the user to remotely activate the device and then increase or decrease its cooling intensity, precisely controlled through feedback from an integrated digital temperature sensor at the site of the nerve. After the device is no longer needed, it naturally absorbs into the body — bypassing the need for surgical extraction.

Clinicians believe the device will be most valuable for patients who undergo routine surgeries or even amputations that commonly require post-operative medications. Surgeons could implant the device during the procedure to help manage the patient's post-operative pain.

"Although opioids are extremely effective, they also are extremely addictive," Rogers says. "As engineers, we were motivated by the idea of treating pain without drugs — in ways that can be turned on and off instantly, with user control over the intensity of relief."

CREATING A CLOSED LOOP OF SENSING AND THERAPY

As for what devices Rogers will develop next — the future is wide open. His team seems to be perpetually in a state of being simultaneously maxed out with existing projects and looking for new ones, working with Feinberg collaborators to identify the most important unmet needs that could be addressed with new technology.

They're also regularly innovating on their wireless sensor platforms, adding in biochemical sensors that could continuously track cortisol levels or inflammatory markers, as examples. They are also hoping to use machine learning to discover new insights in the vast streams of data that their devices record.

"An important goal is to continue to work on systems that combine both sensing and therapeutics — pulling together multiple different technologies that are all wirelessly synchronized to both sense and treat conditions in a closed loop operation," Rogers says. *

Amanda Morris, Kristin Samuelson, and Melissa Rohman contributed to this story.

A dissolving implantable device that relieves pain without drugs.

Surgeons could implant the medicating device during the procedure to help manage the patient's post-operative pain.

The new chair of the Department of Psychiatry and Behavioral Sciences, Sachin Patel, MD, PhD, brings a unique blend of clinical psychiatry practice and neuroscience research. achin Patel, MD, PhD, has been interested in the human brain and "understanding why people behave the way they do" since he was a high school student in Irvine, California, where his family moved from the Netherlands when he was 11 years old.

Patel went on to study biological psychology at the University of California-Santa Barbara and by the time he was headed to the Medical College of Wisconsin, he says, "I knew I was going to end up in psychiatry or at least something very closely related."

Psychiatry, with its focus on the whole person, eventually won Patel's heart, but his scientific training and research into the neurobiological basis of behavior have always been a cornerstone of his career.

"I'm a neuroscientist by training," Patel explains. "I am interested in using research to understand the human brain and how it works and doesn't work — at the individual level."

Patel completed his residency in clinical psychiatry and translational neuroscience at Vanderbilt University. Later, he joined the faculty, earning tenure and becoming director of the university's Division of General Psychiatry. His clinical activity was focused on the treatment of substance use disorders and co-occurring mental illnesses in inpatient and residential treatment facilities.

After more than a decade at Vanderbilt, earlier this year, Patel joined Feinberg as the chair and Lizzie Gilman Professor of Psychiatry and Behavioral Sciences and psychiatrist-in-chief at Northwestern Memorial Hospital's Norman and Ida Stone Institute of Psychiatry. His wife and two teenage children joined him at their new home in Chicago earlier this summer.

This new chapter feels exhilarating for multiple reasons, he says. "For one, I was excited by the opportunity to help sculpt the training of medical students and residents — being in a position to impact many generations of psychiatrists is something I've always wanted to achieve."

Patel's new role will also give him a platform to help more people appreciate mental illness and addiction as conditions on the same plane as physical illnesses. ►



Patel with trainees and colleagues in the Department of Psychiatry and Behavioral Sciences.

"I want to get people to understand that better treatments for patients will be unlocked when we understand the brain and acknowledge that mental illnesses are elements of pathological processes within neural circuits," he says.

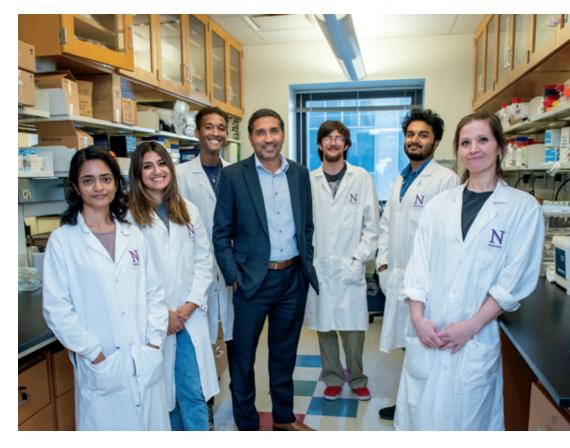
THE IMPACT OF STRESS

Much of Patel's research involves environmental stress and how it can affect brain structure and function. This includes not just post-traumatic stress disorder (PTSD, in which severe stress is a causative agent), but other forms of mental illness exacerbated by stress.

"Patients with substance use disorders can relapse after long periods of abstinence when they're exposed to stress; patients with psychotic disorders can exhibit exacerbations of symptoms under stress; and anxiety disorders and depression get worse when exposed to stress," he says. "Understanding how stress impacts the brain could have broad implications for understanding a lot of mental health disorders. So, I really have focused on that for the vast majority of my career."

In conjunction with studying the impact stress has on the brain, Patel has, for decades, been exploring the involvement of the brain's cannabinoid systems in mental illness and, more specifically, the potential for cannabinoid-based approaches as medicinal treatments.

Cannabinoids naturally produced in the brain are analogous to opioid peptides such as endorphins, he explains. And a greater understanding of the role that these endogenously produced cannabinoids play in mitigating the adverse effects of stress, he believes, may lead to new treatments for substance use disorder and other commonly diagnosed



mental illnesses, such as PTSD, anxiety disorders, and major depression.

When Patel and his colleagues began studying the therapeutic potential of endogenously produced cannabinoids over two decades ago, the therapeutic potential of this system "was not really on anyone's radar," he says.

"We are now at a point where our deep biological understanding of the brain's cannabinoid neurotransmitter systems has resulted in a number of clinical trials using new cannabinoid-based drugs for a variety of psychiatric disorders," he adds.

A BRIGHT FUTURE

Patel is excited to join Northwestern at a time when nationwide interest in psychiatry programs is at an all-time high. "Right now, we have more people than ever going into psychiatry," he says. "The number of applicants is going up. They have been going up for years."

He also looks forward to opportunities for collaboration between psychiatry and other departments across the medical school, building bridges around common goals. To that end, he will lead the new Center for Psychiatric Neuroscience, which is aimed at bringing together basic translational neuroscientists and psychiatrists to study the physiological mechanisms that underlie mental illness. Together, investigators will examine the mechanisms by which current therapeutics work as well as uncover new molecular targets for therapeutic intervention.

"There's a real need to dissect the brain, to understand how it works at a very fundamental level. How does the brain's electrochemical structure result in psychiatrically important constructs like emotion, cognition, and memory?" he says. "A lot of those things are really fundamentally still unknown, and unless we understand them, it's going to be very difficult to understand how those processes get dysregulated and result in disorders like PTSD and depression."

He adds that "working with clinicians and clinical neuroscientists to address these questions in a comprehensive way is really one of the goals of the center."

Another focus for Patel is addressing



"One of the biggest challenges is really the massive national need for mental health care. The need has always been there, but it has become much more acute during the pandemic."

- Sachin Patel, MD, PhD

a larger societal issue: the mental health crisis in the U.S.

"One of the biggest challenges is really the massive national need for mental health care," Patel says. "The need has always been there, but it has become much more acute during the pandemic. People are now much more likely to be talking about these unmet needs. We need to uncover ways we can better meet them."

Patel is encouraged by the investment Northwestern Medicine has already made in ensuring that behavioral health is incorporated more broadly into all areas of healthcare.

"Moving mental health care into primary care settings, increasing access at any point of entry within the health system — whether it's the emergency room or pediatric offices or internal medicine offices — and creating collaborative care models are all great ways to increase access for behavioral health services to people outside of psychiatry departments, per se, and Northwestern Medicine has done that, providing care to folks where they can get it," he says.

While he is heartened by what he sees as a trend toward more open communication

around mental illness, Patel believes that more can be done to help people understand that mental health and addiction are two sides of the same coin and should be treated in a similar manner.

"There shouldn't be a distinction between the two," he says. "We need to talk about these things more openly."

Between broadening the dialogue about mental health, developing new clinical programs that address treatment needs in the community, and increasing Feinberg's research portfolio, Patel has a lot of plans for his new role. Fortunately, he says, all the elements are already in place to make his goals achievable.

"I'm coming into a strong department that has excellent leadership and has made substantial advances," he says. "I view my responsibility as utilizing that growth and capitalizing on investments that have already been made as we enter the department's next phase. No matter where a department is, there is always the next chapter that is bigger and better." \diamond 11:05 4

=

HI PATTY

M

We noticed that your heart rate has dropped a few times the past few days.

While this is not something to be immediately concerned about, Dr. Mutharasan would like to see you and has the following available appointments in the next few days...



"I hope this will improve patients' feelings of being connected to their health provider."

> KANNAN MUTHARASAN, '03 MD

THE CLINIC OF THE FUTURE

Northwestern Medicine is launching a new digital platform to ensure better care and more face time with patients.

t may sound like science fiction, but a new "Clinic of the Future" is about to become a reality – coming soon to Northwestern Medicine Palos Hospital.

Opening in early 2023 at the Palos branch of the Bluhm Cardiovascular Institute, this unique, patient-focused platform will allow providers to spend less time processing medical information and more time addressing the needs of their patients. Powered by unobtrusive digital technology, the clinic will automate the processes of retrieving and storing patient data.

As it stands now, providers spend massive amounts of time inputting information into the electronic health record (EHR) — chronicling medical histories, events between appointments, medications and responses to therapies, images, diagnoses, test results, treatment plans, and more.

Taking that burden off physicians would be monumental, according to Kannan Mutharasan, 'o₃ MD, associate professor of Medicine in the Division of Cardiology, and physician champion of this transformative initiative.

"Physicians and providers typically spend 80 percent of the patient visit gathering data and 20 percent of the visit talking about what they are going to do about it. Now, we hope to flip those ratios," he says. A general cardiologist for 20 years, Mutharasan became excited about the potential for change as cloud-based computing skyrocketed more than a decade ago. And yet, years later, paper and CD records still continue to flood him and his colleagues.

"This is just from today," he says, holding up a four-inch-thick pile.

He is optimistic, however, that the Clinic of the Future will change the status quo.

"I hope this will improve patients' feelings of being connected to their health provider," he says. "A big part of this is going to be getting some of the unnecessary distractions of the clinical environment out of the way so we can increase meaningful interactions with our patients."

ENHANCING THE PATIENT-PHYSICIAN INTERACTION

The Clinic of the Future was born out of Northwestern Medicine's *Patients First* initiative. Experts in artificial intelligence (AI), communications, and patient care came together and envisioned a better hospital experience.

Danny Sama, MBA, vice president of Information Services and chief digital executive at Northwestern Medicine, was among the



key coordinators. He explains that the vision is for technology to be embedded everywhere in the Clinic of the Future, yet the tech will be mostly invisible.

A prime example is the way patient data will be collected. AI "conversational intelligence" combined with ambient microphones in patient rooms could take dictation, pick up key terms, and automatically generate visit summaries and diagnostic code choices, as well as other documentation, and put this data into the electronic record — effectively taking documentation responsibilities away from providers. A smart device would also take patients' vital signs and record them directly in the EHR.

"I think some physicians will be stunned when they have to enter only a few keystrokes >





"I think some physicians will be stunned when they have to enter only a few keystrokes to accomplish everything they want to for an entire appointment." DANNY SAMA, MBA

to accomplish everything they want to for an entire appointment," Sama says.

All the more time for patient-physician interaction — which, too, will be userfriendly. A large wall monitor will show CT scans, graphs showing data over time, or other relevant information, so physicians can explain conditions, treatment plans, or responses to medications, with their patients benefiting from the visual aids.

Ultimately, the Clinic of the Future is designed to help patients get the most out of their visit, Sama says. Even before they enter the clinic, a Northwestern Medicine mobile app will prompt them to think about what they want to discuss and relay it to providers. The app will also ask if they want a family member or loved one to join the appointment; if they do, the participant can attend virtually.

When patients arrive at the clinic, they will get a notification to check in through their phone, then get updates about when the physician will enter their room. Nonetheless, familiar experiences will remain: Nurses will still be present to comfort and assess patients before physicians enter the room.

Not every digital capability described above will be operational when the clinic opens in early 2023. But several smart options will be available for patients to sample. The experimental two-room space will provide the opportunity to try automated functions that might be most beneficial and introduce other digital functions later as they evolve.

A tech-smart space is also planned later next year at Northwestern Medicine's downtown campus for patients with heart disorders.

The Bluhm Cardiovascular Institute was eager to embrace the Clinic of the Future because cardiac care involves gathering substantial information on heart and vasculature function multiple times over years and years. Wearable technology that tracks patients' vitals such as heart rate and blood pressure is becoming common in this "high-touch, hightech" specialty, making cardiology well-suited for piloting the new concept. However, patients don't need wearable technology to participate.

A NATIONAL LEADER

Northwestern Medicine has significantly built up its cloud infrastructure since 2021, empowering rapid adoption of automation and allowing ideas such as the Clinic of the Future to come to life.

Made possible by the generous support of the St. George Corporation, bolstered by a partnership between Northwestern Medicine and Microsoft earlier this year, the Clinic of the Future will enable Northwestern Medicine to lead healthcare's digital transformation in a meaningful way. Elsewhere around the country where digital is envisioned to mesh with healthcare, many ideas remain in the incubation stage.

Efficiency of the clinic will be evaluated to validate that it is actually delivering on its promise. Evidence such as physicians' time spent on the EHR and patient feedback from satisfaction surveys will be gathered. The goal is an 80/20 ratio of patient time to processing time, but "even a 50-50 split would be huge," according to Sama.

"Patients don't come here for our electronic health record," he says. "They come here for our providers." *



Watch this video to see the potential of the Clinic of the Future. **vimeo.com/686077939**

Alumni President's Message

ALUMNI



Standing on the Shoulders of Giants

A letter from Edward S. Kim, '92 BS, '96 MD (HPME)

"A leader takes people where they want to go. A great leader takes people where they don't necessarily want to go, but ought to be." – Rosalynn Carter

"If one is lucky, a solitary fantasy can totally transform one million realities." – Maya Angelou

"Leaders aren't born, they are made. And they are made just like anything else, through hard work. And that's the price we'll have to pay to achieve that goal, or any goal." – Vince Lombardi

These are three of my favorite leadership quotes. They are all similar, but different in their own way. Throughout my career, I have had the privilege of working with some extraordinary leaders: each one different, but similar. In this issue of *Northwestern Medicine*, I want to recognize some great leaders who have served on the Feinberg School of Medicine Medical Alumni Association Board (MAAB). These are folks who influenced me to join the board, to serve, and continue the work "to take a solitary fantasy and transform one million realities."

I am particularly grateful to Jim Kelly, who was MAAB president from 2017 to 2019. Jim recruited me to the board. He was also very active in recreating the board and adding dimensions that include the Business of Medicine subcommittee. Jim and his wife Christine are proud Wildcats who really helped transform the mission of the board. Another key leader is Bruce Scharschmidt, board president from 2015 to 2017. Bruce was instrumental in promoting scholarships for medical students. He and his wife Peggy are big football fans and made sure medical students were able to attend a game. I remember having several meetings with Bruce to hear about his experiences and his distinguished career in medicine and biotech.

Building on the solid foundation and legacy of the MAAB members and leaders who came before me, we currently have a 52-member board actively working together on multiple committees: Engagement, Mentoring, Women in Medicine, and Inclusion and Allyship.

Our alumni association is stronger than ever, based on the work of our board founders, past board members, and an exceptional group of current members. Tremendous leaders, including Ginny Darakjian, ML Farrell ,and now, Babette Henderson, have been essential Feinberg staff partners, guiding our work.

Thank you for all that you have done to help us to get to where we "ought to be."

For more information on sharing your experiences while at Northwestern, getting involved as a MAAB board or subcommittee member, or willingness to host an event in your area, please email us at medalum@northwestern.edu.

MAAB BOARD PRESIDENTS

We thank every board president for their service and their advocacy.

Walter Doren	(1991-1993)
David Sanderson	(1993-1995)
Kenneth Viste, Jr.	(1995-1997)
Richard Heller	(1997-1999)
Howard Traisman	(1999-2001)
Andrew Bunta	(2001-2003)
Suzan Rayner	(2003-2005)
Walter Huurman	(2005-2007)
Bonnie Typlin	(2007-2009)
Douglas Carr	(2009-2011)
Jimmy Hill	(2011-2013)
David Winchester	(2013-2015)
Bruce Scharschmid	dt (2015-2017)
James Kelly	(2017-2019)
Rishindra Reddy	(2019-2021)
Nupur Ghoshal	(2023-2025) President-Designate

ALUMNI **Profile**

BIOTECH BOSS

Sheila Gujrathi, '96 MD, is opening doors for people with diverse perspectives in biotech.

s chief medical officer of Receptos, Inc., Sheila Gujrathi, '96 MD, shepherded Zeposia®, an immune systemmodulating drug, through clinical research trials and on its way to becoming a U.S. Food and Drug Administration-approved therapeutic for the treatment of multiple sclerosis and ulcerative colitis. Now, she is paving the way for others from diverse backgrounds to take on leadership roles in biotech.

The success of Zeposia®, which is now owned and made by Celgene Corporation and is part of Bristol Myers Squibb, helped catapult Guirathi's career in the biotech field. She later co-founded and became the chief executive officer of Gossamer Bio, a clinical-stage biopharmaceutical company working on therapies in immunology, inflammation, and oncology. She now chairs the boards of directors of three companies, serves as a venture advisor to OrbiMed, and is board director, strategic advisor, and co-founder of multiple other companies. These leadership roles make her one of the few women or underrepresented minorities to hold such high-level positions in the field. She is poised to make a permanent mark in the biotech industry as a role model, business executive, and drug developer.

"I have enjoyed a fulfilling career," Gujrathi says. "The companies I work with have excellent chances of getting life-changing drugs approved for patients."

UNCONVENTIONAL PATH

Gujrathi is a graduate of the seven-year honors program in medical education at Northwestern. She loved the program's flexibility and pursued a challenging undergraduate degree in biomedical engineering while working toward a medical degree from Feinberg.



"Those engineering days honed my analytical and problem-solving skills," she says.

At Feinberg, she fell in love with immunology. She was fascinated by the blossoming understanding of the immune system and planned a career in academic medicine researching therapies for autoimmune and other diseases. However, her path would take a few turns along the way.

She took a year off between her second and third years in the program. During that time, she lived in an ashram in the south of India. Taking time for spiritual study helped her reflect on life's larger purpose and commit to living a life of service, she says. It also helped her develop values of respect, humility, and community.

"Establishing a spiritual foundation has been fundamental for my life and career," Gujrathi says.

After finishing the program at Northwestern, she completed an internal medicine residency at Brigham and Women's Hospital in 1996. Then, she completed a clinical fellowship year in allergy/immunology at the University of California San Francisco and Stanford. Exposure to biotech and pharmaceutical industry careers during her training made her reconsider her career path.

"I decided to leave academic and clinical

medicine and ended up finding my way to biotech," she says.

Gujrathi first worked as a management consultant in the healthcare practice at the consulting firm McKinsey & Company. That role gave her business training and helped her decide to pursue a career in biotech.

"That planted the seed for me that I would love to be an entrepreneur and start my own company one day," she says.

To gain experience in her field and learn more about the drug approval process, she worked at biotech company Genentech and then at global pharmaceutical company Bristol Myers Squibb. She says she benefited from learning from experts at both companies. She next took on the chief medical officer role at Receptos and her first oversight position as a director of the Board of Directors of Ambrx and Five Prime Therapeutics.

Gujrathi is poised to make a permanent mark in the biotech industry as a role model, business executive, and drug developer.

In 2017, Gujrathi co-founded Gossamer Bio and later became its chief executive officer. By the time she left the company in 2020, it had \$555 million in assets, two promising drugs in phase 2 trials, and a discovery pipeline.

"Founding and running a successful biotech company is challenging on its own, but especially when doing it as a woman of color." she says. "That is no small feat."

OPENING DOORS

Since then, Gujrathi has served on several boards for biotech and pharmaceutical companies, including Turning Point Therapeutics, Janux Therapeutics, ADARx Pharmaceuticals, ImmPACT Bio, and Ventyx Biosciences. In those roles, she is helping guide the companies and their leaders and protecting the interests of shareholders. She is also helping to increase representation in the biotech industry. She notes that only 2 to 7 percent of the chairs of biotech boards are currently women.

"I am going to keep pushing boundaries for greater representation by women," she says. As a clinician, she is also proud of her role in improving the lives of patients and their families, pointing to the growing understanding of the immune system's role in transplant medicine, autoimmune and inflammatory diseases, cancer, cardiovascular diseases, and infectious diseases.

"We have made great strides in targeting very important immune mechanisms for the treatment of autoimmune disease and cancer," she says. "We are just beginning to elucidate further how to dampen or upregulate the immune system."

In addition to her professional roles, she is a busy mother of two teenagers. She is also the wife of an emergency physician who leads three emergency departments in the San Diego area. She enjoys reading, dancing, exercising, traveling, taking in shows, and spending time with family and friends during her downtime.

"Our goal is to live life to the fullest," she says.

Gujrathi advises both young and midcareer physicians to take time to learn what they are passionate about and what they enjoy doing every day and build a career around that. For some, that may be direct patient care or research. She points out that physicians' training also prepares them for many other fields beyond medicine.

"Find what drives you and makes you excited every day," she says.

Gujrathi is also a strong advocate for women and people from diverse backgrounds in her field. She noted that industry and academia can be daunting for people from underrepresented groups. However, she says it is vital for them to know they belong in the room and at the table.

"There are more doors open than ever before," she says. "We need more people coming forward with diverse perspectives and stepping through these doors. Representation matters because it is critical for real change to occur." *

CAREER HIGHLIGHTS

1988-1992

Completed an undergraduate degree in biomedical engineering from Northwestern's McCormick School of Engineering with highest distinction. Tau Beta Pi engineering honor society.

1991-1996

Earned her medical degree from Feinberg School of Medicine. Alpha Omega Alpha Honor medical society. Received the James Patten Scholarship and Jonathan Philip Reder Award.

1996-2000

Completed a residency in internal medicine at Harvard Medical School and Brigham and Women's Hospital.

1998-1999

Pursued a fellowship in immunology at Stanford University School of Medicine and the University of California, San Francisco.

1999-2002

Worked as a management consultant in healthcare for McKinsey & Company.

1999-2008

Provided medical services as a physician in the urgent care setting for San Francisco's homeless and uninsured population in the city's public health system.

2002-2008

Served as group medical director for immunology clinical development and led the Avastin Franchise Team at Genentech.

2008-2011

Served as vice president of Global Clinical Development and Immunology Therapeutic Area Head.

2011-2015

Worked as chief medical officer at Receptos, Inc.

2016-2020

Co-founded and later served as chief executive officer of Gossamer Bio.

2017-PRESENT

Chaired the boards of directors at several companies, including Turning Point Therapeutics, ADARx Pharmaceuticals, ImmPACT Bio, and Ventyx Biosciences.

PROGRESS NOTES

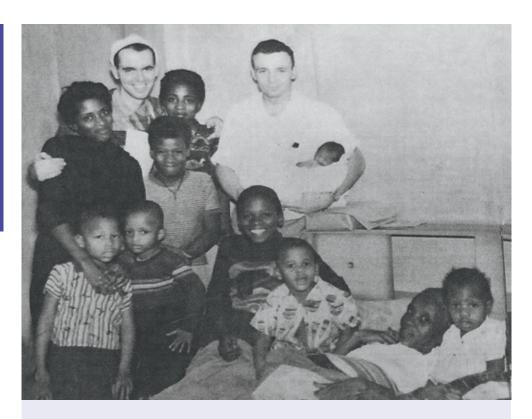
We'd love to hear from you! Please share your recent news, accomplishments, and important milestones with us.

Send your updates and high-resolution photos to **medcommunications@northwestern.edu**. We will publish them in an upcoming issue of the magazine.

1970s

Howard D. Weiss, '68, '71 MD, has authored a digital book titled Parkinson Primer: 'Pearls' to Help Health Care Professionals Provide Better Care for People with Parkinson's Disease. Weiss has been distributing the book in PDF format without charge to general neurologists, internists, nurse practitioners, and other medical professionals to help improve the care of people with Parkinson's disease. The book has received critical acclaim from healthcare professionals in the U.S. and several other countries. Now retired, Weiss serves as adjunct associate professor of Neurology at Johns Hopkins School of Medicine. 1

Leo A. Gordon, '73 MD, presented his ongoing research into presidential illnesses (an interest that began during his medical student surgery rotation at Northwestern) to the Cedars-Sinai Medical Center Alumni



Maynard D. Poland, '61 MD, recently shared this photo from his medical school years. "Seniors rotated through the Chicago Maternity Center in two-student teams for two weeks and delivered carefully-screened multiparous women in their homes," he wrote. Here he is (shown holding a newborn) after one of his deliveries.

Society in Los Angeles. Gordon's presentations have become legendary in the Los Angeles community. "Hail to the Chief Complaint! — A Brief History of Presidential Illnesses" appeals to medical, historical, political, and alumni groups. Gordon enlivens each specific presidential illness by relating the effect of that illness on the political and legislative processes in motion at the time of the illness. (© 2

Jerome C. Cohen, '77, '79 *MD*, '82 *GME*, was recently elected vice president of the Medical Society of the State of New York (MSSNY). Cohen previously served as both speaker and trustee of MSSNY. He has served as a senior attending gastroenterologist for Bassett Healthcare Network since 2015 and is clinical assistant professor of Medicine at the Cooperstown campus of Columbia University Vagelos College of Physicians and Surgeons. A bioterrorism first responder volunteer, Cohen previously served as president of the Broome County Medical Society and as past chair of the American Medical Association's Council on Constitution and Bylaws. Cohen's wife, Elaine V. Drelich, '80 DDS, is also a Northwestern alumna and a graduate of the Northwestern University Dental School. 10

Scott Sarran, '77, '79 MD, '92 MBA, was appointed to the Medicare Payment Advisory Commission by the U.S. Government Accountability Office. Sarran, a geriatrician, is chief medical officer at MoreCare. 10 4

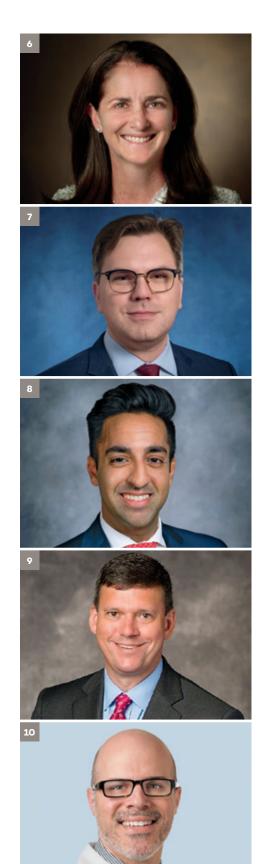
1990s

Sandra Y. Lin, '94 MD, began her position this August as professor and chair of the Division of Otolaryngology, Head and Neck Surgery at the University of Wisconsin School of Medicine and Public Health. Prior to her move to the University of Wisconsin, Lin spent 20 years in the Johns Hopkins Department of Otolaryngology, where she held multiple leadership roles, such as senior vice chair of Clinical Operations, and director of Diversity, Equity and Inclusion. She is excited to be living in Madison and to be returning to the Midwest.

Kelly M. Choi, '94, '98 MD, '02 GME, has been appointed senior vice president of marketing and product management for Element Biosciences Inc. Choi has 20 years SANDRA Y. LIN, '94 MD, BEGAN HER POSITION THIS AUGUST AS PROFESSOR AND CHAIR OF THE DIVISION OF OTOLARYNGOLOGY, HEAD AND NECK SURGERY AT THE UNIVERSITY OF WISCONSIN SCHOOL OF MEDICINE AND PUBLIC HEALTH.



ALUMNI



of commercial leadership experience in product strategy and execution, strategic partnerships, business development, client relations, and operations management for healthcare technology companies. Choi previously served as chief commercial officer at Onegevity of Thorne HealthTech. 10 5

Kris Rehm, '98 *MD*, has been named president-elect of the Society of Hospital Medicine. Rehm is professor of Clinical Pediatrics and vice chair in the Department of Pediatrics at Vanderbilt University Medical Center and the first pediatrician to be named president-elect of the Society of Hospital Medicine. She also serves as director of Outreach Medicine for the Department of Pediatrics and as associate chief medical officer for Children's Services for the Vanderbilt Medical Group. 10 6

KRIS REHM, '98 MD, HAS BEEN NAMED PRESIDENT-ELECT OF THE SOCIETY OF HOSPITAL MEDICINE. REHM IS PROFESSOR OF CLINICAL PEDIATRICS AND VICE CHAIR IN THE DEPARTMENT **OF PEDIATRICS AT** VANDERBILT UNIVERSITY **MEDICAL CENTER AND** THE FIRST PEDIATRICIAN **TO BE NAMED PRESIDENT-ELECT OF THE SOCIETY OF HOSPITAL MEDICINE.**

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 passed away. All dates are in 2022.

ALUMNI

Richard S. Youngs, '45 DDS July 6 Adrian, Mi

Althea Petritz, CERT, '46 June 15 TRAVERSE CITY, MI

James A. Boren, '48 MD July 6 MARINETTE, WI **Loyola Schell, '50 BSDH** May 25 MANHATTAN, KS

William H. Wade, '51 MD July 2 EL PASO, TX

Ledyard E. Ross, '53 DDS June 28 GREENVILLE, NC

Herbert L. Ennis, '54 MS, '57 PhD July 8 LIVINGSTON, NJ D. Keith Whatcott, '55 DDS June 1 PROVO, UT

John B. Roberts, '56 MD June 9 Социмвиз, он

Joan K. Short, '56 MD May 29 WILMINGTON, DE

Richard P. Foth, '56 MD May 16 ST. CHARLES, IL

John Lee Smith, '57 MS June 10 DALLAS, TX

Kenrad E. Nelson, '58 MD April 21 BALTIMORE, MD

2010s

Adrienne H. Long, '15 PhD, '16 MD, received the 2022 American Association for Cancer Research — Conquer Cancer, the ASCO Foundation, Young Investigator Award for Translational Cancer Research.

Brian J. Miller; '11 MD, MBA, MPH, joined the American Enterprise Institute as a nonresident fellow in June 2022. Miller serves as an advisor to members of Congress and their staff and lives in Washington, D.C. He remains a practicing hospitalist at Johns Hopkins Hospital and on the medical school faculty. 107

2020s

Anil R. Wadhwani, '11, '19 PhD, '20 MD, was named to the board of directors for the National Resident Matching Program, one

of the main organizations that helps to place medical students and residency applicants into residency and fellowship training positions. Wadhwani is a neurology resident at the Hospital of the University of Pennsylvania. 10 8

MS/GME/PhD

Karl Y. Bilimoria, '98, '98 MS, '10 GME, is leaving Northwestern Medicine after 20 years to be the chair of Surgery at Indiana University. He will be moving his research program there as well.

Christopher M. Gonzalez, MD, 'oo GME,

'o6 MBA, has been awarded the Barringer Medal from the American Association of Genitourinary Surgeons and was recently named a trustee on the American Board of Urology. Gonzalez is chief of Surgery, as well as chair and the Albert J. Jr. and Claire Speh Professor of Urology at Loyola University Medical Center and Stritch School of Medicine. 10 9

Josh Levitsky, MD, '08 MS, was recently named president-elect of the American Society of Transplantation (AST), the largest transplant organization in North America. In addition to the AST, Levitsky is an active member of the American Association for the Study of Liver Diseases and the International Liver Transplantation Society. He previously served as co-chair of the American Transplant Congress, the AST Cutting Edge of Transplantation Meeting, and the AST Education Committee. Levitsky is professor of Medicine in the Division of Gastroenterology and Hepatology, of Medical Education, and of Surgery in the Division of Organ Transplantation at Feinberg. 10

Yusra Cheema, MD, '11 GME, '14 GME, was

named the recipient of Feinberg's George H. Joost Teaching Award for outstanding teaching in a large-group setting during the M1 year

Pieter H. Smith, '59 DDS June 12 SAN JOSE, CA

Bruce W. Parker, '60 MD, '64 GME June 1 ALBUQUERQUE, NM

Paul E. Schultz, '61 MD, '66 GME June 20 STILLWATER, MN

Richard F. Nice, '62 MD, '64 GME, '70 GME June 24 SIOUX FALLS, SD

Howard C. Joondeph, '61 BSM, '64 MD May 4 ROCHESTER, MI **Edward Robert Johnson, '64 MD** February 5 DALLAS, TX

R. Kent Bryan, '67 MD June 10 PEORIA, IL

Peter M. Maher, '70 PhD July 17 North battleford, sk, canada

Kent C. Hall, '71 DDS May 8 DUNCAN, OK

FACULTY

Michael Altman, MD, professor emeritus, Department of Medicine September 18 EVANSTON, IL Frank L. Frable Jr., '51 MD August 1, 1925 - October 2, 2022 AURORA, INDIANA



Frank L. Frable Jr., '51 MD, passed away on October 2, 2022. Born in New York City, he grew up in Highland Park, Illinois. At 10 years of age, he heard a radio broadcast about sulfa drugs being used to fight infections that sparked his interest in medicine and changed his life. After discharge from the Navy in 1946, he attended Northwestern University for

medical school, and went on to have a long medical career. He is survived by his brother William Jackson Frable, '59 MD, '60, '64 GME, his seven children, seven grandchildren, five great grandchildren, and six nieces.

ALUMNI **Progress Notes**



NORTHWESTERN UNIVERSITY FEINBERG SCHOOL OF MEDICINE

Alumni Weekend is in the fall next year!

SAVE THE DATE! OCTOBER 13-14, 2023

Whether you'll be celebrating your reunion (classes whose graduation years end in 3 or 8), joining us for our Half Century Club programming, taking CME courses, attending our Women in Medicine Tea, or just seeing what's new at Northwestern, we can't wait to welcome you!

11

YUSRA CHEEMA, MD, '11 GME, '14 GME, WAS NAMED THE

RECIPIENT OF FEINBERG'S GEORGE H. JOOST TEACHING AWARD FOR OUTSTANDING TEACHING IN A LARGE-GROUP SETTING DURING THE M1 YEAR DURING THE HONORS DAY AWARD CEREMONY. during the Honors Day Award Ceremony that took place earlier this spring. Cheema is an assistant professor of Medicine in the Division of Nephrology and Hypertension. **© 11**

Yinan Zheng, '12 MS, '17 PhD, is the lead author of a Northwestern Medicine study published in the journal *Circulation* highlighting that epigenetic biomarkers may reflect past cardiovascular health exposures and predict cardiovascular disease in the future. Zheng is an assistant professor of Preventive Medicine at Feinberg.

Jacqueline D. Neal, MD, '13 GME, was

recently awarded the Mark Wolcott Award for Excellence in Clinical Care Delivery by the Department of Veterans Affairs (VA). The award is the highest honor bestowed among the more than 26,000 physicians in the Veterans Health Administration. The Wolcott Award for Excellence is presented to a "VA healthcare practitioner who is deserving of special recognition for their contributions in enhancing clinical care." Neal is a physiatrist in the department of Physical Medicine and Rehabilitation at the Jesse Brown VA Medical Center and assistant professor at both Feinberg and the University of Illinois College of Medicine. © 12

Kelly Foster; MD, '14 GME, '15 GME, '17

GME, has joined the Tampa General Cancer Center of South Florida in Palm Beach County. Foster is a former medical oncologist at Northwestern Medicine, completing her Internal Medicine residency and Medical Oncology and Palliative Medicine fellowship training at Northwestern. She received her undergraduate degree at UCLA and completed medical school at Loyola University. Foster is board-certified in medical oncology, internal medicine, and palliative medicine. She is currently seeing patients with all types of cancer, with a focus on breast and gastrointestinal cancers (gastric, esophageal, pancreatic, hepatobiliary, colon, anal) and is a member of the American Society of Clinical Oncology. 13

ΡΤ

Tasha M. Weatherspoon, '98 MPT, DPT,recently completed her Doctor of PhysicalTherapy degree from the University ofMontana. Weatherspoon is president of theNorthwestern University Physical TherapyAlumni Association. © 15

Stephen Baynai, '10 DPT, Mark Kaufman '89 PT, along with Northwestern University

Physical Therapy and Human Movement Sciences faculty member Babette Sanders, DPT, recently traveled to Washington, D.C., to lobby on issues important to physical therapy. 10 14

Jonathan Tsay, '15, '18 DPT, is the 2022 award recipient of the National Institutes of Health Outstanding Scholars in Neuroscience Award Program (OSNAP). The OSNAP award is designed to recognize those who are conducting exceptional neuroscience research across the nation and have great academic potential in their scientific training. **16**

Sarah E. Rice, '20 DPT, serves as medical support for Chicago musician and cyclist Phil Fox on Race Across America, sponsored by Athletico. Fox rides to support the Multiple Sclerosis Foundation. STEPHEN BAYNAI, '10 DPT, MARK KAUFMAN '89 PT, ALONG WITH NORTHWESTERN UNIVERSITY PHYSICAL THERAPY AND HUMAN MOVEMENT SCIENCES FACULTY MEMBER BABETTE SANDERS, DPT, RECENTLY TRAVELED TO WASHINGTON, D.C., TO LOBBY ON ISSUES IMPORTANT TO PHYSICAL THERAPY.



Transformative Work, Global Impact

t the 15th Annual Robert J. Havey, MD Institute for Global Health Benefit Dinner, more than 250 friends and members of the Feinberg community came together to support an important mission: sustainably combatting healthcare problems in low-income countries across the world.

Leadership shared success stories and updates on projects being carried out around the world — much of the work made possible by philanthropy. Generous donors have funded research, training, and clinical outreach programs led by the institute.

"Whether small, medium, or large, all of us at the institute appreciate every gift we've received these last 15 years — they've all helped expand our global impact," said Robert J. Havey, '80 MD, '81, '83 GME, deputy director of the institute.

In 2009, global health activities at Feinberg involved about 30 faculty and staff, and a student travel program in a handful of countries. Today, the Havey Institute for Global

Health has 300 members, 9 centers, more than 50 partner sites and collaborations across the world, and the top global health rotation program for medical students in the country. In addition, in just the past three years, the institute has funded 71 research projects through its research catalyzer grant, providing up to \$25,000 per project.

One catalyzer project, a portable device called DASH that can deliver accurate 15-minute PCR tests, went on to receive a \$21.3 million



grant from the National Institutes of Health to ramp up production for COVID-19 testing. It received emergency FDA approval earlier this year and could revolutionize testing in countries with poor access to modern healthcare.

"This super achievement couldn't have happened without all of you who supported

Diseases.

our institute," said Robert

Murphy, MD, '81 '84 GME,

executive director of the

institute and the John Philip

Phair Professor of Infectious

Thanks to two leader-

ship donors in particular,

critical healthcare infra-

structure can continue in

perpetuity. Shortly before

the event, Northwestern

the institute's work building

"Whether small, medium, or large, all of us at the institute appreciate every gift we've received these last 15 years – they've all helped expand our global impact."

ROBERT J. HAVEY, '80 MD, '81, '83 GME

University announced a gift from trustees and alumni Patrick G. Ryan and Shirley W. Ryan that will endow the institute's Ryan Family Center for Global Primary Care.

The event was emceed by acclaimed broadcast journalist Bill Kurtis, who also narrated a short documentary about the institute's work. The video showed Northwestern scientists, clinicians, and educators training lab technicians in Peru, Bolivia, and Pakistan to sequence and surveille SARS-CoV-2 variants; establishing long-COVID clinics in Columbia and Nigeria; developing tools to diagnose tuberculosis faster in Mali; and teaching locals in Belize who don't have regular access to electricity how to use ultrasound machines and cell phones to diagnose pneumonias. The video also featured Feinberg medical students working in low-resource settings during their global health rotations, where they strengthened their commitment to health and patient care.

"The more we do, the more we see what needs to be done. We need to build a planet for the next 100 years," explained Havey. "Our children, grandchildren, and great-grandchildren are going to live here. We have a responsibility to build a world for them. That motivates everyone in this institute every day."

Feinberg Faculty Show Support

ore than 4,000 faculty members serve Feinberg every day. They're training the next generation of physicians and scientists in classrooms, clinics, laboratories, and communities and conducting basic, clinical, and translational research to improve the health of people worldwide. In addition to giving their time and expertise, many generously support the medical school through philanthropy. Here, some of these dedicated faculty share why they give to Feinberg.



"I am grateful for the opportunities I have had to become a physician and researcher, and I believe in giving back so that

others can also benefit from the resources of a place like Feinberg. I also know from experience as a physician and researcher that we still have a lot to learn and study in medicine, and so I support key areas of research that are important to me and my extended family to make medicine and medical care better in the future."

Philip Greenland, MD, the Harry W. Dingman Professor of Cardiology, supports research programs in cardiology and heart disease prevention, and other areas of the medical school.



"The exceptional students and colleagues I have had at the Feinberg School of Medicine

and the Department of Pharmacology provided me with inspiration, satisfaction, and joy during my 50-year career here as a researcher and educator. I provide my donation to help maintain that environment for future students and faculty."

Paula Stern, PhD, professor emeritus of Pharmacology, supports the Department of Pharmacology and Feinberg's Annual Fund.

480

FACULTY MADE A GIFT TO FEINBERG LAST FISCAL YEAR (FY22), SUPPORTING 136 AREAS AT THE MEDICAL SCHOOL

\$4,093,873

TOTAL FACULTY GIVING IN FY22

198

FACULTY MEMBERS GAVE AT LEAST \$1,000 IN FY22 TO BECOME MEMBERS OF THE FOUNDERS SOCIETY

100%

GIVING FROM DEPARTMENT CHAIRS FOR SIX YEARS IN A ROW



"I give out of gratitude. Gratitude for the training I received at Northwestern and gratitude for the trust

Northwestern placed in me to train others."

Ann Bidwell, MD, '88 GME, health system clinician of Ophthalmology, planned an estate gift to provide future medical school scholarships and supports the Department of Ophthalmology through outright gifts.



"I support Northwestern Medicine because of its excellence. It's a true triple hit organization: patient care, education,

and research. NM does it all."

James Webster, '56 MD, '60, '63 GME, professor emeritus of Medicine in the Division of Geriatrics, supports the Annual Fund, scholarships, and other areas of the medical school.

WRITTEN BY Lara C. Pullen, '93 PhD

ALUMNI

SCIENTIFIC SOLUTIONS FROM NO MAN'S LAND

My story starts like many of the stories that could make their way into this magazine. I graduated in 1993 from the Feinberg School of Medicine with a PhD in Microbiology-Immunology. I then published my thesis work and proceeded across town to my post-doc at University of Chicago, where I worked on immune cell signaling.

But then my story veered into no man's land: I decided to stay home to raise my children.

Around that time, I quit the lab bench and became a medical writer, returning to Northwestern only to give birth in the rooms above the cafeteria where I used to eat lunch: first, to a girl (now a student in Feinberg's Medical Scientist Training Program, studying in a laboratory close to the same air space as where she was born), then another girl (now working in her first laboratory), and then, 18

l want to use this space.

however, not to rehash what I have done, but rather to talk about what I still want to do. During these past 18 years I have had the opportunity to see the problem of rare disease through a privileged lens: that of a scientist, mother, and successful disruptor. years ago, a boy who stopped moving minutes after he was born.

The boy presented me with a problem that leveraged my biomedical training and propelled clinical progress beyond what I would have achieved had I stayed in the labo-

ratory. Kian has Prader-Willi Syndrome (PWS), a genetic condition that leads to weak muscle tone, poor growth, and delayed development.

The moment we arrived home from Prentice Hospital's NICU, I dove into the medical literature, eventually identifying the histamine 3 receptor as a critical drug target for PWS. I then identified a drug (pitolisant) that had the potential to help my son. At the time, pitolisant was recommended for approval for narcolepsy in Europe, but I had to work with the U.S. Food and Drug Administration to obtain permission for personal importation of the drug.

In the process, I co-founded Chion Foundation, with the mission of improving the quality of life for families touched by Prader-Willi Syndrome and other rare diseases. I also co-authored the first example of patient-initiated real-world evidence in peer-reviewed medical literature and encouraged enrollment in the U.S. phase 2 trial of pitolisant for PWS.

Since my son was the first with PWS to take pitolisant, I also spent a few years in the creation and implementation of a program to help him rebuild his brain and body, which was transformed by the medication. He had noticeable and continuous improvements in language, processing speed, and working memory. His tone normalized, his exercise tolerance improved, and his body composition shifted as he built muscle. Today, I write this from his apartment in Minnesota as he prepares to start college at Hamline University in St. Paul.

I want to use this space, however, not to rehash what I have done, but rather to talk about what I still want to do. During these past 18 years I have had the opportunity to see the problem of rare disease through a privileged lens: that of a scientist, mother, and successful disruptor. I have observed that many bench scientists have good ideas that could save the lives of children, but that these ideas are lost or stall out because scientists have trouble raising the funds necessary to cross the "valley of death" between the laboratory and clinical trials.

My Chion Foundation co-founder Maria Picone and I believe that it should be possible

to create a blended financial model whereby philanthropic funds are given to scientists and/or physicians who would like to develop potential rare disease treatments until they are ripe for transfer to a clinical stage. Such an approach has been advanced in the climate change space and has been used for specific rare diseases such as cystic fibrosis. We intend to use Chion Foundation to raise philanthropic funds to investigate, at the preclinical stage, molecules that target rare disease. We will then transfer those funds to scientific investigators as predetermined pre-clinical milestones are met.

Our hope is that if we can somehow dissociate early-stage drug development from venture capital we can remove the pressure to "prove" a hypothesis and give scientists and physicians a longer runway to test a hypothesis. Such an approach should deliver more and better drugs to clinical trials and the patients who enroll in them.

The author can be reached at lara@chionfoundation.com.

Northwestern Medicine Through the Years

WARD ROUNDS



1996

Princess Diana's Legacy at Northwestern

TWENTY-FIVE YEARS AFTER THE TRAGIC DEATH OF PRINCESS DIANA, HER MEMORY LIVES ON AT NORTHWESTERN, PARTICULARLY FOR HER COMMITMENT TO CANCER RESEARCH. n June of 1996, the Princess of Wales came to the Chicago area for a three-day visit. She toured the Evanston campus, greeted patients at Cook County Hospital, and headlined a black-tie fundraising gala — to which she famously wore a purple Versace gown — to raise money for cancer research.

As part of her visit, Diana was received at the home of then President Henry Bienen for a private reception with breast cancer researchers, Northwestern trustees, the governor of Illinois, and the mayors of Evanston and Chicago and their spouses.

On June 5, Diana also gave the opening remarks at a symposium on breast cancer hosted by the Robert H. Lurie Comprehensive Cancer Center of Northwestern University (then called the Robert H. Lurie Cancer Center of Northwestern University).

"Today is an important opportunity to draw the world's attention to the disease, because there are few subjects which are more likely to raise anxiety and fear than cancer — for some, it remains the dreaded 'C' word," she said in her talk, adding, "And yet in the midst of such negative circumstances there is, today, an amazing amount of hope ... In so many of the seats before me I see specialists who bring hope, pioneers whose work will soon transform the lives of countless individuals ..."

Today, one of these providers of hope is Lurie Cancer Center member Daniela Matei, MD, chief of Reproductive Science in Medicine in the Department of Obstetrics and Gynecology, who joined Feinberg in 2016 and was invested as the Diana, Princess of Wales Professor of Cancer Research. Ann Lurie, president of Ann and Robert H. Lurie Foundation and Lurie Holdings, Inc., spoke during the investiture ceremony about her establishment of this professorship to commemorate Princess Diana's visit to Northwestern. (V. Craig Jordan, PhD, then a professor of molecular pharmacology at Feinberg, whose research led to widespread utilization of tamoxifen for the treatment and reduction of risk of breast cancer, was the first to hold the professorship.)

"Back in 1996, I remember that Diana urged cancer researchers at Northwestern to avoid the other 'C' word — complacency in their work. Today, we have adopted 'urgency' in its place," Lurie said then. "I am happy that through this professorship that exists in perpetuity I could help to leverage the recruitment of someone like Dr. Matei."



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