Northwestern Medicine

SPRING 2022

Extending the Healthspan

Northwestern's new Potocsnak Longevity Institute aims to help people live healthier, longer. · p. 14

INSIDE

Learning from the Best

In January, medical students learned how to perform cleft lip repair under the guidance of Arun Gosain, MD, division head of Plastic and Reconstructive Surgery at Ann & Robert H. Lurie Children's Hospital of Chicago, and professor in the Division of Pediatric Surgery. Gosain and his colleagues lead the Cleft Lip and Palate Repair Program at Lurie Children's.

Photo by Jesse Arseneau

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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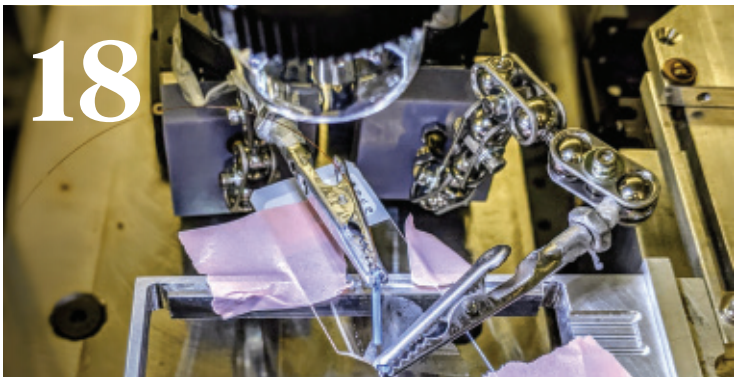
Features

EXTENDING THE HEALTHSPAN

Funded by a very generous gift from Chicago industrialist John Potocsnak and family, Northwestern's new Potocsnak Longevity Institute aims to help people age healthier.



UNLOCKING THE HUMAN PROTEOME

Millions of molecular proteins are coursing through our body's cells at all times. To better understand them, Northwestern scientists are sequencing them the way the Human Genome Project sequenced genes and DNA.

TRANSPLANT TRANSFORMER

Satish Nadig, MD, PhD, plans to usher in a new era of technology in transplantation as director of Northwestern's Comprehensive Transplant Center.

THE RIGHT CARE AT THE RIGHT TIME

Whether it's an acute cardiac episode or chronic unexplained shortness of breath, Northwestern Medicine's cardiac teams have designed protocols for swift intervention.

Departments

ON THE COVER
Evaluations at the Human Longevity Laboratory — part of the new Potocsnak Longevity Institute — will include a blood test that measures DNA methylation and other biomarkers of aging-associated health conditions. The cover shows a 3D illustration of DNA methylation. Getty Images.

Ahead of the Curve

IN A REMARKABLE PLACE SUCH AS OURS — A MEDICAL SCHOOL DESIGNED FOR CONTINUOUS learning, innovation, and discovery — looking ahead is central to our mission. The students we train today will become future leaders; the knowledge we uncover in the now can become treatments and cures for tomorrow.

We believe ideas sparked by collaboration have the power to generate electricity, catalyze people, and drive meaningful change. To this end, at a recent research retreat, over 300 principal investigators gathered to establish priorities that will guide our enterprise for the next five years and beyond, positioning us to better meet the greatest challenges of the future.

Our teaching faculty, likewise, continuously innovate and study the impacts of novel education strategies on learning outcomes and downstream patient-care quality. The field of medicine is undergoing tremendous change, and while our rigorous curriculum has always produced outstanding clinicians, educators, and scholars, we intend to create the next generation of great physician scientists, whose transformational leadership will chart the course.

While we cannot know what the practice of medicine will look like in 30, 40, or 50 years — when our current trainees will be deep into long careers — that is indeed the very period we are shaping now. The questions we pose, the plans we make today, will collectively determine the time ahead.

This issue of *Northwestern Medicine* magazine offers intriguing examples of such visionary thinking and might inspire you to consider what is possible when brilliant minds come together with significant purpose.

Take, for instance, the new Potocsnak Longevity Institute, which signals an ambitious new multidisciplinary approach to the science of aging. Led by Douglas Vaughan, MD, chair of the Department of Medicine, the institute aims to better understand complex biological changes and discover therapies and lifestyle interventions that can expand the healthspan for all people (page 14).

> ***The questions we pose, the plans we make today, will collectively determine the time ahead.***

Another example of forward thinking comes from the Human Proteoform Project, led by Neil Kelleher, PhD, director of the Chemistry of Life Processes Institute and a professor of Medicine at Feinberg. As this global team works to characterize all known proteoforms while systematically discovering new ones, the potential and promise to impact human health and our study of disease is enormous (page 18).

And Satish Nadig, MD, PhD, the new director of the Comprehensive Transplant Center (CTC), arrived this past fall with bold plans to usher in the era of modern immune tolerance following transplantation. At the helm of a stellar team already making strides, his patient-centric approach to innovation and technology may change the paradigm for transplants (page 22).

Finally, we share a quest for a future in which there is equity in healthcare. A report from a group of Black McGaw Medical Center alumni who have changed the face of the Department of Orthopaedic Surgery — and medicine — over the past five decades is inspiring (page 28).

We are forever grateful to the great minds in our midst. We aim to foster an environment in which grand plans are encouraged and people are undaunted by even the loftiest, most intimidating goals. Staying ahead of the curve demands the best of us.

With warm regards,

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

Celebrating Match Day 2022

Torn envelopes littered the floor once again, as fourth-year students resumed the decades-long tradition of celebrating their residency matches in person.

"We've had this pent-up excitement over the last few years, and the fact that we get to be together in one space to share this moment is magical," said Ketan Jain-Poster, who matched in otolaryngology at Kaiser Permanente Oakland Medical Center.

On Match Day, an annual tradition held on the third Friday of March, all fourth-year medical students across the country learn — at the exact same time — where they will train as residents for the next three to seven years.

This year, Feinberg students and their families attended the Match Day celebration at the Louis A. Simpson and Kimberly K. Querrey Biomedical Research Center on Northwestern's Chicago campus.

Match Day continued on the next page →

> ***"We've had this pent-up excitement over the last few years, and the fact that we get to be together in one space to share this moment is magical."***
>
> **KETAN JAIN-POSTER**

Residency matches are made by the National Resident Matching Program (NRMP), which uses an algorithm to pair graduating medical students with available training positions at U.S. teaching hospitals. The model takes into account the top choices of both the students and the residency programs.

This year's graduating class faced enormous adversity due to the COVID-19 pandemic,

according to Marianne Green, MD, the Raymond H. Curry, MD, Professor of Medical Education and vice dean for Education, who spoke to students and their families before the envelope opening.

"You've had a unique medical school experience, and the challenges you've faced and solutions you've provided have made you an inspiration," Green said. "You are an exceptional class."

Match Day is the beginning of the end of medical school for students at Feinberg, many of whom will leave Chicago for training across the country. Zenaida Enchill, a fourth-year student who matched in orthopaedic surgery at the Harvard Combined Orthopaedic Residency Program, said the events conjured up memories of Founders' Day four years ago, where first-year students were welcomed to campus.

"I remember the white coat ceremony, just down the street, and now we're here," Enchill said. "I am very grateful for my mentors and support system, and I'm incredibly excited."

Other students will stay at Northwestern, including Christopher Yang, a fourth-year student who matched into Dermatology at the McGaw Medical Center of Northwestern University. Yang said the backing he received from the Northwestern community was influential in his decision to remain in Chicago.

"Northwestern has been fantastic, the mentors here are incredible, and I could not have done it without them," Yang said.

33 students were inducted into the Feinberg chapter of the Alpha Omega Alpha medical honor society.

Honoring Achievement

In a ceremony on March 15, the Alpha Omega Alpha (AOA) medical honor society welcomed 43 new members into the Feinberg chapter on the basis of outstanding scholastic achievement and significant contributions to medicine.

Prior to the induction ceremony, Elizabeth McNally, MD, PhD, the Elizabeth J. Ward Professor of Genetic Medicine, delivered the Walter G. Barr, MD, Lecture, speaking about the promising future of cardiac risk prediction using genetic variation.

Following the lecture, guests attended the induction ceremony, where Shilajit Kundu, MD, '07 GME, chief of Urologic Oncology in the Department of Urology, welcomed inductees.

"We recognize our students, housestaff, and faculty, who not only provide superb care to patients, but have gone above and beyond to distinguish themselves to be worthy of AOA induction," said Kundu, who serves as AOA councilor for Feinberg.

Susan Goldsmith, MD, '08 GME, associate dean for student affairs and associate professor of Obstetrics and Gynecology in the Division of General Obstetrics and Gynecology, welcomed the 33 new medical student members into AOA.

"My time at Feinberg has been defined by continuously striving for improvement," said Matias Pollevick, a fourth-year student pursuing a residency in internal medicine who was inducted into AOA. "I hope to take this spirit and apply it to my learning as a resident and to serving my patients during practice."

New housestaff inductees were announced by Linda Suleiman, MD, '17 GME, assistant dean of Medical Education, director of diversity and inclusion for the McGaw Medical Center of Northwestern University, and an assistant professor of Orthopaedic Surgery.

"It is an immense honor to be inducted into AOA," said Katherine McGee, chief resident in medicine and AOA inductee. "I owe so much to my mentors, education, and training at Northwestern, which has prepared me for this continued work, and joining the AOA community at Northwestern is an exciting new chapter."

Marianne Green, MD, the Raymond H. Curry, MD, Professor of Medical Education and vice dean for Education, welcomed alumni and faculty inductees into the medical honor society.

"I would like to thank my family for their unrelenting support of my endeavors, and everyone at Feinberg who has encouraged, supported, and challenged me to better myself, both professionally and personally," said Khalilah Gates, MD, assistant dean of Medical Education, associate professor of Medicine in the Division of Pulmonary and Critical Care, and an AOA inductee.

Meron Teklu and Michael Wang, fourth-year medical students and AOA inductees, received the Alpha Omega Alpha Scholarship, an award funded by donors to Northwestern University.

Elizabeth McNally, MD, PhD, the Elizabeth J. Ward Professor of Genetic Medicine, delivered the Walter G. Barr, MD, Lecture, speaking about the promising future of cardiac risk prediction using genetic variation.

Faculty AOA inductees (L-R): **Crystal Clark, MD, MSc**, associate professor of Psychiatry and Behavioral Sciences and of Obstetrics and Gynecology; **Daniela Ladner, MD, MPH**, professor of Surgery in the Division of Organ Transplantation and of Medical Social Sciences; **June McKoy, MD, JD, MBA, '01 GME**, professor of Medicine in the Division of General Internal Medicine and Geriatrics; and **Khalilah Gates, MD**, assistant dean of Medical Education and associate professor of Medicine in the Division of Pulmonary and Critical Care.

Feinberg Among Top Medical Schools

Feinberg School of Medicine was ranked 17th among research-oriented institutions by the latest *U.S. News & World Report*, immediately after a three-way tie for 14th. This is the 15th year in a row Feinberg has placed in the top 20 of research-oriented medical schools.

"Feinberg continues to be recognized as a member of an elite group of world-class institutions, which is a testament to the dedication and drive of our faculty, staff, students, and trainees," said Eric G. Neilson, MD, vice president for Medical Affairs and Lewis Landsberg Dean. "I am proud of the medical school's leading-edge scientific discovery, innovative medical education, and commitment to transforming the future of medicine. I have no doubt that our outstanding reputation will continue to grow in the future."

This year, seven of Feinberg's specialty programs were also recognized among the best in the nation. Obstetrics and gynecology ranked 6th, surgery was ranked 13th, pediatrics ranked 14th, internal medicine and psychiatry each ranked 15th, radiology rose one spot to rank at 16th, and anesthesiology was ranked 17th. Physical therapy, assessed every four years by *U.S. News*, ranked 4th in the nation in 2020. In the *U.S. News* rankings of public health programs, Feinberg's public health program was ranked 24th, the second-highest ranking for a U.S. public health program that is part of a medical school.

OVERALL RANKING

17 in the nation for research-oriented medical schools

15 years in a row that Feinberg has been in the top 20

SPECIALTY PROGRAM RANKINGS

6 in the nation for obstetrics and gynecology

16 in the nation for radiology

4 in the nation for physical therapy

15 in the nation for psychiatry

13 in the nation for surgery

14 in the nation for pediatrics

15 in the nation for internal medicine

17 in the nation for anesthesiology

New Technology in Medical Education

Feinberg is bringing the latest technology into the classroom with its new curriculum enhancements. The Augusta Webster, MD, Office of Medical Education has begun instruction in Digital Health and Data Science, a curriculum being co-developed by David Liebovitz, MD, associate vice chair for clinical informatics in the Department of Medicine and co-director of the Center for Medical Education in Data Science and Digital Health, and Mahesh Vaidyanathan, MD, MBA, assistant professor of Anesthesiology.

Students will meet several core competencies and learning outcomes while learning about the health data ecosystem; the health IT regulatory environment; data science methods and research; digital health decision support; bias, ethics and health equity; and the sociotechnical context for digital health and data science.

"No matter what specialty students choose to practice or where they end up practicing medicine, they will have to utilize digital healthcare and data science every day of their careers. This curriculum is designed to give students the knowledge and skills to optimize their utilization of those technologies, ultimately for the benefit of the patients they treat," Vaidyanathan said.

Anatomy education is, too, getting a boost of new technology. Feinberg is partnering with Case Western Reserve University School of Medicine to integrate its HoloAnatomy software. The software uses Microsoft's HoloLens 2 mixed reality headsets, which allow students to visualize every part of the body as a virtual, three-dimensional hologram. Feinberg's new anatomy curriculum is currently being introduced to first-year and second-year medical students in their Phase 1 Module and to first-year PA students.

"We use this technology not as a replacement for dissection but to augment and enhance the learning of anatomy in a more efficient and effective way," said Patricia Garcia, MD, MPH, associate dean for curriculum and a professor of Obstetrics and Gynecology in the Division of Maternal Fetal Medicine and of Medical Education.

INVESTIGATING PRECISION NUTRITION

Northwestern, the University of Chicago, Illinois Institute of Technology, University of Illinois Chicago, and Rush University are part of a $170 million National Institutes of Health (NIH) program that is the first comprehensive study to investigate precision nutrition. The goal of "Nutrition for Precision Health" (NPH), powered by the All of Us Research Program, will be to develop algorithms to predict individual responses to food and dietary routines.

The Illinois Precision Nutrition Research Consortium — one of six centers around the country — is composed of Northwestern and its partners. Their grant will be $13,321,184 awarded over five years, pending availability of funds.

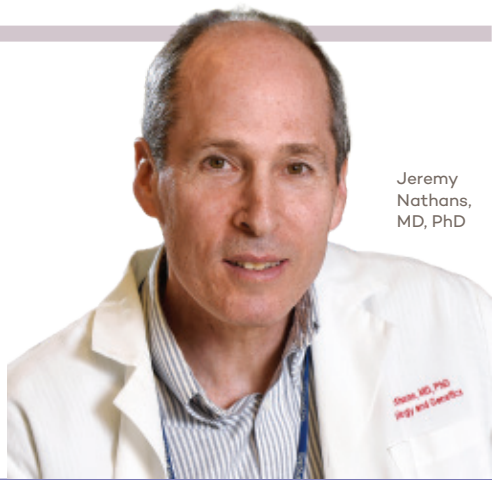
Precision nutrition, also known as personalized nutrition, will move away from one-size-fits-all diet recommendations and create a customized diet plan for individuals based on individual differences, such as genetics and metabolism.

"We will learn more precisely how to match dietary recommendations to the needs of an individual," said Linda Van Horn, PhD, professor of Preventive Medicine in the Division of Nutrition and one of the senior principal investigators.

2022 NEMMERS PRIZE RECIPIENT ANNOUNCED

Jeremy Nathans, MD, PhD, an investigator at the Howard Hughes Medical Institute and the Samuel Theobald Professor of the Wilmer Eye Institute at Johns Hopkins Medicine, known for his landmark discoveries in the molecular mechanisms of visual system development, function, and disease, is the recipient of the 2022 Mechthild Esser Nemmers Prize in Medical Science at Northwestern University.

The award, which carries a $200,000 stipend, is given to a physician-scientist whose body of research exhibits outstanding achievement in their discipline as demonstrated by works of lasting significance. A jury of distinguished scientists from around the country made the final selection. Nathans will deliver a public lecture and participate in other scholarly activities at Feinberg in the coming year.



Jeremy Nathans, MD, PhD

WRITTEN BY *Melissa Rohman and Marla Paul*

RESEARCH BRIEFS

DISEASE DISCOVERIES

INVESTIGATING PREVALENCE RISK OF FAMILIAL HEART FAILURE

Idiopathic dilated cardiomyopathy (DCM) was found to have a familial etiology in 30 percent of individuals diagnosed with DCM, and the overall risk for a family member of developing DCM was nearly 20 percent by the age of 80, according to a family-based, cross-sectional study published in *JAMA*.

"This study is incredibly important because our goal at the outset was to create a large, diverse cohort of patients with DCM and their families to understand the risk of developing heart failure simply by being related to someone who has DCM," said Jane Wilcox, MD, '10, '11 GME, associate professor of Medicine in the Division of Cardiology and a co-author of the study.

In dilated cardiomyopathy, one of the leading causes of heart failure in the U.S., one or both of the heart's ventricles stretches, "dilates," and becomes weaker, and many patients will ultimately require a heart transplant. In the case of DCM, the cause of the heart muscle's dysfunction is often unknown, though recently investigators have learned that many cases are common in families, suggesting a genetic cause.

Furthermore, Black patients, who have a higher risk of heart failure hospitalization and death, have historically been underrepresented in clinical trials exploring heart failure, underscoring the importance of including more diverse patient cohorts in studies, according to Wilcox. The study findings emphasize that heart failure screening should be of the same rigor and consistency as is screening for other genetic illnesses, especially among Black individuals, Wilcox said.

This study was supported by National Heart, Lung, and Blood Institute R01HL128857 and a supplement from the National Human Genome Research Institute.

CLINICAL BREAKTHROUGHS

Patients May Benefit From Atrial Shunt

A Northwestern Medicine-led study published in *The Lancet* suggests that some patients with the most common form of heart failure may benefit from a novel, minimally invasive cardiac implant device called an atrial shunt. The study also offers new insight into the role exercise plays in understanding, diagnosing, and treating this type of heart failure.

Heart failure with preserved ejection fraction (HFpEF), also called diastolic heart failure, affects 3 million Americans. Despite being the most common type of heart failure in the U.S., effective treatments remain elusive, leading to high morbidity and mortality.

"While the overall trial was neutral, in our subgroup analyses we found that what happens in the heart and lungs during exercise is of prime importance in this type of heart failure," said Sanjiv Shah, MD, the Neil J. Stone, MD, Professor of Medicine in the Division of Cardiology and lead author of the study. Shah is also director of research at the Bluhm Cardiovascular Institute and director of the Northwestern Medicine HFpEF Program. "The normal response to exercise is relaxation of the blood vessels in the lungs. Patients with HFpEF who are able to relax the blood vessels in their lungs appear to do well with the device, whereas those whose blood vessels can't relax appear to do worse when an atrial shunt is implanted."

"What we saw in this study suggests that future clinical trials should specifically investigate the subgroup of patients with HFpEF whose pulmonary blood vessels respond normally to exercise," Shah said. "If future trials validate what we found, the potential is enormous. This subgroup comprises two-thirds of

people with this type of heart failure — that is 2 million people who could benefit from this innovative therapy. This simple, one-time procedure could significantly improve quality of life."

Funding for the study was provided by Corvia Medical.

WRITTEN BY *Melissa Rohman*

CLINICAL BREAKTHROUGHS

Neural Stem Cell Therapy May Improve Metastatic Cancer Survival

Neural stem cells (NSCs) engineered by Northwestern Medicine investigators used in combination with the HER2 inhibitor drug tucatinib improved survival in mice with HER2-positive breast cancer brain metastases, according to findings published in *Proceedings of the National Academy of Sciences*.

The study, led by Maciej Lesniak, MD, chair and the Michael J. Marchese Professor of Neurosurgery, demonstrates the therapeutic utility of engineered NSCs for drug delivery to brain tumors and may lead to the development of novel and more efficient therapeutic options against HER2-positive breast cancer brain metastases.

Brain metastases are one of the main causes of mortality for patients with breast cancer. A lack of clinical trials coupled with the presence of the blood brain-barrier, which significantly decreases the efficacy of existing targeted therapies, have long stalled progress to improve patient outcomes.

The overexpression of HER2 is observed in about 30 percent of patients with breast cancer and is known to be associated with advanced disease and decreased overall survival. Additionally, about 50 percent of patients with overexpressed HER2-positive breast cancer will develop central nervous system metastases and are given an average survival rate of 11 to 18 months after diagnosis.

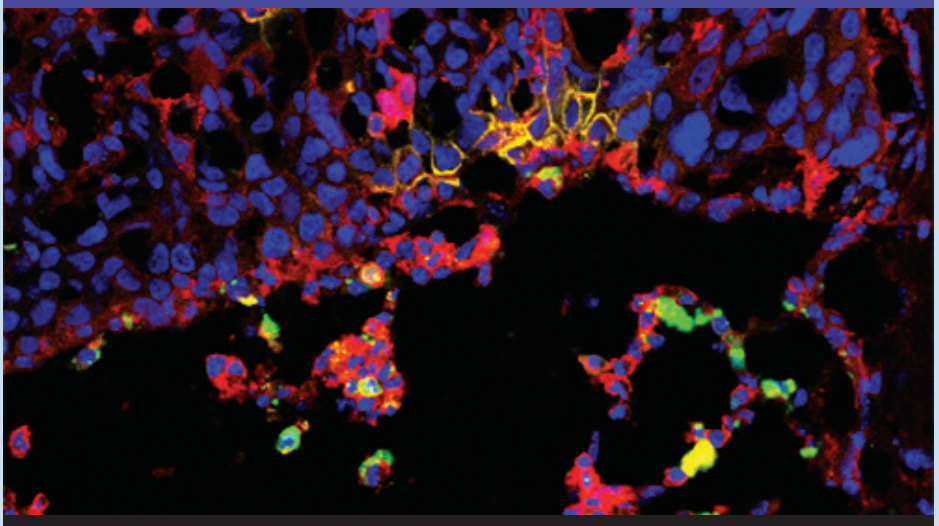
50%

OF PATIENTS WITH OVEREXPRESSED HER2-POSITIVE BREAST CANCER WILL DEVELOP CENTRAL NERVOUS SYSTEM METASTASES.

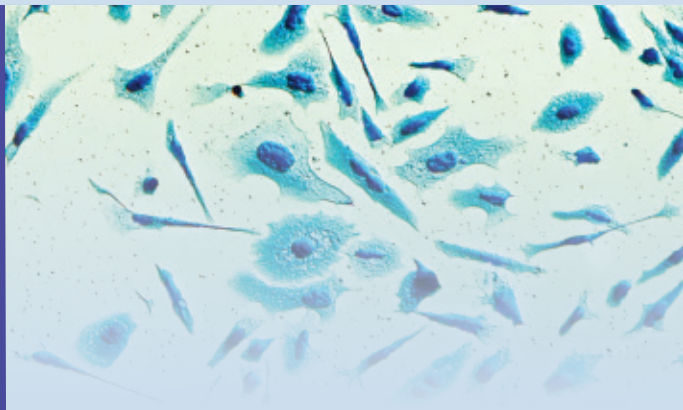
While chemotherapy drugs have improved outcomes for patients with primary breast cancer and patients with systemic metastases, more effective targeted therapies for patients with breast cancer metastases in the central nervous system are desperately needed.

Lesniak is a member of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University.

This work was supported by National Institutes of Health grants R35CA197725, R01NS093903, 1R01NS115955-01, R33NS101150, R01NS106379 and R37CA258426.



Representative immunostainings of brain sections harvested from mice treated with LM008 anti-HER2 neural stem cells (NSCs). The amount of anti-HER2 antibodies released by NSCs (green) was measured with antihuman IgGs (yellow). Presence of HER2 antibodies binding to the membrane of HER2-positive BT474-Br cells (red). Nuclear staining is shown in blue.



CLINICAL BREAKTHROUGHS

NEW TREATMENT FOR METASTATIC HORMONE-SENSITIVE PROSTATE CANCER

A new drug, administered in combination with standard androgen-deprivation therapy (ADT) and docetaxel chemotherapy, increased survival in patients with metastatic hormone-sensitive prostate cancer, according to a trial published in *The New England Journal of Medicine*.

This represents a new strategy for managing metastatic hormone-sensitive prostate cancer (mHSPC), according to Maha Hussain, MD, the Genevieve E. Teuton Professor of Medicine in the Division of Hematology and Oncology, a co-author of the study and study steering committee member. Hussain is also deputy director of the Lurie Cancer Center.

In the current double-blind, phase 3, multi-site trial, investigators enrolled patients with mHSPC, randomizing them to receive either darolutamide with standard ADT and docetaxel chemotherapy or a placebo with standard ADT and docetaxel chemotherapy.

During the three-year trial period, patients receiving darolutamide were 32.5 percent less likely to die compared to patients receiving the placebo. In addition, patients receiving darolutamide experienced significantly delayed time to developing castration-resistant prostate cancer — the terminal state of the disease — and pain progression, helping reduce negative quality-of-life impacts.

"This is a very important and practice-changing finding, but there is more to be achieved," Hussain said.

This study was supported by Bayer and Orion Pharma.

SCIENTIFIC ADVANCES

STUDY FINDS DOPAMINE SIGNALING PROMOTES COMPULSIVE BEHAVIOR

Northwestern investigators have discovered that dopamine signaling in the brain's dorsomedial striatum promotes the development of compulsive behaviors in animal models, according to findings published in *Current Biology*. Talia Lerner, PhD, assistant professor of Neuroscience, was senior author of the study.

Corticostriatal circuits are neural circuits connecting the brain's cerebral cortex to the striatum, a cluster of neurons within the basal ganglia that are responsible for controlling movement and reward-seeking behaviors. Prior research suggested these circuits control the expression of compulsive behaviors commonly observed in obsessive-compulsive disorder (OCD) and substance misuse disorders.

While corticostriatal circuits were thought to be involved, the precise mechanisms that cause compulsive behaviors to emerge have remained unclear. Lerner and colleagues hypothesized that dopamine activity, which regulates the plasticity of corticostriatal circuits, played a crucial role in this process.

For the current study, the investigators studied dopamine activity in two regions of the brain's striatum, the dorsomedial striatum and the dorsolateral striatum, which are involved in different types of reward learning: the dorsomedial striatum is involved with goal-oriented learning behaviors, while the dorsolateral stratum is involved with habitual behaviors.

Although it was previously thought that habit played a role in compulsion, to their surprise, the team found that dopamine signaling activity was actually upregulated in the mice's dorsomedial striatum, where it predicted the development of compulsive reward-seeking behavior.

The study was supported by the National Institutes of Health K99/R00 Award R00MH109569, a NARSAD Young Investigator Award from the Brain & Behavior Research Foundation, and National Institutes of Health Diversity Supplement R00MH109569-04S1.

SCIENTIFIC ADVANCES

Investigators Identify New Connections Between Circadian Rhythm and Muscle Repair

Northwestern Medicine investigators have discovered a novel mechanism that connects circadian rhythm-controlled cellular metabolism and regeneration with muscle repair after injury, according to recent findings published in the journal *Genes and Development*. Clara Peek, PhD, assistant professor of Biochemistry and Molecular Genetics, was senior author of the study. Peek is also an assistant professor of Medicine in the Division of Endocrinology, Metabolism and Molecular Medicine and a member of the Lurie Cancer Center.

Disruptions in circadian rhythm — the body's internal 24-hour clock that regulates rest and wakefulness — have been associated with the pathogenesis of different metabolic disorders, including diabetes and obesity. However, research regarding its association with tissue regeneration and muscle repair has remained limited.

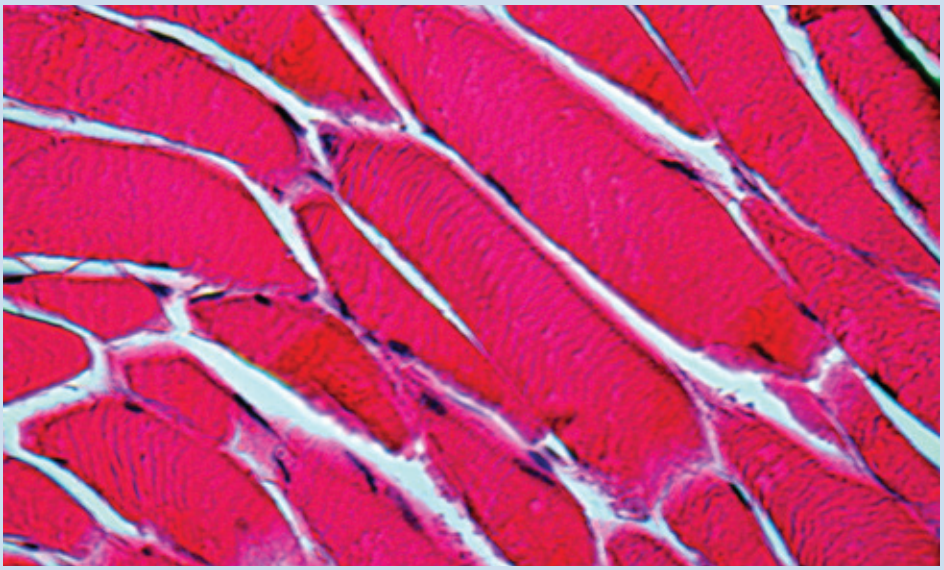
PEEK'S TEAM AIMED TO IDENTIFY THE PROTEIN BMAL1'S EXACT ROLE WITHIN MUSCLE STEM CELLS AND GREATER MUSCLE REPAIR.

In the current study, Peek's team investigated the role of adult muscle stem cell's circadian clock in controlling muscle regeneration and tissue repair after acute ischemic injury in mice. They zeroed in on the protein Bmal1 — a circadian clock regulator protein expressed in virtually all cells in the body — and aimed to identify its exact role within muscle stem cells and greater muscle repair.

Peek and her team found that muscle repair after injury was greater when mice were active or awake compared to when they were inactive or resting. Additionally, the loss of Bmal1 within the muscle stem cells led to impaired muscle regeneration.

Using metabolomic profiling to study approximately 10,000 activated muscle stem cells in vivo and cultured myoblast cells, or premature muscle cells, the investigators demonstrated that the loss of Bmal1 reduced the amount of activated muscle stem cells on the third day after injury.

This work was supported by the National Institutes of Health National Institute of Diabetes and Digestive and Kidney Diseases grant R01DK123358, National Cancer Institute grant R35CA197532 and National Institute on Aging grant P01AG049665.



WRITTEN BY *Melissa Rohman*

DISEASE DISCOVERIES

GENETIC VARIANT OF HIGH-RISK CHILDHOOD LEUKEMIA REVEALED

A genetic variant changing just one base pair of nucleotides greatly increases risk of a high-risk subtype of childhood acute lymphoblastic leukemia (ALL), according to a Northwestern Medicine study published in *Nature Genetics*.

Tracing this oncogenic pathway provides a template for future studies of other types of cancers as well, according to Feng Yue, PhD, the Duane and Susan Burnham Professor of Molecular Medicine and co-senior author of the study.

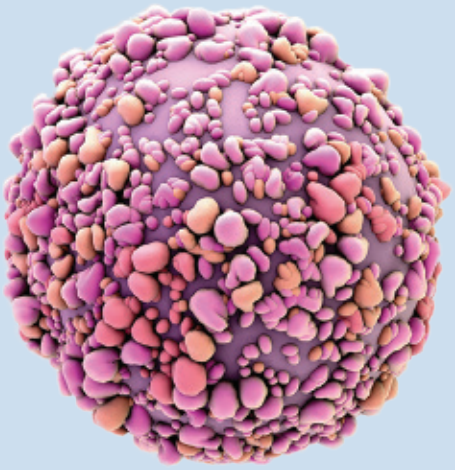
"In this study, we discovered how an inherited gene variation regulates multiple known ALL oncogenes through a cascade of interactions," said Yue, who is also an associate professor of Biochemistry and Molecular Genetics, and of Pathology, as well as director of the Center for Cancer Genomics at the Lurie Cancer Center. "If we can manipulate this pathway, we could potentially prevent the development of this cancer."

Childhood acute lymphoblastic leukemia is the most common leukemia among children. Genetic contributions to childhood ALL have been previously identified, but the mutations that lead to subtypes — such as the more-lethal "Ph-like" ALL — have remained mostly uncharacterized.

This study was supported in part by National Institutes of Health grants 1R35GM124820, R01HG009906, U01CA200060 and R24DK106766.

CLINICAL BREAKTHROUGHS

Locoregional Therapy Does Not Improve Breast Cancer Survival



Treating a tumor in the breast when distant metastases have already occurred does not improve outcomes in women with stage IV breast cancer, according to a new study published in the *Journal of Clinical Oncology*.

Retrospective studies of treatment outcomes had suggested there was a benefit to treating the breast tumor, instead of only treating the metastases, which has long been standard practice, according to Seema Khan, MD, the Bluhm Family Professor of Cancer Research, interim co-vice chair of research in the Department of Surgery and lead author of the study.

"It's possible that some subset of patients will derive a benefit from treatment of the breast tumor, but we were unable to identify such a subset in our trial, so this remains hypothetical," said Khan, who is also a professor of Surgery in the Division of Breast Surgery and a member of the Lurie Cancer Center.

"It appears the positive effects of tumor removal were not greater than the negative quality of life generated by the presence of the breast tumor," Khan said. "This is probably related to the bodily injury caused by surgery or radiation, which can have some long-lasting effects."

While the results are disappointing, they contain an important lesson about retrospective studies. Critical for understanding health and generating hypotheses, retrospective trials do suffer from many types of bias — in this case, selection bias, according to Khan.

"Someone in better overall condition may have been offered surgery for the breast tumor, while only the distant tumor was treated for someone in worse condition," Khan said. "This is one of the cases where the retrospective studies were helpful, but the discussion can only be settled with a randomized trial."

This study was conducted by the ECOG-ACRIN Cancer Research Group and supported by the National Cancer Institute of the National Institutes of Health under the following award numbers: U10CA180821, U10CA180863, Canadian Cancer Society #704970, U10CA180820, U10CA180868, U10CA180822, U10CA180888, U10CA180794, UG1CA189830, UG1CA189859, UG1CA189953, UG1CA232760, UG1CA233180, UG1CA233193, UG1CA233234, UG1CA233277, UG1CA233320, UG1CA233329 and UG1CA233341.

WRITTEN BY *Will Doss*

MEDIA SPOTLIGHT

The New York Times

Rare Virus Lineages Were Predominant in Nigeria in 2021. They Were Hardly Noticed.

Eta, a SARS-CoV-2 variant that circulated in Nigeria in early 2021, may have warranted designation as a "variant of concern" had its growth potential been recognized earlier, according to investigators at Feinberg and the University of Ibadan in Nigeria. Judd Hultquist, PhD, the associate director of the Center for Pathogen Genomics and Microbial Evolution, said worldwide tracking of variants was uneven. "Less than 1 percent of sequences are from the continent of Africa, and less than 3 percent are coming from South America," he told *The New York Times*. "Eta was able to outcompete the Alpha variant in the region before the arrival of Delta."

NBC NEWS

Revamped 'Cancer Moonshot' Could Prevent Deaths and Improve Quality of Life for Survivors

President Joe Biden's ambitious "Cancer Moonshot" relaunch has a goal of reducing the cancer mortality rate by at least 50 percent over the next 25 years for a disease that is expected to kill 609,360 people in the U.S. in 2022 alone. Experts worry that cancers associated with obesity, such as uterine and pancreatic cancer, could rise.

Maha Hussain, MBChB, a medical oncologist and deputy director of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University, said a continued focus on prevention and screening was critical to meeting the rest of the goals in Biden's plan.

"The best thing is to not get cancer, and that's what we need to invest in, so definitely prevention," she said. "And if you get cancer, we want to make it something that can be treated, so early detection. The next step would be making cancer a chronic disease as opposed to an acute, deadly disease."

TIME

Older Americans Are the Ignored Victims of the Opioid Epidemic

In adults ages 55 and older, opioid overdose deaths rose tenfold between 1999 and 2019, surging from 0.9 deaths per 100,000 people to 10.7, according to a new study published in *JAMA Network Open* that analyzed two decades of data. Maryann Mason, PhD, associate professor of Emergency Medicine, was lead author of the study.

In the near-decade she's been involved in opioid overdose research, Mason says she's "almost never" seen older adults' drug use addressed in the media or in academic studies. This lack of attention, plus a culture rife with ageism, can conceal the threat opioids pose to older people, according to Mason. "We have this idea in our mind of what older people are like — what grandma and grandpa are like — and they're not people who use recreational drugs," Mason told *Time*. "I think that keeps a lot of people from looking into this area."

U.S.News & World Report

Most Vaccine-Hesitant Health Care Workers Change Their Minds, Study Shows

Most health care workers at a large U.S. hospital who initially refused COVID-19 vaccines eventually went and got their shots, new research reveals.

"It shows there is opportunity to change people's decisions about not getting vaccinated," said lead study author Charlesnika Evans, PhD, MPH, professor of Preventive Medicine in the Division of Epidemiology.

Her team surveyed nearly 4,200 healthcare workers at Northwestern Medicine when COVID-19 vaccines became available last winter. At that time, three-quarters said they intended to take the shots. By spring, a second survey found that 95 percent had been vaccinated, including 90 percent of those who had been unsure. Of those who initially said they didn't plan to get vaccinated, nearly 60 percent had done so by spring.

The New York Times

The Coronavirus Invades Cells in the Penis and Testicles of Monkeys, Researchers Discover

Studies have reported about 10 to 20 percent of men with the coronavirus have symptoms linked to male genital tract dysfunction. Men infected with the virus are three to six times as likely as others to develop erectile dysfunction.

"The signal that jumped out at us was the complete spread through the male genital tract," said Thomas Hope, PhD, professor of Cell and Developmental Biology. "We had no idea we would find it there."

PHOTOGRAPHY COURTESY OF *Getty Images*

FACULTY AWARDS & HONORS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Peng Ji, MD, PhD, associate professor of Pathology, has been awarded the 2022 Ramzi S. Cotran Young Investigator Award from the United States and Canadian Academy of Pathology, an award that recognizes investigative work that has contributed significantly to the diagnosis and understanding of human disease. 1

Ritu Nayar, MD, professor of Pathology and of Medical Education, was named vice president of the Executive Committee for the American Board of Pathology. 2

Linda Teplin, PhD, the Owen L. Coon Professor of Psychiatry and Behavioral Sciences and of Medicine in the Division of Infectious Diseases, is the recipient of the American Psychology-Law Society Award for Distinguished Contributions to Psychology and Law. 3

Paula H. Stern, PhD, (4) professor emeritus in the Division of Pharmacology, and **Catherine Woolley, PhD**, professor of Neurology in the Ken & Ruth Davee Department of Neurology, have been selected 2021 fellows of the American Association for the Advancement of Science.

Robert Kushner, MD, '80, '82 GME, professor of Medicine in the Division of Endocrinology, was honored by the Clinical Research Forum with a 2022 Top 10 Clinical Research Achievement Award and with the prestigious Herbert Pardes Clinical Research Excellence Award. 5

Lucas Pinto, MD, MS, PhD, assistant professor of Neuroscience, was selected as a Sloan Research Fellow in neuroscience, a two-year $75,000 fellowship that is one of the most competitive and prestigious awards available for young researchers.

Lisa Hirschhorn, MD, MPH, professor of Medical Social Sciences and of Psychiatry and Behavioral Sciences, has been elected to serve on the Consortium of Universities for Global Health Board of Directors. 6

Stephen Miller, PhD, the Judy Gugenheim Research Professor of Microbiology-Immunology, Dermatology and of Medicine in the Division of Gastroenterology and Hepatology, has been named an American Association of Immunologists 2022 Distinguished Fellow. 7

Rola Kaakeh, PharmD, adjunct instructor in the Department of Preventive Medicine, has been awarded the Above and Beyond Pharmacy Champion award from GoodRx, recognizing her advocacy, spirit, and leadership.

Derek Wainwright, PhD, assistant professor of Neurological Surgery, Microbiology-Immunology, Neuroscience, and of Medicine in the Division of Gastroenterology and Hepatology, has been named a NextGen Star by the American Association for Cancer Research.

John Rogers, PhD, the Louis Simpson and Kimberly Querrey Professor of Materials Science and Engineering, Biomedical Engineering and professor of Neurological Surgery, has been awarded the 2022 James Prize in Science and Technology Integration by the Council of the National Academy of Sciences.

Bonnie Spring, PhD, director of the Center for Behavior and Health and chief of Behavioral Medicine in the Department of Preventive Medicine, has been selected by Feinberg's Women Faculty Organization as this year's winner of the fifth annual Paula H. Stern Award for Outstanding Women in Science and Medicine.

Jane Winter, MD, professor of Medicine in the Division of Hematology and Oncology and a highly regarded lymphoma expert, will serve as president of the American Society of Hematology for a year-long term through December 2022.

Each year, Clarivate Analytics releases a list of highly cited investigators who have "demonstrated significant and broad influence, reflected in the publication of multiple papers frequently cited by their peers during the last decade." Below is a list of the Feinberg investigators who made the list in 2021 and the category in which they were identified:

Brian Mustanski, PhD, director of the Institute for Sexual and Gender Minority Health and Wellbeing and professor of Medical Social Sciences, Psychiatry and Behavioral Sciences and in the Weinberg College of Arts and Sciences, in Social Sciences; **Chad Mirkin, PhD**, professor of Medicine in the Division of Hematology and Oncology and in the Weinberg College of Arts and Science, in Cross-Field; **Clyde Yancy, MD, MSc**, vice dean for Diversity and Inclusion and chief of Cardiology in the Department of Medicine, in Cross-Field; **David Cella, PhD**, chair of the Department of Medical Social Sciences and the Ralph Seal Paffenbarger Professor of Medical Social Sciences, Neurology, Pediatrics, Preventive Medicine, and Psychiatry and Behavioral Sciences, in Social Sciences; **Donald Lloyd-Jones, MD**, chair of the Department of Preventive Medicine and the Eileen M. Foell Professor of Preventive Medicine, Medicine, and Pediatrics, in Clinical Medicine; **Navdeep Chandel, PhD**, the David W. Cugell, MD, Professor of Medicine and Biochemistry and of Molecular Genetics, in Molecular Biology and Genetics and Biology and Biochemistry; **Philip Greenland, MD**, the Harry W. Dingman Professor of Cardiology and of Preventive Medicine, in Cross-Field; **Samuel Weinberg, MD, PhD**, in Cross-Field; and **Sanjiv Shah, MD**, the Neil J. Stone, MD, Professor of Medicine in the Division of Cardiology, in Clinical Medicine.

EXTENDING THE HEALTHSPAN

Northwestern's new Potocsnak Longevity Institute aims to help people age healthier.

Written by Emily Ayshford and Marla Paul

The notion of a person's biological or functional age being very different than the number of times they've orbited the sun is nothing new. But the idea that one might be able to find out what actually comprises aging itself has always seemed like science fiction. Until now.

The futuristic-sounding Human Longevity Laboratory at Northwestern — part of the new Potocsnak Longevity Institute — is on a fast track to open later this year.

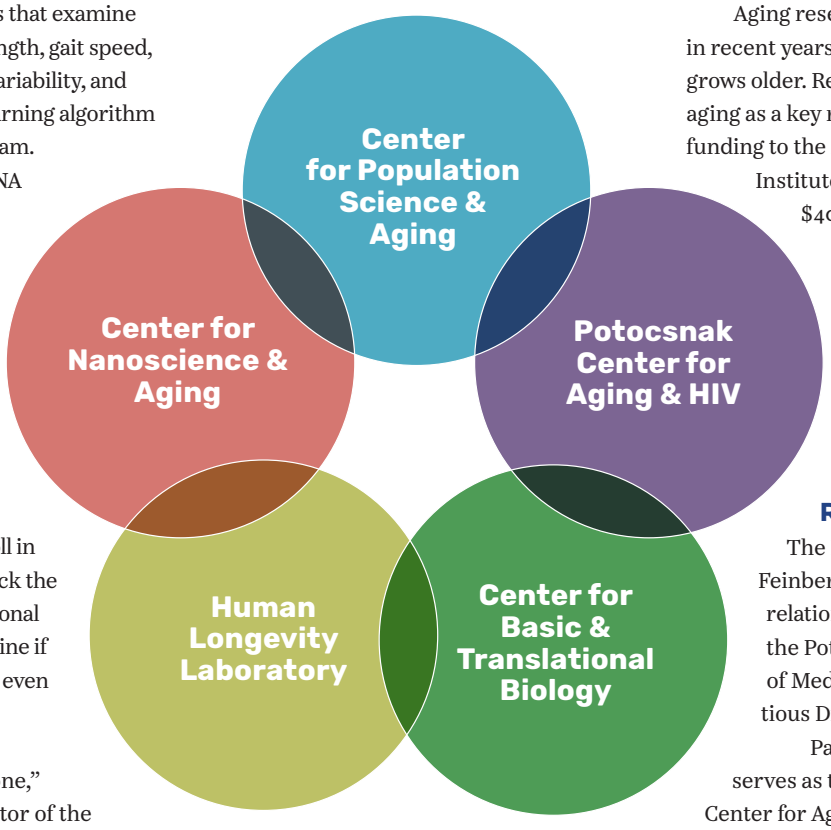
There, a person will find themselves undergoing comprehensive evaluations that examine hearing ability, balance, grip strength, gait speed, pulmonary function, heart rate variability, and cognitive function. A machine learning algorithm will analyze their electrocardiogram. A blood test will measure their DNA methylation and other important biomarkers of aging-associated health conditions, such as levels of inflammation and coagulation.

The result: the revelation of one's actual biological age. But the laboratory will do more than merely measure biological age: It will provide opportunities for patients to enroll in longitudinal clinical studies to track the velocity of aging and in interventional investigative programs to determine if the rate of aging can be slowed or even reversed.

"We now have the tools to measure biological age in everyone," says Douglas Vaughan, MD, director of the new institute and chair and Irving S. Cutter Professor of Medicine. "And we will most certainly have the ability to change the time on your clock face — shift it back a bit, or at least slow it down. With the new Potocsnak Longevity Institute, we will create a multidimensional program unlike any others that currently exist. We will be able to cultivate and build a contemporary dataset to better understand the trajectory of aging while including people from all communities."

The Potocsnak Longevity Institute

The Institute is made up of interdisciplinary centers that work to lengthen the human healthspan.



HELPING PEOPLE LIVE LONGER, HEALTHIER LIVES

The Human Longevity Laboratory is just one part of the ambitious multi-center institute, whose goal is to foster new biomedical discoveries and build on Northwestern's ongoing research in the rapidly advancing field of aging, also called geroscience.

Funded by a very generous gift from Chicago industrialist John Potocsnak and family, the institute aims to extend what Vaughan terms the human "healthspan."

Through centers and laboratories, scientists and clinicians will address the period of life when people are at the greatest risk for aging-related comorbidities — arthritis, dementia, heart disease, diabetes, aging-related cancer, hypertension, frailty — in an effort to help people live not just longer, but in a healthier and more highly functioning way.

Aging research has accelerated significantly in recent years as the Baby Boomer generation grows older. Recently, Feinberg has identified aging as a key research theme, and research funding to the medical school from the National Institute of Aging has risen to more than $40 million since 2016.

"The idea of actually doing something about aging has gone from magical thinking to theoretical thinking to an actual, pragmatic possibility," Vaughan says.

ROOTS IN HIV RESEARCH

The Potocsnak family has supported Feinberg for decades through a close relationship with Frank Palella, MD, the Potocsnak Family – C.S.C. Professor of Medicine in the Division of Infectious Diseases.

Palella has long studied HIV and serves as the director of the Potocsnak Center for Aging & HIV within the Potocsnak Longevity Institute, for which he serves as associate director. When effective combination-antiretroviral therapies to treat HIV were introduced in the late 1990s, physicians found that people living with HIV could live much longer lives than they previously had.

But there was a catch — those living with HIV still died 10 to 15 years earlier than people without HIV as a result of the premature onset of aging-related health conditions that occurred due to having chronically elevated levels of ▸

Center for Applied Health Research on Aging

Since 2019, Feinberg's Center for Applied Health Research on Aging (CAHRA) has brought together investigators who focus on aging issues to conduct research into the cognitive, psychosocial, community, and health system factors that affect a person's ability to manage their health.

To say they have had a busy two years is an understatement. "We have had a very productive launch, especially in terms of research funding," says Julia Yoshino Benavente, MPH, associate director of the center.

MICHAEL WOLF, PhD, '02 MPH
director of the Center for Applied Health Research on Aging

During the COVID-19 pandemic, CAHRA investigators have been conducting novel research into the experiences of older adults with complex care needs — whether they were experiencing isolation and loneliness, how their access to healthcare was affected, if their lifestyle and self-care behaviors changed, and ultimately whether COVID-19 has widened inequities in health outcomes.

The team is also working to serve low-income areas of Chicago to deliver messaging about the need for COVID vaccinations. "Vaccination rates among middle age and older adults in these areas has really lagged behind, and we're trying to address that disparity," says Michael Wolf, PhD, '02 MPH, director of the center, and associate vice chair for research in the Department of Medicine.

CAHRA is also home to Northwestern's Claude D. Pepper Older American's Independence Center, part of a national network of National Institutes of Health centers contributing to aging research. To date, the Pepper Center has supported 10 early career investigators with funding for pilot projects and/or protected time. Now, the center looks forward to working with the Potocsnak Longevity Institute.

"Aging research across the university has always been strong but somewhat fragmented, and we look forward to supporting this long-needed institute in bringing together faculty for meaningful collaborations and helping junior investigators advance their career path in aging research," Wolf says.

inflammation and chronically overstimulated immune systems.

"That means HIV became a good model in which to explore determinants and interventions for aging processes," Palella says. "There is a cross-pollination here between studying what improves and extends the healthspan and lifespan of people with HIV and the aging general population."

Discussions with the Potocsnak family on expanding HIV research led to broader discussions on aging research, and the idea for the institute was born.

"We are grateful for the opportunity to support the vision put forth by Northwestern's leaders, scientists, and physicians to help people live their longest, healthiest lives possible," Potocsnak shares. "The promise of the amazing work being done by Doug, Frank, and many others holds the potential to profoundly impact quality of life for millions. My wife Laura, myself, and my family are proud to support this important work as we strive to make the world a better place than when we got here."

FROM PROTEINS TO NANODEVICES

The institute builds on decades of aging research at Feinberg. A few years ago, Vaughan discovered that a distinct community of Old Order Amish in Indiana have a genetic variant that protects them against multiple aspects of biological aging. Amish people with this mutation have significantly less diabetes and a younger vascular age than those who don't have the mutation.

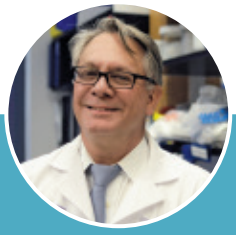
It turns out these individuals have very low levels of PAI-1 (plasminogen activator inhibitor), a protein that comprises part of a "molecular fingerprint" related to aging or senescence (deterioration) of cells.

Northwestern has contributed to the development of an experimental drug with a Japanese company that blocks PAI-1 that is now

being tested in clinical trials, showing that it is clearly possible to lower PAI-1 levels in adults without gene editing. One of these trials is in high-risk patients over age 50 with COVID-19 here at Northwestern. This drug and others will likely be included in clinical trials performed in the Human Longevity Laboratory.

Northwestern investigators are also at the forefront of studying what are known as SuperAgers — adults over age 80 who have the memory capacity of individuals who are at least three decades younger. The institute plans to collaborate closely with the Mesulam Center for Cognitive Neurology and Alzheimer's Disease, the home for this research.

The institute will also build on current research by convening investigators into several centers. In the Center for Population Science & Aging, scientists will utilize and refine existing tools — including well-defined biochemical and genetic markers — to demystify the aging process in large populations of humans at all ages.



"We will be able to cultivate and build a contemporary dataset to better understand the trajectory of aging while including people from all communities."

DOUGLAS VAUGHAN, MD,
director of the new institute
and chair of Medicine

"The ultimate goal is to push back the onset of age-related diseases and give people the opportunity to live healthier, longer."

FRANK PALELLA, MD
Potocsnak Family – C.S.C. Professor of Medicine in the Division of Infectious Diseases

The Center for Nanoscience & Aging will leverage Northwestern's strengths to develop nanotechnological devices, novel diagnostic measures, and innovative anti-aging therapies and drug-delivery platforms.

"It might be wearable devices that track physiological measures, or drug delivery systems that can impact different sites in the body," Vaughan says. "It will bring chemistry, nanoscience, nanotechnology, and engineering all to the table."

EDUCATING STUDENTS AND THE PUBLIC

The institute will also train and educate future clinicians and scientists in aging research disciplines through its Geroscience Academy, which will develop curriculum and educational materials as well as host lectures and community engagement activities.

In fact, community engagement will be a huge priority as the institute gets off the ground, especially for patient-focused initiatives like the Human Longevity Laboratory.

"We want this institute to be relevant to every community in Chicago," Vaughan says. "We are going to be reaching out to our fellow Chicagoans to get as much ethnic, socioeconomic, and educational diversity as we can. All of these factors impact aging, and we want our work to reflect the diversity of our community."

Those who visit the Human Longevity Laboratory will become part of a large dataset that will help investigators track aging processes and clinical events and to discover essential factors with which they can intervene. Patients will also have the opportunity to participate in clinical research trials.

A 'BREATHTAKING OPPORTUNITY'

Work is already underway at the institute, with hopes to open the Human Longevity Laboratory as soon as possible.

"This is a breathtaking opportunity to bring together not just HIV and infectious disease experts, but experts across disciplines to identify and predict aging-related conditions so we can design interventions that can delay, treat, and even reverse them," Palella says. "To have this under one roof is unprecedented."

The ultimate goal is to push back the onset of aging-related diseases and give people the opportunity to live healthier, longer.

"Our aspirations are big, but so are our abilities," Palella says.

Unlocking the Human Proteome

Millions of molecular proteins — the main drivers of all human diseases — are coursing through our body's cells at all times. To better understand them, Northwestern scientists are leading the charge to sequence proteins the way the Human Genome Project sequenced genes and DNA. A recent study in *Science* confirms they are on to something big.

Written by Gina Bazer

Shown here are two related proteoforms of a protein that act together to convert glucose to energy in our cells. The red dot signifies a modification to the protein by an enzyme called a kinase, which increases enzymatic activity by 400 percent, creating the difference between a protein and a proteoform. The proteoform is a modified form of the protein that controls activity and function.

Neil Kelleher, PhD, has been weighing proteins since 1999, when, as a young professor, he opened his independent laboratory at the University of Illinois in Urbana-Champaign. His goal then, he says, was the same as his goal now: "to weigh every human protein."

More specifically, he is aiming to measure the exact molecular composition, or unique proteoform, of 100 million proteins to understand and treat diseases ranging from cancer to neurogenerative and heart diseases. At last count, he's classified about 200,000 unique proteoforms, leaving many millions more to go. This will require a similar, nearly 1,000-fold jump in sequencing technology as occurred in the Human Genome between 1992 and 2002, when the genome was first fully sequenced, he says.

Fortunately, Kelleher, who is now a professor of Medicine at Feinberg and the Walter and Mary E. Glass Professor of Molecular Biosciences and professor of Chemistry in the Weinberg College of Arts and Sciences, is no longer the only one counting. In November of 2021, approximately 400 scientists in a worldwide proteomics research consortium (topdownproteomics.org) launched an initiative known as the Human Proteoform Project. Kelleher serves as the founding president.

"Watch this space, both in the private and public sectors."

NEIL KELLEHER, PhD

"People told me I was leaning in far over my skis when I started, but now momentum is growing steadily," says Kelleher, who is also the director of the Chemistry of Life Processes Institute (CLP) and faculty director of Northwestern Proteomics, a center within CLP that helps clinicians define the proteoform signatures of health and disease. "There are technological leaps that need to be made, and there are many signs that show this could be the decade where it finally happens."

There's a logical reason why the race is on to map the proteome in the same way the Human Genome Project began the quest to map DNA 30 years ago. Since proteins are the mediators of disease phenotypes, they are involved in all diseases, Kelleher explains.

"Today, there is a realization that unlocking protein-level biology is standing between us and a far healthier and more efficient future for interacting with our own proteomes," Kelleher says. "After the genome project, it's an obvious next step toward precision medicine, as proteins underlie all our health and every disease. Our bodies are driven by proteoform biology, so we are talking about the earlier and more precise detection of all human disease, better drug development, and improving healthy lifespans through regenerative medicine."

While still in its early stages, Kelleher and his colleagues' mission to map all proteins is hardly an abstraction. Recently, their efforts moved conceptually from bench to bedside. A recent study published in *Science* describes how Kelleher and his lab, partnering with Northwestern Medicine transplant hepatologist Josh Levitsky, MD, mapped 57,000 new proteoforms and discovered families of proteins in the body that could potentially predict which patients might reject a new liver transplant. The advancement, which Kelleher describes as microcosm of the Human Proteoform Project's macro potential, marks the beginning of a new era for proteomics.

A REVOLUTIONARY TOP-DOWN ANALYSIS OF PROTEIN PATTERNS

Conventionally, scientists have tended to look at shifting patterns of proteins as if through goggles underwater, taking in just a fraction of available information about their unique structures through a "bottom-up" analysis that digests whole proteins into peptides and identifies what remains. The Kelleher lab does a "top-down" analysis using state-of-the-art mass spectrometry to identify proteoforms in cells and blood more precisely (and efficiently) by keeping them intact, rather than cutting them up into tiny pieces.

"Bottom-up leaves major knowledge gaps," says Kelleher, which is why, more than 25 years ago, he led the charge to develop top-down proteomics. At the time, he used a machine the size of a VW bus containing a superconducting magnet, created by his mentor, the late Fred McLafferty, PhD, of Cornell University. "I would manually process each step, including the measurement of intact proteins with a five-ton instrument resembling an MRI machine, and it would take me a whole month to characterize a single proteoform," Kelleher recalls.

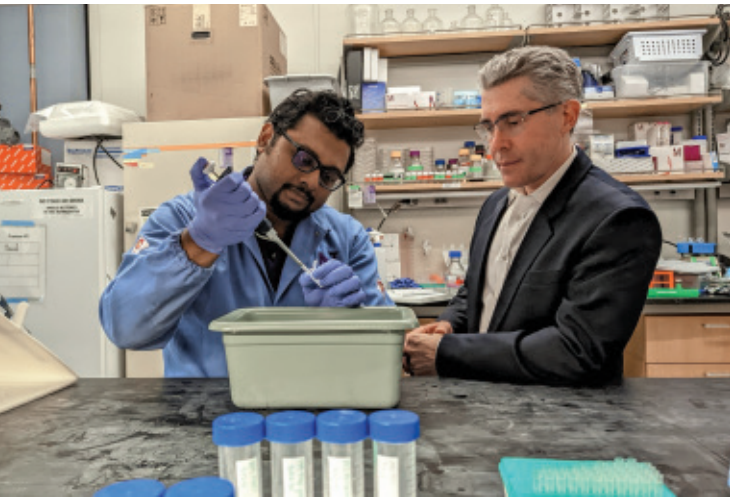
PROGRESSION OF THE HUMAN PROTEOFORM PROJECT

2012
Conceptualized the Human Proteoform Project

2018
Established Technological Capabilities

2020
Framed Coordination With NIH

2022
Created Initial Human Proteoform Atlas



↑ Navid J. Ayon, a postdoctoral scientist, confers with Neil Kelleher, PhD, in the Kelleher lab. Photo by Lisa La Vallee

Fast forward to the present. The Kelleher lab now uses a dozen benchtop instruments that weigh about 200 pounds each. The technology has come a long way from 2012, when Kelleher published his first case for mapping the entire human proteome in the *Journal of the American Society of Mass Spectrometry*. More modern instruments allow scientists in this growing field to measure a few thousand proteoforms in a week. Kelleher predicts scientists will begin mapping proteoforms 100 times more rapidly over the next five to 10 years, using a variety of new technologies now in their infancy.

"Watch this space, both in the private and public sectors," he says.

For the *Science* paper, Kelleher's top-down method allowed the scientists in his lab to take a magnifying glass to 21 human cell types and blood to create a map of protein families. They then held the map up in front of liver transplant recipients and found new indicators in immune cell proteins that changed with acute organ rejection. The result, the Blood Proteoform Atlas (BPA) — "just one specific-use case and a small pilot for the Human Proteoform Project," according to Kelleher — advances the field by 10-fold over any previous study.

A BLOOD TEST FOR LIVER TRANSPLANT REJECTION

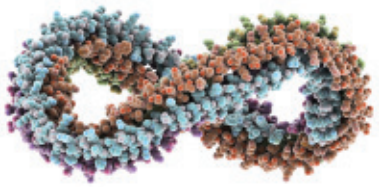
Having team members across disciplines allows the project to conceptualize a clinical application. As Kelleher probes the scientific basis for phenomena in the cell, he works with Levitsky, the study's co-corresponding author, to understand how these could be applied to a specific system. Levitsky, who is also a professor of Medicine, Surgery and Medical Education, originally connected with Kelleher through his leadership in the biomarkers space, in which measurable signs in the blood are used to predict health metrics in patients facing disorders — and in this instance, liver transplant rejection.

"It was really important for Neil that there was a biologically relevant example to contextualize how these proteoform panels can identify diseases non-invasively as markers," Levitsky says. "And there's also a need in my field to have mechanistic biomarkers that are more relevant to their immune biological pathways. This could be the start of a new era in cell-specific markers."

Physicians must suppress the immune system with drug therapy and monitor liver transplant recipients for signs of rejection, often only detected after an episode has begun. Guesswork throughout this process could be eliminated with specific knowledge about what's happening at the most granular level.

> "This could be the start of a new era in cell-specific markers."
>
> **JOSH LEVITSKY, MD**

With the BPA as a reference map, the team took blood samples from participants in one of Levitsky's biomarker collection studies. They examined which proteoforms seemed to activate

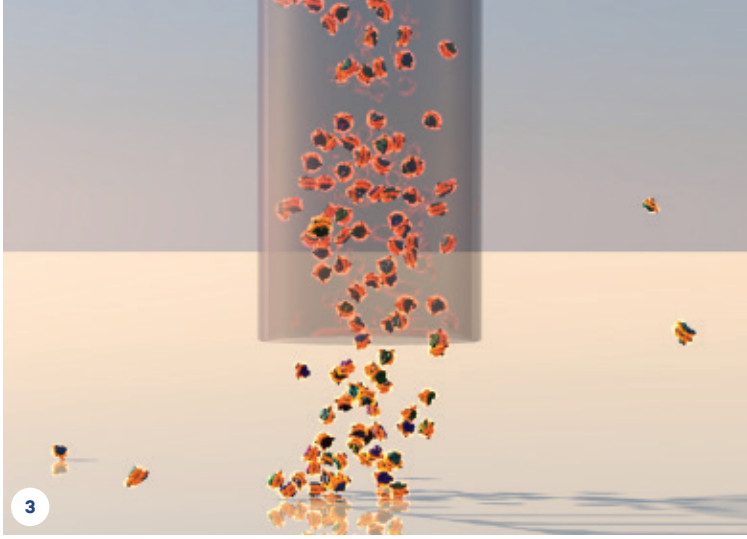


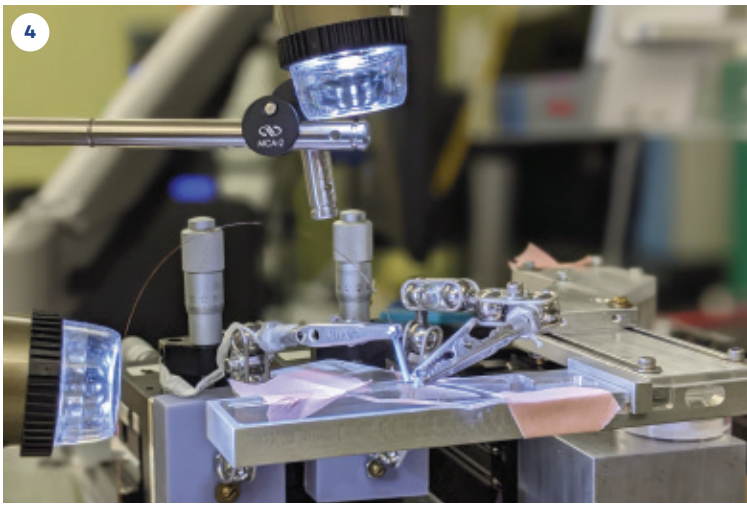
Proteoforms in Cardiovascular Disease

The story of cardiovascular disease risk is often boiled down to the traditional risk factors: cholesterol, blood pressure, insulin resistance, body weight, tobacco use, diet, physical activity, and genetics. But they don't explain all the risk, according to John T. Wilkins, MD, MS, associate professor of Medicine in the Division of Cardiology and of Preventive Medicine in the Division of Epidemiology. He says another factor could be modifications to apolipoproteins, a category of proteins found in the blood that mediate cholesterol metabolism.

Using participants from the Coronary Artery Risk Development in Young Adults (CARDIA) study, Wilkins and Kelleher measured proteoforms of apolipoprotein A1 (apoA1) in 150 participants, comparing specific ratios of proteoforms to cardiovascular risk factors such as waist circumference (a marker of abdominal body fat) and HDL cholesterol. Publishing their findings in the *Journal of the American Heart Association*, the investigators reported a positive association between HDL — good cholesterol — and several proteoform variants of apoA1.

"These findings present opportunities to enhance the understanding of metabolic health and potentially develop better biomarkers," Wilkins says.





in response to the transplant and identified those that changed compared to patients without rejection.

Next, the Levitsky and Kelleher team developed a panel of 24 proteoforms from the initial study and looked at them in transplant recipient samples from across the country. They found the same proteoforms lit up as in the first trial.

"The promise here is to be able to use this panel moving forward to be able to identify patients who have no signs of rejection versus those who have very early evidence of rejection," Levitsky says. "If we can pick up on this several weeks before rejection actually happens, we might be able to modify immunosuppression."

Levitsky continues to examine how proteoforms change in transplant recipients over time to develop additional biomarkers that may inform how he treats patients down the line. Kelleher says as the number of cell types in the atlas grows, so, too, will potential ways to use it. In addition to broadening understandings of human biology, the BPA could have similar applications across immune disorders.

ENDLESS POSSIBILITIES

Each human gene can have from just a few to sometimes over 100 unique proteoforms. And with 20,300 individual genes in the human body, there are millions of proteoforms created by modification or splicing. Kelleher says with a reasonably complete roadmap of each gene's family of proteins, discoveries about disease, aging, and new therapeutics will accelerate significantly.

"We are trying to communicate this potential to the world," Kelleher says. "Feinberg and Northwestern are really at the forefront of this thinking, and I feel fortunate that we have been able to come as far as we have. The arc of history is on our side." ❖

1 Northwestern Proteomics staff analyze intact proteins using mass spectrometry.

2 Members of the Kelleher Research Group and Northwestern Proteomics gather outside of The Richard and Barbara Silverman Hall for Molecular Therapeutics and Diagnostics, the administrative home and intellectual locus of CLP.

3 This image depicts high throughput analysis of nucleosomes (black proteins wrapped in bright orange DNA). Samples are analyzed out of solvent directly into the gas phase for mass spectrometry analysis. Protein separation through the use of capillary electrophoresis has been utilized for native nucleosome mass spectrometry analysis and its subunit characterization.

4 Shown here is Northwestern Proteomics' proteoform imaging mass spectrometry system. It combines Nano-DESI and individual ion mass spectrometry (I2MS) techniques to image proteoforms with high sensitivity directly from tissue. A thin slice of kidney tissue is currently on the glass slide.

Images 1, 2 and 4 by Lisa La Vallee.
Image 3 by Luis Schachner, PhD.

The Science *study was conducted across six institutions with 26 investigators. Rafael Melani, PhD, a research assistant professor in the Kelleher Group, was the first author of the paper, along with Vincent Gerbasi, PhD, also from Northwestern, and Lissa Anderson, PhD, from Florida State University.*

ADDITIONAL REPORTING BY *Win Reynolds and Will Doss*

Written by Bridget Kuehn

Photography by Jose Torres/Gr8y Productions

TRANSPLANT TRANSFORMER

Satish Nadig, MD, PhD, plans to usher in a new era of technology in transplantation as director of Northwestern's Comprehensive Transplant Center.

During his first week of medical school at the Medical University of South Carolina (MUSC), Satish Nadig, MD, PhD, knocked on the door of a transplant surgeon looking for research opportunities. By the end of the week, he had participated in his first organ procurement. It was a liver for a child with less than 24 hours to live. The transplant was successful, and the child survived and was able to go home.

"I never looked back," says Nadig, the Edward G. Elcock Professor of Surgical Research and chief of Organ Transplantation in the Department of Surgery. "I saw the impact the field could make immediately."

That procurement was just the first in a series of fateful moments in his early career. He also participated in an organ procurement on the day he graduated from medical school. Then, during the welcome ceremony for new residents at Beth Israel Deaconess Medical Center at Harvard Medical School, he sat next to Khalid Khawaja, MD, a highly respected transplant surgeon at Beth Israel Deaconess Medical Center. Mid-ceremony, Khawaja received a page and asked Nadig to accompany him on an organ procurement trip to Bangor, Maine.

"Transplant found me, rather than me finding transplant," Nadig says. "It was just meant to be."

Now, he hopes to help lead the field into a new era of transplant medicine as director of the Comprehensive Transplant Center at Feinberg and head of the Northwestern Memorial Hospital Solid Organ Abdominal Transplant Program. To achieve these goals, he plans to work with faculty to better leverage technology to improve organ matching, innovate post-transplant care, and advance transplant equity.

'PUSHING THE ENVELOPE'

Nadig's parents immigrated to the United States from India in the 1970s for his father to attend graduate school. Growing up in Columbia, South Carolina, he had a strong interest in the sciences, which led him to Washington University in St. Louis, where he earned his bachelor's degree in biology and anthropology and conducted undergraduate research. But as the first person in his family to pursue a career in medicine, he wasn't quite sure what specialty to choose.

"I was very interested in research," he says. That interest led him to return home to South Carolina to attend medical school at MUSC and to that pivotal knock on the door.

At the time, the field of organ transplant was still relatively young. Surgeons completed the first transplant in 1954, and the field and techniques used to prevent organ rejection were still evolving.

"By the end of medical school, we were doing transplants differently than when I started," he says.

During his residency at Beth Israel Deaconess Medical School, Nadig met Anthony Monaco, MD, the emeritus Peter Medawar Professor of Surgery at Beth Israel Deaconess Medical Center and Harvard Medical School, a pioneer in ▸

"From molecular biology research to operating room procedures, there are going to be technology-based approaches to change the way we do transplants."

SATISH NADIG, MD, PhD
Edward G. Elcock Professor of Surgical Research and chief of Organ Transplantation in the Department of Surgery

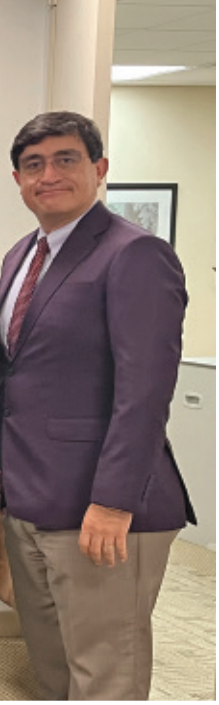
For team bonding, Nadig ordered each surgeon at the Comprehensive Transplant Center a purple jacket with a Northwestern emblem stitched inside.

organ transplant. Nadig credits Monaco with encouraging him to attend the University of Oxford to earn a PhD in transplant immunoregulation. After Nadig completed his PhD and residency, he pursued a fellowship at the University of Michigan in Ann Arbor.

Nadig returned to MUSC in 2013 as an assistant professor. There, he founded the Lee Patterson Allen Transplant Immunobiology Laboratory and the Center for Immunobiologic Therapeutics. He also ran the pediatric and living donor programs while performing transplant surgeries on adult patients. In 2019, he was named the P.K. Baliga Endowed Chair in Solid Organ Transplantation.

Over the past decade, Nadig's research has focused on targeted immunosuppression of the donor organ to reduce or eliminate the need for antirejection medications. Though these medications can help patients live for years, they cause an array of serious side effects, including cancer, metabolic diseases, and life-threatening infections.

"Patients are dying because of the side effects of the antirejection medications and because the organs do not last forever," he explains. "I think we can do better with the technology we have."



Nadig developed and patented a way to encapsulate antirejection medications in nanoparticles and deliver them to donor organs prior to transplant. Preclinical studies in animals have shown that this pre-treatment reduces or eliminates the need for antirejection medications and promotes long-term survival.

"I kept trying to push the envelope, both clinically and academically," he says. That's why when the opportunity to come to Northwestern presented itself, he jumped at the chance to lead a program at a university with robust clinical and research resources.

'PATIENT-CENTRIC IMPACT'

Nadig's mission for the Comprehensive Transplant Center is "patient-centric impact through quality, innovation, and education." That mission starts with optimizing organ utilization so that the right patient gets the right organ, he says. Making better use of the organs available could increase the number of transplants Northwestern Medicine completes each year and help reduce the number of patients on waiting lists.

"There are so many organs that are underutilized or unused for transplant that we can tap into as a resource," Nadig says. "We are going to see more technology-based strategies to improve organ utilization."

1 The Comprehensive Transplant Center team (left to right), in the custom purple jackets that Nadig had made for them: Zach Dietch, MD, MBA, Dinee Simpson, MD, Nadig, Joseph Leventhal, MD, PhD, Daniela Ladner, MD, MPH, Daniel Borja-Cacho, MD, MS, and Juan Carlos Caicedo MD (not pictured: Derrick Christopher, MD, MBA and Vinayak Rohan, MD)

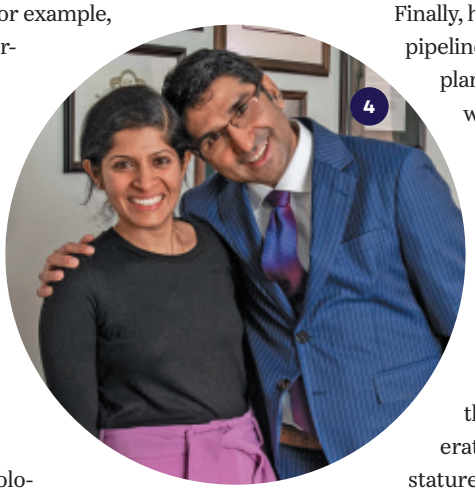
2 Nadig in surgery (Photo by Lauren Hooker)

3 Carla Randles, operations coordinator at the Comprehensive Transplant Center, with Nadig

4 Nadig with his wife, Nandita Nadig, MD, associate professor of Medicine in the Division of Pulmonary and Critical Care

> "I kept trying to push the envelope, both clinically and academically."

He wants to continue to improve the already excellent care Northwestern's transplant patients receive after transplant. To do this, he plans to leverage the health system's research infrastructure to drive technological innovation in transplant care. For example, using machine perfusion of donor organs to deliver therapeutics through nanoparticles can help reduce the need for toxic immunosuppressive drugs post-transplant. Nadig also wants to use new technology-aided techniques, such as CRISPR gene-editing to alter cells in donor organs, to make it easier for recipients' bodies to accept them, as well as deploying robotics and other technologies to improve surgical outcomes.



"From molecular biology research to operating room procedures, there are going to be technology-based approaches to change the way we do transplants," he says.

Nadig also wants to bolster Northwestern's reputation for being a leader in improving transplant equity. In 2006, Juan Carlos Caicedo, MD, professor of Surgery, created the Northwestern Medicine Hispanic Transplant Program to provide culturally competent care for Hispanic patients. In 2019, Dinee Simpson, MD, vice chair for Faculty Development and Diversity in the Department of Surgery and assistant professor of Surgery, created the African American Transplant Access Program.

"We were the first — and we are the largest — and we want to continue to be a model and a beacon for the rest of the country on how we can improve access to transplant care," Nadig says.

Finally, he wants to train a pipeline of new transplant surgeons who will eventually exceed even the accomplishments of their mentors at Northwestern.

"True mentorship is making sure that the next generation exceeds your stature," he says.

Nadig predicts that the next decade will be an exciting time in the field of transplant surgery. Moreover, he believes Northwestern can help lead the way with its multidisciplinary team, ranging from basic scientists to infectious disease specialists to surgeons.

"I want history to look back and say Northwestern was a player in changing the paradigm of how we do transplants," he says. ❖

Listen to our *Breakthroughs* podcast with Nadig at feinberg.northwestern.edu/research/ under the News & Podcasts tab.

Written by Kim Waterman

–The– RIGHT CARE –at the– RIGHT TIME

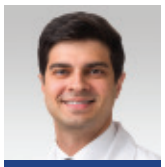
Whether it's an acute cardiac episode or chronic unexplained shortness of breath, Northwestern Medicine's cardiac teams have designed protocols for swift intervention.

Jeff Beck

Jeff Beck was walking on a treadmill when he suddenly felt a tightness in his chest and experienced altered vision. His girlfriend insisted he go to the Emergency Department at Northwestern Medicine McHenry Hospital. Within hours, Beck was in an operating room 50 miles away at Northwestern Memorial Hospital in Chicago for emergency surgery.

Beck had an acute aortic dissection, a potentially catastrophic tear in the largest artery of the body. Upon diagnosis, McHenry Hospital Emergency Medicine Physician Olga K. Sarnov, MD, activated the Northwestern Medicine Code Aorta Program. This rapid-transfer program provides a streamlined pathway for patients diagnosed with aortic emergencies at hospitals across Chicagoland to go directly into the operating room at Northwestern Memorial Hospital.

"By bringing patients directly to the operating room, we are able to provide life-saving surgery almost two hours faster than the traditional approach of bringing patients to the ICU first. The mortality rate of a type A aortic dissection increases 1 percent to 2 percent every hour, so every second counts," says Christopher K. Mehta, MD, director of the Code Aorta Program and a cardiac surgeon at Northwestern Medicine Bluhm Cardiovascular Institute.



CHRISTOPER MEHTA, MD

The Code Aorta Program offers a multidisciplinary team approach. Local emergency departments can contact a referral hotline where physicians connect with Northwestern Medicine cardiac and vascular surgeons within minutes. The physicians review imaging and test results in real time to determine if the patient needs to go directly to the operating room. If emergency surgical care is required, the operating room team is activated, and the patient is transferred.

In Beck's case, the tear was in the lining of the ascending aorta and aortic arch. Blood was pooling between the layers of the wall creating an aneurysm, or bulge, that could rupture. Mehta surgically removed the damaged aorta and replaced it with a synthetic graft, a strong and flexible tube that promotes regular blood flow.

Beck was up and walking the next day and discharged from the hospital five days later. Within a month of his surgery, he was feeling well enough to travel to Baltimore for his daughter's college graduation.

"I am so fortunate to be surrounded by an incredible medical community," Beck says. "I'm keeping an eye on my blood pressure, watching my salt intake and continuing to exercise. My life is pretty much back to normal."

Northwestern Medicine Bluhm Cardiovascular Institute launched the Code Aorta Program in January 2020, and Northwestern Memorial Hospital now repairs more aortic dissections than any other hospital in Illinois. Aortic emergency volume has increased 53 percent since the launch of the program.

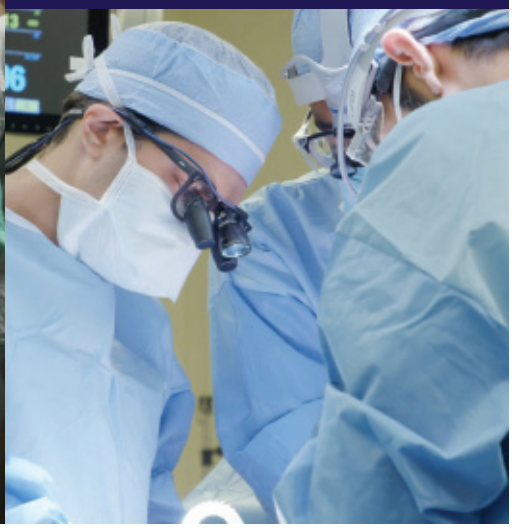
"Our Code Aorta Program delivers swift and comprehensive care to patients in the region who suffer from these catastrophes," says S. Chris Malaisrie, MD, director of thoracic aortic surgery at Northwestern Memorial Hospital. "The Code Aorta Program is a key facet in our specialized aortic center, which offers expert medical care, novel imaging modalities, and complex surgical and endovascular procedures for patients living with aortic disease."

Acute aortic dissections involve the ascending aorta in approximately two-thirds of patients. Chest pain is the most common symptom, but patients may also feel other symptoms, including back pain, abdominal pain or neurological stroke-like symptoms. Beck encourages others to pay attention when something feels off about your health.

"I realized how short life can be," Beck says. "Typically, I'm the guy who doesn't go to the hospital. Had I not gone to the hospital or not listened to the doctor who wanted to run one last test, I could have died in my sleep. Take care of yourself and listen to your body."

Addressing a Lifetime of Suffering With a Single Test

Dona Smith's experience with chest pain was not so sudden — she'd experienced chest pain and shortness of breath for 20 years. At times it was so severe, it would stop her in her tracks. She had two heart surgeries, was prescribed inhalers for asthma, and took numerous medications. However, nothing seemed to address the breathing discomfort until she underwent a multidisciplinary examination at the dyspnea



← Dona Smith, who suffered from chest pain for two decades, completed the iCPET testing program to understand her condition.

↓ Christopher Mehta, MD, director of the Code Aorta Program, performing a surgery.

clinic at Northwestern Medicine Central DuPage Hospital.

Dyspnea, which is labored or difficult breathing, can have many causes. The dyspnea clinic at Northwestern Medicine Central DuPage Hospital was developed specifically to help patients who, despite numerous tests and interventions, still don't have an answer for what is causing their shortness of breath.

"We know patients who have unexplained shortness of breath after a preliminary workup often struggle for a long time without getting a diagnosis to explain their symptoms," said Nauman Mushtaq, MD, medical director of Cardiology for Northwestern Medicine Bluhm Cardiovascular Institute at Central DuPage Hospital, Delnor Hospital and Kishwaukee Hospital. "These patients may be really sick and have been bouncing among specialists to try to figure out what is wrong. Our clinic brings many experts together to get to the heart of the problem," he said.

NAUMAN MUSHTAQ, MD

Physicians who specialize in general cardiology, heart failure, interventional cardiology, heart rhythm disorders, pulmonology, and imaging, along with staff in the cardiac catheterization and respiratory labs, come together to discuss clinical cases and develop a plan to evaluate patients with unexplained shortness of breath.

Innovative Diagnostic Testing

A key component of the clinic evaluation is the invasive cardiopulmonary exercise testing (iCPET) program. The test happens inside an interventional lab so that cardiovascular, respiratory, and metabolic function can be assessed simultaneously during the exercise.

The patient completes a stress test on a bicycle with an electrocardiogram monitor. But it is no ordinary stress test. A catheter is placed in the pulmonary artery through the neck, and a mask is placed over the nose and mouth to measure gas analysis and respiratory mechanics. A team of experts that include an interventional cardiologist, exercise physiologist, respiratory therapist, and others monitors the patient.

"People may have multiple reasons that partially explain the shortness of breath. They could have underlying lung and heart disease, but you don't know which component is the problem," says Mushtaq. "Respiration, gas transport to the tissues and pushing out CO_2 require a great deal of coordination within the body. Testing these functions together helps us discover the limiting factor that is causing the symptoms."

Smith says she jumped at the chance to get the test done. It revealed she had exercise-induced heart failure due to hypertrophic cardiomyopathy, even though everything looked good at rest. Mushtaq adjusted her medications, and Smith is now back to taking long walks with her family.

"For so many years I was frustrated, sitting in doctors' offices in tears because I knew I wasn't fine," Smith says. "It was very clarifying to find out exactly what was going on with my heart. Now I can walk without the fear of going into cardiac arrest." ❖

Landmark Gift

Chicago philanthropist Neil G. Bluhm and the Bluhm Family Charitable Foundation announced a $45 million gift to establish the Northwestern Medicine Bluhm Heart Hospital at Northwestern Memorial Hospital. The gift expands cardiac care capacity and addresses health equity by providing greater access to Northwestern Medicine's world-class cardiovascular care. Northwestern Memorial Hospital is consistently ranked as the top heart program in Illinois and among the top in the country for cardiology and heart surgery.

The Bluhm Heart Hospital will expand to 140 beds and modernize cardiovascular services on Northwestern Medicine's Chicago campus. The gift will also support collaboration with community partners in under-resourced Chicago communities to develop outreach and education efforts to support heart health and address the social determinants of health.

Trailblazers in Orthopaedics

How a close-knit, multigenerational group of Black orthopaedic surgery residents put their mark on Northwestern Medicine

Back row, left to right: Muhammad Mutawakkil, MD, Clarence Woods, MD, Randall Morgan, Jr., MD, MBA. Front row, left to right: Erik King, MD, Audley Mackel, III, MD, James Hill, MD, Linda Suleimain, MD, and Clyde Yancy, MD, MSc, vice dean for Diversity and Inclusion and chief of Cardiology in the Department of Medicine, who toasted the group before dinner.

On a rainy evening in March, seven surgeons, all of whom completed their residencies at McGaw Medical Center of Northwestern University, gathered at a Streeterville restaurant to share a meal with their friends, colleagues, and mentors. Professionally speaking, they were convening for the annual meeting of the American Academy of Orthopaedic Surgeons, but this intimate party was much more than a convention of people in the same specialty — it was a cherished opportunity to reconnect with kindred spirits.

Spanning more than 50 years at Northwestern, this group of six Black men and one Black woman (along with six others who were not present) have helped one another break barriers and climb ranks in what's known as the whitest specialty in medicine: orthopaedic surgery. Trailblazers at Northwestern and in their profession alike, each of them is passing a torch to the next generation as they continue to fight for more diversity and inclusion in their chosen field, which is currently less than 2 percent Black.

MEMORIES OF PREJUDICE, PARTNERSHIP, AND PERSEVERANCE

The first surgeon to enter the room was, fittingly, Clarence Woods '64 MD '72 GME, who in 1973 became the first Black board-certified orthopaedic surgeon in Chicago. Northwestern's first Black resident and a celebrity in the group, he

Clarence Woods, MD, holds a name tag from a past Feinberg reunion, showing his medical school graduation picture.

also received a Bronze Star for distinguished U.S. Army service in Vietnam from 1966 to 1967.

"There is my hero," said Audley Mackel III, MD '86 GME as he entered, making his way to Woods to shake his hand.

Woods retired in 2014 and lives in Sedona, Arizona, after a long, successful career as a general orthopaedic surgeon in Los Angeles. He served as chief of Orthopaedics at Martin Luther King, Jr./Drew Medical Center for 10 years, training more than 30 orthopaedic surgeons.

Yet, during his time as the only Black orthopaedic resident at Northwestern, he put up with frequent indignities, including being prevented from seeing some of the white patients at Evanston Hospital.

"My attending would say, 'You have to understand … that's just the way it is with some people,'" Woods recalled. "It was hard to hear that, but I also experienced plenty of support from faculty and fellow trainees."

With his determination and undaunted spirit, Woods paved the way for others to follow, starting with Randall Morgan, Jr., MD, MBA, '74 GME, who earned his MD degree from Howard University, a historically Black university (HBCU).

WRITTEN BY *Gina Bazer* · PHOTOGRAPHY BY *Teresa Crawford*

Another recognized champion of equity in medicine, Morgan, too, experienced painful humiliations during his residency, such as the time a white patient at Passavant Memorial Hospital refused to allow him to treat her fractured wrist. "This patient told me to call Dr. James Stack, who was doing laps at Lake Shore Athletic Club at the time. So, I did, and I explained the situation," he said. "Dr. Stack told me to tell this patient that if the procedure was too tough for me to do, then it was too tough for him, too, and so she finally let me do it."

"There were other allies, too, like Dr. William Kane, Dr. Michael Schafer, and Dr. David Stulberg, and fellow residents who were truly color blind," Morgan added. "They fought for us."

Morgan would eventually go on to devote more than 40 years fighting for healthcare equity. He currently serves as the founding executive director of the W. Montague Cobb/National Medical Association Health Institute. He was also the 95th president of the National Medical Association and maintained an orthopaedic surgery practice in his hometown of Gary, Indiana, before moving to Sarasota, Florida, where he became that city's first Black orthopaedic surgeon.

As Morgan was finishing his residency, a young James Hill, '74 MD, '79 GME, who had just completed medical school at Northwestern, started an internship in the department. By then, he had already experienced his share of discrimination in medical school — not being able to complete an OB-GYN rotation with his medical school classmates, for example.

"I was the only one in my class to rotate at Cook County Hospital, while the others rotated at Passavant; I guess some of the Passavant patients didn't like the idea of me watching them," he said.

He continued on in the department as a resident, then joined the faculty in 1980, and stayed at Northwestern for more than 40 years and counting. He is now a professor of Orthopaedic Surgery.

During the course of his career, Hill has provided care for the National Football League and Olympic athletes as well as underserved communities in Ethiopia. He was on the board of trustees at Talladega College, Alabama's oldest historically Black liberal arts college, and is a founding member of the J. Robert Gladden Orthopaedic Society, an organization dedicated to increasing diversity in orthopaedic surgery. In 2020, he received the Diversity Award from the American Academy of Orthopaedic Surgeons.

'THE TORCH-PASSING IS ESSENTIAL'

In the 1980s, while they were both at Northwestern, Hill and Morgan met the talented Mackel, who was doing a summer internship at at a hospital in nearby Gary, Indiana. Later, when Mackel applied for his residency at Northwestern, "We knew we wanted him," Morgan said.

"They validated me to other faculty members," Mackel said. "Having that kind of network has helped all of us, and it is why we are working so hard to continue to build that community now."

Mackel is the author of several published articles and book chapters about orthopaedics. He has been in a private orthopaedic surgery practice since 1988 and is a clinical instructor at the Case Western Reserve University School of Medicine as well as division chief of Orthopaedics and the past president of medical staff at St. Vincent Charity Hospital Medical Center in Cleveland.

Decades into their careers, Morgan and Hill were also mentors for Linda Suleiman, MD, '17 GME, who is now an assistant professor of Orthopaedic Surgery and assistant dean of Medical Education at Feinberg, as well as director of Diversity and Inclusion at McGaw Medical Center of Northwestern University. She is making her mark not only on the future of medical education, but also as one of just six Black female surgeons in the country trained to perform joint replacements.

While it was a long road for Suleiman, she knew from the get-go that her predecessors had her back. In 2012, on the first day of her residency, she received a voicemail from Morgan wishing her good luck. A decade later, she still keeps this message saved on her iPhone, and she played it for everyone at the dinner — just before sharing a photo of herself and her own protégé, Muhammad Mutawakkil, MD, '22 GME, seated ▸

The dinner party — all pictured on the previous page — also included Woods' wife Pamela Woods (seated next to Woods) and her son, Shawn Hill (seated across from Woods), along with Angela Mota from Northwestern's office of development (to the right of Pamela Woods) and Gina Bazer, editor of *Northwestern Medicine* magazine (to the right of Morgan).

Hill poses with his souvenirs from the Olympics for the Winter 1988 issue of this magazine.

seated next to her, who was recently hired by the department.

"He is like my little brother," she said, pulling him in for a hug.

"I met Dr. Suleiman when I was doing a trauma rotation during a summer program at Northwestern, and she is one of the biggest reasons I wanted to come here for my residency," Mutawakkil responded affectionately, adding that now that he has completed his training, he feels a sense of duty to pay it forward.

"The torch-passing is essential. Look, it's been more than 50 years since Dr. Woods started his residency, and there have still only been 13 of us," he said. "I have to do my part."

'I GUESS I DO HAVE A PLACE HERE'

Another colleague at the table was Erik King, MD, '98 GME. Now interim division head of Orthopaedic Surgery and Sports Medicine at Ann & Robert H. Lurie Children's Hospital of Chicago and associate professor of Orthopaedic Surgery at Feinberg, he, too, was no stranger to racism during his residency.

"When I was a resident, this was around 1996, I went to see a patient at my attending's private clinic. When I came into the room, the patient told me he didn't want to see me. I didn't want to force myself on him, so I left and told my attending, Dr. Greg Palutsis, what happened. He sent his nurse in to explain that I was the resident and would see him first, and that Dr. Palutsis would follow. When I returned the second time, the man still refused to see me. The nurse communicated to us that the reason was because I was Black. So, Dr. Palutsis went into the room with the man's coat, told him that if he wouldn't see me, then he wouldn't be seen at the clinic, and showed the man the door. The patient left, and that was the end. My attending lost a patient because he stood up for me. And I thought, 'Oh, I guess I do have a place here.'"

King did, indeed, find a place at Northwestern. After serving as chief resident at Lurie Children's (formerly Children's Memorial Hospital), King was recruited, upon the completion of his fellowship in Pediatric Orthopaedic Surgery and Scoliosis at Texas Scottish Rite Hospital for Children, to return to Northwestern as faculty — and has been here ever since. He was the first Black full-time surgeon at Lurie Children's.

Like his fellow alumni, King is proud of his Northwestern affiliation. Together, these pioneers aren't just working to give their best to their patients. They're also out to change the face of orthopaedic surgery — and of all medicine — to give more people of color a place in the profession. They all agree that it will take time, and it will take allies like those they found during their own early days at Northwestern. But they aren't giving up.

"What we accomplished didn't happen in a vacuum," said Morgan. "And there is still plenty of work to do."

THROUGH THE YEARS

Celebrating Northwestern's Black Orthopaedic Surgery Residents

Clarence Woods, '64 MD, '72 GME

Randall Morgan, Jr., MD, MBA, '74 GME

James Hill, '74 MD, '79 GME

Audley Mackel, III, MD, '86 GME

Robert E. Bartley, III, MD, '92 GME (deceased 2021)

Erik King, MD, '98 GME

Bryan Little, MD, '03 GME

Alfred Joseph Cook, '03 MD, '08 GME

Le Don Anthony Robinson, '08 MD, '13 GME

Andre D'Edrick Ivy, MD, '15 GME

George Ochenjele, '10 MD, '15 GME

Linda Suleiman, MD, '17 GME

Muhammad Mutawakkil, MD, '22 GME

Top: Hill and Suleiman with the late Michael Schafer, MD, '72 GME, professor and former chair of Orthopaedic Surgery, the longest-serving chair in the department's history.

Center: King teaching Bryan Little, MD, in 2000; he performed the same surgery with Suleiman in 2017 and Mutawakkil in 2022.

Bottom: Morgan, far right, during his residency days at Northwestern.

Find your Eudaimonia

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

Eudaimonia: Greek for the state or condition of good spirit, commonly translated as happiness or welfare.

The term "happiness" is used in the context of mental or emotional states, including positive or pleasant emotions ranging from contentment to intense joy. It is also used in the context of life satisfaction, well-being, and flourishing. Aristotle said that eudaimonia means "doing and living well."

There are many things that can lead to happiness, cause happiness, or just remind us to be happy. This can include family members and loved ones, memories of events, a hobby or exercise, food, movies, vacations, or amusement parks.

Dogs have also been linked to happiness. In 2019, a study led by Lauren Powell, PhD, a postdoctoral researcher at University of Pennsylvania, looked at whether getting a dog improved the owner's activity level, cardiovascular health, and psychological state.

Powell and her colleagues then compared the dog-owners to members of the two dogless control groups, statistically manipulating factors such as education, age, and appetite for exercise, to make sure that the canine alone accounted for any differences. After three months, people with dogs walked 2,589 more steps a day than the control groups.

"But at eight months there was a drop-off, so the difference was no longer significant," said Powell, speculating that, "People were really excited at first, but maybe the novelty wore off."

The psychological impact of a dog packed a bigger punch. They found that the loneliness in the group that got a dog decreased by 40 percent and stayed at that lower level at eight months. But how exactly do dogs make us happier?

In a previous study, Powell's group had shown that owning a dog promotes the flow of oxytocin, a hormone that decreases our heart rate and fosters feelings of well-being and relaxation. Plus, she adds, dogs "encourage their owners to get out in nature, maintain a sense of routine, and stay in touch with their neighbors."

Even on a neurochemical level, relationships with different sorts of animals have different effects on happiness. Paul Zak, an economist at Claremont Graduate University in California, has found in his research that dogs get a 57.2 percent oxytocin boost when they interact with their owners. Cats get a 12 percent boost. In other words, your dog truly adores you. Your cat accepts your presence … for now.

We derive happiness from many things. One of them is our dog, Louis. From my vantage point, Louis has achieved eudaimonia. He has constant companionship, sleeps in a comfortable bed, is treated with snacks, and even dresses in fancy clothes.

Louis's state of eudaimonia helps with our happiness. Additionally, Louis has a back story. He was gifted to our family by one of my longest surviving patients who beat stage 4 lung cancer. She was diagnosed in 2002 with two large tumors in her brain and another large tumor in her chest. The median survival for this type and stage of cancer was eight months at the time. Miraculously, the chemotherapy and subsequent radiation therapy (after brain surgery and radiation) controlled her cancer for the better of 20+ years.

Being a lovable affectionate companion in addition to inspiring memories of my patient, Louis continues to bring us such joy and happiness — perhaps one day helping us, too, achieve true eudaimonia.

Check out Louis on Instragram!
@LouisVYorkieStyle

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.

From Lab Partners to Life Partners

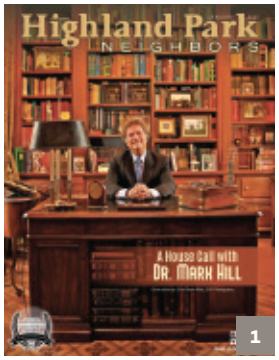
In honor of their 45th medical school reunion, **Philip M. Weinerman '75, '77 MD, '80 GME**, wrote in to share how he and his wife **Julia A. (Davidson) Weinerman '75, '77 MD**, met:

"Julie and I attended the September 1971 Northwestern University HPME (Honors Program in Medical Education) freshman orientation. We met, talked, and she asked if I would like to be her physics lab partner. I said sure, with no clue that this would lead to… dating, marriage, five children, lots of grandchildren, two satisfying careers, countless hours of community volunteering, and many loving memories.

50 years later, we are still partners.

We retired recently from radiology and physical medicine and love spending time with our 19 grandchildren and continuing our volunteer community work. We both are grateful for the excellent education we received at Northwestern and for the friendships we made."

1970s



Mark Hill, '77 MD, FACS, was recently featured as the cover story for the January 2022 issue of *Highland Park Neighbors* magazine. The profile on Hill celebrates his lifelong and passionate dedication to a productive life of service through medicine, civic and community involvement, music, education, and environmental efforts. An accomplished musician, Hill has been in practice on Chicago's North Shore for 40 years. He is professor of Surgery at the Chicago Medical School (now known as the Rosalind Franklin School of Medicine) and the new Kansas College of Osteopathic Medicine, where he is developing a new surgical curriculum. Hill is also president and chief executive officer of his medical practice, North Shore Surgical Associates. 1

1980s

Frank C. Candela, '82 MD, '87 GME, began painting two years ago and recently launched an Instagram page featuring his artwork. Candela is a California-based general and oncologic surgeon. To see Candela's artwork, follow him on Instagram @the_painting_surgeon. 2

Anna M. Kelly, '83 MD, is practicing obstetrics and gynecology at Platte Valley Medical Center in Brighton, Colorado, and occasionally accepts locum tenens work at remote hospitals in need of coverage as they search for permanent medical staff. ***James P. Kelly, '83 MD***, is executive director of the Marcus Institute for Brain Health at the University of Colorado Anschutz Medical Center in Aurora, Colorado, where he is

professor of Neurology. The Marcus Institute is a clinical care and research institute for military veterans and first responders with persistent effects of traumatic brain injury. Anna and Jim have four adult children, one in each time zone across the country, and two grandchildren, one on each coast.

1990s

Christopher S. Kang '92, '96 MD, '00 GME, has been named president-elect of the American College of Emergency Physicians (ACEP). He will serve a one-year term before assuming the presidency next October during ACEP22 in San Francisco, California. Kang has served in leadership roles at multiple professional organizations at both the state and national level, including the Washington State Medical Association and the Disaster Clinical Advisory Committee of the Northwest Healthcare Response Network, as well as being a member of the Board of Directors and president of the Washington Chapter of the ACEP. He was elected to the ACEP board of directors in 2015 and served as treasurer from 2019–2020 and as chair from 2020–2021. Kang is also a diplomate of the American Board of Emergency Medicine. 3

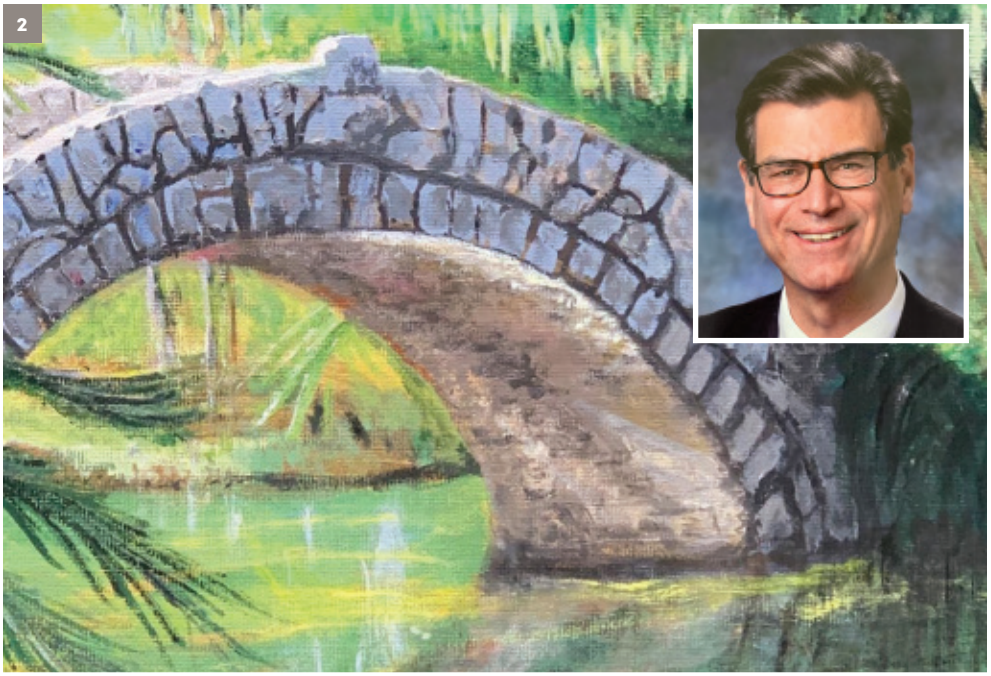
Richard E. Heller, III, '99 MD, '00 GME, '12 MBA, has been elected an at-large director on the Radiological Society of North America's (RSNA) Board of Directors. Heller is associate chief medical officer for Communications and Health Policy and national director of Pediatric Radiology at Radiology Partners. He also serves as clinical associate at University of Chicago Medicine, Comer Children's Hospital in Chicago. Heller will serve on the RSNA Board of Directors for a three-year term. 4

GME

Lyle L. Berkowitz, MD, '95 GME, has joined the board of PatientBond, a consumer-science-driven patient engagement software service provider. Berkowitz is associate professor of Clinical Medicine at Feinberg and editor-in-chief of *Telehealth and Medicine Today*. Berkowitz serves on the board of directors of Oneview Healthcare and as an advisor to a variety of digital health companies and venture firms. Previously, Berkowitz was the founder and chair of Healthfinch and chief medical officer for MDLIVE. 5

Christopher S. Davis, MD, MPH, '14 GME, '16 GMEF, was selected as a director-at-large for the Association for Academic Surgery Foundation (AASF). The AASF serves to support "…the advancement of surgical care by providing resources and education to young surgeon scientists." As a proud surgeon-scientist and educator himself, Davis values this opportunity to impact the future generation of surgeons early in their careers and to give back in a similar way to those who gave a jumpstart to his own early successes. Davis shared that he is "grateful for the opportunity to have learned so much from membership on the MAAB," and that he "looks forward to utilizing this experience to forward the mission of the AASF as well." 6

ANNA M. KELLY, '83 MD, AND JAMES P. KELLY, '83 MD, HAVE FOUR ADULT CHILDREN, ONE IN EACH TIME ZONE ACROSS THE COUNTRY, AND TWO GRAND-CHILDREN, ONE ON EACH COAST.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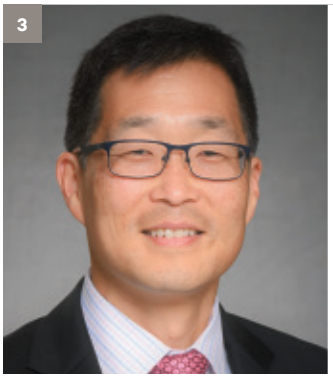
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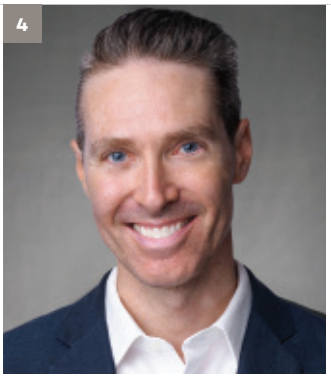
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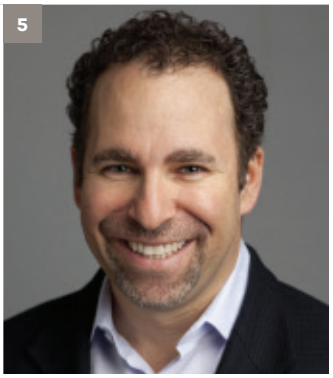
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WELCOME THE NEXT GENERATION OF NORTHWESTERN PHYSICIANS

Where It All Began

Founders' Day celebrates the distinguished history of Northwestern University Feinberg School of Medicine and introduces students to the unique responsibilities that lie ahead for them as physicians.

On this day, the white coat ceremony welcomes the incoming class to Feinberg and honors those who have come before. This fall, our first-year students will embark on their medical journey and don their white coats for the first time.

Your involvement in this momentous occasion bridges the generations of medicine and is symbolic of our incredible medical alumni community.

Make your gift to support a white coat this year at **giving.northwestern.edu/whitecoatfy22**.

JONATHAN TSAY '15, '18 DPT HAS SEVEN PUBLICATIONS, FIVE UPCOMING, AND HAS BEEN A PEER REVIEWER FOR SEVERAL MEDICAL JOURNALS IN THE AREAS OF NEURO-REHABILITATION, MOTOR LEARNING, PROPRIOCEPTION, CEREBELLAR ATAXIA, AND PARKINSON'S DISEASE.

PT

Jennifer Gilbertson '87, MHS, DPT, is the 2022 recipient of the Department of Physical Therapy & Human Movement Science (NUPTHMS) Alumni of the Year Award. Since graduating, Gilbertson has continued her education, culminating in receiving her DPT and orthopaedic clinical specialty certification. She has served as the assistant director of outpatient therapy services at UChicago Medical Center, improving the interdisciplinary relationship of healthcare professionals and fostering a supportive, respectful, compassionate, and empathetic team environment. 7

Jennifer A. Weiss '93, '96 MPT, has been named chief executive officer of the Encompass Health Rehabilitation Institute of Libertyville, Illinois, a 60-bed hospital, expected to open in March 2022, which will provide around-the-clock nursing care and physical, occupational, and speech therapies to patients recovering from major illnesses and injuries. Weiss most recently served in leadership roles at AMITA Health, including regional director of Rehabilitation Services and director of Respiratory Care. She previously served as system director of Rehabilitation Services at Schwab Rehabilitation Hospital and as coordinator of Inpatient Rehabilitation at Ingalls Memorial Hospital. 8


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13

Dawn S. Brown '96, '99 MPT, DPT, is the 2022 recipient of the NUPTHMS Diversity, Equity, and Inclusion Achievement Award. Brown is clinical assistant professor and director of clinical education in the Northern Illinois University Doctor of Physical Therapy Program. With over 21 years of clinical and educational experience, she is currently completing her dissertation in the Doctor of Education Program in Higher Education Administration at Northern Illinois University. Brown earned board-certification in orthopaedic physical therapy from the American Board of Physical Therapy Specialists and uses this content expertise in her teaching and clinical practice. 9

Rodney L. Weir '99 MPT, DPT, DHS, NCS, recently founded the Rodney Weir Marching Band Scholarship, given to the Berrien, Michigan Community Foundation. A 1992 Rose Parade drum major, Weir started this scholarship to celebrate the importance of education and the opportunities marching band provided him. Weir is assistant professor of Physical Therapy at Western Michigan University. 10

Jessica L. LeJeune, '12 DPT, developed an on-demand webinar through the American Physical Therapy Association Section on Pelvic Health titled "Acute COVID-19 and Respiratory Failure in Pregnancy: Physical Therapy Management." LeJeune identified the need for specialized care of these patients during the COVID-19 pandemic through her acute care work in women's health. LeJeune developed this course to help other clinicians provide evidence-based care for this highly specialized population. 11

Kristen Tinlin, '13 DPT, is the 2022 recipient of the NUPTHMS Young Alumni of the Year Award. Since graduating, Tinlin has worked in central Indiana with nursing and therapy staff in critical

KRISTEN TINLIN, '13 DPT, IS THE 2022 RECIPIENT OF THE NUPTHMS YOUNG ALUMNI OF THE YEAR AWARD. SINCE GRADUATING, SHE HAS WORKED IN CENTRAL INDIANA WITH NURSING AND THERAPY STAFF IN CRITICAL CARE, TREATING PATIENTS WHO ARE SEVERELY BURNED.

JESSICA COHEN, '16 DPT, HAS BEEN NAMED HEAD ATHLETIC TRAINER FOR THE PORTLAND TRAIL BLAZERS, BECOMING THE ONLY WOMAN TO CURRENTLY SERVE AS HEAD ATHLETIC TRAINER IN THE NBA.

care, treating patients who are severely burned. She has worked with Harry Dyer and The Harry Dyer Burn Center in Kenya to increase access to patient care in Africa, which has significantly improved patient mortality and recoveries for improved quality of life. Tinlin earned her lymphedema clinical specialty certification and is a certified wound therapist. She also has a love of dogs and is certified in canine rehabilitation, providing orthopaedic care for canines throughout central Indiana at Paws Rehab. 12

Jonathan Tsay '15, '18 DPT, is the 2022 recipient of the NUPTHMS Research Achievement Award. Tsay is pursuing his PhD in Psychology and Cognitive Neuroscience at the University of California, Berkley. He has seven publications, five upcoming, and has been a peer reviewer for several medical journals in the areas of neurorehabilitation, motor learning, proprioception, cerebellar ataxia, and Parkinson's disease. 13

Jessica Cohen, '16 DPT, has been named head athletic trainer for the Portland Trail Blazers, becoming the only woman to currently serve as head athletic trainer in the NBA. Cohen previously served as the team's assistant athletic trainer/physical therapist since her arrival in 2019. She spent seven seasons in the WNBA, serving as head athletic trainer and physical therapist for two seasons with the Atlanta Dreams and for five seasons with the Chicago Sky. Cohen also worked with the National Lacrosse League's New England Black Wolves and toured with celebrity performers. She is a certified performance, strength and conditioning, and sports physical therapy specialist.

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 unless specified below.

ALUMNI

Don Lewis, '47 WCAS, '51 MD
Seattle, WA
DECEMBER 8, 2021

Loren Call Barlow, '51 MD
Eugene, OR
FEBRUARY 2

Everett D. Hendricks, '51 MD
Prescott, AZ
DECEMBER 3, 2021

Thomas J. Williams, '51 MD
Grandview Heights, OH
DECEMBER 6, 2021

Whitney W. Crossman, '51 MD
DECEMBER 11, 2021

Carleton J. Wright, '52 MD, '53 GME
Los Gatos, CA
DECEMBER 8, 2021

Edwin E. Gordon, '52 MD, '52 MS
Bethesda, MD
JANUARY 4

David Fasano, '52 DDS
Norwood, MA
JANUARY 4

Donald W. Ourada, '53 DDS
Western Springs, IL
DECEMBER 16, 2021

Otto O. Stevens, '54 DDS
Spokane, WA
JANUARY 28

George Yen, '54 DDS
Bellevue, WA
NOVEMBER 20, 2021

Suzanne L. Hudson '55 BSN
Madison, CT
JANUARY 27

Harold E. Fromm, '57 MD
Fairburn, SD
DECEMBER 13, 2021

Lenore Sheridan Tsang, '57 MD
Portola Valley, CA
FEBRUARY 14

William H. Hoag, '57 MD
Oro Valley, AZ
FEBRUARY 3

Lois Hulquist Orndorff, '58 BSN
Mequon, WI
NOVEMBER 25, 2021

Thomas G. Soper, '60 MD, '65 GME
Evanston, IL
DECEMBER 17, 2021

Harry A. Osborne, '62 DDS
Canton, OH
JANUARY 23

Robert Buttemiller, '63 WCAS, '66 MD
Litchfield Park, AZ
JANUARY 10

Blaine H. Wilcox, '64 DDS
Salt Lake City, UT
FEBRUARY 20

Richard G. Dedo, '64 MD, '69 GME
Hillsborough, CA
DECEMBER 20, 2021

Daniel S. Duick, '67 MD
Phoenix, AZ
JANUARY 5

Charles R. Martinez, '69 DDS
Hoffman Estates, IL
JANUARY 28

David A. Vagneur, '70 MD
Minneapolis, MN
NOVEMBER 11, 2021

David W. Miles, '72 DDS
Logan, UT
JANUARY 16

Philip K. Newman, '72 MD
Winnetka, IL
NOVEMBER 24, 2021

Dennis D. Riston, '75 MD
Lumberton, TX
JANUARY 4

Frank Olu Apantaku, '75 MD
Skokie, IL
FEBRUARY 22

Silas J. Thomas, '76 MD
MAY 25, 2020

Benedict A. Marchlewicz, '81 PhD
Libertyville, IL
FEBRUARY 2

Cathlyn E. Stephen, '83 WCAS, '87 MD, '90 GME
Algonquin, IL
FEBRUARY 4

Phil Hageman, '21 MD
Chicago, IL
DECEMBER 12, 2021

FACULTY

Edward F.X. Hughes, MD, MPH
professor emeritus
Evanston, IL
JANUARY 23

Miguel Angel Oviedo, MD, '68, '73 GME
assistant professor of Surgery
Northbrook, IL
NOVEMBER 30, 2020

Jeremiah Stamler, MD
Sag Harbor, NY
OCTOBER 27, 1919 – JANUARY 26, 2022

Jeremiah Stamler, MD, founding chair and professor emeritus of Preventive Medicine, passed away on January 26. He was 102 years old. Known as the father of preventive cardiology, Stamler helped transform the understanding of diet and cardiovascular health.

Stamler was born on October 27, 1919 in Brooklyn, New York. He earned his bachelor's degree from Columbia University and his medical degree from State University of New York in Brooklyn in 1943. He completed an internship at Kings County Hospital Center in Brooklyn, New York, in 1944 before serving in the U.S. Army until 1946, where he was honorably discharged.

Stamler joined Northwestern in 1958 as an assistant professor in the Department of Medicine. In 1972, he became the inaugural chair of the newly created Department of Community Health and Preventive Medicine, a position he held for more than 18 years before becoming professor emeritus of Preventive Medicine in the Division of Epidemiology in 1990. In 2014, The Jeremiah Stamler Professorship in Preventive Medicine was established in his honor.

"Jerry was a giant intellect who founded the fields of cardiovascular epidemiology and preventive cardiology and led in defining new prevention concepts right up until his last days. He was also a kind and gentle soul who believed in people. As the current chair of the department he founded 50 years ago, I can say that we are all so grateful to have known him, to have been mentored by him, and to have been inspired by his example," said Donald Lloyd-Jones, MD, ScM, chair of Preventive Medicine and the Eileen M. Foell Professor of Heart Research.

Andrew D. Bunta, '64 BSM, '67 MD, '74 GME
Lake Forest, IL
AUGUST 2, 1942 – FEBRUARY 24, 2022

Andrew D. Bunta, '67 MD, '74 GME, associate professor of Orthopaedic Surgery, passed away on February 24. He was 79 years old. In 2021, he was named a "Pillar of the Orthopaedic Profession" by the American Orthopaedic Association (AOA).

Bunta was born in Chicago on August 2, 1942. After earning his bachelor's degree from Northwestern in 1964, Bunta graduated from Feinberg in 1967. He served as a General Medical Officer with the United States Air Force in Minot, North Dakota, from 1968 to 1970. Bunta then completed his residency training in Orthopaedic Surgery at Northwestern in 1974 and joined the Feinberg faculty the same year.

In 1999, Bunta joined the medical staff at Northwestern Memorial Hospital (NMH) as an attending physician. From 1999 to 2015, he served as vice chairman of the Department of Orthopaedic Surgery and as associate program director of the orthopaedic surgery residency program. Most recently, he served as medical director of the NMH Orthopaedic Unit and then as medical director of Clinical Documentation at NMH and Northwestern Medicine Lake Forest Hospital.

Bunta held various leadership positions with the Medical Alumni Association over the years, including serving as president from 2001 to 2003. In 2012, he was honored with Feinberg's Alumni Faculty Lifetime Achievement Award. He also held leadership roles at the AOA.

Bunta was married to Susanna Guenther Bunta for more than 56 years. He was the loving father of Elizabeth Bunta Haussman Bartels (Gilpin Bartels) of Bryn Mawr, Pennsylvania, and of Maria R. Bunta of Chicago, Illinois. He was the devoted grandfather of Charles B. Haussman and James R. Haussman, both of Bryn Mawr, Pennsylvania.

David Holtzman, MD, is breaking new ground in identifying, treating, and preventing Alzheimer's disease and other disorders that affect memory and thinking.

ON THE CUSP

When David Holtzman, '85 MD, was in his second year of medical school at Northwestern, he was surprised to learn how little was known about Alzheimer's disease.

"I was shocked because it was the most common cause of dementia, yet our understanding and ability to treat the disease was poor," says Holtzman, the Barbara Burton and Reuben M. Morriss III Distinguished Professor in the Department of Neurology at Washington University in St. Louis. But his shock quickly turned into determination to fill that knowledge void.

Since then, Holtzman, who is the recipient of Feinberg's 2022 Distinguished Alumni Award, has emerged as a leader in Alzheimer's disease research. His research has helped reveal how genetic variants of Apolipoprotein E (APOE) contribute to the development of the disease, and his team has brought antibody-based therapies into clinical trials. He has also helped to build and grow two collaborative centers for brain disease research and co-launched a startup that has brought a blood test for Alzheimer's disease to the market.

"It's been incredible," Holtzman says. "When I first started learning about this over 30 years ago, we had absolutely no clue of what caused Alzheimer's disease or how to treat it; now we are on the cusp of having real, powerful treatments."

PLAYING THE LONG GAME

After Northwestern, Holtzman completed his residency at the University of California, San Francisco (UCSF). During his post-doctoral research at UCSF, he became interested in APOE and its role in Alzheimer's disease. Though his post-doctoral research focused on mouse models of neonatal stroke and neurodegeneration, he began collaborating with other scientists at UCSF on APOE research.

In 1994, Holtzman joined the faculty at Washington University in his hometown of St. Louis. He devoted his new laboratory to study what APOE does in the brain and how genetic variants of APOE contribute to the development of Alzheimer's disease.

His laboratory and other groups showed that APOE variants played a central role in the pathology of the disease by causing a buildup of amyloid proteins in the brain. More recently, they've shown APOE variants also contribute to neurodegeneration caused by a buildup of tangled Tau proteins in the brain — a process they believe involves the innate immune system. Holtzman and his team are currently focusing on better understanding the immune system's role in the disease.

While running his laboratory, Holtzman also saw patients at a memory disorders clinic at the university as well as seeing research participants, helping Washington University become a nationally recognized leader in Alzheimer's disease research. He led the Department of Neurology as chair between 2003 and 2021. Early in his tenure as chair, the family of Christopher Wells Hobler, a patient with amyotrophic lateral sclerosis, approached Holtzman with a desire to accelerate research on neurodegenerative disease. Hobler and his family had created a

WRITTEN BY *Bridget Kuehn* • ILLUSTRATION BY *Jacqui Oakley*

CAREER TRAJECTORY

foundation seeking cures for neurological disorders, now called Hope Happens. Along with the family, Holtzman helped launch the Hope Center for Neurological Disorders, which promotes cross-disease, multi-disciplinary translational research. The center offers pilot funding for laboratories collaborating to study brain disease, provides core laboratory resources, and hosts weekly seminars to keep scientists up to speed on the latest developments in brain research. Holtzman has served as the center's scientific director since 2015.

Holtzman is also associate director at the Charles F. and Joanne Knight Alzheimer's Disease Research Center (Knight ADRC), where, he says, investigators started realizing in the late 1980s that the pathology of the disease starts years before the symptoms do — an idea that took a long time to gain traction in the field. According to Holtzman, this inspired Knight ADRC scientists to conduct longitudinal studies comparing individuals with normal aging to those who have Alzheimer's disease, and these studies have yielded important insights. It has also led to additional massive longitudinal research endeavors at Washington University, including the Dominantly Inherited Alzheimer Network, where scientists study rare mutations that cause early onset forms of Alzheimer's disease and test potential therapies.

TESTING INNOVATIVE SOLUTIONS

Fifteen years ago, Holtzman launched a startup called C2N Diagnostics with his former post-doctoral fellow Randy Bateman, MD, who is now the Charles F. and Joanne Knight Distinguished Professor of Neurology at Washington University. One of the goals was to develop a blood test to detect early signs of Alzheimer's disease type pathology in the brain. During his post-doctoral fellowship, Bateman developed a method to measure the production of amyloid proteins in the nervous system of humans, Holtzman explains.

"We started accurately measuring the amyloid protein in the blood and found that the blood levels were related to how much of the protein was building up in the brain," he says. "That ultimately turned into a test that is highly accurate at determining whether someone has a buildup of amyloid in their brain or not."

> **Over 30 years ago, we had absolutely no clue of what caused Alzheimer's disease or how to treat it; now we are on the cusp of having real, powerful treatments.**

Bateman and colleagues recently published results of a multi-center international study in the journal *Neurology* showing that the test accurately detected the presence of amyloid plaques in patients. Holtzman says that the test could be a valuable tool for clinicians trying to determine the cause of early signs of cognitive impairment.

"We know that in people with Alzheimer's disease, the brain changes start occurring about 20 years before symptoms, and the blood test can pick that up," he says, adding that this is already allowing people to enroll in clinical trials of treatments to prevent or delay the disease. The test could also help clinicians rule out Alzheimer's disease in patients who do not have amyloid buildup.

"If the test is negative, then you want to look for other causes of cognitive impairment," he says.

The company, partnering with Holtzman's lab, helped develop an antibody-based potential treatment for Alzheimer's, targeting Tau tangles. According to Holtzman, no beneficial effect was found when the company AbbVie tested the therapy in clinical trials. Since then, Holtzman's laboratory has shifted gears to determine whether APOE protein may be a better target for antibody-based as well as other gene-targeting therapies.

"Antibodies to APOE that is in amyloid plaques might be a better way to remove plaques without some of the toxic side effects seen with some anti-amyloid antibody therapies," he says.

His laboratory is currently studying how disrupted sleep may contribute to the buildup of harmful proteins in the brain.

"We are trying different pharmacologic ways to improve sleep and gauging whether it affects Alzheimer's pathology," Holtzman says.

When he is not working, Holtzman enjoys kite surfing, hiking, and attending cultural events with his wife. Her support, he says, has been pivotal to his career, which often entails putting in extraordinary hours. He also acknowledges life-long friends he made while at Northwestern, who continue to play an important role in his life.

"Northwestern launched my career," he says. "It set up everything that allowed me to be successful afterward." ❖

Alumnus Invests in Digital Health and Data Science

Ed Wu, '02 MD, has not had a traditional career in medicine since graduating from Feinberg. Instead, he has become an entrepreneur, combining his interests in medicine, data science, and technology to improve healthcare.

To help prepare the next generation to innovate and succeed in a rapidly evolving field, Wu and his wife, Joyce, have made a generous $250,000 commitment to Feinberg to expand its digital health and data science curriculum. Northwestern is one of the first medical schools in the nation to emphasize this important area.

"Back in medical school, I was interested in blending patient care, informed decision-making, and technology," Wu says. "Digital health wasn't around yet, but Northwestern gave me the mentors and opportunities to carve my own path. Northwestern was instrumental to my career in digital health, so I wanted to give back and help students pursue this area that today touches every discipline of medicine."

When Wu was in medical school, Northwestern had just adopted an electronic health record (EHR) system, but the digital revolution in healthcare was still decades away. Ahead of his time, Wu got involved in research projects with former Feinberg faculty Greg Makoul, PhD, and David Channin, MD, studying patient-physician communication and medical informatics.

"Healthcare is all about people coming together. If we can all come together to support our medical school, we can make a huge difference across the field of medicine."

ED WU, '02 MD

After graduating with his BS, MD, and MBA from Northwestern, Wu practiced as an internist in New York City and pursued public health research during a fellowship at New York University. He went on to spend a decade advising health systems across the country on the deployment of EHRs. Over the years, he got involved with nonprofits and startups focused on streamlining patient care in specialties spanning mental health to geriatric medicine using digital health technologies.

"Data science can help us heal in a more focused and efficient way. By analyzing large data sets, we can diagnose quicker and create targeted treatment plans for individual patients," Wu explains. In 2020, he cofounded Recora, a company that applies these ideas to improve cardiac care in the home.

Feinberg has already begun to build its digital health and data science curriculum (see page 7 to learn more) and can bring its efforts to the next level with the Wus' gift. For example, the funding will enable faculty in Feinberg's Institute for Augmented Intelligence in Medicine (I.AIM) to create a Health Data Gymnasium. This digital library will contain extensive de-identified and synthetic data for students to engage in hypothesis-driven research and practice clinical decision-making while learning data science skills.

"Healthcare is all about people coming together. If we can all come together to support our medical school, we can make a huge difference across the field of medicine," Wu says. "I've been fortunate to be able to give back to that area that I've cared about so deeply since medical school, and I encourage others to give back to the area that shaped them."

"We are incredibly grateful to Ed and Joyce for their generosity to our Center for Medical Education in Data Science and Digital Health," said Abel Kho, MD, director of I.AIM and a professor of Medicine and Preventive Medicine. "The Wu's philanthropy not only gives Northwestern and our graduates a competitive edge, it also will help us train future leaders in medicine equipped to leverage — and even develop — new information and technologies to better serve patients."

Still in the midst of their careers, the Wus chose to give back to Feinberg now because they believe investment in Northwestern and data science can't wait. Wu continues to integrate Recora's technology at health systems and insurers. His wife works in finance and chairs the Board of Trustees at Central Queens Academy, a school dedicated to serving new immigrant families. They reside in New York City with their three young children.

"The moment is now. Data science will inform primary care, cardiology, dermatology, urology, pathology — you name it. This is an area where we can build overall efficiencies for patient care," Wu explains. "I would love for others to join me in making gifts to support this important cause that will ultimately benefit all of us."

For more information about supporting digital health and data science, please contact Dave McCreery at david.mccreery@northwestern.edu or 312-503-6099.

WRITTEN BY *Jennifer Pien, '01 MD*

THE HEALING POWER OF STORYTELLING

Every month, I am visited by Ozzy Osbourne incarnate. This patient has enough tattoos and gothic jewelry to adorn an entire heavy metal band. He arrives accompanied by several attentive staff, there to keep him safe, and brings his guitar with him, clutching it like a warrior would his sword.

As "Ozzy" settles in for our session, a helpful staff member sets the guitar aside, while carrying on a steady stream of chatter with my patient. Yet when I ask Ozzy to tell his story, he falls silent.

> **As medical practitioners, we can all benefit from incorporating self-expression in our work.**

I understand that he will need a different approach, but it takes me a little while to figure out exactly what that will be. Years ago, I swapped out Virginia Woolf and Kazuo Ishiguro (heroes of my undergraduate years) for Drs. Glen Gabbard and Irvin Yalom, turning my focus to the field of psychiatry. At my medical school interview, an oncologist asked me what drew me to medicine. Jettisoning my rehearsed statement, I said, "I am interested in the story of each person, not just about their illness and recovery, but about who they are."

A few years ago, I undertook a quest many of you may be familiar with after the hyper-focused rigors of medical school and residency — rediscovering lost passions. In the process, I decided to write a novel, and in doing so I stumbled upon the field of narrative medicine. Dr. Rita Charon, the founder and executive director of the Program in Narrative Medicine at Columbia University, describes the discipline as "melding aspects of how we approach literature and writing to clinical care." Early qualitative data shows that this approach to clinical care can increase therapeutic alliance, empathy, and reduce health provider burnout. Patients feel better cared for. Providers give better care.

The field of narrative medicine draws upon principles similar to Rogerian centeredness, mindfulness, and the fundamental psychiatric skills of attentiveness and empathy, reminding us to be present and open to the story of each individual patient we encounter. Narrative medicine combines my medical practice with my love of writing, giving me a framework in which to draw out the stories found within each of my clients, and at the same time, fight back against the gravity-like pulls of burnout and eventual complacency.

Back to the guitar-wielding warrior, my patient who cannot tell his story.

One day, I have an idea. I stop the staff from setting aside my patient's guitar. I wonder aloud whether the patient would like to play something for us. Without a word, he obliges. As he strums, his muteness transforms. Gone is his inability to convey his story. With the chords as his backdrop, my patient tells me about the abuse of his childhood. He tells me that without his music, he is agitated, consumed by a powerful distress that all too often culminates in police encounters and self-mutilation. His story is entwined ineradicably with his music, and we have learned to sit back, giving him his space to share his story in the medium most suited to him.

Music is the backbone of his story. Writing is the fundamental element of mine. As medical practitioners, we can all benefit from incorporating self-expression in our work. Whether it is sketching, sculpture, or any other form of creative self-expression, I recommend taking a moment to reflect on your patients and channeling those encounters into a creative outlet. Then, share the process with your patient or a trusted colleague. Studies show that co-creation of an illness narrative reminds us of and reinforces the individuality of our patients.

Every day, my writing informs my work. My work informs my writing. Challenges are invigorating rather than stultifying. I push myself to figure out how to capture the psychological effects of trauma through fiction. And I have come to believe that honoring the stories that grow out of our patients' lived experiences can only benefit us in our professions.

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