WINTER/SPRING 2021

EINSTEIN

THE MAGAZINE FOR ALUMNI AND FRIENDS OF ALBERT EINSTEIN COLLEGE OF MEDICINE

20 YEARS AFTER 9/11

In response to tragedy, a groundbreaking research program monitors the health of first responders

A Message From the Dean

For more than a year now, the COVID-19 pandemic has upended our lives in unimaginable ways. I offer my condolences to everyone who suffered the loss of a loved one during a most difficult year. Yet, even during these challenging times, we have been fully engaged in combating the coronavirus and the disease it causes—and we have some significant achievements to show for our efforts.

We have opened a new COVID-19 unit at Einstein and Montefiore to test the effectiveness of vaccines. We have evaluated coronavirus treatments, including convalescent plasma, corticosteroids, and monoclonal antibodies. And we have studied how COVID-19 affects children and why it causes psychiatric problems in adults. You can learn more about our COVID-19 research on pages 8 and 9.

A different tragedy, the collapse of the Twin Towers, continues to disrupt the health and lives of many New Yorkers. Our cover story, "20 Years After 9/11" (page 18), begins with David Prezant, M.D.—an Einstein graduate and chief medical officer for the Fire Department of the City of New York—who arrived at Ground Zero shortly before the towers fell. Dr. Prezant would go on to establish a groundbreaking program to monitor the health of first responders and obtain lifelong support for their care. A section titled "The Ones Who Ran Toward Danger," beginning on page 26, recounts the heroism and health problems of three of those first responders.

Our second feature article, "Gut Reactions" (page 36), describes the promising microbiome research that Einstein and Montefiore scientists are conducting. Their studies suggest that altering the makeup of the gut may lead to treatments for intestinal problems as well as diseases such as sickle cell anemia and diabetes.

I am heartened by what we've accomplished these past several months. And as we begin to recover from the pandemic, I'm optimistic about what can be achieved as we work together for a better future.

GORDON F. TOMASELLI, M.D.
The Marilyn and Stanley M. Katz Dean
Albert Einstein College of Medicine
Executive Vice President, Chief Academic Officer
Montefiore Medicine

EINSTEIN
Science at the Heart of Medicine

Winter/Spring 2021

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ON THE COVER: David Prezant, M.D. '81, pictured second from right, is a professor of medicine and of epidemiology & population health at Einstein and a pulmonologist at Montefiore. He is the FDNY's chief medical officer and helped create the World Trade Center Health Program.

Visit **magazine.einsteinmed.org** or scan code

Two Prominent Researchers Take Helm of PRIME

Vilma Gabbay, M.D., M.S., and **Jelena Radulovic, M.D., Ph.D.**, have been named co-directors of the Psychiatry Research Institute at Montefiore Einstein (PRIME).

Dr. Vilma Gabbay

Dr. Jelena Radulovic

The new center will integrate research in psychiatry and neuroscience to tackle urgent problems such as trauma and stress disorders, substance-use disorders, schizophrenia, depression, and anxiety, as well as multicultural health and mental health disparities. PRIME is a joint initiative of the departments of psychiatry and behavioral sciences and of neuroscience, and exemplifies Einstein and Montefiore's commitment to basic, translational, and clinical research.

Dr. Gabbay, associate professor of psychiatry and behavioral sciences and in the Dominick P. Purpura Department of Neuroscience at Einstein, and a clinical psychiatrist at Montefiore, studies the neurobiological basis of mood and anxiety disorders in young adults. She directs the Pediatric Mood and Anxiety Disorders Research Program at Einstein and Montefiore, and recently received a $4 million grant from the National Institutes of Health to study the neurobiology of depression in teenagers.

"PRIME is committed to pursuing meaningful advances in understanding and treating mental illness," Dr. Gabbay says. "Together, Dr. Radulovic and I will support and mentor teams of investigators—from medical and graduate students and postdoctoral fellows to early-career scientists."

Dr. Radulovic, professor in the Dominick P. Purpura Department of Neuroscience and of psychiatry and behavioral sciences, uses animal models to study how memories of stressful events cause fear, anxiety, and depression. Her research has been funded by the National Institute of Mental Health since 2006.

She is leading a research project focusing on the molecular, cellular, and circuit mechanisms involved in the brain's processing, storage, and recall of negative memories and the roles they play in the development of depression.

"The challenges of researching these questions connected to mental health disorders are big—but so is the excitement and promise of our work at PRIME," Dr. Radulovic says. "If we can discover more about the mechanisms in brain circuits that are affected, we can work toward developing treatments."

New Chief of Dermatology Appointed

Beth McLellan, M.D., has been named chief of the division of dermatology at Einstein and Montefiore. An associate professor of medicine at Einstein and a clinical dermatologist at Montefiore, she previously served as director of dermatology at Jacobi Medical Center.

Dr. McLellan specializes in oncodermatology—diagnosing, treating, and managing the complications of cancer. She has previously worked at New York University's Grossman School of Medicine and the NYU Langone Medical Center.

"Dr. McLellan is an exceptional leader, outstanding educator, and role model," says Yaron Tomer, M.D., professor and chair of the department of medicine at Einstein and Montefiore and the Anita and Jack Saltz Chair in Diabetes Research at Einstein. "She created the oncodermatology program at the Albert Einstein Cancer Center, leads an annual free skin cancer screening in the Bronx, and helped start a committee for diversity, inclusion, and cultural competency in dermatology."

A graduate of Wayne State University School of Medicine in Detroit, Dr. McLellan completed her internal medicine internship at Loyola University in Maywood, Illinois, followed by a dermatology residency at the Henry Ford Health System in Detroit, where she was chief resident. She is currently collaborating with Montefiore and Einstein researchers in infectious diseases, bioinformatics, and radiation oncology.

Tenure for 10 Einstein Professors

Jacqueline M. Achkar, M.D., M.S.
Professor of Medicine and of Microbiology & Immunology

Edward Chu, M.D.
Professor of Medicine and of Molecular Pharmacology

Tim Q. Duong, Ph.D.
Professor of Radiology

Louis Hodgson, Ph.D.
Professor of Anatomy and Structural Biology

U. Thomas Meier, Ph.D.
Professor of Anatomy and Structural Biology

Michal L. Melamed, M.D., M.H.S.
Professor of Medicine and of Epidemiology & Population Health

Jelena Radulovic, M.D., Ph.D.
Professor in the Dominick P. Purpura Department of Neuroscience and of Psychiatry and Behavioral Sciences

Julie Secombe, Ph.D.
Professor of Genetics and in the Dominick P. Purpura Department of Neuroscience

Duncan W. Wilson, Ph.D.
Professor of Developmental and Molecular Biology and in the Dominick P. Purpura Department of Neuroscience

Zhengdong Zhang, Ph.D.
Professor of Genetics

Einstein students, faculty, and staff members package produce for Montefiore's Project BRAVO Food Pantry on Bainbridge Avenue in the Bronx.

Honoring Martin Luther King Jr. Through Service Work

On Jan. 18, for the first time, Einstein joined other organizations nationwide in a day of service in memory of civil rights leader Martin Luther King Jr. The federal holiday honoring Dr. King's legacy is unique in being observed as a "day on, not a day off," to encourage Americans to volunteer to improve their communities.

"The difficulties of the past year have reinforced the importance of community," says Nerys Benfield, M.D., M.P.H., senior associate dean for diversity and inclusion. "Dr. Martin Luther King Jr. had a vision of a 'beloved community' where all people can live free from poverty and racism," says Dr. Benfield, who is also an associate professor of obstetrics & gynecology and women's health at Einstein and director of family planning at Montefiore. "Our hope is that students, faculty, and staff members continue to serve the community throughout the year, and we look forward to making this an annual opportunity."

As part of Einstein's inaugural MLK Service Challenge, dozens of students, faculty, and staff members donated their time in person and virtually throughout the week. The office of diversity and inclusion partnered with three local organizations, including Montefiore's Project BRAVO, HERO High School, and the Bronx Community Foundation, as well as Einstein's Food Justice and Medicine group, to offer volunteer events.

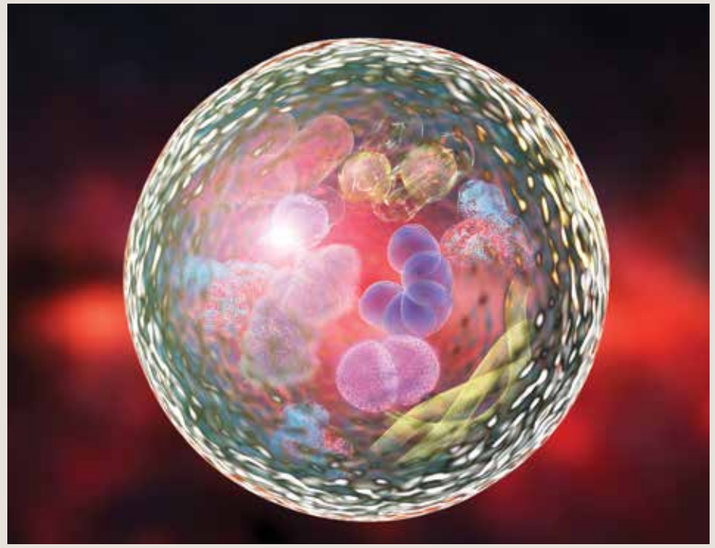
Those included packaging groceries at a Bronx food pantry, helping younger students online with health and science projects, delivering bags of groceries by car to people's homes, and distributing food and personal protective equipment to Bronx community members from Einstein's campus.

RESEARCH
NOTES

Bolstering the Health of Blood Stem Cells

As we age, our hematopoietic (blood-forming) stem cells (HSCs) become less efficient and less able to make healthy new blood cells. In a study published in January 2021 in *Nature*, Einstein researchers found that this reduction in HSC efficiency results in part from deterioration of chaperone-mediated autophagy (CMA), the housekeeping process that removes and recycles damaged proteins and other waste materials that interfere with our cells' ability to function.

"While the aging of HSCs in our bone marrow is inevitable, the good news is that it may be reversible," says study co-leader Ana Maria Cuervo, M.D., Ph.D., professor of developmental and molecular biology, of anatomy and structural biology, and of medicine, and the Robert and Renée Belfer Chair for the Study of Neurodegenerative Diseases at Einstein.



This illustration depicts autophagy. The large red area inside the cell is a lysosome—a membrane-bound, enzyme-filled structure that degrades a cell's waste products.

In previous studies, Dr. Cuervo discovered that the decline in CMA allows waste to build up in cells, contributing to Parkinson's, Alzheimer's, and aging in general, and that revving up CMA can help prevent those processes. The current study investigates whether CMA's age-related decline plays a role in the falloff of HSC activity.

Dr. Cuervo's team first established that CMA in the HSCs of mice does indeed become less efficient with age. The researchers then showed that HSCs depend on CMA for their vitality—both to maintain a healthy balance of proteins and to switch from their normally quiescent state to their active, blood-cell-forming state.

The team found that blocking CMA in the HSCs of young mice duplicates many of the features observed in the HSCs of aged mice. Conversely, young mice genetically engineered to prevent CMA in their HSCs from declining with age were able to repopulate bone marrow with healthy blood cells even into old age. "Even more interesting is that when we pharmacologically activated CMA in old mice, we were able to restore their HSC activity," Dr. Cuervo says.

These studies in mice may also be relevant to human health. The researchers took HSCs from people over 65 and treated them with a CMA-activating drug developed by study co-author Evripidis Gavathiotis, Ph.D., professor of biochemistry and of medicine. The result: The HSCs recovered the ability to make healthy blood cells.

Dr. Cuervo notes that some blood cancers, such as acute myeloid leukemia and myelodysplastic syndromes, almost always affect older people and evolve from mutations that accumulate in HSCs; revving up CMA in HSCs, she says, could help prevent those blood cancers from occurring.

WATCH THE VIDEO
See Dr. Cuervo describe the cellular process of autophagy:
magazine.einsteinmed.org/Cuervo21

Sensory Nerves Mobilize Blood-Forming Stem Cells

Hematopoietic (blood-forming) stem cells (HSCs) are stimulated to leave their "homes" in the bone marrow and enter the bloodstream, where they differentiate into all the body's blood cells. The signals that activate this mobilization of HSCs have not been well defined.

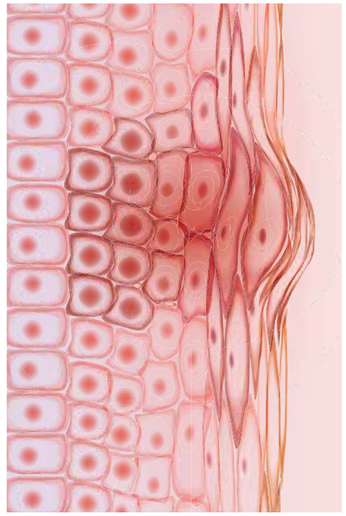
In research published online in December 2020 in *Nature*, Paul Frenette, M.D., and colleagues found that nociceptive (pain-sensing) nerves in the bone marrow play a key role in regulating HSCs. Those nerves secrete peptides into the bone marrow, turning on a cascade of signals that instruct the stem cells to migrate from the bone marrow to the bloodstream.

Interestingly, the research team found that feeding mice food containing capsaicin (the "hot" component of chili peppers) significantly enhanced HSC mobilization. These findings could help to increase the yield of HSCs that are harvested from the blood for use in bone-marrow transplants for treating blood cancers and other life-threatening diseases.

Dr. Frenette is a professor of medicine and of cell biology and the chair and director of the Ruth L. and David S. Gottesman Institute for Stem Cell Biology and Regenerative Medicine at Einstein.

A hematopoietic stem cell surrounded by red blood cells.

Overcoming Melanoma Drug Resistance



Melanoma cancer cells as they appear in a cross section of the skin.

The so-called MAPK signaling pathway regulates cell proliferation by transmitting chemical signals to cells' nuclei from outside the cells. Ten percent of all human cancers and half of all metastatic melanomas result from mutations in *BRAF*, a gene that codes for the protein BRAF in the MAPK pathway. By far the most common melanoma *BRAF* mutation is *BRAFV600E*—a single-nucleotide mutation that causes glutamic acid to substitute for valine in the BRAF protein.

The U.S. Food and Drug Administration (FDA) has approved several BRAF-inhibiting drugs for treating tumors possessing the *BRAFV600E* mutation. Unfortunately, nearly all tumors eventually develop resistance to the drugs. A principal reason is reactivation of the MAPK pathway, which induces BRAF to form drug-resistant dimers (two BRAF molecules linked together).

A study published in September 2020 in *Nature Communications* by Evripidis Gavathiotis, Ph.D., and colleagues describes a drug that shows promise for inhibiting BRAF dimers. The researchers designed a BRAF-dimer inhibitor based on the molecular structure of a drug called Ponatinib, approved by the FDA for treating chronic myelogenous leukemia. Since BRAF dimers encourage melanoma tumors to develop drug resistance, this BRAF-dimer-inhibiting drug may help extend the lives of melanoma patients.

Dr. Gavathiotis is a professor of biochemistry and of medicine at Einstein.

Lab Chat

Britta Will, Ph.D., studies hematopoietic (blood-forming) stem cells and their role in driving two age-related and largely incurable blood cancers: acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS). A native of Germany, Dr. Will earned her doctorate in biology at the Albert Ludwig University of Freiburg and came to the United States in 2005 for advanced training at Harvard. She has been a member of the Einstein faculty since 2013, where she is an assistant professor of medicine and of cell biology. In 2020, she was awarded the prestigious Pershing Square Sohn Prize for Young Investigators in Cancer Research.

What attracted you to biomedical research?
I had a passion for nature at an early age, which led me to study biology. But for a long time, I didn't know about research as a career option. I didn't have any role models. My uncertainty made my parents quite nervous. While they were supportive of me, they thought, "Aside from teaching, what can you do, really, with a biology degree?"

Did that experience influence how you run your lab?
I believe so. My first goal is to make an impact scientifically, of course. But in addition, I feel honored to be in a position where I can help young scientists remain on their paths, especially when they experience difficulties.

How do you boost their spirits?
When they're having a bad streak with their research, for example, I tell them, "Whatever you do today, just make sure to come back tomorrow." If they've made it this far, they can work through the ups and downs. It's in the nature of research to be wrong. You continue asking questions and pushing forward until things fall into place. That takes an open mind, courage, persistence, and time.

What led you to study blood cancers?
It was a natural trajectory, growing out of my interest in stem cells and my desire to address diseases for which we have few treatments or cures.

What brought you to the United States, and why did you stay?
I wanted to see how research was done in another country. I came to appreciate how the system here supports young scientists and is completely open to novel ideas. I stayed because I had an opportunity to do a postdoc with Einstein's Ulrich Steidl [an expert in stem-cell research, AML, and MDS]. He instilled in me the confidence that you can discover something new by pushing boundaries.

Is pushing boundaries what you hope to do with the funding you've received from the Sohn Prize—$600,000 over three years?
Yes, the Sohn Prize will allow me to explore completely uncharted territory: the role of iron in creating and sustaining the cancerous blood stem cells that lead to AML and MDS.

Britta Will, Ph.D., likes exploring "completely uncharted territory" in her research.

Photo by Jonathan Heisler

Have you read anything interesting lately?
The Power, a dystopian science fiction novel by Naomi Alderman. It's my very first novel of this genre, and a deeply moving—and in parts disturbing—story about gender and power.

Do you have any hobbies?
Currently I like doing anything that is making our son, who is 2, happy. Also, my husband and I love to go on hikes.

WATCH THE VIDEO
Dr. Will talks about why she went into stem-cell research:
magazine.einsteinmed.org/Will21

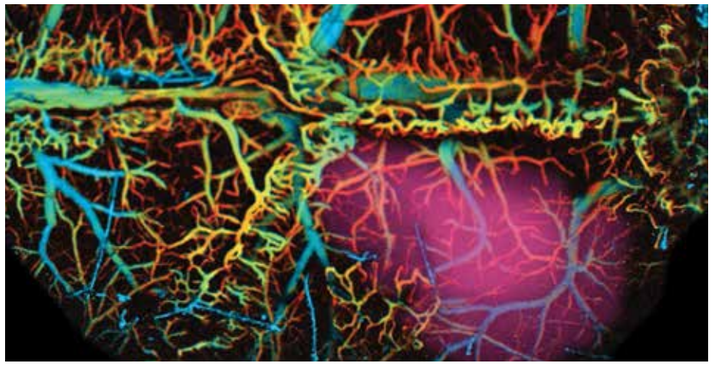
Detecting Neural Activity in Near-Infrared Light

The ability of fluorescent proteins (FPs) to serve as building blocks of biosensors allows scientists to observe normal and pathological biological processes in live cells in real time. FPs that emit visible light were previously available, but only recently have FPs glowing in the near-infrared spectrum been developed, thanks to the work of Vladislav Verkhusha, Ph.D., professor of anatomy and structural biology at Einstein, and his lab.

In a study published online in October 2020 in *Nature Biotechnology*, Dr. Verkhusha and colleagues report the next advance in optical imaging. Using two near-infrared FPs, they have engineered a calcium biosensor that can detect evoked and spontaneous calcium fluxes in the brain, which is an indicator of neural activity. The biosensor is stimulated by and emits near-infrared light, which penetrates deeply into biological tissues with minimal scatter; this allows scientists noninvasively to observe activity in neurons deep within living animals.

The near-infrared calcium biosensor can be combined with biosensors functioning in visible light, which allows for spectral "crosstalk-free" imaging of several simultaneous biochemical intracellular processes.

Dr. Verkhusha and his team constructed a hybrid microscope combining fluorescence and photoacoustic imaging. The hybrid microscope can "see through" the skulls of living mice, simultaneously using the near-infrared calcium biosensor to monitor neuronal activity as well as photoacoustics to track blood oxygen levels in the brain. The new calcium biosensor should prove useful in preclinical studies involving animal models.


This image shows the overlay of near-infrared fluorescence of a calcium biosensor (purple pseudocolor) and blood oxygenation (rainbow pseudocolor) in the brain of a living mouse. It was made using a hybrid fluorescence and photoacoustic microscope developed by Einstein's Vladislav Verkhusha, Ph.D., and Junjie Yao, Ph.D., of Duke University. Oxygenation levels range from low (blue) to high (red).

Microbial Diversity May Affect Lung Cancer Risk in Never-Smokers

Although tobacco products cause most lung cancer deaths, one-fourth of lung cancers occur in people who have never smoked. In a study published in December 2020 in *Thorax*, H. Dean Hosgood, Ph.D., associate professor of epidemiology & population health at Einstein, and colleagues analyzed the diversity of microbiota that had been collected from the respiratory tracts of men and women in Shanghai, China, who had never smoked. The researchers found that lower bacterial diversity was associated with a greater risk for subsequent occurrence of lung cancer among never-smokers.

In addition, the researchers found that increased abundance of bacteria in the *Firmicutes* phylum, and *Lactobacillales* in particular, in the respiratory tract may be associated with an increased risk of lung cancer in never-smokers. The findings provide further insight into the causes of lung cancer in the absence of active tobacco smoking.

Dr. Hosgood is also the director of global environmental health for the Global Health Center at Einstein and the associate director for population and clinical sciences in Einstein's Clinical Research Training Program.

Einstein and Montefiore Scientists Continue to Tackle COVID-19

Since our coverage of the COVID-19 crisis in the Summer/Fall 2020 issue of *Einstein* magazine, physician-scientists at Einstein and Montefiore have made further progress in understanding the disease and developing strategies for preventing and treating it. Here are some recent highlights.

VACCINE UNIT

In November, Einstein and Montefiore opened a new COVID-19 vaccine unit, enrolling people in a phase 3 clinical trial to test the efficacy of the AstraZeneca-University of Oxford vaccine. The unit is led by Barry Zingman, M.D., professor of medicine at Einstein and clinical director of infectious diseases at the Moses division of Montefiore.

In recruiting people for the vaccine trial, Dr. Zingman and his team required that more than half the participants were adults most affected by COVID-19, with a focus on people of color and people older than 65.

The randomized, placebo-controlled, double-blind trial vaccinated two people with the vaccine for each person who received a placebo injection. Two injections were given to each participant over 29 days. "To the healthcare providers and investigators who enthusiastically joined the effort and to the people who come in to participate in these critically important trials, we thank you for your role in helping the world end this pandemic," Dr. Zingman says.

MONOCLONAL ANTIBODIES AND BLOOD THINNERS

Einstein and Montefiore have become a testing site for trials funded by the National Institutes of Health (NIH) known as ACTIV-3 and ACTIV-4. The ACTIV-3 trial is evaluating the safety and effectiveness of Eli Lilly's monoclonal antibody (bamlanivimab) in patients hospitalized with COVID-19.

ACTIV-4 is assessing several blood-thinner drugs for treating people with COVID-19, particularly patients with life-threatening blood clots. The principal investigator for both trials is Michelle Ng Gong, M.D., M.S., chief of the divisions of critical care and of pulmonary medicine at Montefiore and Einstein and professor of medicine and of epidemiology & population health at Einstein.

COMBINATION THERAPIES

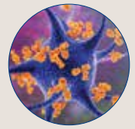
Montefiore is also the testing site for the NIH-funded ACTT-4 clinical trial assessing combination therapies for COVID-19. Those enrolled are people hospitalized with moderate to severe COVID-19 who are on oxygen but are not intubated.

All participants receive the antiviral drug remdesivir, and are randomized to receive one of two anti-inflammatory drugs: baricitinib and dexamethasone. ACTT-4 seeks to compare the safety and effectiveness of the anti-inflammatory drugs, both of which have shown promise in treating COVID-19. Each of the patients receiving combination therapy is matched with a patient receiving remdesivir alone. The principal investigator is Robert M. Grossberg, M.D., associate professor of medicine (infectious diseases) at Einstein and medical director of the Montefiore Center for Positive Living/Infectious Diseases Clinic.

COVID-19 AND CHILDREN

In the first-ever study comparing the immune responses of adults and children with COVID-19, researchers at Einstein and Montefiore and at Yale University detected key differences that may explain why children usually have a milder course of disease. The findings, which were published in September 2020 in *Science Translational Medicine*, suggest that children's stronger innate immunity protects them against SARS-CoV-2, the novel coronavirus that causes COVID-19. Betsy Herold, M.D., chief of pediatric infectious diseases and vice chair for research in the department of pediatrics at Einstein and Children's Hospital at Montefiore, was one of the senior authors of the study.

NEUROLOGICAL SYMPTOMS



People hospitalized with COVID-19 who have neurological problems have a higher risk of dying than other COVID-19 patients, according to a study that Einstein and Montefiore researchers published in December 2020 in *Neurology*.

The research is the first to show that the presence of neurological symptoms, particularly stroke and confused or altered thinking, can predict a more serious course of illness even when problems with breathing aren't severe. The study looked at data from 4,711 people admitted to Montefiore with COVID-19 between March 1 and April 16, 2020.

The findings could potentially help medical workers identify and focus their treatment efforts on individuals most at risk, and could decrease COVID-19 deaths. The study's co-authors were David Altschul, M.D., chief of the division of cerebrovascular neurosurgery at Einstein and Montefiore, and Emad Eskandar, M.D., M.B.A., the Jeffrey P. Bergstein Chair in Neurological Surgery in the Leo M. Davidoff Department of Neurological Surgery at Einstein and the David B. Keidan Chair of Neurological Surgery at Montefiore and Einstein.

CONVALESCENT PLASMA

A study published in January 2021 in *JCI Insight* found that plasma donated by people who've recovered from COVID-19 is effective in treating younger patients hospitalized for the disease.

Einstein and Montefiore researchers administered convalescent plasma to 103 severely ill patients with COVID-19 who were admitted to Montefiore between April 13 and May 4, 2020. Seventy-three of those patients were matched with 73 COVID-19 patients admitted during the same period who did not receive plasma. The authors found no difference in mortality between the people who received convalescent plasma and those who had not at 28 days following admission.

However, when patients were stratified by age, those plasma recipients under age 65 had a fourfold lower mortality after 28 days compared with similarly aged control patients. Liise-anne Pirofski, M.D., was the study's senior author. She is the chief of infectious diseases at Einstein and Montefiore and holds the Selma and Dr. Jacques Mitrani Chair in Biomedical Research at Einstein.

PSYCHIATRIC PROBLEMS

In a letter published in the *Journal of Psychiatric Research* in August 2020, members of Einstein and Montefiore's department of psychiatry and behavioral sciences added to evidence indicating that COVID-19 may cause psychiatric problems.

The authors described two adults with COVID-19 admitted to the emergency department with severe psychosis and mania. Neither patient had a prior psychiatric history or significant medical or pulmonary symptoms; both were discharged following treatment with antipsychotic drugs. The authors speculated that the patients' psychiatric problems may have resulted from immune-system activation and its effect on the central nervous system. Vilma Gabbay, M.D., was the corresponding author. She is an associate professor of psychiatry and behavioral sciences and in the Dominick P. Purpura Department of Neuroscience and a co-director of the Psychiatry Research Institute at Einstein, and a clinical psychiatrist at Montefiore (see page 2). E

Supporting a Culture of Openness in Urology

Q&A with Dr. Mark Schoenberg

Mark Schoenberg, M.D., is the chair of urology at Einstein and Montefiore and an internationally recognized authority on the treatment of bladder cancer. Dr. Schoenberg came to Einstein and Montefiore in 2014, after 20 years at the James Buchanan Brady Urological Institute at the Johns Hopkins University, where he served as the director of urologic oncology.

Both your father and grandfather were physicians. Did they influence your career choice?
Not at first. In college, at Yale, I was interested in Russian history and went to Russia to study and learn the language.

Was there family pressure to study medicine?
The only one who pressured me at all was my paternal grandmother. She told me that studying Russian was a waste of time because I was going to be a doctor. I laughed and told her it wouldn't happen.

What changed?
After I got back from Russia, I started reexamining my professional options. I was curious about medicine and took premed courses to figure out if that's what I wanted to do. With no prior background in science, I really struggled. I applied to several medical schools but didn't get in.

How did you wind up going to the University of Texas School of Medicine in Houston?
On my father's advice I moved to Texas, which had a surplus of medical schools and a shortage of qualified applicants. I took additional science courses, improved my grade-point average, and worked in a couple of research labs, including one at MD Anderson Cancer Center. The combination of those extra experiences and Texas residency was enough to get me into the med school there.

How did you become interested in urology?
At first I was attracted to psychiatry, but ended up liking surgery and urology even more—to the amazement of my father, who was a urologist.

And cancer research?
I always wanted to do clinical research, but the question was, what field? Cancer seemed to be the most exciting choice. This was the early '90s, when scientists were just starting to understand the genetics of cancer, which had enormous implications for diagnosis and treatment. That led me to a fellowship looking at the genetics of prostate cancer at Johns Hopkins.

Why did you switch your focus to bladder cancer?
After my fellowship, I was offered a position at Hopkins to work on bladder cancer. When I said I didn't know anything about it, I was told, "You'll learn." And I did. Hopkins, like Einstein, has a tremendous bench of scientists with whom clinicians can do translational research. It turned out to be a very productive time. I promised my wife we'd stay just a few years and then we'd return to Philadelphia, where both of us are from. But we stayed in Baltimore for 20 years.

What are the greatest challenges in treating bladder cancer today?
First of all, we need more therapeutic options to offer patients with bladder cancer. Checkpoint inhibitors have transformed how we manage individual patients with metastatic bladder cancer, but we're still not able to markedly change the clinical course of disease for most of them.

Your department has a high percentage of female urologists. Was that a conscious decision?
They weren't recruited because they are women, but because they are excellent clinicians and researchers. Our department is about 40% female—five times the national average. This has paid tremendous dividends. It has introduced different points of view and pushed all of us, male and female, to rethink work-life balance, which of course is a particular challenge for female surgeons in training who are considering having children. We don't have all the answers, but at least we're grappling with it.

Does having more women on staff affect patient care?
Women in general want to see female doctors. Oncology was once the fastest-growing subspecialty within urology, but today it's female pelvic medicine—problems such as female urinary incontinence, pelvic pain, and recurrent urinary tract infections. In collaboration with obstetrics and gynecology, we now have a Pelvic Floor Center at Montefiore, which is dedicated to these health issues.

How do you envision your role as department chair?
My goal is to support a culture of openness and the habit of clear-eyed questioning. I want our faculty and trainees to ask, "Why are we doing what we're doing?" Don't accept as gospel what you're told. We have a young faculty, and it's important to get this message across early in their careers. I also tell my faculty, "I don't care what you work on, so long as you really dig into it." That's the path to a fruitful career in academic medicine, to personal intellectual growth, and to innovation.

In retrospect, your grandmother knew you best.
Maybe. But I do use my Russian now and then, when treating patients here in the Bronx. E

THE POWER OF A PARTNERSHIP

Einstein's global health program in Kisoro, Uganda, benefits both patients and students

BY TERESA CARR

Photo by Aravind Addepalli

Last spring, residents of Kisoro, a remote district of Uganda, heard that a new illness called COVID-19 was approaching. They feared it would be like the Ebola virus—a death sentence that would wipe out people in hundreds of villages.

Kisoro hospital workers braced for an overwhelming flood of patients. They knew that the virus responsible for COVID-19 was easy to transmit. And in a society where six people might sleep in one room and go to the market every day, suppressing COVID-19's spread was going to require some work.

Fortunately, a program for handling this kind of challenge was already in place, developed over the years by Kisoro District Hospital leaders, Einstein faculty and students, and the nongovernmental organization Doctors for Global Health. Ugandan village health workers—people who knew their neighbors best and had their trust—had been trained to deliver medical care to people in their homes.

Now, they traveled throughout the region to give half-hour talks using flip charts to explain how COVID-19 could be transmitted and how to prevent the illness. Working with four adults at a time, the workers reached more than 14,000 village residents in three months.

"People told us the home talk was the most valuable source for increasing their understanding of COVID-19, more than what they were hearing on the radio," says Shombit Chaudhuri, a fourth-year medical student at Einstein who spent a year in Kisoro as part of a global health initiative.

The village health workers also began a home drug-delivery initiative so that older patients with chronic diseases could continue to take their medications and would not have to go to the hospital-based clinic and risk exposing themselves to COVID-19.

A WINNING COMBINATION

Einstein and Montefiore's connection with the people of Uganda began two decades before the pandemic arrived, with senior medical residents traveling to the western city of Mbarara to supervise interns and medical students at one of the country's two medical schools.

Gerald Paccione Jr., M.D., a professor of medicine at Einstein, the director of global health education for the primary care and social internal medicine residency program at Einstein and Montefiore, and an internist at Montefiore, had been traveling around Uganda searching for another community with which to partner on sustainable local healthcare programs. Kisoro, in Uganda's southwest corner, fit the bill. Though it is a breathtakingly beautiful region of mountains and dense forests, it is also a place of stark poverty, with per

Nursing assistants Emilly Betty Niyonshuti, standing at left, and Hadijah Kabaganda, seated at right, wear face masks as they prepare for patient visits at Kisoro District Hospital last summer.

Photos by Aravind Addepalli and Jill Raufman and courtesy of Gerald Paccione Jr., M.D.

capita income of less than $2 per day and the highest prevalence of chronic malnutrition in the country.

Dr. Paccione launched Einstein's global health partnership with Kisoro in 2005 with help from local hospital leaders, and since then some 15 Einstein medical students and 25 Montefiore residents have worked in the district every year, closely supervised by Einstein global health faculty members.

Students and residents first spend a month at Kisoro District Hospital, the only public (free) medical facility in the region, with more than 150 inpatient beds, and at the Chronic Care Clinic, which sees up to 200 patients a day. At the Chronic Care Clinic, students and residents work alongside Ugandans trained by the program to treat patients with hypertension, diabetes, chronic lung diseases, heart disease, neurologic disorders, and more.

Students then spend another month shadowing village health workers who deliver primary and preventive care to remote villages. (Like Mr. Chaudhuri and fellow fourth-year medical student Aravind Addepalli, some students will stay for a year.)

The program has grown tremendously since its creation 16 years ago. "We've invested in developing health resources in the hospital, clinic, and surrounding communities," Dr. Paccione says. "In turn, those communities welcome our students, helping ensure that they receive top-notch medical training and have an excellent experience. It's a win-win." (See page 17.)

LIVING, LEARNING IN KISORO

To prepare for their stays in Uganda, students and residents take an intensive monthlong global health elective. Still, says Alyssa Yeung, M.D. '20, a Montefiore obstetrics and gynecology resident who spent much of 2019 in Kisoro, walking into the hospital for the first time was an eye-opener. "Wards are large, open rooms lined with basic bed frames topped with camp-type mattresses," she says. "And families are expected to help take care of their relatives while they are in the hospital. On a nice day, you will see patients and their families out on the lawn, sharing a meal out of a common pot or doing laundry."

This page, from top left: Gerald Paccione Jr., M.D., rides with Sam Musominali, Einstein's site director and head of the village health worker program; Vanice Ntambara, a village health worker, weighs a baby; and a view of the large, open rooms of Kisoro District Hospital.

From a clinical standpoint, one of the biggest differences from American healthcare facilities is the lack of diagnostic tools, says Gloria Fung Chaw, M.D. '08, who spent years in Kisoro as a medical student, resident, and faculty member for the program.

"We have access to only four or five basic lab tests," says Dr. Fung Chaw, an assistant professor of medicine at Einstein, an internist at Montefiore, and the associate director of the Global Health and Clinical Skills Fellowship program. "The ultrasound is old and often out of service. The X-ray machine functions only if you have film and electricity—and we were often without either."

The challenging setting demands that clinicians pay close attention to their patients. "Students learn to rely on their clinical skills—talking to patients, doing a thorough physical exam, using clinical reasoning," Dr. Fung Chaw says. "That's not the type of medicine that is deeply taught in the United States, where we emphasize technology—sometimes to the detriment of both students and patients."

Charles Moon, M.D. '20, says he found it valuable to reach a likely diagnosis based on just the basic information available. "Coming back and practicing in U.S. hospitals now, I think I'm much better at that," says Dr. Moon, who worked in Kisoro between his third and

Clockwise from top right: Einstein fourth-years Aravind Addepalli and Shombit Chaudhuri take a coffee break; Gloria Fung Chaw, M.D., and senior translator Moses Dushime talk to a group of village health workers; a microscope is used to analyze cell cultures; and a socially distanced group of village health workers discusses COVID-19.

Photos by Shombit Chaudhuri and Mark Scheflen

fourth years of medical school and is now a resident in pediatrics at Children's Hospital at Montefiore. "I will be a better provider for my patients, no matter where they are."

Dr. Moon is careful not to sugarcoat the difficulties faced by the villagers he cared for. "Life is hard there," he says. "People come to the hospital with advanced cases of tuberculosis and rheumatic heart disease—things you don't see much here in the States. People die because of a lack of access to medicines and modern surgical care. Sometimes there's little we can do."

Asked what they liked best about their time in Kisoro, Drs. Moon and Yeung both cited bumping along steep dirt roads on the backs of motorbikes as they accompanied village health workers on home visits. Since 2005, Einstein has trained about 80 village health workers, and most are still on the job. They work, on average, two days a week, educating people about topics such as nutrition and family planning, and monitoring discharged hospital patients, the elderly, and those with chronic diseases.

"The village health worker program is the foundation for a lot of community programs that have been developed," Dr. Fung Chaw says. "One of the biggest accomplishments of our partnership has been training and supporting Ugandans who can provide important health services, particularly for chronic diseases. They connect with their Ugandan clinical supervisors when cases are complicated, and the supervisors, in turn, can take over on-site at Kisoro District Hospital or virtually. This is a unique infrastructure for delivering primary care and chronic-disease services in a rural district where resources are scarce."

A MODEL FOR GLOBAL HEALTH

The Kisoro village health worker program could be a model for improving health in resource-poor countries, research has shown. It is also a model many think would work well in underserved areas of the United States, including rural communities and urban areas such as the Bronx.

For example, Kisoro-area patients with high blood pressure who were monitored by village health workers maintained consistently lower readings than patients treated only in the clinic, according to a 2016 study published in *Health Policy and Planning*.

Thanks to the low cost of living in Kisoro, the village health worker program manages to operate on a modest budget. On average, village health workers are paid $250 to $300 per year, and Einstein and Montefiore participants volunteer their time. Einstein supports about 75% of the cost of student experiences through global health fellowships, with much of the money going to community projects the students participate in. Other funding comes from Karen's Tots Fund (money raised for disadvantaged children through friends and family of Dr. Paccione in memory of his sister) and Hofstra University, a recent partner in the initiative.

Einstein and Montefiore's long-term collaboration of more than 15 years with the people of Kisoro is a model for what global health can be, says Jill Raufman, M.P.H., M.S., director of medical student global health programs and associate director of the Global Health Center at Einstein.

"It's a key reason why we have been able to develop successful programs and the infrastructure for healthcare delivery. Our current faculty were once Einstein students or Montefiore residents themselves," she says. Ms. Raufman notes that Einstein will participate only in global health programs that are ethical, collaborative, and sustainable. "Our Kisoro model fulfills all of that," she says. "Plus the people, who open their communities to Einstein's young doctors in training, give as much as or more than they receive. It's a real partnership." E

From top: Fourth-year Aravind Addepalli prepares to distribute a box of medication with senior translator Moses Dushime; pills from the Kisoro Hospital pharmacy; and Jill Raufman, M.P.H., M.S., director of Einstein's medical student global health programs, is surrounded by, from left, Christopher Pina, M.D. '18; fourth-year Sadia Ahmed; Galit Benoni, M.D. '20; Michael Kornblit, M.D. '20; and fourth-years Akarsh Vijayashanka, Shombit Chaudhuri, Aravind Addepalli, and Shahaharyar Ilyas.

Photos by Shombit Chaudhuri and courtesy of Jill Raufman

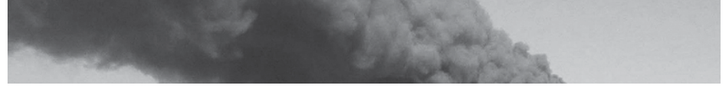
MEETING LOCAL HEALTH NEEDS

Einstein and Montefiore have worked with partners in Kisoro to create an ever-expanding array of services:

- Community care programs, such as Chronic Disease in the Community and the Elders Program, involve village health workers who visit senior citizens and those with chronic diseases at home, saving people the arduous trip to the clinic.
- Women's health initiatives reduce mortality and foster healthier lives for women and their families. The women's clinic and a community outreach program provide treatment, screenings for HIV infection and cervical cancer, counseling on family planning and domestic violence, postpartum care, and health education. Einstein students team with midwives to host a popular call-in radio program focused on women's health.
- Nutrition programs feed infants in the pediatric ward and children in their homes. The programs help up to 800 children yearly, and the Ugandan parliament has recognized them as one of the country's most effective nutrition initiatives.
- Treatment for psychiatric disorders, one of the leading causes of disability in Africa, is made possible.
- A health census collects demographic, medical, and behavioral information from people in the surrounding villages every two years to identify health risks.
- Patients with life-threatening heart conditions are referred to medical centers outside Kisoro equipped to care for them. Surgeries for up to four patients yearly are supported, and the program has a growing waiting list.
- The Follow-Up Project, involving a team of four trained staff members, reaches out by motorcycle to reengage with patients from remote villages who need continuous care but have stopped returning to the clinic—patients with tuberculosis, HIV, high-risk chronic diseases, and cervical cancer, and malnourished children.
- Educational scholarships help high school–age orphans and former employees pursue careers in healthcare.

20 YEARS AFTER

In response to tragedy, a groundbreaking research program monitors the health of first responders



Neville Elder via Getty Images; Michael Foran; Wally Gobetz; Jörg Meyer; Millrock Productions, Inc. via Getty Images

The collapse of the Twin Towers forever transformed many lives—including that of an Einstein graduate who experienced a brush with death at Ground Zero. He would go on to document the health effects of exposure to World Trade Center dust, help establish a groundbreaking healthcare program for first responders, and help win lifelong federal support for their care.

BY GARY GOLDENBERG

On that impossibly clear blue September morning in 2001, David Prezant, M.D. '81, was driving to his office at Montefiore and listening to the radio when he heard reports of a plane hitting one of the World Trade Center (WTC) towers. His other job, as deputy chief medical officer for the Fire Department of the City of New York (FDNY), required him to respond to major emergencies. He spun around and sped toward lower Manhattan.

"I arrived downtown shortly after the second plane hit and started triaging first responders and civilians coming out of the South Tower," Dr. Prezant recalls. "When debris—and, horrifically, people jumping—started falling near us, Charlie Wells, one of the EMS [emergency medical services] chiefs, told us to move away from the tower. By the time we'd walked maybe 10 steps, everybody started running and, instinctively, I did too. Before I knew it, [the tower collapsed and] I was blown across West Street and landed under a pedestrian bridge, partly covered in rubble." Battered and bruised, he dug himself out and returned to duty, directing a triage unit on Broadway just east of Ground Zero.

He recounts a second story, about an encounter later that terrible day, when a young woman in hospital scrubs came rollerblading over to the triage unit and asked for the physician in charge.

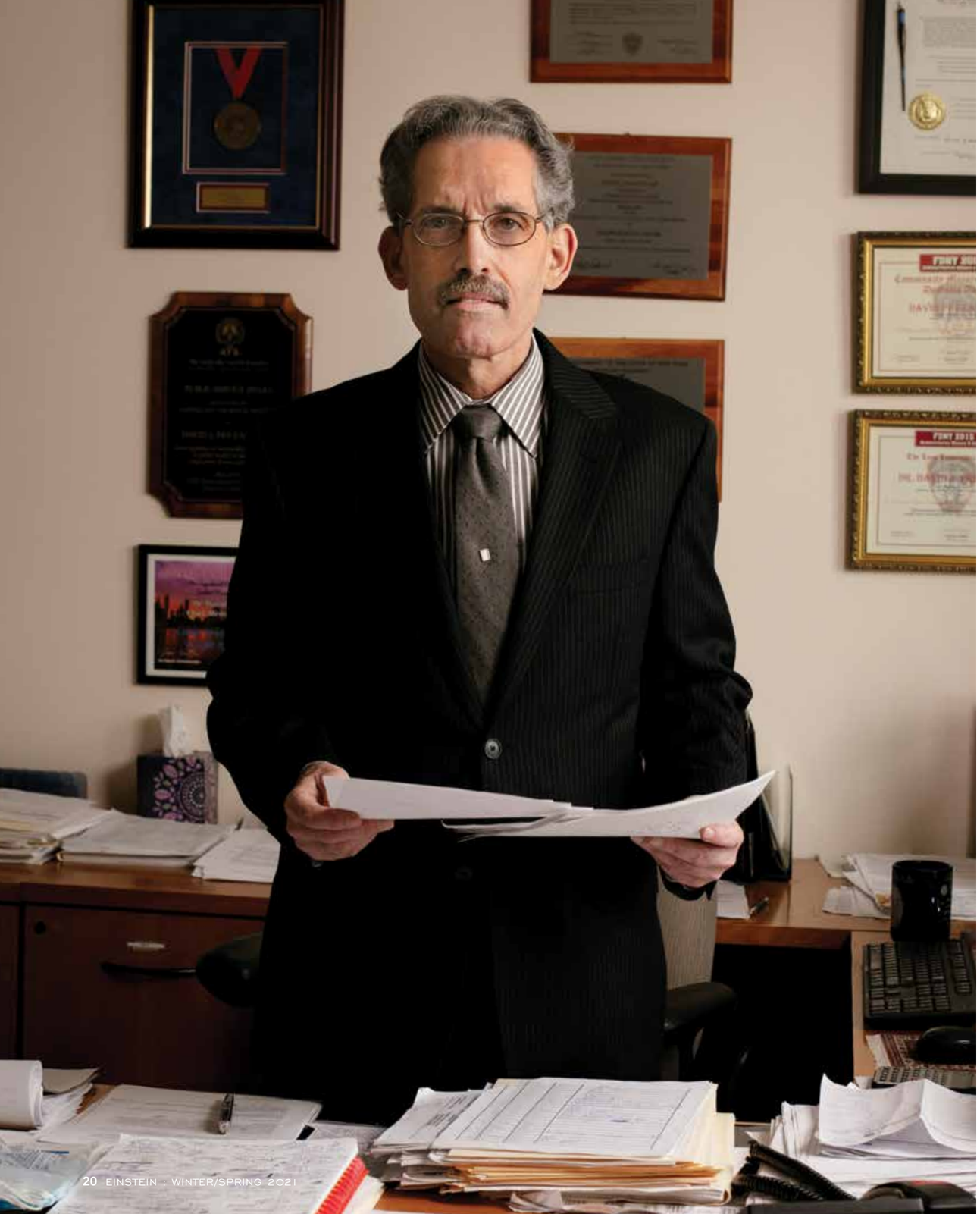
"'I'm Doctor So-and-So, a veterinarian, and I'm here to help,'" Dr. Prezant recalls her saying. "I replied something like, 'We've been attacked and I don't know how many thousands are dead and injured. This is not a time to worry about cats and parakeets!' She gave me a look that I soon found out I deserved and replied, 'Listen up—by federal statute all rescue dogs must stop working after four hours unless a veterinarian is present. So you need to get me to the rescue dogs or I'm shutting them down.'"

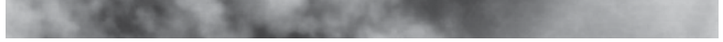
It was a humbling—and eye-opening—moment, he says. "Due to pure ignorance, I almost wound up shutting the site down," he says. "Later it occurred to me, 'The dogs had to be monitored every four hours, but we let human beings work at the disaster site for God knows how many hours.' Something to remember."

BRONX BEGINNINGS

Dr. Prezant, professor of medicine and of epidemiology & population health at Einstein and a pulmonologist at Montefiore, grew up two blocks away from the Moses campus of Montefiore, the child of an elementary school teacher (his mother) and a high school teacher and administrator (his father).

Science came naturally to their son, and after college at Columbia University he intended to pursue a Ph.D. in biochemistry, with designs on a career in bench research. Yet he couldn't shake the feeling that his talents were better suited to medicine. He enrolled at Einstein in 1977, less than confident about his decision.





"For the first two years, I wasn't a very motivated student—average at best," he admits. But in his third-year clinical rounds, he found an affinity for pulmonary medicine and intensive care.

"The ICU [intensive care unit] is very much like working in a lab, with lots of data to process, plus the challenge of caring for patients and interacting with their families—complete strangers with whom you form this incredible bond and who are forever scarred if the ICU experience doesn't go well," Dr. Prezant says. "The responsibility is immense. It was then I began to realize how engaging it could be to care for patients, and how much of a privilege it is."

After Einstein, he began a residency in internal medicine at Harlem Hospital, preferring to work with underserved populations as he'd done in the Bronx. Dr. Prezant returned to the Bronx for fellowships in pulmonary care and pulmonary research in a joint program at Montefiore and Jacobi hospitals. All the while he moonlighted at Harlem Hospital, regularly working six or seven days a week—a schedule he still keeps. "I'm the most boring person on Earth," he insists. "Other than going to the gym, I have no hobbies. I like working. My goal is to die at work. Seriously."

CONNECTING WITH THE FDNY

In the mid-'80s, Dr. Prezant joined the Einstein and Montefiore staffs in a role that combined clinical research and patient care. With a new wife and two stepchildren to help support, he also applied for a part-time position with the FDNY. He seemed a shoo-in for a newly opened pulmonologist position, only to be told by the then-fire commissioner that physicians with military experience were preferred. Walking out of the commissioner's office, he tried one last gambit, mentioning that he'd been a Boy Scout. "And the commissioner goes, 'Well, that involves a uniform. Great—you're hired!'" Dr. Prezant recalls.

Over the years, Dr. Prezant became more and more involved with the FDNY's first responders, made up of EMS providers (paramedics and emergency medical technicians) as well as firefighters. That meant treating first responders in the field and in the hospital, evaluating new firefighting gear and personal protective equipment, developing new health initiatives—and gradually winning the trust of the rank and file.

By 1996, Dr. Prezant had hit his stride: He was appointed deputy chief medical officer at the FDNY, was placed in charge of the pulmonary clinic at Montefiore and, at Einstein, took over the second-year course called Pulmonary, Critical Care, and Disaster Medicine, which is now in its 25th year. His professional life was full and relatively uneventful. And then came 9/11.

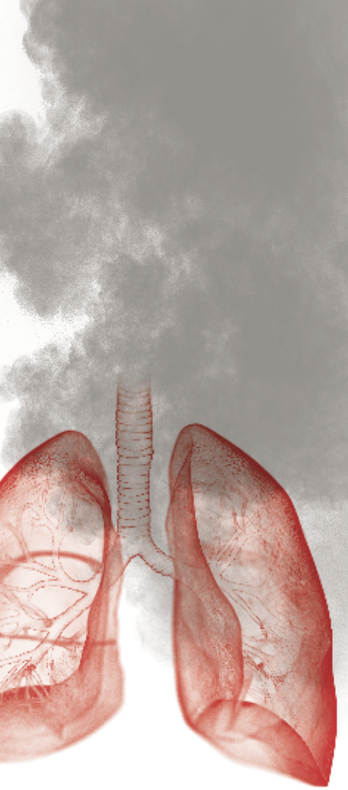
EXAMINING HEALTH EFFECTS

Dr. Prezant escaped Ground Zero with cuts and bruises and a sore back, and quickly returned to work. His one lingering complaint was a case of "World Trade Center cough syndrome," an all-too-common legacy of the noxious mix of asbestos, burning plastics, jet fuel, and other toxins that fouled the air around lower Manhattan for weeks on end. He fully recovered after a few months, but many others didn't, as he would eventually document.

> "I have no hobbies. I like working. My goal is to die at work. Seriously."
>
> — DR. DAVID PREZANT

Photos by Jörg Meyer; Andrea Booher/ FEMA; U.S. Navy

At left, David Prezant, M.D., at his FDNY office in New York City.



As time went on, first responders experienced an increasing number of serious WTC-related health problems.

Following the attacks, Dr. Prezant and his team—including staffers at the FDNY and at Einstein, Montefiore, and other medical centers—launched the Fire Department's WTC Medical Monitoring and Treatment Program under a multimillion-dollar grant from the U.S. Centers for Disease Control and Prevention. (See "Teaming Up to Study First Responders," page 23.)

"We expected an increase in upper and lower pulmonary disease and other health problems," he says. "But to this day, I am amazed at the magnitude of those issues."

In a 2006 paper in the *American Journal of Respiratory and Critical Care Medicine*—one of the first of more than 100 attack-related papers in his curriculum vitae—he reported that 9/11 first responders lost substantial lung function in the year following the attacks; they suffered more than 12 times the decline expected with normal aging.

The largest lung-function decline occurred in workers who arrived at the WTC site the morning of 9/11, when the dust cloud was most intense. Before 9/11, the FDNY had expanded its annual medical exams to include lung-function tests and other critical health measures—a move championed by Dr. Prezant and one that provided crucial clinical baselines for the WTC studies and gave them added weight.

Dr. Prezant and his team described findings that were even more disturbing in a 2010 *New England Journal of Medicine (NEJM)* paper. A significant portion of FDNY rescue workers who'd experienced acute lung damage still had not recovered normal lung function a full seven years after 9/11. For 13% of the firefighters and 22% of the EMS providers, lung function was below normal for their ages.

Previous studies of firefighters had found that the lung-function impairments caused by inhaled pollutants were mild and reversible. The serious lung damage inflicted on 9/11 rescue workers, the 2010 study concluded, most likely stemmed from repeated daily exposure to high concentrations of airborne particles and gaseous chemicals.

The *NEJM* study was remarkable for its findings and for its size and scope. It remains the largest longitudinal study of occupational influences on lung function ever reported. The researchers performed 62,000 spirometry (lung-function) tests on nearly 13,000 first responders, or 92% of those present at the WTC site during the first two weeks after the attacks—a testament to the trust that firefighters and EMS providers had placed in Dr. Prezant and the WTC Medical Monitoring and Treatment Program at FDNY's Bureau of Health Services.

"Many people affected by the attacks suspected that researchers were the enemy—that we were just trying to prove that WTC dust had no lasting health impacts," Dr. Prezant says. "But that wasn't the case within the FDNY, where they realized we were partners, that we would call it the way it is."

PTSD, CANCER, HEART DISEASE, AND MORE

As time went on, first responders experienced an increasing number of serious WTC-related health problems.

In 2010, Dr. Prezant found that first-responding firefighters had elevated rates of post-traumatic stress disorder (PTSD). More than 10% of them had signs of PTSD four years after the WTC attack, creating significant difficulties at work and at home, he reported in *Public Health Reports*.

A 2011 study in *The Lancet* reported that firefighters exposed to the WTC site were at least 19% more likely than their nonexposed colleagues to develop cancer in the seven years following the disaster. "We expected we might see an increase in cancers after 20 years, but not after just seven," he says.

The results, Dr. Prezant said at the time, "support the need to continue monitoring firefighters and others who responded to the World Trade Center disaster or participated in recovery and cleanup at the site. This monitoring should include cancer screening and efforts to prevent cancer from developing in exposed individuals." As he had recommended, the federal WTC Health Program (the new name for the WTC Medical Monitoring and Treatment Program following passage of the James Zadroga 9/11 Health and Compensation Act in 2011) was expanded in 2012 to include cancer screening and prevention efforts.

In 2016, the team reported in *Mayo Clinic Proceedings* that autoimmune diseases had also increased. First responders were 34% more likely to suffer from diseases such as systemic lupus erythematosus, Sjögren's syndrome, and psoriatic arthritis than a comparison group of Midwestern men.

In 2018, Dr. Prezant and colleagues published a study in *JAMA Oncology,* reporting their findings that firefighters faced an increased risk for developing myeloma precursor disease, which in some people leads to the blood cancer multiple myeloma.

A 2019 paper in *JAMA Network Open* linked WTC exposure to an increase in heart disease among the first responders. Those who arrived first at the site had a 44% higher risk of cardiovascular complications than those who arrived later in the day. Similarly, those who worked at the WTC site for six months or longer were 30% more likely to have experienced a primary or secondary cardiovascular event than those who worked less time at the site.

"An important message is that new chest pain in this group should not automatically be attributed to well-known WTC-related illnesses, such as acid reflux or obstructive airway disease. It might very well be associated with CVD [cardiovascular disease]," Dr. Prezant said at the time.

AN FDNY ADVOCATE

Before 9/11 and especially afterward, Dr. Prezant saw that his role as an

TEAMING UP TO STUDY FIRST RESPONDERS

Dr. Prezant has had many collaborators, including:

The late Thomas Aldrich, M.D., professor of medicine and director of the Pulmonary/Critical Care Training Program at Montefiore and Einstein and of the Pulmonary Function Laboratory at Montefiore

David W. Appel, M.D., associate professor of medicine and director of the Pulmonary Sleep Center at Montefiore

Krystal Cleven, M.D., assistant professor of medicine and a pulmonologist at Montefiore

Hillel Cohen, Dr.P.H., M.P.H., professor of epidemiology & population health at Einstein

Charles Hall, Ph.D., professor of epidemiology & population health and in the Saul R. Korey Department of Neurology at Einstein

Simon D. Spivack, M.D., M.P.H., professor of medicine, of epidemiology & population health, and of genetics at Einstein and a pulmonologist at Montefiore

Amit Verma, M.B.B.S., professor of medicine and of developmental and molecular biology at Einstein and director of hemato-oncology at Montefiore

Mayris Webber, Dr.P.H., professor of epidemiology & population health at Einstein

Rachel Zeig-Owens, Dr.P.H., research assistant professor of epidemiology & population health at Einstein

Firefighter Terrence Jordan, circled, helps carry seriously injured colleague Alfredo Fuentes to safety. Lt. Jordan and Capt. Fuentes are both spotlighted in this article, and their stories begin on page 26.

FDNY physician stretched beyond medical care into policy and politics—a challenge he approached with a blend of empathy and science.

"I'm especially proud of our transition from compassion-driven advocacy to data-driven advocacy," he says. "The idea was that knowing what went on down there on 9/11 would result in the right treatment for our responders and would enable us to advocate better for government support. Eventually all that came true, but not without a struggle. And while we now have cancer covered, we are still working on getting certain autoimmune diseases covered under the federal WTC Health Program."

As early as 2002, Dr. Prezant began lobbying members of Congress for money to care for 9/11 first responders.

"During those first trips to the Hill, naysayers in the hearing rooms would tell us, 'Oh, they have symptoms and our hearts go out to them, but most people with symptoms will get over it,'" Dr. Prezant says. "But starting in 2006, after we had strong objective evidence, no one doubted that the first responders were actually suffering. Then the legislators switched to saying, 'We don't know how we're going to pay for this. We don't know if it's a priority.'"

In 2008, Dr. Prezant testified before the U.S. House of Representatives' Appropriations Committee on behalf of what is now called the WTC Health Program. After listing the many health issues plaguing the first responders, he told the representatives that a commitment to long-term funding was needed "to ensure that we can continue necessary treatment, monitoring, and research into the future. As we know in environmental-occupational medicine, there is often a significant lag time between exposure and emerging diseases. … The actual effect of the dust and debris that rained down on our workforce on 9/11 may not be evident for years to come."

He testified again in 2010, this time in support of the proposed Zadroga Act, which would provide more funding for health monitoring and financial aid for the first responders, volunteers, and survivors of the attacks.

"These healthcare findings—they really don't speak to the heart of the matter, to what our patients are suffering on a daily basis," he told the Senate Committee on Health, Education, Labor & Pensions. He went on to describe one such sufferer:

"On 9/11, when the Twin Towers were burning, FDNY firefighters ran into those buildings. By the time the second plane hit, most realized that this was not going to be just a fire; this was an attack. And yet they continued to run in. I have a patient who told a younger firefighter, 'You go left, I'll go right.' That younger firefighter died. And that older firefighter, because of that decision, feels he was responsible for that firefighter's death. He woke up every night screaming for the first six months. And now he wakes up screaming less, but still so often that his wife sleeps in a separate room. That's not the way things should be."

Soon after, comedian Jon Stewart dedicated an entire episode of *The Daily Show* to the Zadroga Act, more or less shaming Congress into passing the proposal, which President Barack Obama signed into law in January 2011. Four years later, the act was reauthorized and extended through 2090—essentially providing lifelong care for health-impaired first responders. Mr. Stewart got much of the credit, but it could be said that Dr. Prezant and other scientists softened up the hardened lawmakers for the comedian's final punch.

Millrock Productions, Inc. via Getty Images; U.S. Navy

"David's lobbying skills are legendary and were seminal in landing the Zadroga Act," says Simon D. Spivack, M.D., M.P.H., professor of medicine, of epidemiology & population health, and of genetics at Einstein and a pulmonologist at Montefiore. "He has been a model of highly effective and caring medicine, science, and advocacy—a very challenging juggling act. We are truly fortunate to have him as part of the Einstein community."

Dr. Prezant "has always been a tireless advocate for the health and safety of every FDNY member," says Fire Commissioner Daniel A. Nigro. "Through his work with the WTC Health Program, he has honored the memory of all those innocent lives taken on Sept. 11 and fought for the health of FDNY members—and really, every first responder—who bravely served in the rescue and recovery effort at the World Trade Center. His work has been key to ensuring early intervention for our members battling illness and in proving that funding is needed to care for the men and women who sacrificed so much to protect our city."

In 2010, Dr. Prezant was appointed the FDNY's chief medical officer and special adviser to the fire commissioner on health policy. He is responsible for the WTC Health Program at the FDNY, its Bureau of Health Services, and its Office of Medical Affairs. His 9/11 studies earned him the American Thoracic Society's Public Service Award (2011) and the American College of Chest Physicians' Presidential Honor (2012).

THE GREATEST JOB

Apart from his 9/11 studies, Dr. Prezant has played major roles in the FDNY's responses to Hurricane Sandy, the Ebola virus, and, most recently, COVID-19.

"Dr. Prezant has been an essential member of my team during the pandemic," Fire Commissioner Nigro says. "He has provided daily, and even hourly, updates to ensure our members were always armed with the latest information and operating with the highest level of personal protective equipment."

In his teaching role at Einstein, Dr. Prezant over the years has mentored almost three dozen epidemiologists, biostatisticians, and pulmonary fellows in his lab. And for one month each year, he supervises the training of young doctors in pulmonary and critical care medicine at Montefiore.

"When I joined Dr. Prezant's research team in 2008 as a newly minted epidemiologist, I knew I could make a difference under his leadership," says Rachel Zeig-Owens, Dr.P.H., research assistant professor of epidemiology & population health at Einstein, director of epidemiological research at the FDNY's WTC Health Program, and a co-author on many of Dr. Prezant's papers. "But I didn't know that 13 years later I'd still be at it with a colleague who truly cares about his patients, his collaborators, and the research as a whole."

Dr. Prezant still cares for patients (see firefighter profiles starting on next page). "That's what I live for," he says. "Being a physician is, without a doubt, the greatest job on the planet."

> "David's lobbying skills are legendary and were seminal in landing the Zadroga Act."
>
> — DR. SIMON D. SPIVACK

THE ONES WHO RAN TOWARD DANGER

Studies assessing the health of 9/11 first responders conducted over the past 20 years are driven by data and as a result are inherently dry and impersonal. Yet such studies can have profound effects—on health policy as well as on the health of the people studied. Here are the stories of three World Trade Center first responders, whose health data was used to inform studies performed by David Prezant, M.D., and who benefited from their findings. The three men ran toward Ground Zero while most others fled, but they paid heavily for their heroism.

A DAY OF TWO 'HAIL MARYS'

In the span of 29 minutes on 9/11, Capt. Alfredo Fuentes, the acting chief of the marine division of the Fire Department of the City of New York (FDNY), escaped death not once but twice.

His first brush with mortality occurred at 9:59 a.m. While awaiting orders at a command post next to Ground Zero, the then-50-year-old Capt. Fuentes noticed that the South Tower had begun to buckle. He warned his colleagues and then sprinted into an underground parking lot. "There was a noise like an oncoming freight train, and everything turned black," he remembers. "I bent down, put my hands over my head, and said the 'Hail Mary' because I thought it was over."

Miraculously, Fuentes emerged unscathed, ready to resume his duties. He then heard that people were trapped inside the Marriott Hotel, and he joined the rescue efforts there. Standing in the middle of the street, he used hand signals to let the other rescuers know when debris from the North Tower had temporarily stopped falling and it was safe to evacuate people from the hotel.

When one group struggled to make its way across the street, Fuentes started toward them—and then at 10:28 a.m. came a second roar. "I looked up and the North Tower was collapsing," he says. "I couldn't run because of all the rubble. I just bent over, covered my head, said the 'Hail Mary' again, and got ready for the hit."

RESCUED FROM THE RUBBLE

That was Capt. Fuentes' last memory of 9/11—which is just as well. The avalanche of debris broke nine of his ribs, collapsed his left lung, scorched his airway, fractured his skull, and nearly tore off his scalp. Somehow, he managed to radio for help. FDNY rescuers, including Lt. Terrence Jordan (page 28), dug him out from the rubble and sent him to a Jersey City, New Jersey, hospital, where he was put into a medically induced coma for two weeks.

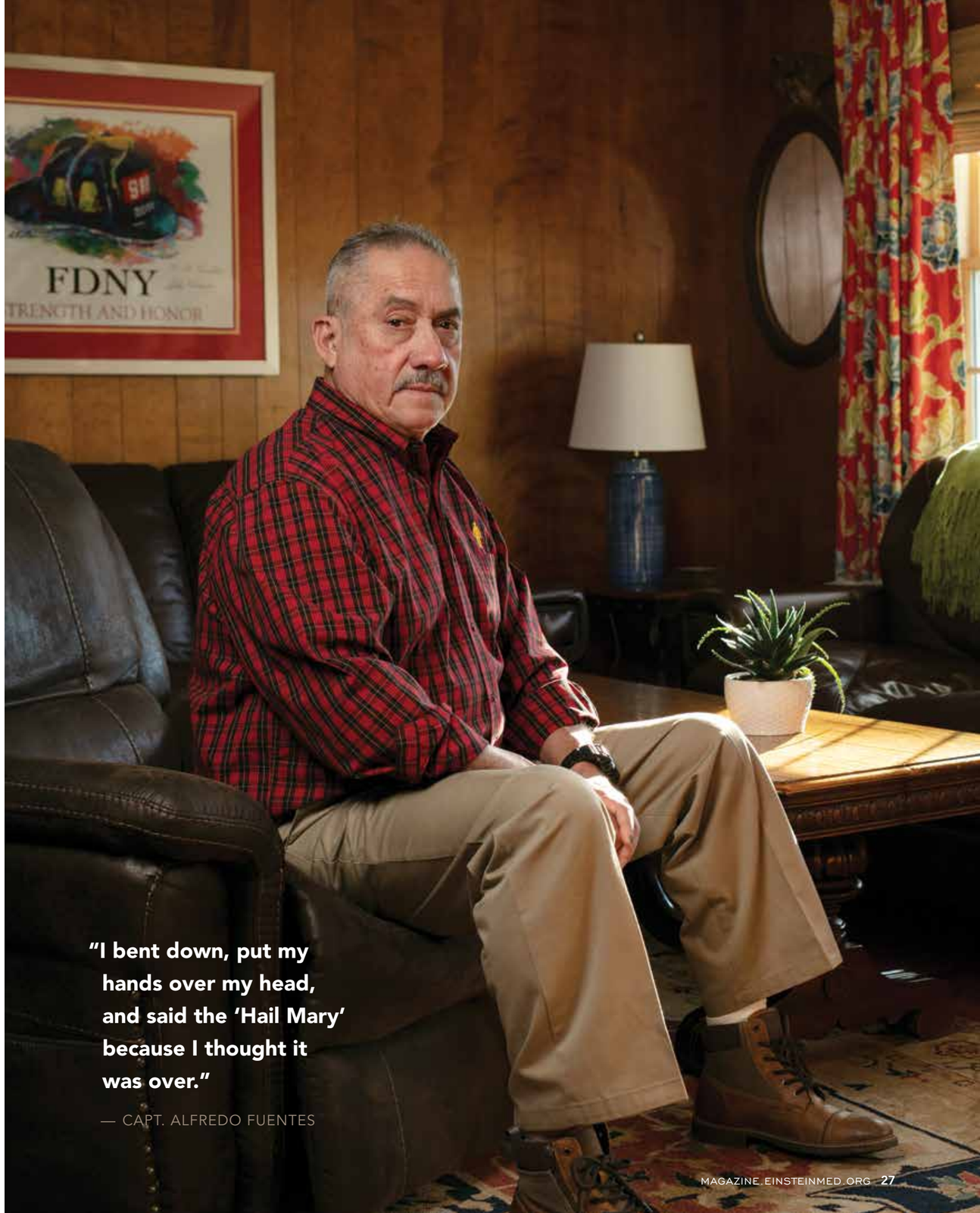
Meanwhile, the FDNY's then-deputy chief medical officer, David Prezant, M.D., who was recovering from his own 9/11 wounds, arranged for Capt. Fuentes to be transported to Montefiore, where it was thought he'd get better care.

One of Capt. Fuentes' first requests on awakening was to see the FDNY chaplain, the Rev. Mychal Judge, a close friend. "I said, 'I need to talk to somebody, about the people jumping and everything.'" When his wife started crying, Capt. Fuentes knew that Rev. Judge hadn't survived.

Then came news of the death of his friend and colleague FDNY Deputy Chief Ray Downey, who was near him when the North Tower collapsed. It was more than he could take.

Capt. Alfredo Fuentes at Montefiore, where he was treated for his injuries.

Photo at right by Jörg Meyer



"I bent down, put my hands over my head, and said the 'Hail Mary' because I thought it was over."

— CAPT. ALFREDO FUENTES

STILL STRUGGLING

Sept. 11 would be Capt. Fuentes' last day on the job. In the months that followed, he underwent numerous surgeries and procedures—more than he can remember. He spent the better part of a year confined to a recliner because of inner-ear damage that had compromised his balance. He's still recovering 20 years later, struggling with lung disease, chronic sinusitis, and memory loss.

"With help from the World Trade Center Health Program and Dr. Prezant, we're keeping everything at bay," says Capt. Fuentes, who was born in Ecuador and lives in Woodside, Queens. "Dr. Prezant sees me once or twice a year, goes over my case, and makes sure I get to the right doctors. I have to credit him for the quality of life that I have now."

Capt. Fuentes has every right to be bitter about the day that cost him so much, but he sees only the good that came of it. "What I witnessed that day was incredible, the way people responded, and not just the firefighters but also the civilians. I can't say enough about the City of New York and the country," he says.

"Who's got it better than me?" he asks. "I survived. I got to see my wife and family and my grandson."

'I'M LUCKIER THAN SO MANY OTHER PEOPLE'

Like thousands of other first responders, Lt. Terrence Jordan of the FDNY would never be the same after 9/11.

Lt. Jordan, then in his early 40s and a member of the FDNY's Marine Company 9, was on Randall's Island for compulsory training when the planes hit the towers. He made his way to the Brooklyn Navy Yard, commandeered a boat named (of all things) *Smoke*, loaded it with medical supplies, and raced at full throttle to the North Cove Marina near Ground Zero, arriving shortly after the buildings collapsed.

"The air was filled with an incredibly thick cloud of dust—you couldn't see two feet in front of you," Lt. Jordan recalls. He had bypassed his firehouse and so hadn't brought his mask and respirator. That hardly mattered to him in the heat and dust of the moment—especially after overhearing radio calls from a fellow FDNY mariner, Capt. Alfredo Fuentes, who was buried somewhere under the rubble (page 26).

A SEARCH FOR SURVIVORS

Moving through the eerie quiet, Lt. Jordan and his team followed the periodic beeps of fire safety equipment programmed to emit a distress signal when the wearer stops moving. The rescuers

Lt. Terrence Jordan on a visit to the 9/11 Memorial in Manhattan.

found Capt. Fuentes, pulled him from the rubble, administered first aid, and carried him to the docks for transport across the Hudson River to a New Jersey trauma center.

Lt. Jordan returned to the debris piles to search for more survivors. "We'd find an arm or a leg," he says. "It was horrible." A few people were found alive, and so he pressed on, staying on site for three straight days.

His own troubles started on day one, with an asthma-like attack. Lt. Jordan gulped a few mouthfuls of bottled oxygen, caught his breath, and rejoined the rescue effort. More asthma attacks followed, prompting him to contact Dr. Prezant, who implored him to come for testing at the first opportunity.

"I made him promise he wouldn't put me on medical leave," says Lt. Jordan. "There was so much work to be done."

But when Lt. Jordan went for testing a few days later, the news was grim. His lungs were severely damaged, probably beyond repair. "Dr. Prezant told me, 'Terry, you won't be going to another fire. You'll have to retire.'"

TETHERED TO A TANK

Twenty years of service in the FDNY were followed by 20 years of pain and suffering. Since 9/11, Lt. Jordan has struggled with chronic obstructive pulmonary disease, severe emphysema, bronchitis, and asthma. In 2010 he had a stroke, which partially paralyzed his right side. "I go to more doctors than you could imagine," says Lt. Jordan, who is tethered via a tracheal tube to an oxygen tank 24 hours a day. "It's like I'm 140 years old."

Yet he remains remarkably upbeat. "I have my issues," says Lt. Jordan, the father of seven. "But I'm in reasonably

Photo on this page by Theresa Jordan; photo at right by Jörg Meyer

"The air was filled with an incredibly thick cloud of dust—you couldn't see two feet in front of you."

— LT. TERRENCE JORDAN

good shape because of the World Trade Center Health Program and Dr. Prezant, who stays on top of my health. Just this past November, I had another breathing episode, and he treated me over the phone for 10 weeks until it resolved. He never gives up."

And neither does Lt. Jordan. Three years after his stroke, he participated in the annual Stephen Siller Tunnel-to-Towers Run & Walk, pushing a walker with a battery-powered oxygen concentrator. After last December's nor'easter, he could be found clearing the driveway of his Floral Park, Long Island, home with a snowblower, over the objections of his wife and neighbors. And he still rides his motorcycle.

"I don't want my life to be defined by a terrorist incident," he says. "I have a pretty good life. I just had my ninth grandchild. I never would have seen any of my grandchildren had I not survived 9/11. I'm luckier than so many other people."

ASSIGNED TO THE MORGUE

One thing was clear after both World Trade Center towers collapsed on 9/11: The tragedy would claim the lives of many firefighters. Fire Marshal Conrad Tinney of the FDNY was dispatched to the chief medical examiner's office in Manhattan later that day to expedite the handling of the remains. Mr. Tinney had seen his share of death and destruction as a Navy sailor in Vietnam and then as a firefighter in New York. Yet nothing he'd experienced had prepared him for the task at hand.

"It was pure madness, like a scene out of the movie *M*A*S*H*," he says. "We identified the first 20 bodies by sight, because we had worked with these guys before." The remains kept arriving at the morgue, body part after body part. A total of 343 firefighters died that day.

Mr. Tinney stayed at the morgue for five days, until Charles Hirsch, M.D., the chief medical examiner, threatened to have him physically removed if he didn't go home.

"I gave the neighbors a free show," he says. "I took off all my clothes on the front steps, walked into the house, and showered. After I started shaving my beard, which had absorbed the smell of death, I looked in the mirror and broke down."

WORKING ON THE 'PILE'

Mr. Tinney soon returned to duty and spent the following weeks shuttling back and forth between the morgue and the "pile"—the term coined by rescue workers to describe the 1.8 million tons of smoldering debris left from the towers' collapse. He didn't wear a mask or respirator. "We were told [by the U.S. Environmental Protection Agency] that the air was fine," he says.

It wasn't, of course, and neither was Mr. Tinney. "Every morning, I'd walk over to my kitchen window, where I could see the smoke from the towers—and I knew I had to go down there," he says.

Three months in, disobeying direct orders, he reported to headquarters instead of to the pile—no small decision for a person in uniform. "I told them I just couldn't take it anymore—that the human mind is not meant to handle such traumatic events," he says. "It took me two years of therapy to come to terms with it."

As fall turned to winter, Mr. Tinney came down with bronchitis, which persisted for months. A scan administered the next spring picked up a small nodule in his left lung. Dr. Prezant recommended that Mr. Tinney undergo periodic scans to keep a close eye on the growth.

A BATTLE WITH LUNG CANCER

Seven years later, soon after he retired, Mr. Tinney was told that the growth on his lungs looked suspicious and would have to be removed. "Let the dance begin," he said, the fight still left in the firefighter.

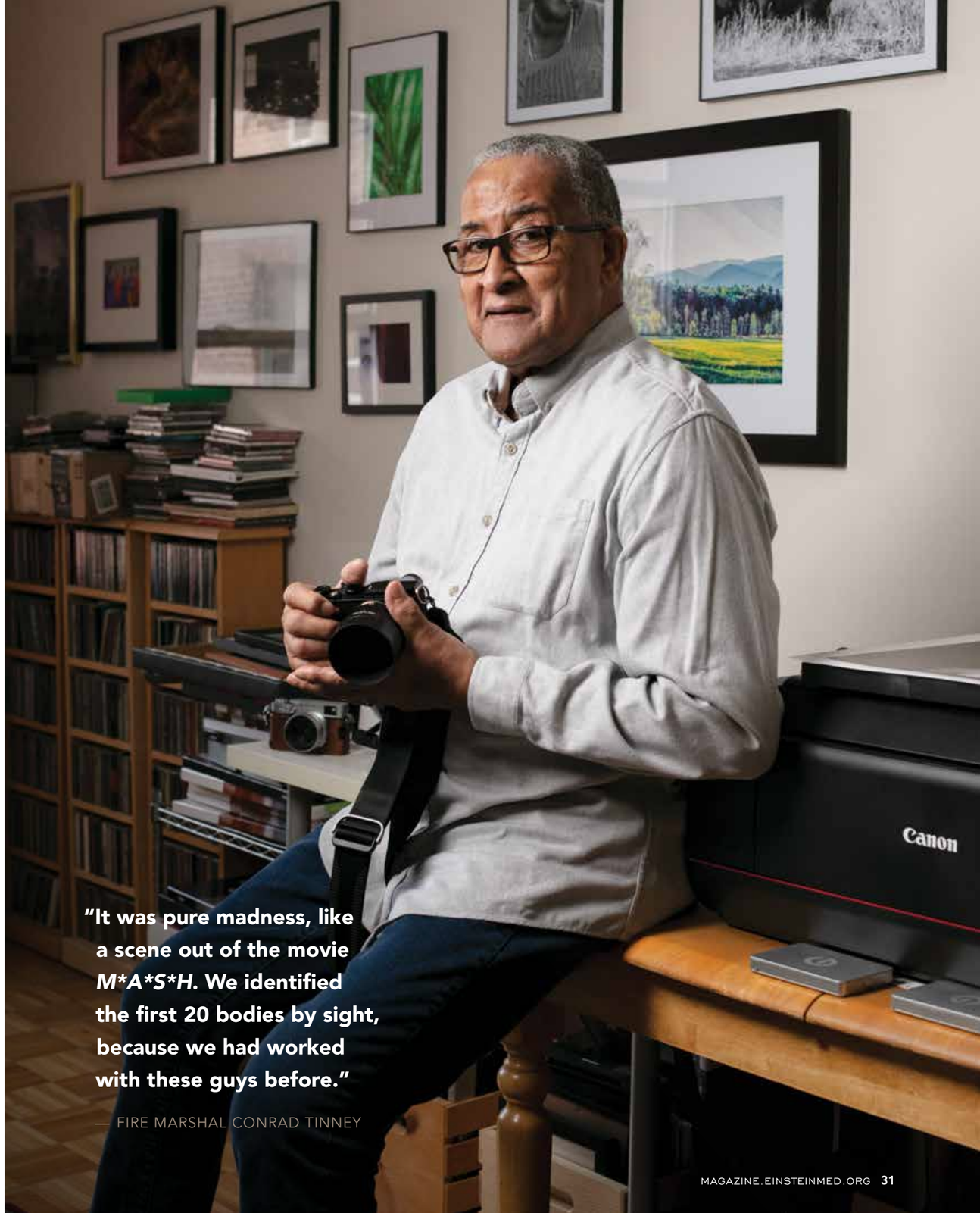
A biopsy confirmed that the growth was cancerous, and a surgeon successfully removed it from Mr. Tinney's lung. But his ordeal was just beginning.

After enduring several rounds of chemotherapy for the lung cancer, Mr. Tinney went into renal failure. Then his immune system crashed, and he was prescribed an experimental immune-boosting therapy that saved his life. Next came 36 rounds of radiation therapy aimed at eliminating any lingering cancer in his chest.

All the while, Mr. Tinney strove to live as fully as possible, indulging in his passions of photography and travel, including journeys to Vietnam, Kenya, and Namibia. That all came to a halt last year, and not just because of the pandemic. His "good" lung started filling with fluid, which doctors found was the result of lymphoma. The dance continues.

"I'm still here," Mr. Tinney says. "You have to look at the good part of it. People ask, 'How's your day?' and I say, 'I got up this morning.'" E

Photo by Jörg Meyer



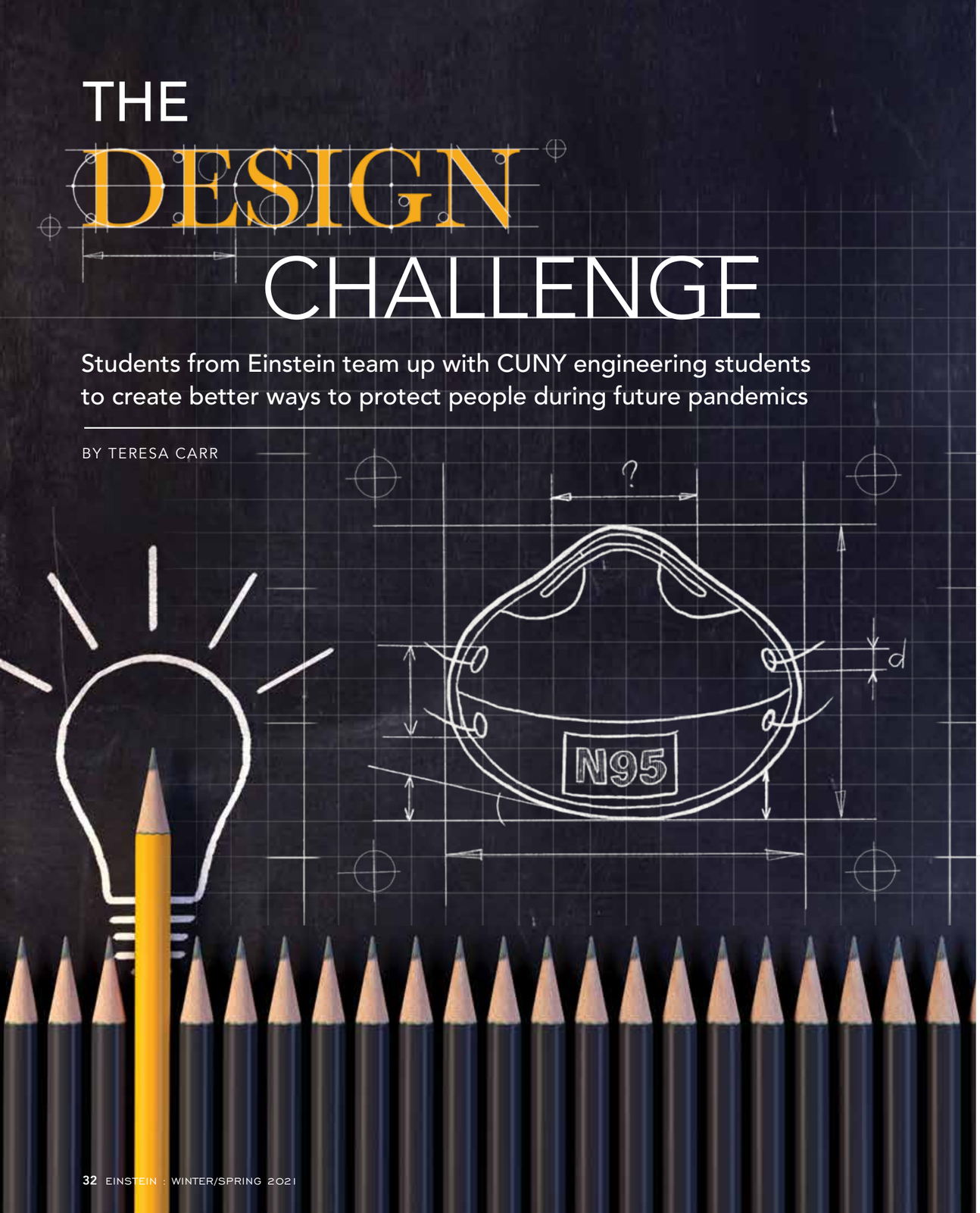
"It was pure madness, like a scene out of the movie *M*A*S*H*. We identified the first 20 bodies by sight, because we had worked with these guys before."

— FIRE MARSHAL CONRAD TINNEY

THE DESIGN CHALLENGE

Students from Einstein team up with CUNY engineering students to create better ways to protect people during future pandemics

BY TERESA CARR



Xueting "Hattie" Zhang, a second-year medical student at Einstein, was intrigued but nervous. She was looking for a way to help out during the pandemic, and an email announcing a new summer educational offering had just popped up on her computer screen. Called the "COVID-19 Design Challenge," it asked students to devise innovative solutions for making healthcare workers and the public safer in a future wave of COVID-19 or another infectious disease. And it gave them just eight weeks to do it.

"I wanted to register for it, but I was worried that if my design required engineering, I wouldn't have the skill that was needed," she says. Then she learned that participants would work in multidisciplinary groups that included engineering students from the City University of New York (CUNY). So she took a deep breath and signed up—along with 16 others from Einstein, including medical students and Ph.D. candidates, all eager to help fight a virus that was ravaging the Bronx.

"If motivated, interested, and excited students get together to work on a challenge from different vantage points, good things will happen," says Todd Cassese, M.D., associate dean for medical education, an associate professor of medicine at Einstein, and a hospitalist at Montefiore. "These types of experiences can be transformational."

OPPORTUNITY AMID CRISIS

The idea to create a design challenge arose from conversations between Dr. Cassese and Joshua Nosanchuk, M.D., senior associate dean for medical education at Einstein and an infectious-diseases clinician at Montefiore, about how designs for personal protective equipment (PPE) for healthcare workers hadn't progressed much over the years. "This moment seemed like an opportunity to reframe what's really important during an outbreak—not just PPE, but all the challenges we were facing—and get some really bright minds to think about it," Dr. Cassese says.

While Einstein students had the medical know-how, Dr. Cassese realized that engineering expertise would also be needed. Since Einstein already had a relationship with CUNY with existing master's of public health and Centers for AIDS Research programs, it seemed like a good place to start.

Dr. Cassese pitched the idea of a design challenge to the dean of the Grove School of Engineering at the City College of New York/CUNY, where Sabriya Stukes, Ph.D., caught wind of it. Dr. Stukes, who earned her doctoral degree in microbiology and immunology at Einstein in 2014, is the associate director of CUNY's master's in

"If motivated, interested, and excited students get together to work on a challenge from different vantage points, good things will happen."

— DR. TODD CASSESE

Above, Einstein second-year medical students Kevin Batti, left, and Hattie Zhang examine an N95 mask while collaborating on the COVID-19 Design Challenge.

translational medicine (MTM) program. "MTM blends engineering, science, and business concepts to teach scientists and engineers how to design and commercialize medical technologies," Dr. Stukes explains. "So it felt like a very good fit."

Faculty members from Einstein and CUNY then divided students into 10 teams, with most containing a mix of engineering and medical students. Each team's goal was to identify an unmet public health need and come up with a possible solution. There was also an incentive: Winning teams would be invited to submit a budget to develop and refine their concepts and could be awarded up to $5,000, paid from an Einstein educational fund for curriculum innovations.

Initially, many medical students worried about their technical skills, while the engineers felt they lacked medical training. "The light-bulb moment was when they realized that wasn't a weakness," Dr. Stukes says. "They found they could work across disciplines and admit, 'I don't know about this, but here's what I do know, and I am willing to learn.'"

CUNY engineering faculty created a curriculum that taught students how to sift through possible solutions, develop prototypes, make an initial proposal, build a business case, and craft a compelling narrative about their technology.

Einstein brought in experts with medical backgrounds, including pulmonologists, who explained how ventilators work, and microbiologists and infectious-disease experts, who covered molecular virology. "There's no way this would have happened without the generous donation of time and energy from a series of experts in engineering, entrepreneurship, design, science, and medicine," Dr. Cassese says.

Photos by Jason Torres

Einstein medical student Hattie Zhang discusses design modifications with other members of her team on a videoconference call.

FROM PAPER TO PROTOTYPE

Ms. Zhang's team included fellow second-year Einstein medical student Kevin Batti and three CUNY engineering students. The challenge they chose was reducing healthcare workers' risk of exposure to the coronavirus when putting on, taking off, or storing their PPE.

The pandemic required the team members to discuss their concepts on videoconference calls. "It was definitely tricky, not being able to pass around tangible objects such as masks," Mr. Batti says. "We'd hold drawings up to the camera and point."

At the first meeting, Ms. Zhang came up with what she recalls as "a very rough idea": a device for allowing people to efficiently and safely put on and take off face masks while minimizing the risk of contamination. One of the engineering students then sketched a design on paper.

The team kept returning to Ms. Zhang's concept for several weeks—only to abandon it in favor of devising something more impressive. "But when it came to implementing our design, we decided that simplicity was our best friend," Mr. Batti says. The team soon crafted a working prototype from inexpensive parts ordered from Amazon.

"We were excited to arrive at something we felt could actually scale and go to market," Mr. Batti says.

> "Teamwork is so crucial to being a healthcare provider. ... We can teach our students facts, but we need them to be able to apply them at the bedside and in innovative research."
>
> — DR. HELEN RHIM

IDEAS WITH LASTING IMPACT

When the eight-week challenge was up, each group presented its project to a panel of five experts. The judges from Einstein were Peter Bernacki, senior director of business services, and Helen Rhim, M.D., M.P.H., director of educational innovations in the office of medical education and the fellowship director for pediatric hospital medicine at Children's Hospital at Montefiore. Other judges were Lola Brown, Ph.D., assistant dean for research at Weill Cornell Medicine; Aaron Kyle, Ph.D., a senior lecturer in biomedical engineering design at Columbia University; and Lawrence Levy, former chief financial officer of Pixar Animation Studios.

"I was so impressed by the creativity and the breadth of products—from things people could use in daily life to specific medical equipment to help protect frontline workers," Dr. Rhim says. "The high quality of the projects made it difficult to decide on the finalists."

While proud of their design, Ms. Zhang and Mr. Batti didn't expect to be among the finalists. "I didn't think we would win because everyone in the competition was really impressive—talented and smart," Mr. Batti says. "We were going up against some amazing stuff like new types of ventilators." Much to their surprise, their face-mask device earned the top score among the four groups chosen as finalists.

"An important takeaway for the students is that sometimes the simplest ideas are best," Dr. Stukes says.

Members of the winning Design Challenge team convene via videoconference. They are, clockwise from top left: Renato Vilca Valderrama of CUNY, Hattie Zhang of Einstein, Oliver Brannigan of CUNY, Kevin Batti of Einstein, and Andrea Ozuna of CUNY.

Other winning ideas included two safer ways for healthcare workers to deliver oxygen to patients and a method for disinfecting taxis and car services to reduce virus transmission. Members of the winning teams are using the money given to them to revise their prototypes and file patent applications.

Ultimately, the first-ever design challenge also exceeded the expectations of those who had created it. "The degree of innovation really surprised me," Dr. Cassese says. But he says the primary goal of the course was to enrich students' educational experiences. "We think about how we can give learners the tools and confidence to pursue ways to improve our healthcare system and to help their patient community, to really make a difference," he says. "By that measure, the design challenge was an incredible success."

Dr. Rhim wholeheartedly agrees. "Teamwork is so crucial to being a healthcare provider," she says. "That application phase is so important to what we are trying to achieve in the medical school curriculum. We can teach our students facts, but we need them to be able to apply them at the bedside and in innovative research."

Ms. Zhang, who wants to specialize in internal medicine, says that she's excited about tackling more problems. "This experience showed me that I don't have to be an engineer or a coder to be an innovator. I can do it with everyday projects, and I can find a great group of people to help perfect my idea."

Mr. Batti, who hopes to become an orthopedic surgeon, agrees. "Realizing you can take an idea from a vision to a tangible product is really cool," he says. "I feel like I can go on to improve operations in the future." E

Illustrations: ©Tatyana Starikova Harris

Gut Reactions

Einstein and Montefiore researchers are finding that the intestinal microbiome may hold the key to good health—and that altering it may help treat sickle cell disease, diabetes, obesity, and more

BY GARY GOLDENBERG

Our microbiome consists of a vast array of bacteria, viruses, fungi, and other microbes living on us and in us. Our gut microbiome alone contains an estimated 38 trillion bacterial cells belonging to 500 to 1,000 species. Some of those species perform useful functions, such as those that synthesize folate and other vitamins or that protect us against pathogens. While most gut bacteria cause no harm, disturbances in the levels of certain species contribute to a wide range of health problems—some extremely serious.

"Doctor, this disease is ruining my bank account, it's ruining my social life, it's ruining me. I'm coming to you as a last resort. Is there anything you could do?"

While it's common for a seriously ill patient to plead for help, it's rare for a physician to come up with a eureka moment on the spot. Yet that's what happened in 1991, when a new patient with a devastating intestinal infection came to the office of Lawrence J. Brandt, M.D., professor of medicine and of surgery at Einstein and a gastroenterologist at Montefiore.

The elderly woman's problems started with a bout of pneumonia. Antibiotics cleared her lungs but left her infected with *Clostridioides difficile*, a gut bug that is resistant to many antibiotics, causes severe diarrhea and inflammation of the colon, and is often lethal. *C. diff*, as it is commonly referred to, and the accompanying diarrhea would both return as soon as the woman's antibiotic treatment was halted.

"I have an idea," Dr. Brandt told his patient after she'd explained her predicament. "I think the antibiotics did something to the bacteria in your gut that were protecting you. But you're sitting right next to a guy [her husband of 50 years] who likely has the same bacteria in his gut as you had. Maybe we could replace what you lost by taking some of his stool and putting it in your colon."

The couple immediately agreed to the therapy, odd though it may have seemed. Days later, Dr. Brandt took a

stool sample from the woman's husband, diluted it, and used a colonoscope to inject the solution into her colon. "She called me at home that night and said, 'I don't know what you did, but I haven't felt this good in months,'" remembers Dr. Brandt. "She never had a recurrence."

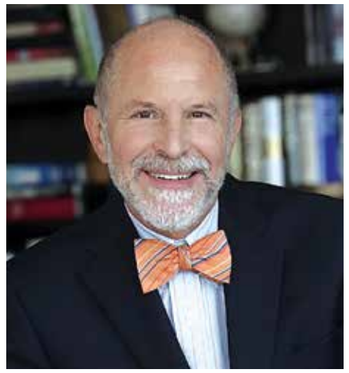
Only later did Dr. Brandt learn that his "novel" therapy—now known as fecal microbiota transplantation (FMT)—actually dates to the fourth-century Chinese healer Ge Hong. He touted fecal material for food poisoning or severe diarrhea in *Handy Therapy for Emergencies*, China's first handbook of emergency medicine.

The Western experience with FMT can be traced to 1958, when Ben Eiseman, M.D., a Colorado-based surgeon, used fecal enemas to cure four patients with infectious colitis. Despite these and several other treatment successes, FMT garnered little attention until decades later, when Dr. Brandt starting curing his Montefiore patients who suffered from recurrent *C. diff*.

IN SEARCH OF A MECHANISM

The first clinical trial of FMT occurred in 2013, when researchers in Amsterdam compared FMT with antibiotic therapy in patients whose *C. diff* infections had relapsed after one round of antibiotics. FMT cured 15 out of 16 patients, while antibiotics cured just 7 out of 26, according to a report in the *New England Journal of Medicine*. Every patient in the antibiotics group who relapsed was subsequently cured with FMT.

Dr. Brandt co-led a clinical trial in 2014, also involving patients with antibiotic-resistant *C. diff*. A single FMT treatment produced lasting cures in 15 of 17 patients, and a 16th was



"She called me at home that night and said, 'I don't know what you did, but I haven't felt this good in months.'"

— DR. LAWRENCE BRANDT

cured after two treatments, for an overall cure rate of 94%, as reported in the *Journal of Clinical Gastroenterology*.

How does FMT work? "*C. diff* and the antibiotics used to treat it reduce the diversity of bacteria in the gut," says Dr. Brandt. "FMT immediately restores this diversity and prevents disease-causing bacteria from infecting and colonizing the GI tract." But how?

"We know that FMT works, but not the mechanism responsible," Dr. Brandt acknowledges. "We think the benefits result from the presence of metabolic products of bacteria found in healthy stool that maintain and regulate our metabolism."

Better treatments for *C. diff* are certainly needed. *C. diff* infections are growing at an alarming rate, particularly among nursing home residents. Roughly a half million people in the United States are affected annually, with a recurrence rate of about 20%, leading to an estimated 29,000 deaths each year.

The U.S. Food and Drug Administration (FDA) still classifies FMT as an investigational procedure but allows its use for patients with *C. diff* who do not respond to conventional treatment. (In November 2019, the FDA hosted a meeting to obtain public input on the state of the science regarding FMT, which could lead the agency to reclassify the therapy.)

The FDA's limitations aside, the major barrier to wider FMT use is the therapy's "yuck" factor.

"In our society, stool is seen as something dirty," says Dr. Brandt. "We make light of it with scatological humor. When I tell people I'm infusing stool as a medical treatment, they laugh and think I'm crazy." He's now encouraging the field to rechristen the treatment as IMT, for intestinal microbiota transplant.

"It is the microbiota that is transplanted … not feces!" he wrote in a recent issue of the *American Journal of Gastroenterology*. "The term 'fecal transplant' is often puzzling to patients and awkward for providers."

In the meantime, Dr. Brandt cautions that physicians prescribing FMT should obtain microbiota from rigorously tested sources, such as OpenBiome, a nonprofit stool bank, to reduce the risk of transmitting disease-causing microbes—a rare but potentially deadly complication. Another worry: No one knows the long-term consequences of using FMT to manipulate the gut microbiome.

"It's one thing to treat older patients who might die if they don't get their

Lawrence Brandt, M.D., checks on the image clarity of an endoscope before beginning a procedure at Montefiore.

C. diff under control," he says. "It's quite another to treat younger patients with non-life-threatening conditions. We don't know if FMT may set them up for other problems later in life."

FMT may work for other conditions as well. Researchers are currently studying the technique in Crohn's disease, ulcerative colitis, irritable bowel syndrome, obesity, diabetes, Parkinson's disease, and autism.

THE MICROBIOME, METABOLISM, AND COVID-19

To a great extent, obesity and type 2 diabetes result from what we put into our stomachs. Our microbiome also has a major influence—and is itself influenced by a third variable: acculturation. Where we were raised appears to influence our microbiome and hence our risk for metabolic disease.

Research at Einstein on the acculturation connection can be traced to 2016, when the National Institutes of Health

"The question is, how do you make favorable changes to the microbiome? With probiotics? With regular foods? With medications?"

— DR. ROBERT KAPLAN

awarded Einstein researchers a five-year, $3.9 million grant to investigate the role of the gut microbiome in type 2 diabetes among Hispanics and Latinos—the fastest-growing segment of the U.S. population—enrolled in the long-running Hispanic Community Health Study of Latinos (HCHS/SOL). The study has been following 16,000 participants ages 18 to 74 since 2010, and Einstein is one of four HCSH/SOL sites nationwide.

The Einstein researchers analyzed the microbiomes of more than 3,000 adult HCHS/SOL participants who either were born here or came to the United States later in life. In a study published in 2019 in *Genome Biology*, they reported that the composition of people's microbiomes was related to their degree of acculturation. People who relocated to the United States at an early age had a lower diversity of intestinal microbes compared with those who relocated after age 45.

Acculturation's influence on the microbiome may have major health implications. The study found that people with lower microbiome diversity were more likely to be obese (a major diabetes risk factor), which is consistent with results from other studies. In addition, a reduced ratio of *Prevotella* to *Bacteroides* bacteria was significantly associated with obesity among the HCHS/SOL participants—a link not seen in other populations.

"These findings from our study are important since they tie population-specific microbiome associations to clinical outcomes," says Robert Burk, M.D. He is the co-principal investigator of the HCHS/SOL gut microbiome study and also vice chair for translational research in the department of pediatrics, professor of medicine, of microbiology & immunology, of pediatrics, of obstetrics & gynecology and women's health, and of epidemiology & public health at Einstein, and a pediatric geneticist at Montefiore.

Robert Kaplan, Ph.D., the other co-principal investigator of the HCHS/SOL gut microbiome study, notes that its findings also suggest that manipulating the gut flora could help in treating or even preventing metabolic diseases such as type 2 diabetes—which usually results from obesity and is especially common among Hispanics, who have a 66% higher rate of diabetes than non-Hispanic U.S. whites (11.8% versus 7.1%). "The question," he says, "is how do you make favorable changes to the microbiome? With probiotics? With regular foods? With medications? These are all things to be learned in the years ahead." Dr. Kaplan is also a professor of epidemiology & population health, the Dorothy Manealoff Foundation and Molly Rosen Chair in Social Medicine, and the principal investigator for the HCHS/SOL at Einstein.

Earlier this year, Carmen Isasi, M.D., Ph.D., the co-principal investigator for the Einstein HCHS/SOL site, took the lead in rapidly redesigning the entire HCHS/SOL project to encompass the COVID-19 pandemic.

"We have already begun collecting data on our study participants' COVID-19-related diagnoses and hospitalizations, including how the pandemic has affected them personally from a health, emotional, and employment standpoint," says Dr. Isasi, who is an associate professor of epidemiology & population health and of pediatrics at Einstein. That effort also includes analyzing stool specimens to determine whether the gut microbiome—which can profoundly

The Microbiome Facts & Figures

TYPES OF MICROBES IN THE MICROBIOME: **BACTERIA, VIRUSES, FUNGI, ARCHAEA, AND EUKARYOTES**

NUMBER OF BACTERIA IN THE HUMAN GUT:
38 TRILLION

NUMBER OF CELLS IN THE HUMAN BODY:
30 TRILLION

WEIGHT OF THE HUMAN MICROBIOME:
0.44 POUND

PROPORTION OF THE MICROBIOME LOCATED IN THE G.I. TRACT:
>99%

"MICROBIOME" WAS COINED IN 2001 BY JOSHUA LEDERBERG, THE NOBEL PRIZE–WINNING MICROBIOLOGIST, "TO SIGNIFY THE ECOLOGICAL COMMUNITY THAT LITERALLY SHARES OUR BODY SPACE AND HAS BEEN ALL BUT IGNORED AS DETERMINANTS OF HEALTH AND DISEASE."

NUMBER OF GENES IN HUMANS:
20,000–25,000

NUMBER OF GENES IN HUMAN MICROBIOME:
>8 MILLION

affect the immune system—influences the body's response to SARS-CoV-2, the coronavirus that causes COVID-19.

"We could be dealing with the effects of COVID-19 long after this pandemic is over," Dr. Kaplan says. "We're hopeful that our ongoing HCHS/SOL trial—and its recent redesign to study the intersection of the gut microbiome, COVID-19, and overall health—can shed light on risk factors that can lead to long-term complications and on what can be done to prevent them."

In addition to his gut microbiome research involving HCHS/SOL participants, Dr. Burk is investigating the role of microbiomes in health problems including human papillomavirus (HPV) infection, osteosarcoma (a pediatric bone cancer), kidney stones, HIV infection, and cognitive impairment.

A decade ago, he says, he was skeptical about the importance of the microbiome in human health. "We've learned a lot since then," he adds. "Now I think we have to take a step back and consider that there may be a role for the microbiome in almost every disease."

PREVENTING SICKLE CELL COMPLICATIONS

Paul Frenette, M.D., is the principal investigator on a study involving the gut microbiome and sickle cell disease (SCD). Dr. Frenette is a professor of medicine and of cell biology and the chair and director of Einstein's Ruth L. and David S. Gottesman Institute for Stem Cell Biology and Regenerative Medicine.

People with SCD have an inherited gene mutation that leads them to produce abnormal hemoglobin, the oxygen-carrying protein in red blood cells. Red blood cells with abnormal hemoglobin become sickle-shaped and less flexible, which causes them to clog small blood vessels, triggering attacks of severe pain called sickle cell crises, or vaso-occlusive episodes. These episodes cause major organ damage over time and contribute to the decreased life expectancy (now in the mid-40s) of people with SCD.

In 2002, Dr. Frenette found that SCD vessel blockages occur when sickled red cells bind to neutrophils (a type of white cell) that have adhered to the vessel walls. "This early work indicated that not all neutrophils are the same," says Dr. Frenette. "Some appear to be inert while others appear overly active in promoting inflammation—which is useful for attacking microbes but causes neutrophils to capture sickled red cells inside vessels, leading to blockages."

The hows and whys of neutrophil activation became clearer in 2015. While studying a mouse model of SCD, Dr. Frenette's lab found that neutrophils become more active and pro-inflammatory as they grow older in the blood, suggesting they receive signals that tell them to age—signals, it turns out, that come from the gut microbiome.

"Since the body's microbiota seem to 'educate' neutrophils to age," Dr. Frenette says, "we realized that purging those microbes with antibiotics might help against SCD."

In fact, when the researchers used antibiotics to deplete the microbiota of SCD mice, they observed a striking reduction in neutrophils but not in other white cells. Moreover, the antibiotics appeared to prevent sickle cell crises in SCD mice—markedly suppressing interactions between neutrophils and red cells, improving local blood flow, and increasing the rodents' survival.

> "What was most surprising and exciting was that the antibiotics greatly reduced chronic tissue damage in the spleen and liver."
>
> — DR. PAUL FRENETTE

Deepa Manwani, M.D., director of the Sickle Cell Disease Program at Children's Hospital at Montefiore, listens to the heart of a young patient.

"What was most surprising and exciting was that the antibiotics greatly reduced chronic tissue damage in the spleen and liver," says Dr. Frenette, whose study appeared in *Nature*. "This is the first time that something was found to have an impact on the organ damage that can be so devastating in SCD."

With help from the Sickle Cell Disease Program at Children's Hospital at Montefiore (CHAM), Dr. Frenette and colleagues investigated whether their mouse findings might be relevant to people. They obtained blood samples from nine healthy children and from 34 patients with SCD. Of the 34 SCD patients, 11 were taking penicillin daily to ward off infections, as is recommended for children 5 or younger with SCD; 23 had been off penicillin for at least two months. Consistent with the mouse findings, children with SCD who were not taking penicillin had many more circulating aged neutrophils compared with healthy controls.

"Daily penicillin for patients with SCD younger than 5 works really well in preventing infections," Dr. Frenette says. "Our study suggests that older people with SCD could potentially benefit from preventive antibiotic therapy as well."

His team is currently collaborating with Deepa Manwani, M.D., who directs CHAM's Sickle Cell Disease Program, on a study evaluating penicillin's effect on the gut microbiomes of young SCD patients. Children are enrolled and their microbiomes evaluated at age 4 to 5, while they are still taking daily penicillin; their microbiomes are sampled again around age 5 to 7 (when they have stopped taking penicillin for at least six months) to compare the microbiomes of the children while they were taking penicillin and after they stopped taking the antibiotic.

Dr. Frenette is also trying to understand how the microbiome combines with psychological stress to cause sickle cell crises. Using a mouse model of SCD, he has found that the path to sickle cell crises begins in the brain.

Stress triggers the secretion of hormones in the brain that travel to the gut and increase its permeability. The greater permeability allows gut microbes known as segmented filamentous bacteria to interact with immune cells, which are stimulated to produce pro-inflammatory molecules that enter the bloodstream. These molecules promote the aging and accumulation of neutrophils that drive sickle cell crises. The findings were published in July 2020 in *Immunity*.

"Importantly, we found we could markedly reduce sickle cell vaso-occlusive episodes in mice through several different interventions: inhibiting glucocorticoid synthesis, depleting segmented filamentous bacteria, or blocking the inflammatory molecules induced by these bacteria," Dr. Frenette says. "Each of those actions could potentially limit the impact of psychological stress on people with SCD."

MAKING CHEMOTHERAPY SAFER

Patients who develop colorectal cancer often are prescribed irinotecan—a chemotherapy drug found on the World Health Organization's List of Essential Medicines. However, up to 40% of patients who receive irinotecan experience severe, potentially life-threatening diarrhea.

"As you can imagine, such patients

"Microbes are nature's chemists, capable of producing and metabolizing a diverse array of compounds."

— DR. LIBUSHA KELLY

Libusha Kelly, Ph.D., at work in her Einstein lab.

are already quite ill, so giving them a treatment that causes intestinal problems can be dangerous," says Libusha Kelly, Ph.D., associate professor of systems & computational biology and of microbiology & immunology at Einstein.

Dr. Kelly wondered if the gut's microbiome might be to blame for adverse reactions to irinotecan. "We've known for years that variations in genetic makeup can affect how people respond to a medication," she explains. "It stood to reason that microbiome variations might also play a role. Microbes are nature's chemists, capable of producing and metabolizing a diverse array of compounds. That's beneficial in some cases—when gut bacteria make vitamin B12, for example. But the microbiome can also turn otherwise helpful drugs into toxins."

Irinotecan is administered intravenously in an inactive form. Certain liver enzymes metabolize the drug into a compound toxic to cancer cells. Other liver enzymes later convert the drug back to its inactive form, which makes its way to the intestine for elimination.

But some people possess gut bacteria that use part of inactivated irinotecan as a food source by digesting the drug with enzymes called beta-glucuronidases. That's good for the bacteria but terrible for the intestines. This enzymatic action reactivates irinotecan into its toxic form, which damages the intestinal lining.

To minimize irinotecan-related toxicity, doctors have tried using oral antibiotics to kill the offending bacteria but found that the antibiotics killed off protective gut bacteria as well.

In a search for an alternative treatment, Dr. Kelly and her colleagues collected fecal samples from 20 healthy individuals and treated the samples with inactive irinotecan. They then used metabolomics (the study of the unique chemical fingerprints that cellular processes leave behind) to group the fecal samples according to whether they metabolically reactivated the drug. Four of the 20 people were found to be "high metabolizers," and the other 16 were "low metabolizers."

The two groups of fecal samples were checked for differences in microbiome composition, with a focus on beta-glucuronidase-producing bacteria. The microbiomes of high metabolizers contained significantly higher levels of three previously unreported types of bacteria capable of producing beta-glucuronidases compared with low metabolizers.

The 2017 findings, published in *npj Biofilms and Microbiomes*, a *Nature* journal, suggest that analyzing the composition of patients' microbiomes before giving irinotecan might predict whether intestinal side effects will occur. Thus forewarned, physicians would know when to prescribe diarrheal treatment preventively and to monitor patients more closely for irinotecan side effects. Dr. Kelly is now testing her hypothesis in a study involving colorectal cancer patients who are receiving irinotecan, in collaboration with Montefiore oncologist Sanjay Goel, M.B.B.S., M.S., professor of medicine at Einstein.

The findings also suggest that the use of drugs that inhibit specific beta-glucuronidases might prevent adverse irinotecan reactions—and that prebiotics (nondigestible fiber that gut microbes feed on) might help, too. "Beta-glucuronidases have an appetite for the carbohydrates found in the inactive form of irinotecan," Dr. Kelly says. "If we feed patients a competing source of carbohydrates when we administer irinotecan, perhaps we could prevent those enzymes from metabolizing the drug."

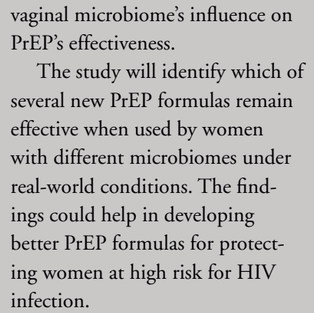
In a project with even broader clinical implications, Dr. Kelly and two members of her lab (Leah Guthrie, Ph.D., and postdoctoral fellow Sarah Wolfson, Ph.D.) developed MicrobeFDT, a tool that groups 10,000 drugs, foods, and other compounds according to their chemical structure and links them to gut microbial enzymes that interact with them. The goal: predicting adverse health effects from exposure to those compounds.

MicrobeFDT correctly predicted how gut microbes might alter the structure of altretamine, an ovarian cancer drug that can cause diarrhea and kidney damage. "When we incubated altretamine in fecal samples from healthy volunteers, the drug was altered as the tool predicted," says Dr. Kelly, whose findings were published in 2019 in the journal *eLife*.

"We hope this research will ultimately enable us to improve people's health by monitoring and potentially altering their microbiomes," Dr. Kelly says.

In an *npj Biofilms and Microbiomes* paper published last October, Dr. Kelly and her postdoctoral fellow William Chang, Ph.D., devised an analytical method that was able to distinguish between gut microbe dynamics found in "healthy" and "sick" people, despite the continually changing microbiome compositions in both conditions over time.

"How does one's microbiome respond to a trip outside the country? Does the state of your microbiome today tell us anything about your health tomorrow, or next week? We have so many questions," says Dr. Kelly. "It's early days for this field, but I'm excited about the potential to translate this basic research into the clinic and hopefully help improve people's lives." E



Betsy C. Herold, M.D.

THE MICROBIOME AND VAGINAL HEALTH

Studies show that PrEP, the two-drug-combination pill taken daily for preventing HIV infection, can be highly effective—capable of reducing the risk of sexual transmission of HIV by more than 90%. In 2019, the Eunice Kennedy Shriver National Institute of Child Health & Human Development awarded a five-year, $2.6 million grant to Betsy C. Herold, M.D., to study the vaginal microbiome's influence on PrEP's effectiveness.

The study will identify which of several new PrEP formulas remain effective when used by women with different microbiomes under real-world conditions. The findings could help in developing better PrEP formulas for protecting women at high risk for HIV infection.

Dr. Herold is professor, chief of infectious diseases, and vice chair for research in the department of pediatrics at Einstein and Children's Hospital at Montefiore, and the Harold and Muriel Block Chair of Pediatrics.

PASSIONATE
PURSUITS

The Thrill of the Climb

BY WAYNE COFFEY

It's a Tuesday night in Long Island City, and a sinewy septuagenarian is making a sure-footed ascent up a rock-studded wall, his muscles taut as a rope. Three times a week, Steven Cohen, M.D., M.P.H., morphs into rock climber extraordinaire, scaling walls for hours at The Cliffs, an indoor facility where he evokes awe among his fellow climbers.

"He's the most focused and driven person in the gym," says Judy Aschner, M.D., a fellow climber and an Einstein professor of pediatrics and of obstetrics & gynecology and women's health. "He pushes himself every single climb, every single time, to do more-challenging things and to do them perfectly. It's astonishing to watch him. He's the strongest person his age I've ever seen."

OLYMPIAN GYMNAST

At 5 feet 7 inches and 150 pounds, the 75-year-old Dr. Cohen has a physique that would be envied by people half his age. That's no surprise, given his previous athletic life. Growing up in Philadelphia, Dr. Cohen was a two-time city champion as an all-around gymnast before going on to become a Penn State University All-American and member of the 1968 U.S. Olympic gymnastics team in Mexico City.

Steven Cohen, M.D., M.P.H., adjusts his footing as he scales a steep vertical wall in the White Mountain National Forest in Rumney, New Hampshire, in 2018.

Clockwise from top: Dr. Cohen balances on one arm before being named the NCAA all-around gymnastics champion while competing for Penn State University in 1966; at Rattlesnake Mountain in Rumney, New Hampshire, he hugs the face of the rock during an ascent in 2018; at The Cliffs in Long Island City, New York, an indoor rock-climbing facility, he perfects his skills in 2020.

More than a half-century later, he works full time as a professor of dermatology at Einstein and is chief emeritus of the division of dermatology at Einstein and Montefiore, specializing in rare skin diseases.

Still, he makes time to climb. He typically travels twice a year to such iconic climbing destinations as Red Rock Canyon National Conservation Area in Nevada's Mojave Desert and Joshua Tree National Park in California. Closer to home, he enjoys climbing in the Shawangunk Mountains in New York's Hudson Valley. His goal is to become the oldest person to climb El Capitan, the 3,000-foot granite monolith in California's Yosemite National Park.

"My energy level is high," Dr. Cohen says with a soft laugh.

THE APPEAL OF CLIMBING

An avid runner, cyclist, and swimmer as a younger man, Dr. Cohen had to undergo a full hip replacement at age 40, after doctors discovered a tumor. Though he stayed active, he didn't find an enduring athletic passion until decades later when, at age 69, he talked to a rock climber at a party and was instantly intrigued. The climber invited Dr. Cohen to stop by his climbing gym in Brooklyn.

Dr. Cohen

Climbing, like gymnastics, requires strength, balance, and the ability to handle technical challenges. It immediately appealed to Dr. Cohen, along with the sport's demand for "interdependence" with climbing partners—a quality Dr. Cohen refers to as "part of the gestalt of climbing."

He also loved climbing's adrenaline rush. "I was climbing in the crib," Dr. Cohen says. "My parents couldn't put enough bars on it to keep me in it. I climbed telephone poles, chimneys, anything I could find. I think it was built into my consciousness from birth. After I went [to the Brooklyn gym] once, I never turned back."

Dr. Cohen now enjoys introducing the sport to friends and students. Several have become dedicated climbers themselves. He says medicine will always be at the core of who he is, because "taking care of people is really what I love doing." But he's grateful to have found an outside pursuit that keeps him vigorous and sharp.

He may be the oldest man on the rock-climbing wall, but he's fine with that. "To me," Dr. Cohen says, "climbing is part of the joy of living." E

VIEW MORE
Find additional photos of Dr. Cohen's climbing adventures: magazine.einsteinmed.org/photos21

Exploring the Science of Longevity

Nir Barzilai, M.D.
Founding director of the Institute for Aging Research at Einstein, the Ingeborg and Ira Leon Rennert Chair in Aging Research, professor of medicine and of genetics at Einstein, and an endocrinologist at Montefiore

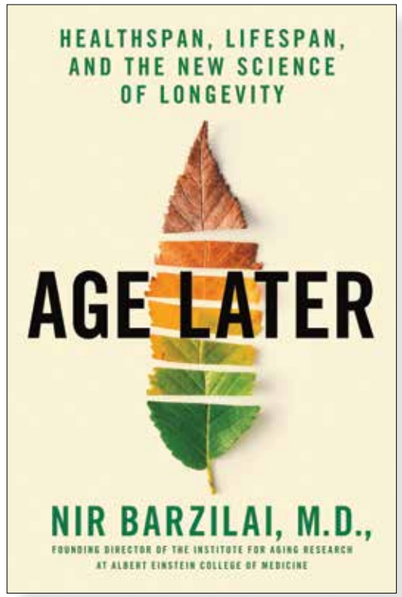
Every year, trees signal their leaves to change color and die. Are people programmed to deteriorate in a similar way? Or is it possible to stave off mortality? Nir Barzilai, M.D., who has spent the past few decades researching the mechanisms that drive aging, addresses that question in his new book, *Age Later*.

Growing old, after all, not only transforms us but makes us susceptible to one or more of the "big four" illnesses: Alzheimer's, cancer, diabetes, and cardiovascular disease. Dr. Barzilai had long wondered whether the aging process could be targeted like a disease, to slow it down and lengthen the human "health span."

In 1998, to gain insight into the biology of aging, Dr. Barzilai launched a study of "Super Agers"—people living independently at age 95 and beyond who had not experienced diseases that plagued their peers. Dr. Barzilai and his team focused on Ashkenazi Jews, who are more genetically uniform than other groups, making it easier to spot gene differences and similarities that might be present. The Longevity Genes Project enrolled nearly 3,000 men and women, about 750 of whom were ages 95 to 109 and the rest either offspring of the Super Agers or older adults with no longevity in their backgrounds. Participants were mainly from the New York metropolitan area and had similar education and income levels.

Most of these exceptionally long-lived individuals possessed at least one of the following genetically influenced traits:

• High levels of good cholesterol—high-density lipoprotein—which protects them from heart attacks and dementia;



Courtesy of St. Martin's Press

• Unusually low levels of the growth hormone IGF-1 (insulin-like growth factor 1), a protein produced in the liver; and

• Unusually high levels of mitochondrial-derived peptides, which provide resilience against the stresses of aging.

Many of the Super Agers also benefited from healthy lifestyles and healthy environments. But their most significant common denominator was possessing gene mutations that seem to confer long life spans. Dr. Barzilai and his colleagues have so far identified dozens of such "longevity genes."

So how can the rest of us improve our chances of becoming centenarians, especially if we haven't inherited the right genes? Dr. Barzilai is working on that. He co-founded a biotech company that is targeting several hallmarks of aging, and he serves as chief medical consultant for several other companies with a shared goal: developing drugs to prevent Alzheimer's, diabetes, and other diseases of aging.

In the meantime, he says, the best antidote for aging is exercising for at least 25 minutes three to five times a week. What else helps? Don't eat too much or too often, and focus on the positive things in life—one of which, in the near future, he assures us, will be drugs that mimic what longevity genes can do.

PUBLISHED BY: St. Martin's Press, 2020

Stories of Pregnancy, Birth, and the Unexpected

Chavi Eve Karkowsky, M.D.
Associate professor of obstetrics & gynecology and women's health at Einstein and medical director and clinical liaison of outpatient obstetrics at Montefiore Medical Center

"Pregnancy" is often used as shorthand for "happily ever after." But the experience is almost never that simple, as maternal-fetal medicine specialist Chavi Eve Karkowsky, M.D., describes in her new book, *High Risk*.

Some women—those with an autoimmune disease or a history of miscarriages, for example—already know they'll need a maternal-fetal medicine specialist, also known as a high-risk-pregnancy doctor, when they get pregnant. But plenty of others might be having a completely routine pregnancy—until they're not. Maybe their water breaks at 27 weeks. Maybe an ultrasound picks up something not quite right about the shape of the fetal heart.

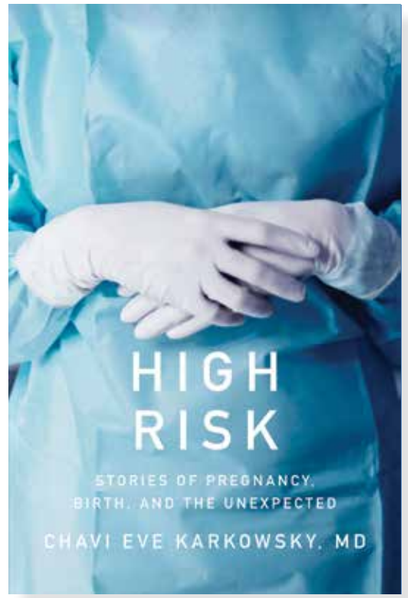
High Risk offers insights into those complications, but also covers a wide spectrum of reproductive health issues—genetic testing, ultrasounds, miscarriages, preterm births, the dramatic rise in cesarean sections, and the diagnosis of stillbirth.

Pregnancy, Dr. Karkowsky explains, often produces plenty of surprises, and almost nobody (not even some doctors) knows what can happen before, during, and after. "I wish someone had told me" is what she hears often from patients, she writes.

Dr. Karkowsky aims to do just that by telling compelling stories of some of the patients she has seen in her years of practice, in well-written chapters organized like a pregnancy itself: trimesters one, two, and three; full-term pregnancy; going into the hospital (or staying out); and postpartum and beyond.

She also shares her own experiences, including the nausea and vomiting (which affects 70% to 90% of pregnant women) that had her "hating every moment" at six weeks and grabbing the sides of her bed "as if I were shipwrecked on an unstable raft."

A chapter is devoted to maternal mortality and racial disparities.



Courtesy of Liveright

From 2011 to 2014 in the United States, pregnancy-related mortality rates for Black women were 3.2 times those for white women, a "shameful truth," Dr. Karkowsky notes. The medical establishment is beginning to understand the scope of the problem, she writes, but countering physicians' implicit biases (subconscious prejudices) is going to take hard and constant work.

The book concludes with a night on the labor and delivery floor, "routine and amazing, everyday and earth-shattering, all at once." It begins at 5:05 p.m. after an already busy day at the clinic, when Dr. Karkowsky and her colleagues divvy up the evening's patients. One has chronic hypertension and three prior cesarean sections; another, eight days past her due date, came in because her water broke; a third patient had just fallen down stairs at 27 weeks; a fourth is already 5 centimeters dilated; and a fifth is recovering from a cesarean and being monitored after a blood transfusion.

Dr. Karkowsky runs from patient room to operating room and back all night, until the morning team arrives at 7:30. She exits the hospital exhausted but upbeat. After all, she notes, she has had "a front-row seat to the most interesting and compelling parts of human experience." E

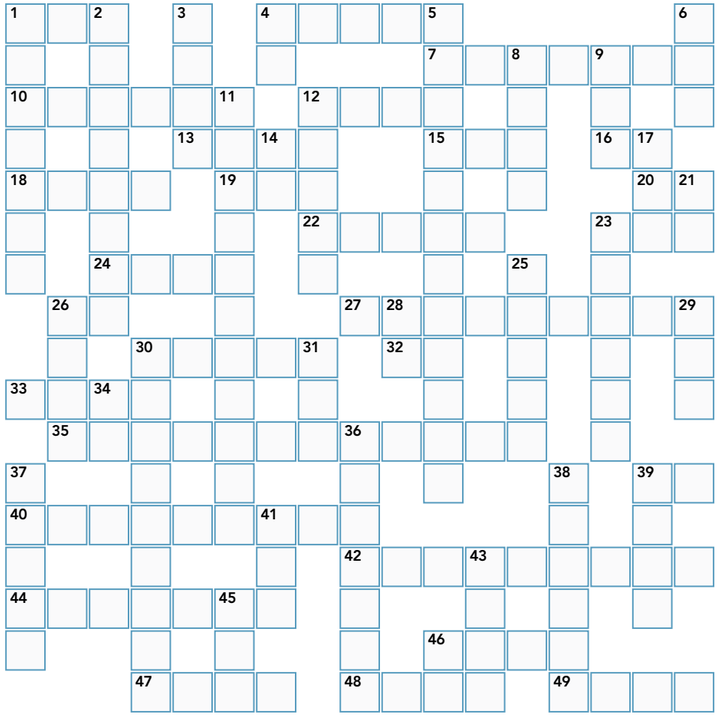
PUBLISHED BY: Liveright, an imprint of W.W. Norton, 2020

ALBERT'S

PUZZLER

BY DEIRDRE BRANLEY

It Was 20 Years Ago Today*



Across

1 Gaping mouth
4 She wore a swan dress to the Oscars
7 This pioneering peer-to-peer music-sharing site was shut down
10 Pop singer Billie ____ was born
12 When Destiny's Child broke up, Beyoncé went ___
13 Quiet
15 Shortened term to describe people whose gender identity corresponds to their sex assigned at birth
16 Allison Janney took home an Emmy for playing this character on *The West Wing*
18 *Smallville* began, which featured this reporter friend of Superman
19 This Russian space station was decommissioned
20 Lithium on the periodic table
22 This infamous energy company went bankrupt
23 The ginger best friend of Harry, in the top movie of the year
24 This filmmaker released *Ali*, starring Will Smith
26 Not true
27 This first transdermal birth control patch was released
30 Pediatric surgery that redirects blood flow from upper body directly to the lungs
32 This satellite radio service launched
33 ____ Rudd starred in *Wet Hot American Summer*
35 These Arizona snakes beat the Yankees in the World Series
39 Iron's atomic symbol
40 This open-source encyclopedia was launched
42 He and Nicole Kidman divorced
44 She sang "I'm a Slave 4 U" at the MTV Video Music Awards
46 NWA rapper Ice ____ released his greatest hits
47 This future secretary of state became the first Black female national security advisor
48 A warm, shallow bath that cleanses the perineum
49 Justin Timberlake's band, 'N ____

Down

1 This future special counsel for Russian election interference was named FBI director
2 These sisters met in a Grand Slam final
3 He was inaugurated as president in January
4 Bromine's atomic symbol
5 The Lasker Award honored this model of human disease
6 Limb where humerus is located
8 This leaning tower reopened after 11 years
9 Habitual muscle spasm
11 First drafts were simultaneously released by Craig Venter and Francis Collins
12 This cartoon ogre's first movie was released
14 Silicon, for short
17 This Latina released an eponymous album
21 Not out
23 They won the Super Bowl, besting the New York Giants (as our dean will know)
25 This Barry broke the season home run record, which he still holds
26 ____ Pitt starred in *Ocean's Eleven* and *The Mexican*
28 Prescription abbreviation
29 It merged with Time Warner
30 Winner of Best Picture Oscar
31 Simpsons' neighbor ___ Flanders was on the cover of *Christianity Today*
34 Short for user interface
36 This Lonely Hearts Club Band had the No. 1 album of the year
37 Tools to get COVID-19 test sample
38 Apple's digital music service was launched
39 The car film franchise *The ____ and the Furious* began
41 Not night
43 She starred with 42 Across in *Vanilla Sky*
45 Yadda, yadda, yadda
46 A type of scan that uses X-rays

* *Note: Many clues refer to 2001, a nod to our cover story.*

See how well you did at: magazine.einteinmed.org/puzzler2021

MOTIVATIONS

The Front Line of Philanthropy at Einstein and Montefiore

Image: Justin C. Wheat, M.D./Ph.D. candidate

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64 Class Notes
68 In Memoriam

To learn more, please visit montefiore.org/giving and einsteinmed.org/giving

A Message From the Senior Vice President of Development and Chief Philanthropy Officer

KATHLEEN KEARNS

Kathleen Kearns

What motivates philanthropists to give? Throughout my decades-long career, those reasons—from the personal to the visionary and beyond—have always moved me. When I came to Albert Einstein College of Medicine and Montefiore Health System at the end of 2020 as the new senior vice president of development and chief philanthropy officer, hearing from so many generous and passionate Einstein supporters confirmed what I had long known: Einstein is a special place, made more so by the people who hold it so close to their hearts.

This devotion is evident in the latest issue of *Motivations*. You will read about John Braver, M.D., from Einstein's Class of 1970, who joined forces with fellow alumnus Gordon F. Tomaselli, M.D. '82, the Marilyn and Stanley M. Katz Dean at Einstein and executive vice president and chief academic officer at Montefiore, to fund the renovation of the Education Center in the Forchheimer Building (page 54). You'll learn how UJA-Federation of New York has partnered with Einstein to care for Holocaust survivors coping with the COVID-19 pandemic (page 56). And you'll take a look inside the emerging Blood Cancer Institute, where researchers are gaining crucial knowledge about the causes of blood cancers and more-effective treatments for them (page 60).

In this issue we also pay tribute to one of the most inspiring humanitarians I've had the honor of knowing, however briefly: the late Roger W. Einiger (see facing page). A committed chair of the Board of Trustees and notable thought leader, Mr. Einiger created a legacy for Einstein that will forever fill chapters of Einstein's history—and indeed, our future.

The Einstein community is exceptional, composed of dynamic individuals motivated to make the world a better place. That mission binds us all through our vocations, volunteerism, and philanthropy.

As our namesake said, "Only a life lived for others is a life worthwhile." That philosophy guided Albert Einstein in his brilliant work and still guides many of us here today. With that, I'll open up the conversation: What motivates *you* to give?

With gratitude,

Kathy Kearns

Kathleen Kearns

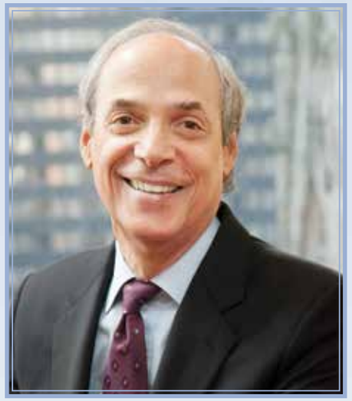
REMEMBERING EINSTEIN BOARD CHAIR ROGER W. EINIGER

The Einstein and Montefiore communities lost a devoted and loyal friend on Dec. 9, 2020. Roger W. Einiger, chair of the Einstein Board of Trustees and trustee of Montefiore Medicine and Montefiore Health System, died peacefully at his home in New York City at age 73 after a courageous, two-and-a-half-year battle with pancreatic cancer.

STEADY LEADERSHIP

"Few people have played a more important role in the recent history of Einstein and Montefiore," says Philip O. Ozuah, M.D., Ph.D., president and chief executive officer of Montefiore. "Over his lifetime, Roger provided important leadership and generous support for all aspects of Einstein's mission, strengthening its position as a research powerhouse, top-ranking academic destination, and force for social good." Mr. Einiger's service continued his family's long relationship with Einstein: His parents, Jack and Glory Einiger, were among the College of Medicine's earliest supporters and were members of the Society of Founders.

Mr. Einiger joined the Einstein Board in 2005 and served in numerous roles, including treasurer, chair of the executive committee, and chair of the budget and finance committee, tapping into three decades of experience in finance and investment banking and providing Einstein's leadership with invaluable strategic and financial advice. He joined the Montefiore Board in 2014 and was instrumental in finalizing the historic partnership between Einstein and Montefiore one year later. Mr. Einiger became Einstein's board chair in 2015, succeeding Ruth L. Gottesman, Ed.D., and



led the recruitment in 2018 of Gordon F. Tomaselli, M.D., the Marilyn and Stanley M. Katz Dean at Einstein and executive vice president and chief academic officer at Montefiore.

Among his many other contributions, Mr. Einiger led the Campaign to Transform Einstein, which raised nearly $200 million for the College of Medicine. In 2020, Mr. Einiger was the trustee lead for the search committee that recruited Edward Chu, M.D., M.M.S., as the new head of the Albert Einstein Cancer Center. Dr. Chu holds the Carol and Roger Einiger Professorship of Cancer Medicine.

"Roger was an unrelenting supporter of the medical school and a stalwart friend and, most recently, he helped steer us through the turbulent challenges of the COVID-19 pandemic," notes Dr. Tomaselli. "For these and many other reasons, I was privileged to present him with an honorary doctorate of humane letters during our 2020 virtual commencement ceremony."

HIS LIFE AND CAREER

Mr. Einiger spent more than 30 years at Oppenheimer & Co. and its successor companies, ultimately serving as executive vice president, chief administrative officer, and vice chairman. He began a second career in 2001, devoting his time to serving on the boards of numerous nonprofit organizations important to him, helping to advance their missions and strengthen their finances. In addition to Einstein and Montefiore, these included UJA-Federation of New York, Big Brothers Big Sisters of NYC, the Anti-Defamation League, the University of Pennsylvania School of Design, and The Washington Institute, among others.

Born in New York City in 1947, Mr. Einiger earned his bachelor's degree in economics from the Wharton School of the University of Pennsylvania and his M.B.A. from New York University's Stern School of Business. He is survived by his wife of 51 years, Carol; their son, Joshua; their daughter-in-law, Julie; their grandson, Jacob; and Mr. Einiger's sister, Ellen, and brother-in-law, Mitch. E

DR. JOHN BRAVER
CLASS OF '70

A lifelong physician and educator helps the Einstein Education Center meet the future

BY JOAN LIPPERT

Less than a decade ago, Einstein's Education Center was a state-of-the-art technology hub for learning about everything from anatomy to zoonoses. But 10 years is a lifetime when it comes to today's increasingly wireless teaching spaces.

Low ceilings and cement columns were causing audio and connectivity challenges. Outdated equipment made it harder to project information from newer computers onto large screens. And smartphones, tablets, and laptops were straining the Wi-Fi system. The Education Center needed a reboot.

PAYING IT FORWARD

Fortunately, Einstein alumnus John Braver, M.D. '70, had been thinking for a while of making a gift to his alma mater, to express his gratitude to the College of Medicine. "I got a terrific education and a career for life," he says.

Dr. Braver had retired in 2016 as chief of gastrointestinal radiology and co-director of abdominal imaging at Brigham and Women's Hospital in Boston. He had not, however, retired from his longtime dedication to medical students. A beloved and skilled educator, he was voted Brigham's Teacher of the Year in 1982 and again in 2010. Even after retiring, he still teaches Brigham residents once or twice a week.

In June 2019, Dr. Braver attended a brunch for Boston-area Einstein alumni hosted by Janina Galler, M.D. '72, and Burton Rabinowitz, M.D. '72. There he met fellow alumnus Gordon F. Tomaselli, M.D. '82, Einstein's Marilyn and Stanley M. Katz Dean, who shared campus updates and answered questions about admissions, student life, residency matching statistics, and other details. "We talked about supporting students, and I left impressed by the dean's enthusiasm and vision," Dr. Braver says.

That meetup inspired Dr. Braver to make a generous donation at the end of 2019 to benefit medical students and to support education. "I trusted Einstein's leaders to know how my contribution could best be used to help students learn and engage most effectively," Dr. Braver says.

IMPROVED INFRASTRUCTURE

Dr. Braver's gift came at a crucial time. Costs for repairing and replacing Education Center equipment were running as high as $60,000 per year. Plus, the surge in digital communication caused by the COVID-19 pandemic was stressing the aging educational facility. "The pandemic meant that our third-years couldn't see patients in the hospital, so we created a nine-week virtual course with lessons from the clerkship," says Joshua Nosanchuk, M.D., senior associate dean for medical education. Also, all first- and second-year lectures were being delivered virtually. Dependable digital communication with Montefiore and beyond was more essential than ever.

John Braver, M.D., standing next to a security robot in Silicon Valley, says he sees great value in new technologies for use in education, medicine, and more.

Dr. Braver's donation allowed work on massive technology upgrades to begin quickly. The vastly improved Education Center now offers a new Wi-Fi system, a refined broadcast frequency to prevent outside interference, and improved microphone audio that uses Bose technology. Small tables have replaced large ones to accommodate more test-takers

GUIDING ELDERLY SURVIVORS OF THE HOLOCAUST

With support from UJA-Federation of New York, Montefiore is bringing vital mental health services to those who endured the World War II concentration camps

BY GARY GOLDENBERG

After her husband's death, 90-year-old Sarah L. of Washington Heights* moved to a new apartment to be closer to her children. Sadly, the combined loss of her spouse, home, and neighbors was too much to bear, leaving her depressed and confused. Worse yet, she struggled with nightmares about her childhood in Eastern Europe, where she was deported to Auschwitz, along with her four siblings, all of whom perished in Nazi concentration camps.

Sarah's decline seemed unstoppable—until she connected with an unusual alliance of caregivers from Montefiore and Selfhelp Community Services, a local agency, bolstered by a philanthropic partnership with UJA-Federation of New York.

"It was heartbreaking," says Alessandra Scalmati, M.D., Ph.D., associate director of geriatric psychiatry at Montefiore and associate professor of psychiatry and behavioral sciences at Einstein, who oversaw Sarah's care. "But with her family's assistance, we got her started on antidepressants and psychotherapy, and arranged for in-home care. After a while, her nightmares and other symptoms began to ease."

The caregiver alliance—dedicated to addressing the mental health of Holocaust survivors and their families—has provided help to hundreds of people like Sarah. "This is our last opportunity to ensure that the survivors can live out their years with dignity," says Briana Hilfer, L.M.S.W., a planning executive with UJA-Federation of New York, the alliance's founder and funder. "By providing this care, along with other critical support services, we can help survivors remain safely and comfortably in their homes, which is what most prefer."

WHEN THE PAST IS PRESENT

New York City's 36,000 Holocaust survivors are an incredibly resilient group. They've endured the camps, built new lives in a foreign land, and lived well into old age. But their survival has exacted an emotional toll.

"Most Holocaust survivors have been able to cope with the lingering effects of their trauma," says Gary Kennedy, M.D., director of geriatric psychiatry at Montefiore and professor of psychiatry and behavioral sciences at Einstein, who has been involved with the alliance since its inception. "But with aging, they tend to lose their natural filters to contain the horrors they experienced."

Cognitive impairment affects about one in four individuals over age 85 and tends to make matters worse. "With dementia, people can get trapped in their early memories," Dr. Scalmati says. "They might not remember what they had for breakfast, but they

* Some details have been changed to protect the family's privacy.

"If they remember being confined in the camps, that can rekindle nightmares and flashbacks."

— DR. ALESSANDRA SCALMATI

can usually recall every detail of their childhood. If they remember playing in the fields, fabulous. But if they remember being confined in the camps, that can rekindle nightmares and flashbacks and trigger other symptoms of post-traumatic stress disorder, increasing their vulnerability and risk of institutionalization."

Further complicating matters, many survivors are reluctant to seek support. "Some don't want to be at the mercy of strangers, while others fear being stigmatized by psychiatric care or being forced into a nursing home or hospital," Dr. Scalmati adds.

AN ALLIANCE IS CREATED

In 2012, the United Jewish Appeal (UJA)—long a sponsor of programs for Holocaust survivors—realized that survivors were declining in number but that their needs, particularly their mental health concerns, were rising. To help address that problem, the UJA found an ideal partner in Montefiore, established more than a century ago to care for poor Jewish immigrants.

Today, Montefiore's geriatricians are among a handful of specialists nationwide with expertise in aging and trauma. The third partner in the alliance is Selfhelp, the organization operating the oldest and largest support program for Holocaust survivors in North America.

"UJA, Selfhelp, and Montefiore's collective goal is to ensure that Holocaust survivors are treated with the utmost dignity, compassion, and respect," says Alisa Doctoroff, a member of the boards of trustees of Montefiore Medicine, Montefiore Health System, and Einstein, as well as a past president of UJA-Federation of New York.

"Montefiore and Einstein's caregivers pay attention to all vulnerable people within their community, whether they are aging Holocaust survivors or members of often-overlooked or disadvantaged groups," she says. "This mission makes Montefiore and Einstein the ideal partners to lead this work."

The collaborative's guiding philosophy—person-centered, trauma-informed (PCTI) care—recognizes the impact of violence and trauma and promotes people's dignity, strength, and empowerment. While PCTI may sound dry in principle, it's deeply humanistic in practice.

"You need to have extra sensitivity for people who have experienced trauma," Dr. Kennedy says. "You cannot force people to address their issues. The challenge is to convey the message 'If you want to talk, I want to listen.' These patients are naturally cautious about new relationships and can come across as 'difficult.' Caregivers need to understand and respect this or they won't be able to help. But once we earn the patients' trust, we can help them understand what is triggering their fears and assure them they are safe."

Montefiore Medicine trustee Alisa Doctoroff and her husband, Daniel.

"We can help them understand what is triggering their fears and assure them they are safe."

— DR. GARY KENNEDY

36,000 HOLOCAUST SURVIVORS
live in the New York area.

SINCE COVID-19 STRUCK ...

36% OF NEW YORKERS
reported symptoms of depression and anxiety, with elderly and Holocaust survivors acutely affected.

HOLOCAUST SURVIVORS
are coping with resurfaced trauma from early lives spent in hiding and years of food scarcity.

Source: UJA-Federation of New York

Both Magda Goodman, above right, and Bernard Igielski, pictured with his daughter and grandson, are Holocaust survivors and program participants. Mr. Igielski often gives talks about his experiences to students.

understand what is triggering their fears and assure them they are safe."

The program team also offers care to family members, who can feel the effects of a parent's trauma. "We call this 'vicarious traumatization,' in which trauma passes from one generation to the next through a parent's behaviors," Dr. Kennedy says.

The COVID-19 pandemic has heightened the challenge of caring for Holocaust survivors. "Social isolation is hard on older people," Dr. Scalmati says. "It can provoke memories of wartime, when survivors had to go into hiding or were separated from family."

Adds Ms. Hilfer: "As the pandemic intensified, our partner agencies sprang into action. Social workers were in touch with their clients, some almost daily, when in the past clients would be in touch with social workers only a few times per month. These efforts were not only appreciated, but also crucial to boost mental health. These conversations are an opportunity to adopt telehealth techniques that will have lasting utility after the pandemic has passed."

A MODEL FOR TREATING OTHERS

While caring for local Holocaust survivors is their primary goal, Drs. Kennedy and Scalmati also want to conduct training programs for Selfhelp's staffers and caregivers and to share findings with the geriatrics and psychiatry community.

"In a decade or two, there will be no more Holocaust survivors," Dr. Scalmati says. "But sadly, there is no shortage of people who need this specialized care. Having generous and devoted partners to support communities who need their help gives me hope for these people and for future generations."

Mrs. Doctoroff has a similar vision. "My hope is that this program will not only improve the lives of Holocaust survivors but also inspire others to reach out to underserved and marginalized populations—and inspire motivated donors to support these efforts through their philanthropy." E

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NEW BLOOD CANCER INSTITUTE TO LEAD THE SEARCH FOR CURES

Einstein's new research center will build on recent successes to create lifesaving treatments

BY TERESA CARR

In 2010, Amit Verma, M.B.B.S., and Ulrich Steidl, M.D., Ph.D., were spending hours in their Einstein labs studying cellular mechanisms linked to a group of blood cancers called myelodysplastic syndromes (MDS). This cancer of the bone marrow leaves people with too many defective blood cells and too few normal ones, leading to life-threatening anemia. "Treatments at the time could reduce levels of defective blood cells for a while, but we needed therapies that could attack the root cause of MDS," Dr. Verma says.

A few years earlier, these researchers had been among the first to show that MDS arises from abnormalities in hematopoietic stem cells (HSCs)—cells in the bone marrow that produce all of the body's blood cells. Dr. Steidl's lab went on to identify novel targets against these disease-causing malignant stem cells in both MDS and a related disease, acute myeloid leukemia.

Dr. Verma and his team were homing in on a signaling pathway in HSCs that inhibits the cells from developing into mature red blood cells. They discovered that this pathway, known as SMAD2/3, was overactive in MDS patients. "We theorized that blocking the SMAD2/3 pathway with a drug would allow blood cells to develop normally, preventing the debilitating and even deadly anemia that accompanies MDS," says Dr. Verma, now associate director for translational research at Albert Einstein Cancer Center (AECC), professor of medicine and of developmental & molecular biology at Einstein, and director of hematologic malignancies at Montefiore.

The researchers' hunch proved correct. Scientists across the globe soon began testing potential therapies, first in animals and then in human clinical trials. The payoff came in January 2020 when the *New England Journal of Medicine* published a study they participated in showing that the drug luspatercept significantly reduced the need for blood transfusions to treat anemia in MDS patients.

Three months later, the U.S. Food and Drug Administration approved the drug (brand name Reblozyl)—the first new therapy for MDS in 12 years. "It's gratifying when you can see how the basic science eventually leads to life-changing treatments," Dr. Verma says. "That's the driver for everything we do."

FINDING TREATMENTS FASTER

"Nearly all therapeutic breakthroughs have a similar story—arising from ideas born in labs and then worked on for 10 to 15 years before their use in the clinic,"

"We would like to bring innovative therapies to patients at a rapid pace ... actual fundamental advances."

— DR. ULRICH STEIDL

says Dr. Steidl, who is associate director for basic science at AECC, professor of cell biology and of medicine, and the Diane and Arthur B. Belfer Faculty Scholar in Cancer Research at Einstein, and associate chair for translational research in oncology at Montefiore. But it can be challenging, he says, to obtain research grants and government funding, "especially for ideas that are outside of the mainstream."

To speed the development of new therapies, Drs. Verma and Steidl are helping to launch the first-of-its-kind Blood Cancer Institute within AECC, of which they will be the co-directors. "We would like to bring innovative therapies to patients at a rapid pace," Dr. Steidl says. "And by that, I don't mean variations on tried-and-true treatments but actual fundamental advances."

The institute will kick-start the early stages of both basic and translational research, when outcomes are less certain, Dr. Verma says. "We will focus on areas where we can make a unique contribution to the field—basic bench research

AECC Director Edward Chu, M.D.

and also early-phase clinical trials with novel compounds, for instance," he says. "Then we can take the next step and bring the state-of-the-art science into the clinic."

Achieving that vision will require a $6 million-plus philanthropic investment. Marilyn and Stanley M. Katz, both longtime members of Einstein's Board of Trustees and staunch supporters of AECC, believe in the vision of these researchers and in the powerful role philanthropy plays in elevating influential cancer research. "This is about hitting the home run, finding the cure," Mr. Katz says. "But to get there, you need enough charitable gifts to get the preliminary work done, so you can land funding for larger-scale investigations."

COLLABORATION IS KEY

The AECC is ideally suited to take the lead on blood-cancer research, says Edward Chu, M.D., M.M.S., director of the AECC, professor of medicine and of molecular pharmacology, and the Carol and Roger Einiger Professor of Cancer Medicine at Einstein, and vice president for cancer medicine at Montefiore. "Our cancer center is at the forefront both in the lab and in the clinic," he says. "The

Below and pictured on the cover of *Motivations* (page 51): Mouse blood-forming stem cells. Colored dots are single RNA molecules corresponding to different cancer-relevant genes.

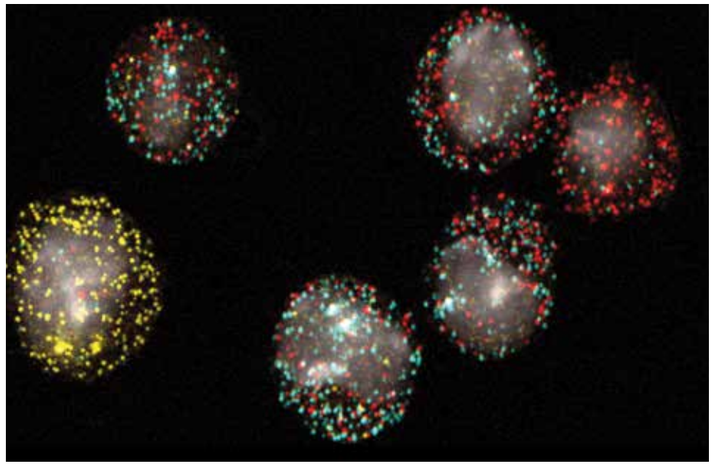
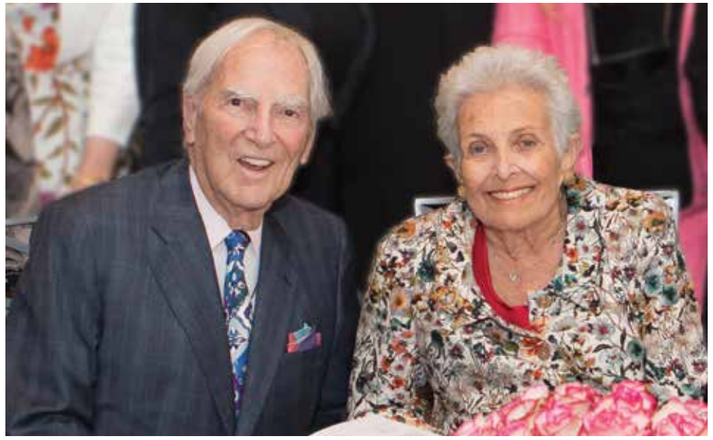


Image: Justin C. Wheat, M.D./Ph.D. candidate



Stanley M. and Marilyn Katz, longtime members of the Einstein Board of Trustees, at the 65th Spirit of Achievement Luncheon in 2019, when the Women's Division recognized Mrs. Katz as an honoree.

Aditi Shastri, M.D.

synergy between our research scientists and clinicians helps us translate lab findings into clinically applied solutions for changing the course of cancer medicine and to improve the lives of our cancer patients."

ON THE CUSP OF CURES

The discovery about 20 years ago that genetic mutations in HSCs could lead to cancer "changed everything when it comes to treating blood cancer," says Aditi Shastri, M.D., assistant professor of medicine and of developmental & molecular biology at Einstein, an oncologist at Montefiore, and a member of AECC. "We realized that we could design treatments that target those mutations and spare healthy cells."

One prime example is the targeted therapy imatinib (Gleevec) that has transformed chronic myeloid leukemia—once nearly always fatal—into a manageable disease for many patients. And CAR T-cell therapy, which involves reprogramming the immune system's T-cells to attack cancer cells, has given new hope to patients with certain forms of leukemia and lymphoma. But further progress is vital.

"Many types of blood cancer remain hard to treat," Dr. Shastri says. "And older people—the people most likely to develop blood cancers—are often too frail to undergo aggressive blood-cancer therapies, such as stem cell transplants."

Philanthropic giving will support the people and projects needed to get the state-of-the-art Blood Cancer Institute off the ground. Initial funds will endow a directorship, provide seed funding for research projects, and support the recruitment of junior faculty to conduct research and mentor the next generation of scientists.

For Marilyn Katz, who served as a trustee chairperson for the AECC from 1995 to 2020, the commitment to cancer research and the AECC's expansive work is personal. She talks of people in her life stricken by cancer—a close friend who recently died from leukemia; her daughter-in-law, who had breast cancer; and her sister, who died of brain cancer at age 52. "My hope for the new institute is that it makes enough progress for more people to live healthy, full lives," she says.

Dr. Verma says that he is more optimistic about realizing Mrs. Katz's vision now than at any point in his career. "This new institute will provide resources and access to technologies, but most important, it will foster collaborations," he says. "That's how science advances." E

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CLASS NOTES

1960s

Mervyn (Bud) Goldstein, M.D. '60, has had a varied career, from providing material assistance to Israel during the 1973 war to treating a man who was gored by an African cape buffalo. He has received numerous honors, including the Montefiore Staff and Alumni Award of Appreciation, the Montefiore President's Award, the Einstein Lifetime Service Award, and the Scarsdale-Edgemont Community Service Award.

Sidney Levitsky, M.D. '60, lives in Boston and is a cardiac surgeon and the senior vice chair of the department of surgery at Beth Israel Deaconess Medical Center and the David W. and David Cheever Professor of Surgery at Harvard Medical School. Dr. Levitsky has practiced for more than 50 years. He and his wife, Lynne, formerly chief of pediatric endocrinology at Massachusetts General Hospital, have three children and seven grandchildren. He still remembers Bill Metcalfe arranging a surgical elective at Johns Hopkins Hospital for him.

Melvin Scheinman, M.D. '60, and his wife, Margaret, live in San Francisco, where he heads the genetic arrhythmia unit at the University of California. He has received the American College of Cardiology Outstanding Scientist Award and the Distinguished Alumnus Award for his internationally recognized expertise in cardiac arrhythmias. Dr. Scheinman also performs an annual mission to Phnom Penh, Cambodia, to care for the indigent and teach at a hospital and medical school. He reports he is the "proud grandpa of three talented children and nine wonderful grandchildren."

Henry H. Wortis, M.D. '60, is still working in the department of immunology at Tufts. He is engaged in teaching in the graduate programs in immunology and genetics, and he maintains a small research footprint in genetic regulators of aging. He is involved in antiracist workshops, training in implicit bias and passive racism, and increasing diversity among faculty and trainees.

Morton Schatzman, M.D. '62, trained as a psychiatrist at Mount Sinai and Montefiore hospitals in New York and then moved to London. He lives in Highgate with his wife, Vivien. He has two sons: Daniel, who lives in Manhattan, and Gideon, who lives next door to him in London. Each son has three children.

Steve Weissman, M.D. '63, is, he reports, "in good health and happily married." He is still practicing psychiatry in Washington, D.C. He is writing a family history for his grandson, Sam. Sam's mother—Dr. Weissman's daughter Annie—represents the third generation of psychiatrists in their family. He was saddened to learn that his good friend and Einstein classmate **Arnold Goldschlager, M.D. '63**, passed away.

David White, M.D. '63, is living in Eugene, Oregon, with his wife of 56 years. They are "happy to be together and enjoying each other," he reports.

Stanford M. Goldman, M.D. '65, who received the Dominick P. Purpura Distinguished Alumnus Award in 1996, recently had his photo and biography published in the *Marquis Who's Who* magazine millennium second edition. He is a professor of radiology emeritus, a professor of urology at the University of Texas School of Medicine in Houston, a professor of radiology at MD Anderson Medical Center, and an adjunct professor of radiology and urology at Baylor College of Medicine.

Daniel Nussbaum II, M.D. '67, has practiced in Minnesota; Rochester, New York; and Massachusetts. He did a fellowship in developmental pediatrics at the University of Minnesota. Dr. Nussbaum and his wife, Alice, have returned to Rochester, and he's enjoying retirement. Alice is a Judaic needlework designer. His daughter, Yapha, directs a school library in Los Angeles; his son, Joe, is an Emmy-nominated producer/director in Hollywood.

David H. Abramson, M.D. '69, serves as the chief of ophthalmic oncology at Memorial Sloan Kettering Cancer Center and received a U.S. patent in November 2020 for a bionic ocular prosthesis. Existing prostheses had poor movement and no pupillary response; Dr. Abramson's new one incorporates microelectronics with a screen that mimics ocular motility. His 700th publication appeared this past year, and his work has been cited more than 13,000 times.

Robert Hoffman, M.D. '69, tested positive for COVID-19 last summer. He went to the emergency room at the University of California, Los Angeles, 13 days later; an X-ray revealed COVID-19 pneumonia. Over the next four days he was treated with oxygen until discharge. He received convalescent plasma, monoclonal antibodies, dexamethasone, and Lovinox. Dr. Hoffman was back at work the next week and gradually recovered completely. He has resumed daily exercise with interval training, hikes, and resistance training.

1970s

Douglas Drossman, M.D. '70, is a professor emeritus of medicine and psychiatry in the division of gastroenterology. He has been developing programs that teach communication skills

STAY IN TOUCH

Keep your classmates up to date by submitting your news to *Einstein* magazine. We look forward to including you. Email us at einsteinalumni@einsteinmed.org.

2021. She continues to write jokes and do stand-up comedy, and enjoys acting and writing plays. Dr. Mausner played a psychiatrist on *The Sopranos* (episode 48). Her play *Prescriptions* was published, and she appeared in a documentary called *Vegucated*, available on Amazon Prime.

Judith Lustig, M.D. '82, has retired from practicing neurology. She has been doing volunteer work, including teaching neurology to adults at Bergen Community College. Dr. Lustig has "been blessed with three boys," and now has three grandchildren. Her passion is cycling. She would love to hear from her classmates.

David Tal, M.D. '85, has continued his geriatrics work at St. Joseph's Health Centre in Toronto, Ontario, Canada, and is enjoying his grandchildren. He offers his warmest wishes to all.

Etta May Eskridge, M.D. '86, Ph.D. '95, has been a palliative-care physician, board-certified in internal medicine and palliative and hospice medicine, at Rochester General Hospital since 2013. She has been a board member for the Global AIDS Interfaith Alliance, which organizes trips to Malawi to train medical students and clinical officers in a resource-poor country. She says Einstein prepared her well for her work as we face a rapid increase in the number of elderly patients.

Daniel Hyman, M.D. '86, returned to the Philadelphia area and is serving as the chief safety and quality officer at the Children's Hospital of Philadelphia. After he spent 12 years working in Colorado and living apart from his wife, **Martha J. Sack, M.D. '86**, they are happy to be in one home. Martha continues her work as an attending cytopathologist at Abington Hospital in the Jefferson Health system.

Rafael Pelayo, M.D. '88, has been promoted to associate division chief for the sleep medicine division at Stanford University. He has published a new book, *How to Sleep*.

1990s

Barry Kraushaar, M.D. '90, is busy in Nanuet, New York, practicing orthopaedic, sports, and joint medicine. He serves on the National Board of Councilors at the American Academy of Orthopaedic Surgeons and the board of the New York State Society of Orthopaedic Surgeons. His twin boys are finishing college, focusing on engineering, and his eldest is applying to dental schools. Dr. Kraushaar and his wife, Helene, say they hope their classmates are well, and they would like to hear from their Einstein friends.

Lisa Moreno, M.D. '90, M.S., is a professor of emergency medicine at the Louisiana State University in New Orleans. The American Academy of Emergency Medicine elected Dr. Moreno to be its president; she is the first woman ever to hold that position.

David Rauch, M.D. '91, just published his second book, *Challenging Cases in Pediatric Hospital Medicine*, and has started work on the third edition of *Caring for the Hospitalized Child*. He is happy at Tufts Children's Hospital in Boston with his wife, **Mindy Stimell-Rauch, M.D. '90**.

Jonathan Lewin, M.D. '93, reports that he "is weathering COVID-19" and that in some ways he has gotten stronger. His private orthopaedic/pain/spinal surgery practice in Englewood, New Jersey, and New York, the Center for Musculoskeletal Disorders, has not closed during the pandemic, which is allowing for a smoother recovery phase. If anyone with those specialties is looking for a change of venue, drop Dr. Lewin a line at drjdlewin@gmail.com; his practice is expanding. He says he'd love to reconnect with fellow alumni.

Hugh Bases, M.D. '94, completed his residency in pediatrics and then did a fellowship in developmental-behavioral pediatrics. He is currently the program director of the fellowship at the NYU Grossman School of Medicine. He also has a small private practice. His wife, Randi Asher, Psy.D., has a busy clinical psychology practice on the Upper West Side.

Justin Greisberg, M.D. '95, is a professor of orthopaedic surgery at Columbia University. He is also the chief of foot and ankle orthopaedics at NewYork-Presbyterian and the chief of orthopaedic trauma at NewYork-Presbyterian Lawrence Hospital. He misses his time at Einstein and his great friends from the Class of 1995, and hopes to reconnect.

Kim Starer Landzberg, M.D. '95, and her husband, **Brian R. Landzberg, M.D. '95**, have been happily married since 1992. They have three children: Zachary (24), Renée (22), and Eddie (18), and an English shepherd named Dash. She has practiced in Riverdale, the Bronx, since completing her glaucoma fellowship in 2000. She enjoys forging relationships with whole families of patients; one spans four generations. She has found implanting trifocal intraocular lenses during cataract surgery tremendously rewarding.

Brian Blaufeux, M.D. '96, was on the panel of a NODE.Health webinar about digital health, telehealth, and primary care post-COVID-19. He was also interviewed by the *Westchester Senior Voice* about telehealth, and conducted a virtual live session to take questions from its readers. Read more at: nodehealth.org/tag/digital-health.

IN MEMORIAM

Chair Emeritus of Medicine, Chief of Cardiology

James Scheuer, M.D., distinguished professor emeritus of medicine (cardiology) and university chair emeritus of medicine at Einstein, died Feb. 17, 2021, at age 89, following a brief illness.

Since arriving in the Bronx in 1972 and even after retiring in 2011, Dr. Scheuer served Einstein and Montefiore in numerous roles, including vice chair, interim chair, and the Ted and Florence Baumritter Professor and Chair in Medicine; physician-in-chief; chief of cardiology; director of medical service and of the medical house staff program; professor of physiology; and principal investigator.

"Dr. Scheuer was one of the giants of cardiology and a consummate physician, serving as a role model to generations of physicians," says Yaron Tomer, M.D., chair of medicine at Einstein and Montefiore, and a professor of medicine and of microbiology & immunology and the Anita and Jack Saltz Chair in Diabetes Research at Einstein. "He left an incredible legacy."

Adds Gordon F. Tomaselli, M.D., Einstein's Marilyn and Stanley M. Katz Dean, "Although I didn't have the good fortune to train under him directly, Dr. Scheuer was renowned in American cardiology. His colleagues, trainees, and many other physicians would flock to his presentations at national meetings." Dr. Tomaselli is also a professor of medicine (cardiology) at Einstein and executive vice president and chief of academic affairs at Montefiore.

In addition to being a highly respected clinician and mentor, Dr. Scheuer was a noted scientist who studied basic aspects of heart muscle function. "He was continuously funded by the NIH [National Institutes of Health] for 40 years, which is unheard of in cardiology," says Mark Menegus, M.D., Einstein professor of medicine (cardiology) and director of the cardiac catheterization lab at Montefiore. "He ran his lab and trained lots of cardiac researchers, many of whom are leaders in the field today."

He and his wife established the Ruth and James Scheuer, MD, Endowment in Cardiology to support special training in research for future cardiologists at Montefiore; the division of cardiology on Montefiore's Moses Campus bears his name. The couple also created the James and Ruth Scheuer Fund at Einstein, which provides an annual award for a graduating M.D. or Ph.D. student whose disciplinary focus will be internal medicine.

A native New Yorker, he earned his bachelor's degree at the University of Rochester and his medical degree at Yale School of Medicine. He completed his medical internship at Bellevue Hospital in New York and residency at Mount Sinai.

Dr. Scheuer is survived by his wife, Ruth Lucas Scheuer; their children, Kim Scheuer, M.D. (Derek Olsen), Jeff Scheuer, and Greg Scheuer; his grandson James; his brother Robert; and many nieces and nephews. His brother Thomas predeceased him.

Philip Aisen, M.D., age 91, professor emeritus, physiology & biophysics and medicine at Einstein, April 10, 2020, New York City.

Peter Davies, Ph.D., age 72, clinical professor of pathology at Einstein, director of the Litwin-Zucker Center for the Study of Alzheimer's Disease and Memory Disorders, and a leader in the field of Alzheimer's disease research, Aug. 26, 2020, Greenwich, Connecticut.

Hiltrud Mueller, M.D., age 94, retired professor of medicine at Einstein, former associate chief of the division of cardiology at Montefiore, and a trailblazing physician-scientist, Dec. 23, 2020, New York City.

L. Juden Reed, M.D., age 86, associate professor of medicine (hematology) at Einstein and an oncologist at Montefiore, Dec. 11, 2020, Pelham, New York.

Bernard "Bern" Slosberg, M.D. '67, M.P.H., age 79, retired regional medical director for Aetna Health Insurance, volunteer physician and medical school instructor, Dec. 12, 2020, Silver Spring, Maryland.

Tyr O. Wilbanks, M.D., age 64, assistant professor of surgery and former medical student clerkship director at Einstein and a surgeon at Montefiore, Dec. 3, 2020, Old Greenwich, Connecticut.

Albert Einstein College of Medicine Archives

Ullmann and Einstein

Sixty years ago, on May 7, 1961, Albert Einstein College of Medicine welcomed a special guest: Hans Albert Einstein, Ph.D., a son of the school's namesake. Dr. Einstein, a professor of hydraulic engineering at the University of California, Berkeley, had come to the Bronx to represent his father (who had died six years earlier) at the groundbreaking for the Ullmann Research Center for Health Sciences. Dr. Einstein, center, joined Samuel D. Belkin, Ph.D., president of Yeshiva University, left, and Dean Marcus D. Kogel of Einstein to initiate construction of the 10-story, 12-sided biomedical research tower.

Siegfried Ullmann, a noted industrialist and philanthropist, and his wife, Irma, donated $2 million to help build the facility, which was intended to attract top-notch molecular biologists, cell biologists, and geneticists. The National Institutes of Health provided an additional $2 million toward construction of the $8.5 million building. Its circular design was meant to allow natural light to illuminate all laboratories and to encourage collaboration among scientists. E

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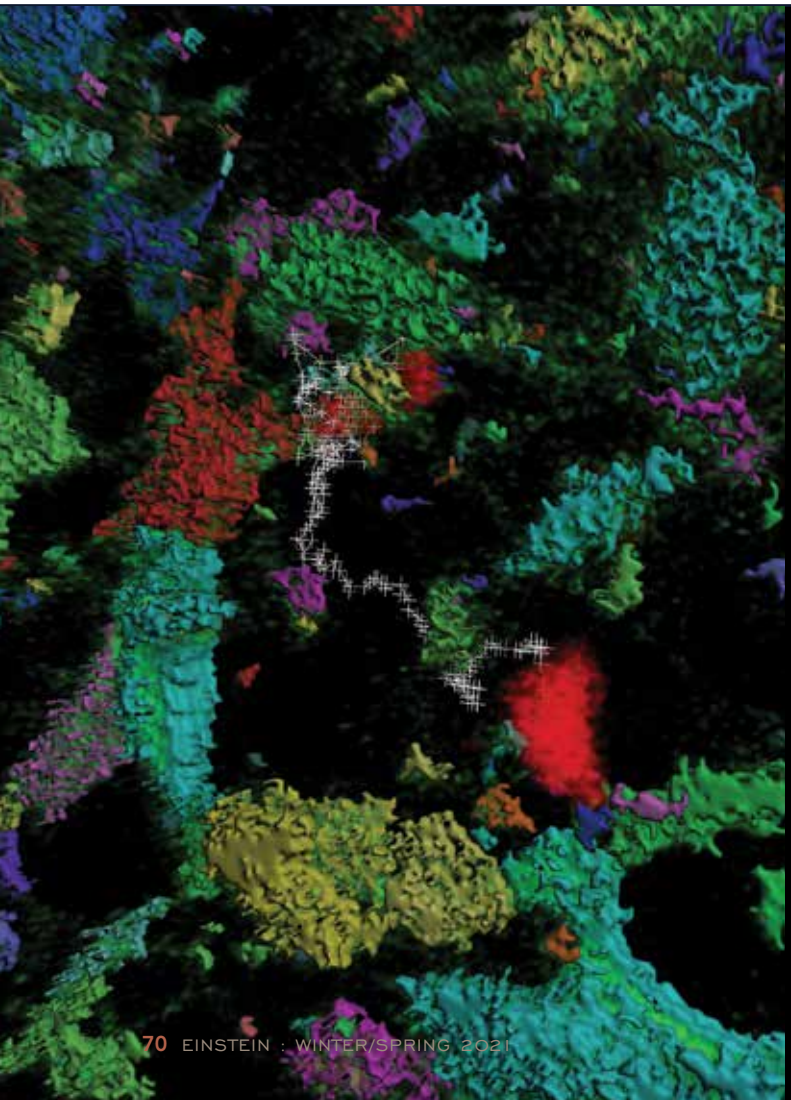

EINSTEIN IMAGE

Hematopoietic stem cells (HSCs) are self-renewing cells that reside in the bone marrow and generate all of the body's blood cells. Clinicians can stimulate HSCs to enter the bloodstream, where they can be harvested and used in bone marrow transplantation to treat cancers and other conditions. But scientists have long assumed that HSCs otherwise remain immobile within their bone marrow niches. In a study published last June in *Cell Stem Cell*, researchers led by David Fooksman, Ph.D., found that HSCs move constantly—probably to maintain their survival. The researchers used two-photon laser-scanning microscopy to observe HSCs in the bone marrow of living mice over several hours. This image shows the white tracks of an HSC (labeled bright red) as it wanders the bone marrow and interacts with differently colored stromal (niche) cells that nourish the HSC by expressing growth factors such as SCF-1. Dr. Fooksman is an associate professor of pathology and of microbiology & immunology.

Image credit: The Fooksman lab