weillcornellmedicine

SUMMER 2019

OUTCOME EQUALITY

Lisa Newman, MD, and Melissa Davis, PhD, aim to help more African American women survive breast cancer

Weill Cornell Medicine

Alumni Association Award of Distinction 2020

Dean Augustine M.K. Choi; 2019 Award of Distinction recipient Allan H. Ropper, MD '74; Alumni Association President Natasha Leibel, MD '98

Call for Nominations

Do you know an alumna or alumnus who demonstrates exceptional achievement as a physician, scientist, or educator, and who has brought honor and acclaim to Weill Cornell Medical College? Would you like to honor a former classmate who has made a difference in science and medicine?

You can help the Weill Cornell Medical College Alumni Association recognize alumni by nominating worthy candidates for the 2020 Award of Distinction.

All nomination packets must be received by Friday, November 1. Please include letters of recommendation and a CV for the nominee. To learn more about the Award of Distinction, past award winners, and the nomination process, visit the Alumni Association's website: weill.cornell.edu/alumni.

Alumni Association Award of Distinction Recipients

1949 – William S. McCann, MD 1915
1950 – David P. Barr, MD 1914
1951 – Connie M. Guion, MD 1917
1952 – Niles P. Larsen, MD 1916
1953 – William C. Menninger, MD '24
1954 – Samuel Z. Levine, MD 1920
1955 – Irving S. Wright, MD '26
1956 – Preston A. Wade, MD '25
1957 – Henry H. Kessler, MD 1919
1958 – Paul F. Russell, MD 1921
1959 – Ida S. Scudder, MD 1899
1960 – Dean F. Smiley, MD 1919
1961 – Irvine H. Page, MD '26
1962 – Paul Reznikoff, MD 1920
1963 – May G. Wilson, MD 1911
1964 – Milton Helpern, MD '26
1965 – S. Bernard Wortis, MD '27
1966 – Armand J. Quick, MD '28
1967 – Thomas P. Almy, MD '39
1968 – Philip Levine, MD 1923
1969 – Alexander D. Langmuir, MD '35
1970 – William D. Holden, MD '37
1971 – Harry Gold, MD 1922
1972 – Harriet L. Hardy, MD '32
1973 – Thomas H. Ham, MD '31
1974 – Charles G. Child II, MD '34
1975 – Gustave J. Dammin, MD '38
1976 – David E. Rogers, MD '48
1977 – Alfred E. Maumenee, Jr., MD '38
1978 – Charles A. LeMaistre, MD '47
1979 – Edwin D. Kilbourne, MD '44
1980 – W. Clarke Wescoe, MD '44
1981 – Walter F. Riker, Jr., MD '43
1982 – William A. Barnes, MD '37
1983 – Fred Plum, MD '47
1984 – Harry M. Rose, MD '32
1985 – Robert C. Hickey, MD '42
1986 – J. Robert Buchanan, MD '54
1987 – Robert J. Haggerty, MD '49
1988 – C. Everett Koop, MD '41
1989 – Joseph F. Artusio, MD '43
1990 – George A. Wolf, Jr., MD '41
1991 – Forrest C. Eggleston, MD '45
1992 – Anthony S. Fauci, MD '66
1993 – John H. Laragh, MD '48
1994 – Mary Ann Payne, MD '45
1995 – Roy C. Swan, MD '47
1996 – Carlton C. Hunt, Jr., MD '42
1997 – Gerald David Fischbach, MD '65
1998 – Heinz F. Eichenwald, MD '50
1999 – Merlin K. DuVal, Jr., MD '46
2000 – Thomas Killip III, MD '52
2001 – Albert Z. Kapikian, MD '56
2002 – Gerald L. Mandell, MD '62
2003 – Elizabeth Barrett-Connor, MD '60
2004 – Francis V. Chisari, MD '68
2005 – John Allen Clements, MD '47
2006 – George H. McCracken, Jr., MD '62
2007 – Jay N. Cohn, MD '56
2008 – Elizabeth G. Nabel, MD '81
2009 – John Ross, Jr., MD '55
2010 – William Schaffner, MD '62
2011 – Anne A. Gershon, MD '64
2012 – Michael D. Gershon, MD '63
2013 – R. Gordon Douglas, Jr., MD '59
2014 – Kathleen M. Foley, MD '69
2015 – Steven G. Gabbe, MD '69
2016 – Stephen L. Hoffman, MD '75
2017 – W. Michael Scheld, MD '73
2018 – Thomas H. Lee, MD '79
2019 – Allan H. Ropper, MD '74

The honoree is celebrated during Commencement and at the annual Award of Distinction Dinner in May.

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(646) 962-9560

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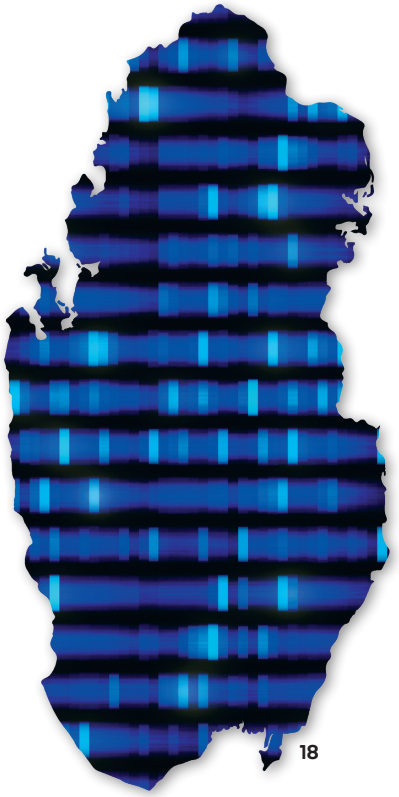
THE MAGAZINE OF
WEILL CORNELL MEDICINE

SUMMER 2019



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Case Notes

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ON THE COVER: LISA NEWMAN, MD (LEFT), AND MELISSA DAVIS, PHD. PHOTO BY JOHN ABBOTT

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PUBLISHER
Jenny Barnett

EDITOR
Beth Saulnier

CONTRIBUTING EDITORS
Alexandra Bond
Chris Furst
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Laura Britton

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Lisa Banlaki Frank

ACCOUNTING MANAGER
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EDITORIAL AND BUSINESS OFFICES
401 E. State St., Suite 301
Ithaca, NY 14850
(607) 272-8530; FAX (607) 272-8532

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Departments

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Augustine M.K. Choi, MD
Dean of Weill Cornell Medicine

Diversity: The Path to Excellence in Medicine

At Weill Cornell Medicine, diversity is a vital part of our mission. We are proud to be an institution that values students, trainees, faculty, and staff from a wide range of backgrounds—not only because we are committed to nurturing the best physicians and scientists, but because each patient's healthcare is improved when it includes practitioners with different perspectives, proficiencies, and life experiences. To advance scientific knowledge and patient care, we also need to do all we can to encourage diverse participants in research, and to reach patients who are typically underserved.

Deepening our understanding of why certain diseases affect populations differently will equalize outcomes for patients who suffer worse effects. Sometimes those patients are ethnic or racial minorities, and for complex reasons, scientists have not discovered why their disease courses run as they do—or how they might best be treated or cured. But some of the reasons may lie in their genetics. In this issue, we describe elegant work led by surgical oncologist Lisa Newman, MD, who has spent decades examining why African American women die of breast cancer more often than women from any other racial and ethnic group; among the clues are similarities between their trajectories and those of women in Western Africa.

The work we're doing around diversity is so tremendous, it is being recognized by prominent funders, especially the U.S. government.

Investigations like those of Dr. Newman and her colleague molecular geneticist Melissa Davis, PhD, will accelerate the development of precision medicine: by studying a broader array of individuals, physicians may ultimately be able to personalize care for all patients. To that end, we are tapping New York City's diverse population as a leader of All of Us, an NIH-sponsored program to establish a national research database by gathering DNA and other medical information from more than 1 million people nationwide, with a focus on those who have been underrepresented. Our Cornell Center for Health Equity works with local organizations and providers in New York City and central New York State to study differences in outcomes among demographic groups, which we expect will lead to novel interventions that narrow the gap in minority communities where conditions like heart disease can be more prevalent. And Harold Varmus, MD—a Nobel Prize winner and former director of the National Cancer Institute who's now the Lewis Thomas University Professor of Medicine at WCM—co-chairs the New York Genome Center's Polyethnic-1000, a project that aims to improve cancer treatment by studying ethnically diverse populations in the city.

The work we're doing around diversity is so tremendous, it is being recognized by prominent funders, especially the U.S. government. With a $2.7 million grant from the Health Resources and Services Administration, Susana Morales, MD, associate professor of clinical medicine, has established a Diversity Center of Excellence within the Center for Health Equity. Two additional grants from the National Institutes of Health—to Senior Associate Dean for Diversity and Inclusion Said Ibrahim, MD, and Weill Cornell Graduate School of Medical Sciences Deans Marcus Lambert, MS '18, PhD, and David Christini, PhD—will increase the number of trainees and doctoral students from backgrounds typically underrepresented in the STEM fields. Last year, we also earned a HEED Award from *INSIGHT into Diversity* magazine, which recognizes excellence in diversity in undergraduate, graduate, and health professional schools. Dr. Ibrahim's leadership on diversity will ensure that we will sustain this momentum to continue to improve representation in academic medicine.

Of course, it is vital that underserved communities have improved access to quality healthcare now. We are deepening partnerships with groups throughout New York City to emphasize the importance of screening and prevention, and to enable more people to receive the most cutting-edge, investigational therapies through clinical trials. Among other hands-on initiatives to address disparities is WCM's student-led community clinic that provides care for uninsured patients in New York City. Likewise, our Wellness Qlinic—which medical students launched earlier this year—offers free psychiatric services for members of the LGBTQ+ population, who often face a disproportionate burden of mental health issues.

These inequities and disparities underscore why it's so important for us to strengthen our culture of inclusion: so the next generation of physicians and researchers comprises many unique voices who will work together to solve complex health problems in innovative ways. As New York City—and the nation—become increasingly multicultural, diversity emerges as the winning formula for excellence in healthcare. Humanity is diverse, and with Weill Cornell Medicine's leadership, medicine is evolving to better serve it. ■

Support for Research
Drives Dynamic Growth

Bolstered by the generous support of donors, Weill Cornell Medicine has experienced dramatic growth in its research enterprise over the past five years – an achievement that advances the institution's goal of providing patients with the most advanced treatments and therapies.

U.S. News & World Report's 2019 top-10 ranking of Weill Cornell Medicine in its Best Medical Schools for Research underscores our continued excellence in research and educational ventures.

Since 2014, Weill Cornell Medicine's research funding from the National Institutes of Health (NIH) has surged more than 40 percent. This expansion in the research enterprise coincides with the opening of the Belfer Research Building, which serves as the hub for our translational research efforts and has led to the recruitment of more than 40 accomplished biomedical researchers to augment the thriving community of existing faculty.

> "All of our endeavors are guided by the essential principle to **improve the health and lives of our patients."**
>
> **Dean Augustine M.K. Choi, MD**

Biomedical investigators at Weill Cornell are targeting some of the most formidable health challenges of the 21st century, seeking to translate breakthrough discoveries into cutting-edge treatments. Increased collaboration between researchers and clinicians is helping accelerate the development of new diagnostics and therapies to benefit patients.

ROGER TULLY

Weill Cornell Medicine

Thanks to the generosity of donors, Weill Cornell Medicine has established numerous interdisciplinary centers, institutes and programs that have bolstered our research enterprise, including the following:

HRH Prince Alwaleed Bin Talal Bin Abdulaziz Al-Saud Institute for Computational Biomedicine

Ansary Stem Cell Institute

Helen and Robert Appel Alzheimer's Disease Research Institute

Cardiovascular Research Institute

Dalio Institute of Cardiovascular Imaging

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Caryl and Israel Englander Institute for Precision Medicine

Feil Family Brain & Mind Research Institute

Friedman Center for Nutrition and Inflammation

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Sean Parker Institute for the Voice

Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine

Jill Roberts Institute for Research in Inflammatory Bowel Disease

Starr-Greenberg Program in Arrythmia Biology

Tri-Institutional Therapeutics Discovery Institute (Tri-I TDI)

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From left: Dr. Manuel Hidalgo, Dr. Sara Czaja, Dr. Anthony Hollenberg and Dr. Brad Jones of the Weill Department of Medicine, the institution's largest clinical and research-focused department.

Commencement Celebrates the Class of 2019

MAJOR MILESTONE: Cornell President Martha E. Pollack (right) greets Ngozi Monu, MD '19, and her children as they walk across the Carnegie Hall stage at Commencement. For more photos of the festivities, see Notebook starting on page 39.

The annual Commencement ceremony in Carnegie Hall marked the accomplishments of 371 graduates: new MDs (from both New York and Doha, Qatar), PhDs, masters of science, and physician assistants. "In thinking about the healthcare challenges we face, it's clear that there are no easy solutions," Dean **Augustine M.K. Choi, MD**, said in his address. "Yet I feel strongly that as graduates of Weill Cornell Medicine, you have the ability to make an impact on this complex world we live in. It's in your DNA."

In her remarks, Cornell President **Martha E. Pollack** noted that the drive to give back to humanity is a distinguishing characteristic of Cornellians, tracing its roots to the University's founding. "As graduates of Weill Cornell Medicine," she said, "the good that you will do will affect others in ways that are not abstract, but concrete; not theoretical, but exquisitely and profoundly human, as you work to enhance human health and wellbeing."

Earlier in May, the Qatar branch celebrated its own Commencement in Doha—graduating forty-nine new MDs, twelve of whom are Qatari nationals. "Becoming a physician is no easy task," said **Javaid Sheikh, MD**, dean of WCM-Q, "and the Class of 2019 has demonstrated great commitment to their studies, intellectual curiosity, and compassion for their patients."

Among the highlights at the New York celebration was the presentation of annual awards for distinguished alumni—giving this year's graduates a glimpse at the accomplishments to which they might aspire. The Weill Cornell Medicine Alumni Association Award of Distinction went to **Allan Ropper, MD '74**, a professor of neurology at Harvard Medical School and the Raymond D. Adams Master Clinician and executive vice chairman of the Department of Neurology at Boston's Brigham and Women's Hospital. A 1970 undergraduate alumnus of Cornell, where he studied engineering and math, Ropper helped open Massachusetts General Hospital's Neurological-Neurosurgical Intensive Care Unit—the first neurologic ICU in an academic medical center—in 1978. He's the lead author of *Adams and Victor's Principles of Neurology* and is a deputy editor at the *New England Journal of Medicine*. He has also penned two neurology books aimed at a general audience: *Reaching Down the Rabbit Hole* and the recently released *How the Brain Lost Its Mind*.

This year's Weill Cornell Graduate School Alumni Award of Distinction was given to **Katharine Hsu, MD '94, PhD '93**, professor of medicine and attending physician at Memorial Sloan Kettering Cancer Center. Through her work as a physician-scientist, Hsu—whose WCM doctorate is in cell biology—has defined the roles of natural killer (NK) cells and the immune receptors on their surface, which regulate how NK cells recognize and kill cancer and virally infected cells. She and her team have written numerous high-impact papers in such publications as the *New England Journal of Medicine* and the *Journal of Clinical Oncology*. As a clinician, she treats patients with bone marrow disorders, leukemias, and lymphomas.

PHOTO: AMELIA PANICO

Nephrologist Leads Korean American Group


Mary Choi, MD

Mary Choi, MD, a professor of medicine at WCM and a nephrologist at New York-Presbyterian/Weill Cornell, has been elected president of the Korean American Medical Association (KAMA). The organization provides guidance and networking opportunities to Korean American medical students, trainees, and physicians, among other activities. Choi's family left Korea when she was eight, ultimately settling in rural Kansas. Her aims as KAMA president include advancing the organization's mission to mentor and support female Korean American students, trainees, and early career physicians. "I think there are some cultural differences, and women in medicine still greatly lag in leadership positions in Korea, and in the United States as well," Choi observes. "I'd like to raise awareness of this issue during my term, and I'm passionate about advancing the careers of all women in medicine through mentorship and mutual support."

PHYSICIAN-SCIENTISTS: Four distinguished members of the WCM faculty have been selected for Crain's Notable Women in Health Care in New York City, which honors individuals who have outstanding professional and philanthropic achievements, as well as proven commitments to mentorship and the promotion of diversity and inclusion in the workplace. They are (from left) Laura Riley, MD, chair of ob/gyn at WCM and obstetrician and gynecologist-in-chief at NewYork-Presbyterian/Weill Cornell; Barbara Hempstead, MD, PhD, dean of the Weill Cornell Graduate School of Medical Sciences; Silvia Formenti, MD, the Sandra and Edward Meyer Professor of Cancer Research and chair of radiation oncology at WCM and radiation oncologist-in-chief at NewYork-Presbyterian/Weill Cornell; and Lisa Newman, MD, chief of the Section of Breast Surgery at NewYork-Presbyterian/Weill Cornell and WCM.

TIP OF THE CAP...

Lawrence Casalino, MD, PhD, chief of the Division of Health Policy and Economics in the Department of Healthcare Policy and Research and the Livingston Farrand Professor of Public Health, appointed to the Medicare Payment Advisory Commission by the U.S. Government Accountability Office.

Joseph Fins, MD '86, the E. William Davis Jr., MD, Professor of Medical Ethics and chief of the division and an attending physician at NewYork-Presbyterian/Weill Cornell, invited to the Pontifical Academy of Sciences' workshop on personalized medicine in Vatican City.

Matthew Greenblatt, MD, PhD, assistant professor of pathology and laboratory medicine at WCM and a pathologist at NewYork-Presbyterian/Weill Cornell, awarded the Pershing Square Sohn Prize for Young Investigators in Cancer Research.

Said Ibrahim, MD, chief of the Division of Healthcare Delivery Science and Innovation, senior associate dean for diversity and inclusion, and professor of healthcare policy and research, named a member of the National Arthritis and Musculoskeletal and Skin Disease Advisory Council of the NIH.

Maria Jasin, PhD, a professor in the cell and developmental biology program at the Weill Cornell Graduate School of Medical Sciences, awarded a Shaw Prize in Life Science and Medicine.

Matthew Laghezza, MBA '19, MS '19, chief physician assistant in the Department of Emergency Medicine at WCM and the Lisa Perry Emergency Center at NewYork-Presbyterian/Weill Cornell, named Physician Assistant of the Year by the Society of Emergency Medicine Physician Assistants.

Gina Lee, PhD, a former postdoc in the Sandra and Edward Meyer Cancer Center who's now an instructor in pharmacology at WCM, winner of a Tri-Institutional Breakout Award for Junior Investigators.

John Leonard, MD, associate dean of clinical research and the Richard T. Silver Distinguished Professor of Hematology and Medical Oncology at WCM and an oncologist at NewYork-Presbyterian/Weill Cornell, winner of the Lymphoma Research Foundation Distinguished Service Award.

B. Robert Meyer, MD, professor of clinical medicine at WCM and an internist at NewYork-Presbyterian/Weill Cornell, winner of WCM's Siegel Family Faculty Award.

Robert Peck, MD, assistant professor of medicine and of pediatrics, winner of the American Medical Association Foundation's Dr. Nathan Davis International Award. Peck is based at Weill Bugando School of Medicine in Tanzania.

Anthony Rosen, MD '10, assistant professor of emergency medicine at WCM and an attending emergency physician at NewYork-Presbyterian/Weill Cornell, winner of a Young Investigator Award from the Society of Academic Emergency Medicine.

Jonathan Shoag, MD, a urologic oncology fellow and instructor of urology who studies the molecular underpinnings of prostate cancer, winner of a Physician-Scientist Training Award from the Damon Runyon Cancer Research Foundation.

PHOTOS: CHOI, TORI MUMTAZ; CRAIN'S, ROGER TULLY

Brooklyn Methodist Names Urology Chief

Alfred Winkler, MD

Alfred Winkler, MD, has become chief of urology at NewYork-Presbyterian Brooklyn Methodist Hospital, a 591-bed teaching hospital in Park Slope. Winkler, also an assistant professor of clinical urology at WCM, was previously chief of urology at NewYork-Presbyterian Lower Manhattan Hospital. An undergrad alumnus of Princeton, he holds an MD from the Renaissance School of Medicine at Stony Brook University and an MBA from the Stern School of Business at NYU. He completed his internship, general surgery residency, and urology residency at Albert Einstein College of Medicine and Montefiore Medical Center, where he was chief resident. Winkler's areas of focus include men's health, kidney stones, and bladder dysfunction. With the aim of spreading awareness about urologic diseases, he has organized educational and screening programs on prostate cancer and bladder health and conducted outreach events at places of worship and community centers—efforts he plans to continue in Brooklyn. "Today, patients have more access to information than ever before, but they often only hear about extremes that create fear and may delay them from seeking treatment," he says. "That's why it is so important to spend time understanding patient concerns inside and outside the office."

MBA/MS Program Graduates First Class

Last spring, a joint program by the Weill Cornell Graduate School of Medical Sciences and the Ithaca campus's Samuel Curtis Johnson Graduate School of Management marked the graduation of its first class. Thirty-nine people earned the combined degree, an Executive MBA/MS in Healthcare Leadership, after two years of study. The program is co-chaired by **Rainu Kaushal, MD**, chair of the Department of Healthcare Policy and Research at WCM, and **Mark Nelson, PhD**, dean of the Johnson School. "When we launched this program two years ago, we set out with a unique mission," Kaushal said at a June dinner in the graduates' honor. "We wanted to train the most innovative future leaders of healthcare."

GLOBAL HEALTH: Tanzania has the world's lowest ratio of physicians to patients, one per 50,000—and in mental health the lack is particularly marked, with just one psychiatrist for every two million people. That reality inspired Abigail Benudis, MD (center left), a second-year psychiatry resident at NewYork-Presbyterian/Weill Cornell, to join an educational exchange that sends some three dozen WCM physicians to Weill Bugando School of Medicine each year. Given Tanzania's dearth of healthcare resources, fields like general medicine have historically been prioritized; Benudis, who spent a month caring for patients and teaching med students, was the first psychiatry resident to participate in nearly a decade.

Grant Aids PhD Diversity

The Weill Cornell Graduate School of Medical Sciences has won a five-year, $2.4 million grant aimed at increasing the number of doctoral students from underrepresented backgrounds—including African Americans, Hispanics, Native Americans, and Pacific Islanders. The award, from the NIH's National Institute of General Medical Sciences, will fund the Weill Cornell Initiative to Maximize Student Development. Each year, the program—intended to increase diversity in the biomedical workforce—will support four incoming students from minority backgrounds for the first two years of training, with additional funds from the Graduate School partly supporting them for their third and fourth years. The program will also offer mentorship opportunities, an eight-week summer research rotation at WCM before their first semester, and the chance to attend a national medical meeting during their second year.

Mental Health Startup Has Top Business Plan

A company co-founded by two faculty members has won the Biomedical Business Plan Challenge, sponsored by WCM's BioVenture eLab. **Jyotishman Pathak, PhD**, the Frances and John L. Loeb Professor of Medical Informatics and chief of the division, and **Alison Hermann, MD**, assistant professor of clinical psychiatry, founded a firm called Iris. It aims to improve treatment of women who suffer from mood and anxiety disorders related to pregnancy and childbirth by using data-driven methods to identify those at high risk. Iris won the $75,000 first prize in the annual challenge, held at the end of the BioVenture eLab's nine-week mentoring program designed to help WCM clinicians and researchers better commercialize their ideas. Seven companies competed this year, presenting their plans to a panel of judges who are investors specializing in early-stage firms. The $25,000 second prize went to Pelex, founded by **Jeremy Wiygul, MD**, an assistant professor of clinical urology at WCM and director of pediatric urology at NewYork-Presbyterian/Queens; it has developed a noninvasive medical device to treat disorders of the pelvic floor.

PHOTOS: WINKLER, PATRICIA KUHARIC; BUGANDO, PROVIDED

FROM THE BENCH

New Form of RNA Will Aid Research

SAMIE JAFFREY, MD, PHD

A technique developed by WCM investigators that creates an unusually stable form of RNA may illuminate many cellular processes and enable new kinds of gene therapies. The work concerns short strands of RNA, called aptamers, that can be useful tools for scientists because they can bind to proteins and block or control their activity. But scientists haven't had much success using them in human or other mammalian cells, in part because they break apart too quickly. But as **Samie Jaffrey, MD, PhD**, the Greenberg-Starr Professor of Pharmacology, and colleagues describe in *Nature Biotechnology*, investigators have overcome this problem by developing a system that makes circular RNAs, whose form prevents them from being broken by enzymes that latch on to the ends of linear RNA strands. Says Jaffrey: "It's a dramatic improvement."

Genetic Heart Defect Explored

Noonan syndrome (NS) is a genetic disorder whose characteristics include unusual facial features, short stature, and a variety of heart defects. Researchers from WCM, Masonic Medical Research Institute, and Beth Israel Deaconess Medical Center have discovered that two molecular signaling pathways underlie an NS defect that is often lethal in infancy or childhood: hypertrophic cardiomyopathy, a severe thickening of the heart muscle. In the study, the investigators reproduced the hallmark features of this defect in the lab using skin cells from an NS patient. They determined that aberrations in two pathways together cause the cells to become enlarged and exhibit other structural defects, a discovery that could point the way toward targeted treatments. The work was published in *Circulation*, with **Fabrice Jaffré, PhD**, instructor of cell and developmental biology in surgery at WCM, as first author.

Drug Shows Promise in Urinary Cancers

BISHOY FALTAS, MD

A newly available drug may improve the effectiveness of immunotherapy in hard-to-treat cancers of the upper urinary tract, reports a study in *Nature Communications*. Exploring the biological characteristics of a type of cancer called upper tract urothelial carcinoma, researchers found that its tumors have a lower number of cancer-killing immune cells called T cells. That could make the tumors particularly susceptible to erdafitinib, a drug that the FDA approved in April, since it inhibits a gene that's hyperactive in cancers with low T-cell signatures. The paper's senior author was **Bishoy Faltas, MD**, the Gellert Family–John P. Leonard, MD, Research Scholar, an assistant professor of medicine and of cell and developmental biology, a member of the Sandra and Edward Meyer Cancer Center, and director of bladder cancer research at the Caryl and Israel Englander Institute for Precision Medicine at WCM, and an oncologist at NewYork-Presbyterian/Weill Cornell.

Can Selenium Prevent Stroke Damage?

The chemical element selenium, an essential nutrient for humans and other animals, protects the brain after a stroke and may be a basis for future therapies, finds a study by scientists at WCM and the affiliated Burke Neurological Institute. The team found that selenium drives a molecular response in brain cells that protects them from a cell-killing process, called ferroptosis, arising in the hours after stroke; in mouse models, a selenium-based therapy prevented brain damage and motor and sensory impairment. "The next step is to see how our results replicate in other laboratories," says senior author **Rajiv Ratan, MD, PhD**, Burke's executive director and a professor of neuroscience in the Feil Family Brain and Mind Research Institute at WCM, "and if that goes well, then we'll want to move toward testing this in humans." The investigators published their work in *Cell*.

Cardiac MRI Aids in Diagnosis

The use of cardiac MRI may improve treatment for patients who experience a type of heart attack caused by a severely narrowed artery, a condition known as an NSTEMI. As a study of 114 patients published in *Circulation* notes, MRI is typically considered only if the results of coronary angiography are unclear. "We sought to learn whether an MRI performed first could improve clinicians' ability to identify the affected artery," says lead author **John Heitner, MD**, director of non-invasive imaging and co-director of cardiovascular research at NewYork-Presbyterian Brooklyn Methodist Hospital and associate professor of clinical medicine at WCM. "Many patients with NSTEMI have diseases in several blood vessels or have no significant blockages at all that make it difficult to identify the correct artery that caused the heart attack. We suspected the MRI's ability to directly visualize the heart muscle that was affected could improve accuracy, and our research suggests that to be the case."

Powerful Tool for Gene Mutation Studies

DAN LANDAU, MD, PHD

A new technology devised by scientists at WCM and the New York Genome Center (NYGC) enables the measurement of gene mutations and their effects on gene activity within individual cancer cells biopsied from patients. The advance, known as genotyping of transcriptomes (GoT), allows researchers to study, in unprecedented detail, the complex dynamics of cancerous cell populations during the course of disease and in response to therapies. "This tool allows us to get multiple dimensions of information from single cells, for tens of thousands of cells at a time—and that in turn should allow us to address some central questions about how cancers develop," says corresponding author **Dan Landau, MD, PhD**, an assistant professor of medicine and a member of the Sandra and Edward Meyer Cancer Center at WCM, a core member of the NYGC, and an oncologist at NewYork-Presbyterian/Weill Cornell. As reported in *Nature*, the scientists used GoT to study blood cancers called myeloproliferative neoplasms; they're now expanding to other cancer types.

Training Clinicians to Curb Obesity

With obesity affecting nearly 38 percent of adults and 17 percent of children and adolescents in the U.S., an alliance of professional medical societies has developed the first competencies for training medical students, residents, and fellows on how to prevent, assess, and treat it. The new standards were published in *Obesity* and highlighted as an Editor's Choice article. "There is an obesity crisis today, and we need more and better training for specialists in obesity medicine as well as physicians, nurse practitioners, and physician assistants in general," says **Leon Igel, MD**, an assistant professor of clinical medicine and program director of the obesity medicine fellowship at WCM. Igel helped draft the standards, leading a group that focused on the medical knowledge and skills needed to address obesity.

Gene Stymies Cancer Treatment

LEANDRO CERCHIETTI, MD

In *Cancer Discovery*, WCM researchers report that a gene that originally evolved to help vertebrates' early ancestors respond to stress is co-opted by many cancers to help them resist treatment. The gene, BCL6, helps cancer cells overcome the DNA damage caused by chemotherapy, radiation, or other therapies. The study showed that blocking that defense in the lab makes cancers more vulnerable. "Understanding this mechanism is very important because you can administer drugs to inhibit BCL6," says senior author **Leandro Cerchietti, MD**, an assistant professor of medicine and member of the Sandra and Edward Meyer Cancer Center at WCM. The research team included **Ari Melnick, MD**, the Gebroe Family Professor of Hematology/Oncology and a member of the Meyer Cancer Center, as co-senior author.

PHOTOS: JAFFREY AND CERCHIETTI, JOHN ABBOTT; FALTAS, TRAVIS CURRY; LANDAU, RENE PEREZ

PHOTOS: JOHN SAMPLES

Kid Friendly

Each year, through a program called Cornell Stars, WCM-Q faculty and staff bring their own children to the Clinical Skills and Simulation Lab to help train third-year medical students in pediatric physical exam techniques. "We are trying to give our students the chance to experience what it is genuinely like to engage a child and perform a basic physical examination of a child, but also to pass on hints and tips that may help with that examination," says the program's organizer, Amal Khidir, MD, associate professor of pediatrics. "For example, we show the students how to keep the children calm, maybe let the children listen to their own hearts through the stethoscope, and generally build up a rapport with them. We want them to learn how to negotiate, communicate, and be creative in engaging the children and their caregiver in a relaxed environment." Held during the clinical orientation week in June, the program gives future physicians some hands-on experience in interacting with and examining infants, toddlers, and children up to age seven. "The kids were so cute," says medical student Rozaleen Aleyadeh '21. "Obviously this won't be exactly how it is in the hospital, but it was very good practice."

MAN ON A MISSION: Scott Kelly during his record-setting tenure on the International Space Station. Opposite page: The cover of *Science* featuring the Twins Study.

Heavenly Bodies

After extensive data gathering and analysis—plus a worldwide media frenzy—NASA's famed Twins Study has begun to yield results

It has been called the most comprehensive analysis of individual human beings ever conducted in scientific history. In March 2015, astronaut Scott Kelly rode a Soyuz spacecraft to the International Space Station and proceeded to spend 340 days in orbit as part of an in-depth study of the long-term effects of space travel on the human body. As rare and valuable as that effort was—representing the longest-ever space mission for a NASA astronaut—it was all the more remarkable thanks to a tantalizing offer from Kelly's identical twin brother: Mark Kelly, himself a retired astronaut. Since Mark was staying on terra firma, he volunteered to serve as an experimental control, allowing scientists to compare two genetically identical men—one on Earth, the other in zero gravity some 220 miles above it, traveling at almost five miles per second.

During Scott's time on the space station (as well as six months before and after his mission), the brothers underwent physical and cognitive testing and contributed numerous blood, urine, saliva, and fecal samples for analysis. Dubbed the NASA Twins Study, the effort comprised ten interconnected research projects—on such topics as cognition, cardiovascular health, genomic changes, immune response, and the composition of gut, skin, and oral bacteria—funded by a total of $1.5 million in agency grants and involving dozens of investigators around the country and abroad.

One of those projects, which focused on how Scott's environment affected how his genes were expressed and regulated, was led by Weill Cornell Medicine's Chris Mason, PhD—and along with the nine others, it would make headlines around the world. In April, the Twins Study landed on the cover of the journal *Science*, which featured a twenty-page article summing up the results—the first publication of what's expected to be many, as researchers continue to parse a mother lode of data. "Overall, the Twins Study is a tour de force about how the body's adaptability extends to outer space," says Mason, the WorldQuant Foundation Research Scholar in physiology and biophysics and an associate professor of neuroscience, of physiology and biophysics, and of computational genomics in computational biomedicine. "The vast majority of changes we saw returned to normal—but about 8 or 9 percent remained. So it also shows that the body was still to some degree adapting to terrestrial life, even six months after Scott Kelly returned to Earth."

Among the Mason Lab's findings were that thousands of genes became active in Scott while remaining dormant in Mark—an effect that became more marked the longer Scott stayed in space. Those genes included ones that play a role in repairing damaged DNA—which may reflect the fact that while in space, Scott was exposed to nearly fifty times as much radiation as his brother was on Earth. Also active were genes related to inflammation, which could be due to the inherent stresses of space travel on the human body; these include the effects of being in zero gravity, such as fluid shifts and bone loss. For Francine Garrett-Bakelman, MD, PhD, who was the first author on the *Science* paper, the findings made sense. "I'm a physician-scientist, and as a physician, I thought, 'Yes, an astronaut is under significant stress,' " says Garrett-Bakelman, who completed her research and medical postgraduate training at WCM (where she was an instructor and an assistant attending physician at NewYork-Presbyterian/Weill Cornell while working in Mason's lab and that of Ari Melnick, MD, the Gebroe Family Professor of Hematology/Oncology) and is now an assistant professor of medicine and of biochemistry and molecular genetics at the University of Virginia School of Medicine, as well as an adjunct assistant professor of medicine at WCM. "He gets launched into space, spends a year in a foreign environment, then comes down to Earth subjected to a tremendous amount of g-forces. It tells us that the human body is resilient and responding normally to a stressful situation."

'Overall,' says geneticist Chris Mason, PhD, 'the Twins Study is a tour de force about how the body's adaptability extends to outer space.'

As Mason notes, a particularly striking finding was the extent to which Scott's immune system was on high alert once he went to space: every type of immune cell the researchers measured was active at levels that are practically unheard of. And in fact, Mason says, the response was even more dramatic when Scott came home. "In his memoir, he says that when he landed back on Earth he didn't feel well—and we could see why very clearly, in his blood work and gene expression data," says Mason, who is also a cofounder, equity stakeholder, and consultant for Onegevity Health, a company that provides a comprehensive molecular portrait and customized ›

PHOTO: NASA / JOHNSON

MIRROR IMAGES: Twins Mark (left) and Scott Kelly. Opposite page: Scott on a spacewalk—his third—in December 2015.

recommendations for an individual's health based on integrated analysis of longitudinal blood, genetics, and microbiome profiles. "There were all these markers for inflammation and for immune cells kicking into high gear. His body was basically having this moment of, 'Wow, I'm back in gravity'—these markers in the bloodstream were sometimes 4,000 percent higher than normal. So we could see that while going to space was hard on the body, returning to gravity was, in some ways, even harder."

One of the Twins Study's most surprising discoveries related to telomeres, sections of DNA located at the ends of chromosomes. Normally, as people get older their telomeres get shorter—and researchers had expected to see that happen in space, possibly even faster due to stress and radiation exposure. But in fact—as an investigator at Colorado State University discovered and the Mason Lab confirmed with new DNA sequencing and analysis methods—Scott's telomeres got longer, though they reverted to normal after he came home. Why? Researchers don't yet know. "We need to do a lot more science on this," says Cem Meydan, PhD, a research associate in the Mason Lab and a co-first author on the *Science* paper. "We need to find out why this is happening, and whether we can prevent it or study it for other health-related purposes, such as to fight cancer or aging."

Mason and his colleagues emphasize that when it comes to understanding how the human body reacts to being in space, the Twins Study had an obvious and inherent limitation: it had only one subject who actually went aloft. Furthermore, says Garrett-Bakelman, "this was a single study of one white male; what happens in women, or in people from other racial or cultural backgrounds, we have no idea. Trying to infer anything at all is very difficult without having additional subjects' data to look at." And of course, given that the Kelly brothers were NASA's first (and so far, only) identical twin astronauts, in many ways the study was a one-of-a-kind

PHOTO: ROBERT MARKOWITZ / NASA / JOHNSON SPACE CENTER

opportunity. "As a geneticist, I wish every person was a twin or a triplet so we could study them," Mason says with a laugh. "It's unclear if or when this will happen again. It's going to be hard to match this study anytime soon." Still, when it comes to figuring out whether humans could survive a mission to Mars or beyond, he and his colleagues call the study's findings highly encouraging. "Obviously it's a sample size of one, so it's hard to make generalized statements—but if we saw similar results in multiple people, I think it bodes well for long-term space travel," Meydan says. "Most of the changes we saw can potentially be targeted; in the next five or ten years, we could develop drugs, interventions, or other technology such as shielding for radiation or clothing for reversing fluid shifts in the body."

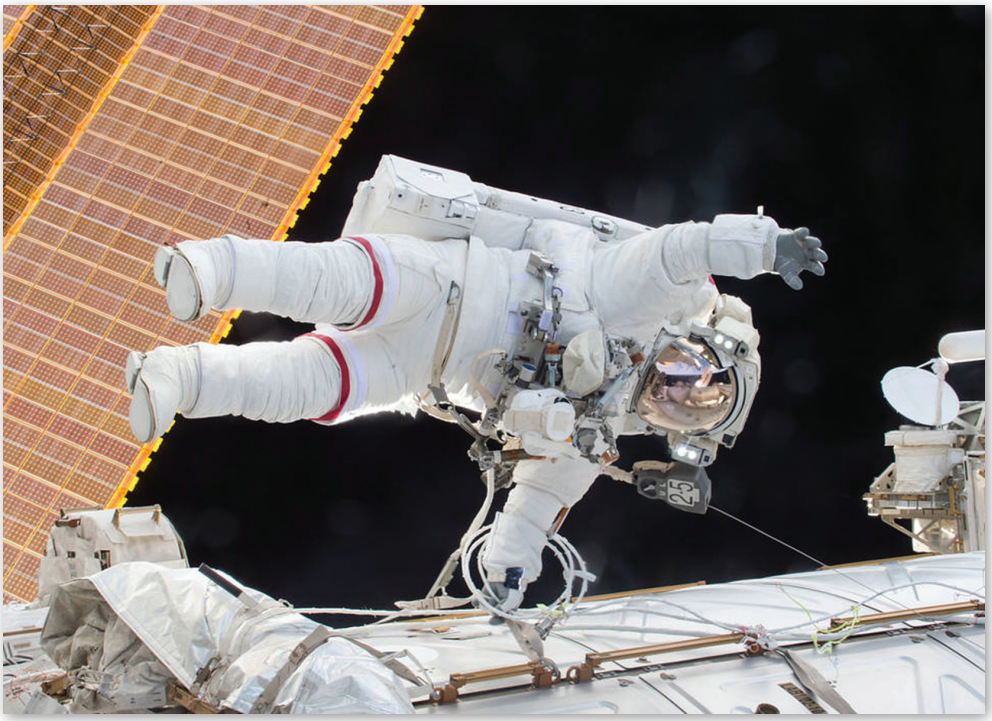


PHOTO: NASA

Mason also points out that the Twins Study could have benefits beyond the findings themselves; some of the procedures and analytic techniques its researchers developed could be a boon to terrestrial medicine. "It forced us to be nimble with limited numbers of cells and to sequence really quickly," he says, noting that their methods could inform rapid diagnosis of infectious pathogens or genetic analysis of a cancer patient's tumor. Working with some of the same collaborators as in the Twins Study, Mason's team also helped pioneer the first-ever DNA sequencing experiments on the International Space Station. Plus, Garrett-Bakelman says, the study stands as a prime example of how broad scientific questions can be answered through large-scale collaboration. "If you think about it, there were over eighty authors on the *Science* paper—from multiple institutions, locations, and countries—in addition to all the support staff at NASA that helped us do this," she says. "It was truly a challenging project to complete, and it wouldn't have been possible without that entire team. That's how these projects should be done: you bring in expertise from many different areas, think outside the box, and piece things together that you would have never thought about unless you were with all those people in the same room."

With the overarching *Science* paper out, the Mason Lab has another half dozen publications in progress—continuing to explore what research associate and co-author Daniela Bezdan calls "the most comprehensive and integrated molecular view to date of how a human responds to spaceflight." For Bezdan and many of her colleagues, just working on a space-related project was a wish come true. The first time she got an e-mail from NASA, she was so excited that she took a screenshot of the header; now, every tenth message in her in-box is from the agency. "We can contribute to making space exploration possible, which could be important for the survival of the human species; it's something bigger than ourselves," Bezdan says. "When I think of space travel, I think of three compartments: we are now describing what happens in space; the next step is to understand it—and the third step is to use it for our advantage."

Mason and his colleagues emphasize that when it comes to understanding how the human body reacts to being in space, the Twins Study had an obvious and inherent limitation: it had only one subject who actually went aloft.

In Scott Kelly's 2017 memoir—entitled *Endurance: A Year in Space, a Lifetime of Discovery*—he describes his record-setting tenure on the space station, the longest-duration mission for a NASA astronaut. Toward the end of the book, he contemplates his contribution to the Twins Study, noting that he expects to continue to be a test subject for the rest of his life. "Science is a slow-moving process," he writes, "and it may be years before any great understanding or breakthrough is reached from the data. Sometimes the questions science asks are answered by other questions. This doesn't particularly bother me—I will leave the science up to the scientists. For me, it's worth it to have contributed to advancing human knowledge, even if it's only a step on a much longer journey." ■

— Beth Saulnier

Coming to Terms

Lupus can cause severe pregnancy complications—but a recent study offers hope for better outcomes

When Betty Delgado got pregnant in 2016, she and her doctors had serious concerns. The thirty-six-year-old Queens resident has lupus, an autoimmune disease that predominantly affects women and carries an elevated risk of complications during pregnancy. Approximately one-fifth of pregnant lupus patients face serious problems that include miscarriage, preterm birth, stillbirth, and preeclampsia, a condition involving high blood pressure that can jeopardize the health of both the mother and unborn child. Delgado was one of those who developed preeclampsia and other difficulties, delivering a baby boy by emergency C-section at twenty-five weeks' gestation. "He didn't make it past three days," she says. "I can't even explain how awful it was—it's the hardest thing my husband and I have ever had to go through."

Though Delgado and her son weren't treated at Weill Cornell Medicine, she's now helping researchers there who are studying the lupus-related pregnancy complications that she endured. It's an issue that has long concerned pediatric rheumatologist Virginia Pascual, MD, who treats girls and young women with the disease, which affects an estimated 1.5 million Americans and at least 5 million people worldwide. As Pascual notes ruefully, she has had to explain to far too many teenage patients that lupus might curtail their fertility—and if they do conceive, the outcome could be dire. "It's a heartbreaking conversation," says Pascual, director of the Gale and Ira Drukier Institute for Children's Health and the Ronay Menschel Professor of Pediatrics at WCM.

So Pascual was eager to collaborate with Jane Salmon, MD,

PHOTO: ISTOCK/ADENE SANCHEZ

Jane Salmon, MD (left), and Virginia Pascual, MD

a professor of medicine at WCM and the Collette Kean Research Professor at Hospital for Special Surgery. Salmon had led an eleven-year, NIH-funded study (known by the acronym PROMISSE) of more than 700 pregnant women—most of whom had lupus or another autoimmune disorder—that sought to identify who had a higher risk for complications and who could be expected to have a healthy pregnancy. Among that study's major findings: that most women have good pregnancy outcomes if their lupus is inactive, contradicting a misconception that all women with the disease should not have children. With that data in hand, Pascual, Salmon, and several colleagues designed a new investigation that analyzed blood samples and other information from a subset of the larger study's patients, including ninety-two pregnant women who had lupus and forty-three who did not. Their results, published in April in the *Journal of Experimental Medicine*, showed that there are distinct molecular changes that happen in the immune systems of lupus patients during pregnancy that may determine the likelihood of major problems like preeclampsia.

In a normal pregnancy, the immune system—through a process that scientists don't yet fully understand—helps prevent a mother's body from rejecting a developing fetus. In their study, Pascual and Salmon learned that in women who don't have lupus, certain immune pathways are suppressed early in pregnancy and remain that way until after delivery. They were surprised to find that there was a similar immune modulation in lupus patients who had uncomplicated pregnancies, while there was little or no pathway suppression for those with the illness who had difficult pregnancies. "This is helping us better understand what happens during pregnancy for women with lupus," says Pascual, "as well as during pregnancy in general."

These findings could aid in developing early diagnostic tests for lupus patients that would allow physicians to better monitor and manage their pregnancies—and, eventually, point the way toward preventive therapies to improve outcomes for at-risk patients with the disorder. Plus, says Salmon, the ability to predict that a mother-to-be with lupus will likely have an easy pregnancy has immense value—not only reducing or eliminating unnecessary interventions, but helping put patients' minds at rest. "All pregnant women with lupus are considered high-risk, even though only about 20 percent have complications, some of which are minor. These women are getting obstetric sonograms every month; they're very anxious, and their care is expensive," says Salmon. "To be able to tell a woman that her pregnancy is likely to be at the same risk as the women down the street with no medical problems—that's enormous for the patient and for allocation of healthcare resources for society."

There may be broader implications, too. The study also looked at twenty-five healthy women undergoing in vitro fertilization and found that the same suppressed immune patterns emerged just days after a pregnancy was detected. More work needs to be done in this area, but Pascual says it's possible such information could eventually help forecast which IVF implantations will be successful. Salmon is also spearheading a trial at HSS to evaluate whether the drug certolizumab—which is FDA-approved for use in rheumatoid arthritis, psoriasis, and Crohn's disease—will significantly decrease the rate of preterm delivery due to preeclampsia or placental insufficiency in women with antiphospholipid syndrome, an autoimmune disorder that can lead to dangerous blood clots and frequently affects lupus patients.

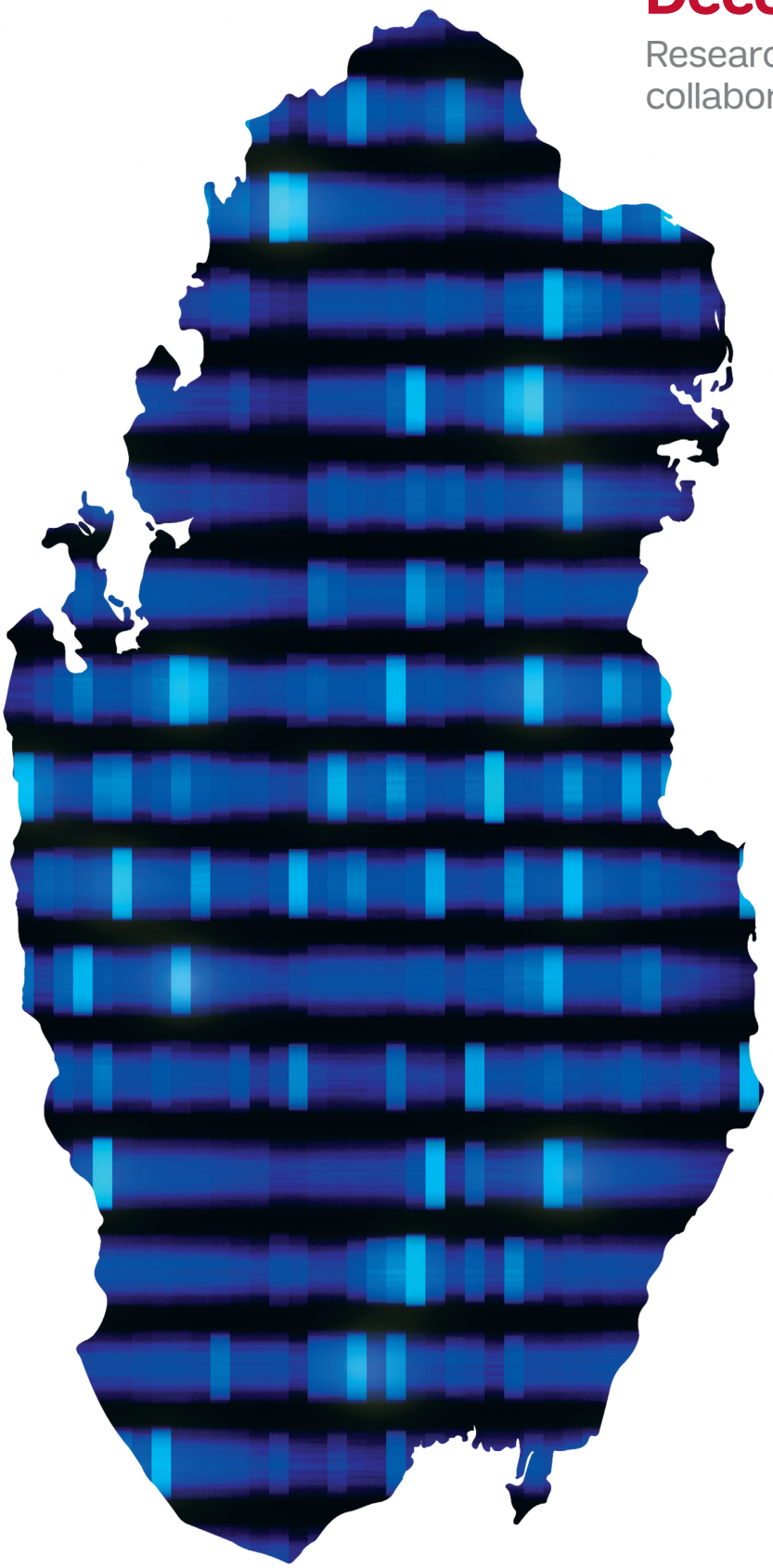
'This is helping us better understand what happens during pregnancy for women with lupus,' says Virginia Pascual, MD, 'as well as during pregnancy in general.'

Delgado enrolled in that trial when she became pregnant again last year. Her son, Miles, was born in February, weighing seven pounds, two ounces—and although he arrived at thirty-six weeks and had some early respiratory issues, he's now thriving. Salmon can't yet say whether the drug played a role in bringing him safely into the world, but Delgado says that just participating in the trial made her feel optimistic. "We had our happy ending," Delgado says. "And I hope that because of the work these doctors are doing, others like me will have their happy endings, too." ■

— Heather Salerno

Salmon has received an investigator-initiated grant from UCB Pharmaceuticals.

PHOTO: JOHN ABBOTT



Decoding DNA

Researchers in Doha and New York collaborate to explore the Qatari genome

There's a rare hereditary disorder of the connective tissue that causes abnormal twists and turns in the blood vessels. This condition, known as arterial tortuosity syndrome (ATS), can lead to serious aortic complications—including narrowing (stenosis), bulging (aneurysms), and tearing (dissection) of the wall—and can be fatal in early childhood, although individuals with milder forms of the disease can live into adulthood. ATS is an autosomal recessive disease, meaning that those who suffer from it have received a faulty gene from each parent. And like many such conditions, the mutation that causes it is more common in one particular population—in this case, the people of Qatar, the Middle Eastern nation that's home to a branch of Weill Cornell Medicine. "ATS is mapped to a mutation that is observed in one large Qatari family," explains Juan Rodriguez-Flores, PhD, an assistant professor of research in genetic medicine at WCM in New York. "Distant relatives intermarry, and so the disease occurs more often than expected."

The higher incidence of ATS in Qatar illustrates an issue with genetic screening tests, which have become an important tool for diagnosis and a popular option for couples who worry about passing on hereditary diseases to their children. Given that the human genome has 3 billion base pairs, including 4 million that vary, it would be prohibitively expensive and time-consuming to test every individual for every possible mutation. Basic genetic screening tests therefore look for only the most common disease-causing mutations—but these have been identified primarily through studying Western populations, which means diseases that are more common outside the U.S. and Europe are easily missed.

That's where a long-standing project to study the Qatari genome comes in. Over the past ten years, Ronald Crystal, MD, the Bruce Webster Professor of Internal Medicine and chairman of genetic medicine (who is based in New York) has been working with colleagues in Doha to investigate details of Qatari DNA. That work recently led to the creation of a customized microarray—a chip that can indicate the presence or absence of certain mutations in a DNA sample—to screen Qataris for hereditary conditions more likely to affect them. "It's Qatari-specific," Crystal says, "but it has implications for everyone."

PHOTOS: QATAR, ISTOCK/VERPEYA; SEQUENCE, ISTOCK/KTS IMAGES; OPPOSITE, PROVIDED

CUTTING-EDGE TECHNOLOGY: Hanan Mohamed al-Kuwari, PhD (seen at right in photo at left), Qatar's minister of public health, presents a model of the Q-chip to Her Highness Sheikha Moza bint Nasser, chairperson of the Qatar Foundation, at the World Innovation Summit for Health in November 2018. Above: A close-up of the chip.

Around the world, Crystal explains, different mutations occur in different groups of people at different rates. Qataris, a small and historically isolated population, offer the perfect example of this phenomenon. "The conventional ways that we screen for hereditary disorders in the United States or Europe are not relevant to the Qataris, because that would miss a lot of their mutations," Crystal says, noting that the same could be said for many other populations. People with African backgrounds, for example, suffer from sickle cell anemia at higher rates, while Eastern European Jews have a higher incidence of Tay-Sachs disease, a degenerative neurological disorder.

By late 2018, a Qatar Foundation initiative known as the Qatari Genome Project—a collaboration between WCM, Qatar Biobank, Hamad Medical Corporation, Sidra Medicine, and the Ministry of Public Health—had sequenced 10,000 citizens' DNA. Meanwhile, Rodriguez-Flores analyzed the frequency of different alleles, or gene variations, in the genomes and helped design the Qatari gene chip ("Q-chip" for short) to efficiently and inexpensively test an individual for the presence or absence of some 360,000 mutations with a known or potential role in causing diseases, and which are particularly likely to appear in Qataris. "Eventually, our vision is that this would be used for newborn screening for thousands of diseases," Crystal says. "The ultimate goal is to do the same kind of thing in different populations—study those populations, take the genomic information, and then design similar approaches."

The Genome Project will evolve into a broader nationwide initiative called Qatar Precision Medicine, which the country's leaders hope will improve healthcare for its citizens and ultimately make it a magnet for biomedical research and innovation. "It's part of the 2030 vision of the government of Qatar," explains Khaled Machaca, PhD, associate dean for research at Weill Cornell Medicine–Qatar. "But it also has immediate, real clinical applications: it will help personalize treatment for Qatari patients. And the nice thing about the chip is instead of doing extensive, time-consuming whole genome sequencing, you can do it quickly."

'The conventional ways that we screen for hereditary disorders in the United States or Europe are not relevant to the Qataris,' says Ronald Crystal, MD, 'because that would miss a lot of their mutations.'

It's a local solution to a local problem—but as Machaca notes, the Q-chip also shows what can happen when WCM investigators work together from opposite sides of the globe. "At the research level, we have a very tight relationship between Weill Cornell Medicine labs here and in New York," he says. "This is the fruit of multiple years of collaborations, both within Qatar and across oceans." ■

— Amy Crawford

Machaca is a co-founder of Valdia Health SL, a company focusing on precision health solutions.

Blame the Messenger?

Hagen Tilgner, PhD, is exploring how faulty building instructions for brain cells may give rise to depression, schizophrenia, Alzheimer's disease, and more

Hagen Tilgner, PhD

By now there's no question that genetics contributes to many brain diseases, including Alzheimer's, autism, and depression. But exactly how genetic malfunctions translate into disorders remains unclear, rendering cures elusive. Hagen Tilgner, PhD, an assistant professor of neuroscience in the Center for Neurogenetics of Weill Cornell Medicine's Feil Family Brain and Mind Research Institute (BMRI), is working to shed light on the genetic roots of brain diseases. His lab does so by decoding the secret communications that occur inside our genes—as Tilgner puts it, "listening to what genes are saying." The research could pave the way to highly targeted—and effective—treatments for conditions affecting the brain, and potentially other parts of the body as well.

Tilgner's work builds upon a fundamental quandary in biology: almost all our cells have the same DNA, yet our bodies are made of different cell types. One important player in this diversity, Tilgner says, is a process called gene expression. The vast majority of cells indeed contain the same genes, but inside each individual cell

PHOTO: ABBOTT

some genes are awake, while others stay asleep. When genes are awake (or in scientific terms, "expressed"), they can facilitate the production of proteins—hard-working molecules that may transport oxygen, fight infections, or serve as building blocks of various tissues. Slumbering genes, on the other hand, cannot participate in protein generation. By waking up some sets of genes and keeping others asleep, developing cells eventually differentiate into skin, muscle, or brain tissue.

Scientists have long associated abnormalities in gene expression with disease, but now they're finding that there's more to the story. When a gene is awake, a cell copies its material into RNA molecules, which then become messengers that carry and relay protein-building instructions—called isoforms—to the cell's internal constructors. A growing body of research is suggesting that faulty isoforms cause glitches in these communications, giving rise to diseases from cancer to diabetes. When such glitches occur in brain cells, researchers now theorize, it can contribute to such conditions as Alzheimer's and autism, and possibly depression and schizophrenia as well. "If we could target the isoforms at the root of the problem," Tilgner says, "then perhaps we could treat the disease."

Tilgner's aspirations are bolstered by recent advances in the field of gene therapy. By tinkering with a specific isoform in motor neurons (brain cells essential to movement), he notes, scientists at Cold Spring Harbor Laboratory were able to find a novel treatment for spinal muscular atrophy, a debilitating genetic disorder that causes sufferers to become wheelchair-bound; although not a cure, the discovery not only enabled patients to walk but also extended their lifespans. Tilgner is now learning more about isoforms in other types of brain cells—ones that may play a role in disorders such as Alzheimer's disease and depression—a step that could be key to treating such conditions. As BMRI director Costantino Iadecola, MD, the Anne Parrish Titzell Professor of Neurology, observes: "You need to know how the engine works before you try to fix it."

Tilgner and his team have developed a technique that lets them "eavesdrop" on isoforms in the brain, where at least a third of the 20,000 total genes in the body are expressed. These particular genes bear a tremendous amount of responsibility. Some facilitate the production of proteins that give rise to the insides of brain cells and to the tissues that connect them, while others make proteins that yield the chemicals that allow neurons to "talk" to one another. It is therefore no wonder that these genes can make or break the brain's development and function—ultimately directing our thoughts, emotions, behaviors, and physical movements. Adding to the pressure is the fact that, unlike their cousins that inhabit the skin or gut, brain cells cannot be replaced. This means that any glitches in protein generation caused by unruly isoforms in brain cells' genes can have particularly dramatic—and currently irreversible—consequences that manifest themselves through debilitating disease.

In a study published in *Nature Biotechnology* in October 2018, Tilgner and his team zeroed in on the genetic intricacies of brain cells in mice by recording their isoforms. Their technique involved trapping different types of brain cells—such as neurons and glia—in minute droplets of liquid, then tagging intercellular messengers with mini "barcodes" that identified the cells that the messengers came from, allowing the investigators to "listen" to the isoforms produced in each of thousands of single cells. By grouping individual cells according to similarity in gene expression, they showed that the technique could be used to study isoforms in tens of types of brain cells simultaneously—an important finding, because neurodegenerative and psychiatric disorders may affect various brain cell types in different ways. The scientists are now planning to use the same method to compare isoforms in animal brain cells affected by diseases such as Alzheimer's with those produced in healthy cells.

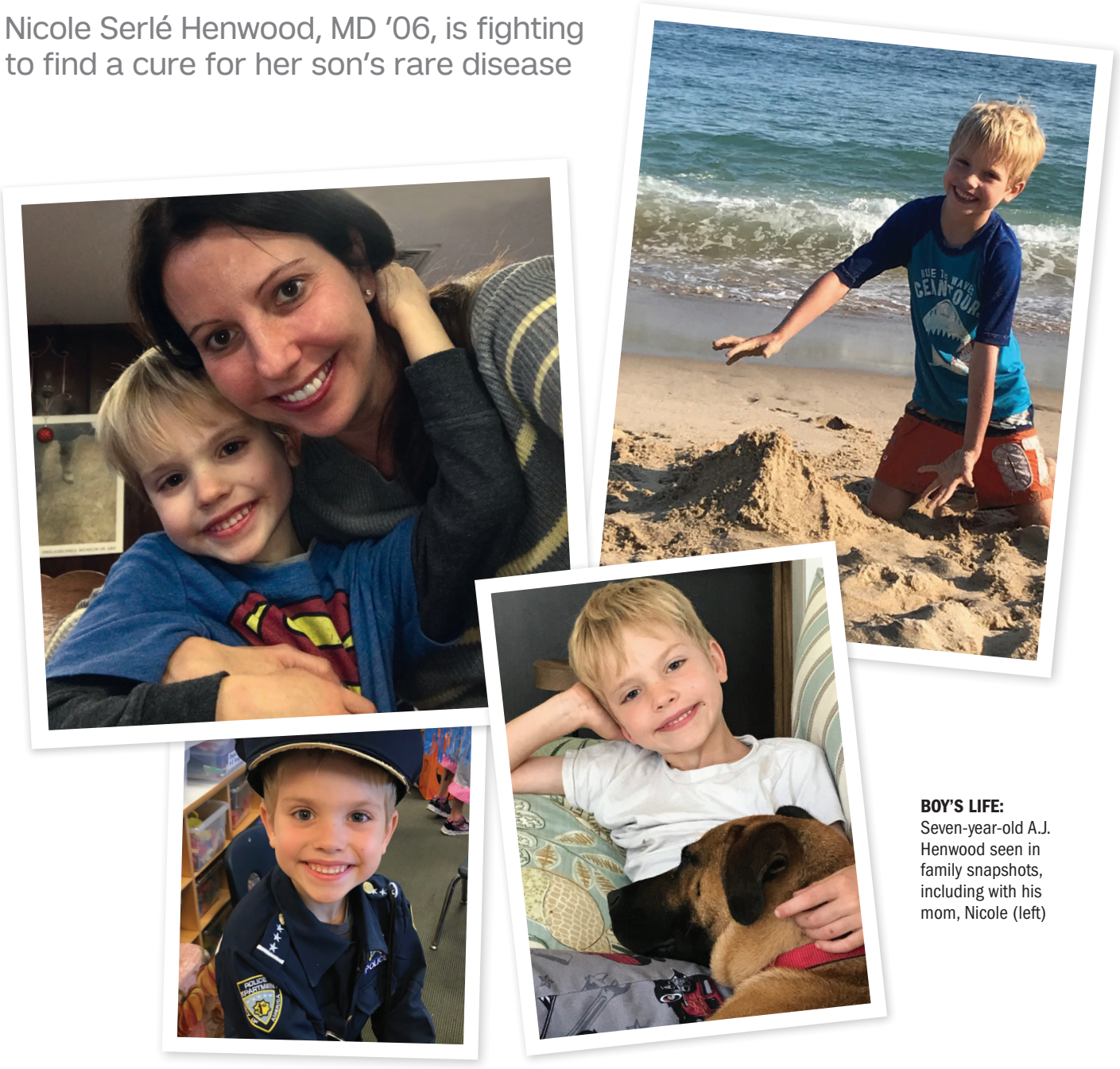
'If we could target the isoforms at the root of the problem,' Tilgner says, 'then perhaps we could treat the disease.'

In the long run, Tilgner would like to apply his research to devising more precise treatments for diseases—both those affecting the brain and other organs—that are driven by faulty isoforms. The key, he says, is to figure out exactly in which cell types disease-causing isoforms act, and to target them precisely there. "We don't want to hit all the cells," Tilgner says. "We just want to hit the ones where it matters, and not cause collateral damage." ■

— Agata Boxe

A Mother's Mission

Nicole Serlé Henwood, MD '06, is fighting to find a cure for her son's rare disease



BOY'S LIFE: Seven-year-old A.J. Henwood seen in family snapshots, including with his mom, Nicole (left)

In many ways, A.J. Henwood is a typical seven-year-old. He loves his family, nurtures big dreams of playing professional baseball, and has a penchant for bringing home stray animals. Aside from slightly imperfect vision and some occasional pain in his left leg, he has always led an ordinary life—which is why his diagnosis came as such a shock. During an eye exam in March 2018, an ophthalmologist saw a freckle-like spot on A.J.'s retina. That, combined with some irregular pigmentation on his body that his pediatrician had deemed benign, indicated that he might have neurofibromatosis 2 (NF2), a rare genetic mutation that causes the growth of benign tumors in the nervous system. A follow-up MRI confirmed it. "I'll never forget that day," says A.J.'s mom, Nicole Serlé Henwood, MD '06. "It was the scariest, most devastating day of my life."

The outlook for patients with NF2 can be bleak. While some are managing relatively minor symptoms well into their eighties, others are wheelchair-bound by the time they're teenagers. Because these non-cancerous tumors can grow anywhere along the nervous system, symptoms vary and can include numbness or pain in the arms and legs, deteriorating eyesight, fluid build-up in the brain, seizures, and paralysis. For unknown reasons, the tumors have a strong preference for growing on auditory nerves—and as a result, nearly everyone with NF2 becomes deaf by their twenties. Patients generally receive MRIs every six months to monitor the tumors, and especially large or obstructive growths are surgically removed. But because NF2 is so rare—striking just one in 33,000 people worldwide—there is little financial incentive for drug companies to fund the research that could lead to a cure.

Henwood is an attending anesthesiologist at Crozer-Chester Medical Center outside Philadelphia. But she says that despite her medical training, in many ways she reacted to her son's diagnosis like any other parent. "Appointments were a blur," she recalls. "They throw all this information at you, and you're like, 'What just happened?' " Faced with her son's potentially dire prognosis due to the many tumors already growing in his body—and the realization that medical science didn't have the answers she so desperately wanted—Henwood decided to take matters into her own hands. She started researching the literature and reaching out to specialists, professional fundraisers, and other families affected by the disease. "I read everything I could find on the subject," she says. "That's what you have to do. You have to *become* the expert." When it comes to research and outreach, she admits, her medical background gives her a leg up. "I think the letters at the end of my name help get people's attention," she says. "They respond to my e-mails more than they would otherwise."

In summer 2018, just a few months after A.J. was diagnosed, Henwood and four others—including her brother and some other parents of kids with NF2—founded NF2 BioSolutions, a nonprofit with the ultimate goal of finding a cure. It has since raised more than $200,000 and grown into a vibrant grassroots organization including a scientific advisory board, a regional support network, and a cadre of volunteers. In late March, it held a workshop attended by some forty biomedical professionals (including surgeons, neurologists, and biotech researchers) focused on outlining a pathway to a cure—which, Henwood says, will entail funding gene therapy research and partnering with industry to manufacture the resulting treatment. Though the nonprofit lacks the funding that major drug companies would bring to bear on the problem, she notes, "we're using manpower to make up for it."

NF2 is just one of thousands of diseases designated as rare by the NIH, meaning that it affects fewer than 200,000 people in the U.S. Some are well-known—like cystic fibrosis, a life-threatening disease that damages both the respiratory and digestive systems, and spina bifida, in which the spinal cord doesn't develop correctly in the womb. Others are more obscure, such as progeria, which causes rapid aging beginning in childhood and affects less than one in 4 million people worldwide. But as Henwood notes: "One in ten people across the U.S. population is affected by a rare disease—so, actually, they aren't that rare."

Many of these diseases are considered "orphans" because, due to a small potential market, private companies aren't inclined to develop treatments for them. The U.S. government has taken steps to incentivize research—notably the 1983 Orphan Drug Act, which provides tax credits and other breaks to drug manufacturers—and institutions such academic centers, nonprofit foundations, and the NIH are actively investigating the causes of many rare diseases and developing clinical trials to treat them.

'One in ten people across the U.S. population is affected by a rare disease,' Henwood points out, 'so, actually, they aren't that rare.'

But Weill Cornell Medicine pediatrics professor Virginia Pascual, MD, says it's not enough. "When you realize that there are close to 7,000 rare diseases, and these institutions are looking at fewer than 200 of those," says Pascual, the Gale and Ira Drukier Director of Children's Health Research at the Gale and Ira Drukier Institute for Children's Health, "you start to understand that there is so much more work to do." She notes that numerous investigators at WCM are researching such ailments, including autoimmune diseases, forms of anemia, and cancers of the brain and blood. Says Pascual: "Every patient deserves to have their disease studied."

That's where grassroots organizations such as Henwood's come in. As she and Pascual note, such patient-driven activism is becoming more common—and it's having demonstrable success in promoting and funding research. For example, gene therapies for two orphan diseases—adrenoleukodystrophy and Sanfilippo syndrome (which both cause fatal brain damage)—have been developed and are being tested in pediatric patients, thanks in large part to their parents' efforts. "We're building on each other," Henwood says. "Every time a parent fights for a cure, they're seeing results faster because some of the research problems have already been solved." ■

— Alexandra Bond

PHOTOS: PROVIDED

Risk Factor

For patients with a genetic syndrome that predisposes them to many cancers, a new vaccine could be a lifesaver

PROTECTIVE MEASURE: Clinical geneticist Steven Lipkin, MD, PhD, and colleagues are developing a vaccine to prevent Lynch syndrome.

One of the most common causes of hereditary cancer, Lynch syndrome affects some 1.1 million Americans, who face a lifetime risk of colorectal cancer as high as 80 percent as well as elevated rates of many other cancers, including of the endometrium, kidneys, ovaries, and prostate. Patients seldom learn they carry the mutations associated with Lynch syndrome until they or a relative have cancer—and that diagnosis may affect their entire family. "You have a fifty-fifty chance of passing it on to each of your children, so the likelihood that other people in the family would have it is enormously high," says Felice Schnoll-Sussman, MD, professor of clinical medicine and director of the Jay Monahan Center for Gastrointestinal Health at NewYork-Presbyterian/Weill Cornell Medical Center. "This is one of those diseases where the patient can feel like they have a target on their back, especially because these are often people who have seen family members succumb to cancer."

It's a diagnosis that haunts patients throughout their lives and requires constant vigilance, explains Schnoll-Sussman, who works to ensure her patients and their affected relatives have regular cancer screenings. "I like to say to a patient when we initially meet, we are basically attached at the hip," she says. "For a lifetime."

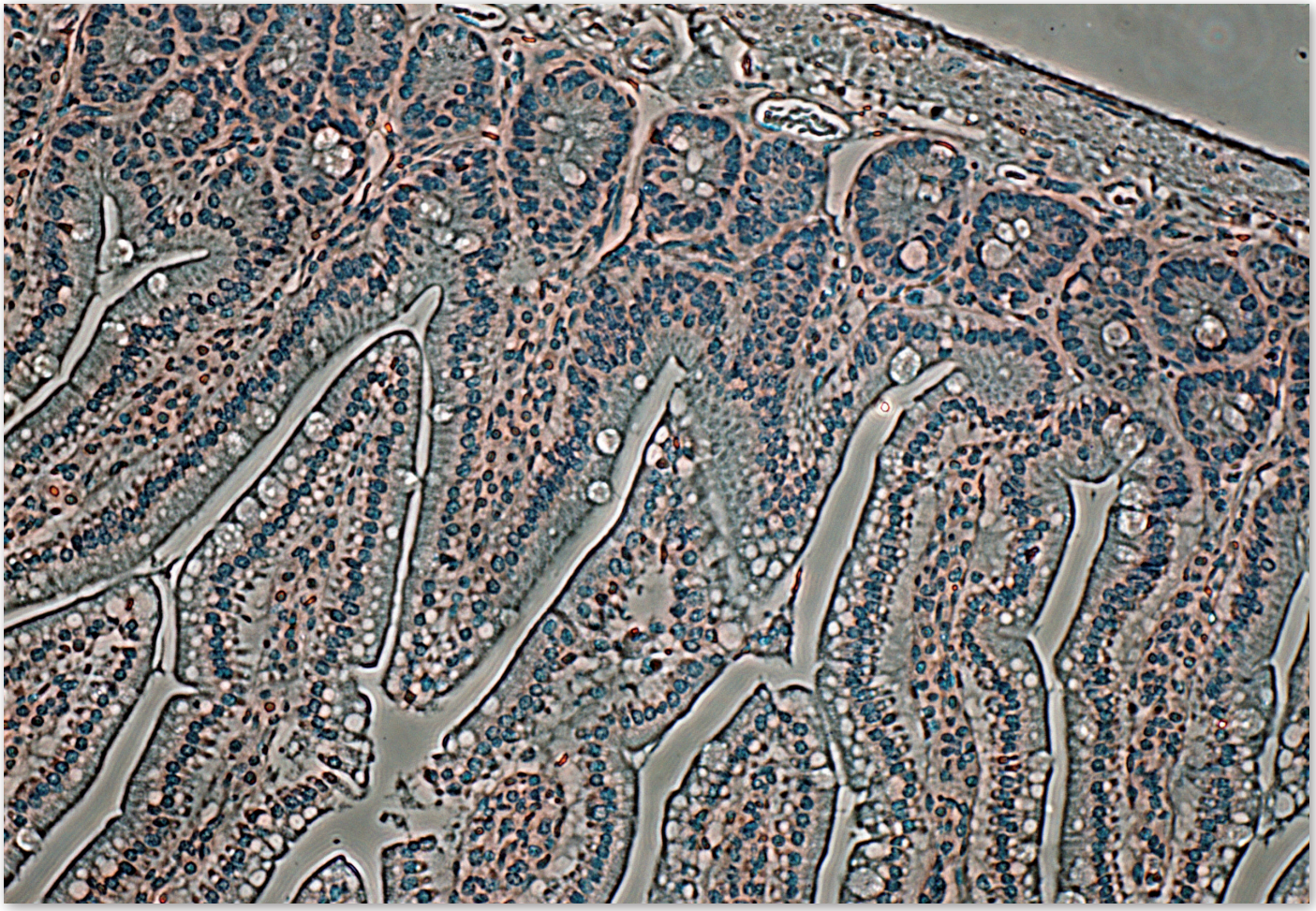
But patients may one day be spared that anxiety, thanks to a vaccine that could effectively train the immune system to stop Lynch-associated cancers before they develop. At the annual meeting of the American Association for Cancer Research last spring, Weill Cornell Medicine clinical geneticist Steven Lipkin, MD, PhD, presented the promising results of a study that showed a vaccine he developed, in partnership with Schnoll-Sussman and other WCM colleagues, could prevent colorectal tumors in mice genetically engineered to have Lynch syndrome. That preclinical study has paved the way for the development of a human vaccine, the first of its kind that would target hereditary cancer. "We think that this approach is something that can actually be used for people at risk of many genetically linked cancers, not just those with Lynch syndrome," explains Lipkin, co-leader of the Cancer Genetics, Epigenetics, and Systems Biology Program at WCM's Sandra and Edward Meyer Cancer Center. "But we have to start somewhere."

Lynch syndrome is caused by mutations in genes that encode proteins responsible for repairing mismatches when DNA is replicated during cell division. (As Lipkin puts it, these proteins act like a "molecular spellchecker.") A faulty mismatch repair protein permits DNA replication errors that lead to changes in parts of the genome called "coding microsatellites," certain tracts of repetitive DNA that may have many different functions. Mutated DNA encodes modified proteins, some of which may cause cells to become cancerous. And while the immune system is able to recognize some irregular proteins as so-called "neoantigens"—protein fragments stemming from mutations in tumor cells' DNA—it is generally unable to mount a response sufficient to stop cancer in its tracks.

A vaccine, however, provides the immune system with advance training, allowing it to recognize and attack cancer cells with mutations common in Lynch syndrome—before a tumor has a chance to grow and spread. "It's the same basic technology used for vaccines against measles or influenza," explains Lipkin, also the Gladys and Roland Harriman Professor of Medicine at Weill Cornell Medicine and an attending physician at NewYork-Presbyterian/Weill Cornell.

Creating the Lynch vaccine involved loading some 200 common mutations found in mice's colorectal tumors into a hollowed-out

PHOTO: ABBOTT



A STRONG DEFENSE: This magnified cross-section of the lower gastrointestinal tract of a mouse genetically engineered to have Lynch syndrome shows that the vaccine Lipkin is developing increases production of molecules (seen in pink) that recruit immune cells to fight tumor cells. Cell nuclei are seen in blue, while the thick gray lines are gastrointestinal epithelial cells.

IMAGE: PROVIDED

virus, which was then given to other mice in the form of an injection. The researchers found that the rodents' immune systems apparently learned to recognize the neoantigens before cancer got a foothold, activating T-cells to attack mutated cells. Vaccinated mice had lower rates of cancer and therefore longer lifespans—380 days, compared to 241 days for a control group. "From mice, we have data that this causes the immune system to recognize cancers even as small as single cells," Lipkin says. "Cancer is very good at suppressing the immune system, but if you catch it very early, it's much easier to cure."

If eventual human trials are successful in preventing Lynch patients from developing cancer, the basic technology behind the vaccine could ultimately be used to combat other hereditary cancers, including breast cancer linked to the BRCA gene. In the meantime, he and Schnoll-Sussman stress the importance of education about Lynch syndrome and expanded genetic testing for all patients with significant family history who are diagnosed with colorectal or endometrial cancers, the two most commonly associated with the condition. While early, regular, and vigilant cancer screenings can save Lynch patients' lives, less than 5 percent of people with the syndrome know they have it. But if the vaccine proves successful, that diagnosis will be an essential step toward preventing the syndrome's potentially dire consequences. "There are some things that are incredibly special in medicine, things that we consider disruptive technology," Schnoll-Sussman says. "For someone with a genetic mutation that can affect every cell in their body, this vaccine could be a life-altering proposition." ■

'We think that this approach is something that can actually be used for people at risk of many genetically linked cancers, not just those with Lynch syndrome,' says Steven Lipkin, MD, PhD. 'But we have to start somewhere.'

— Amy Crawford

For Kids' Sake

WCM-affiliated program empowers New York City nannies to better care for children—and themselves

CARING FOR THE CAREGIVERS: Pediatrician Zoltan Antal, MD, leads a workshop for nannies on issues affecting children's health.

All kids run a temperature from time to time. But as a pediatrician, Zoltan Antal, MD, is well aware that detecting fevers in young children can be tricky—and vitally important. That's why the topic was a key part of a pediatric healthcare workshop he taught in Manhattan's Washington Heights neighborhood one Saturday afternoon in March. "How do you check for a fever?" he asked the nine students, all women currently working as nannies or trying to enter the field. Several responded that they would first press a hand to a child's forehead to see if he or she feels hot. "Many people do that," Antal said with a smile.

But as he went on to explain, children can still be sick when they don't seem warm. Plus, he noted, in infants even a slight fever can be a sign of a potentially serious infection, and keeping a careful watch is imperative. Antal encouraged the women to use a thermometer to ascertain a child's temperature, adding that popular models placed in the ear may not give an accurate reading in newborns. The gold standard, he said, is a rectal temperature, acknowledging that it can be difficult to get a child to cooperate—and at that, the women all laughed and nodded. Antal then suggested certain techniques—like putting a baby belly-down across your lap—to make the process easier. For Melquisedec Mejia, who cares for an infant with a heart condition, this was valuable information. "I have to take his temperature a lot," she said, "and now I know I have to take it differently."

PHOTO: ABBOTT

For those attending that day, Antal's pediatric workshop was the last of seven they had to take to complete a thirty-five-hour training program developed by Cornell Cooperative Extension and the Worker Institute at Cornell's School of Industrial and Labor Relations, in collaboration with Weill Cornell Medicine and the National Domestic Worker Alliance. Intended to improve skills among childcare providers in New York City and Westchester County, the program also covers such subject areas as CPR, nutrition, social-emotional development, workers' rights, and guidance on how nannies can effectively communicate with parents. Such training, organizers say, can benefit not only the nannies but the youngsters they nurture and the children's families. "Caregivers are often the first to identify a problem, sometimes even before a child's parents," says Antal, an associate professor of clinical pediatrics and chief of pediatric endocrinology at NewYork-Presbyterian/Weill Cornell. "They are on the front lines every day."

'Caregivers are often the first to identify a problem, sometimes even before a child's parents,' says Antal. 'They are on the front lines every day.'

According to its organizers, the program is aimed to enhance the quality of services that nannies provide and boost their chances of being hired, while raising industry standards and elevating the value of an occupation that is frequently underappreciated and underpaid. More than 350 participants have graduated so far, each earning a professional development certificate from Cornell's ILR school. In a recent survey of program alumni—most in their thirties and forties, nearly all from underrepresented groups—63 percent felt the training was a strong factor in helping them secure and retain jobs. Three-quarters reported that the program had a positive impact on wages, and 79 percent said it had a positive effect on relationships with employers. The majority also said that they use the medical, nutrition, and child development knowledge gained during their training "frequently" or "all the time." "Hopefully, having this kind of education helps their ability to take care of children," says Antal, "but it also gives them the opportunity to get better jobs or work in them more confidently."

Antal has been involved with the program since 2011, when he volunteered to create its pediatric health curriculum—which also covers such topics as the best ways to spot common illnesses, what to do if a child sustains a head injury or swallows a poisonous substance, and how to use an EpiPen in the case of a severe allergic reaction. Once a month, he travels to various organizations for domestic workers around the city that offer the training—such as Adhikaar, a social justice nonprofit based in Woodside, Queens, that advocates for the Nepali-speaking population, and Beyond Care, a childcare services cooperative in Sunset Park, Brooklyn, whose members are mostly Latina. Course fees vary according to each organization, and some offer the program as a free benefit to members. Interest has increased so much that Antal is helping train two registered nurses and an MD from a community health center who will eventually take over some pediatric classes; nannies who already have their certificates are also being coached as peer educators on other topics. "There's been this wonderful ripple effect," says Antal.

Classes are largely held in areas with a high concentration of immigrants from the Caribbean, Asia, and Latin America; in cases where English is a second language, an interpreter is always present. For instance, for Antal's session in Washington Heights—at a class hosted by NannyBee, a nanny-owned childcare service in Upper Manhattan that offers the training for free—Antal conveyed his expertise in English, which was interpreted into Spanish for the nannies, who eagerly asked questions and shared opinions. Participants like Mejia, who came to the U.S. nine years ago from Honduras, say the training has already opened doors. Before landing two part-time nanny positions earlier this year, Mejia worked as a waitress—but, she says, "I feel like I have more opportunities now."

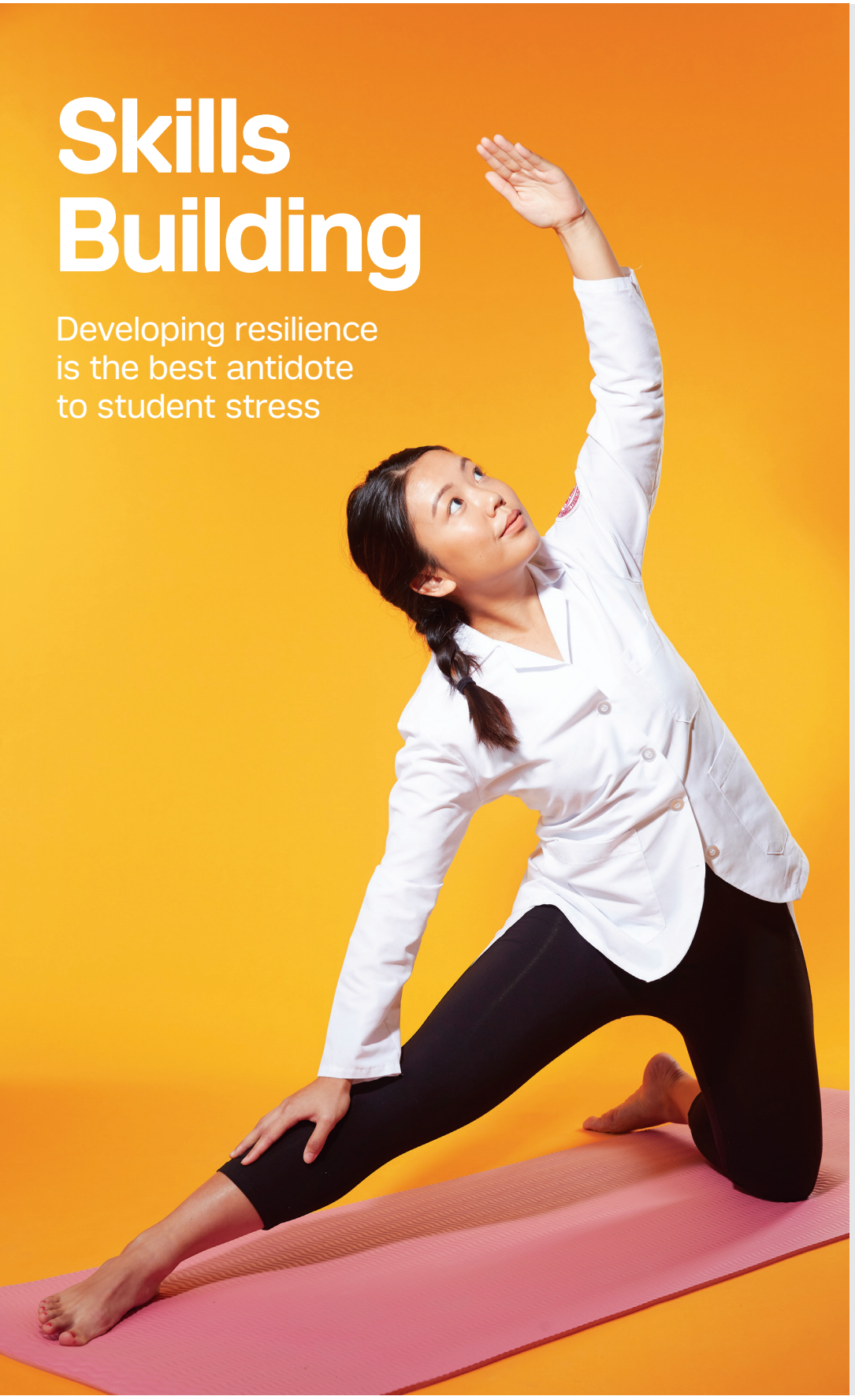
Rose Maria Peña, who completed the program last year and is now a nanny for two boys under five, agrees. She was a schoolteacher in the Dominican Republic before moving to the U.S. in 2016. In New York City, she worked as a home health aide for the elderly, but didn't find it as satisfying. She learned about the training workshops at an English class and immediately signed up; NannyBee helped Peña get her current childcare positions while she finished the coursework. "I feel as though I've regained my life," she says of working with kids. "I feel so happy and completely renewed."

For Antal, the program's mission is close to his heart. His family came to the U.S. from Romania when he was nine, and his mother worked as a child caregiver to make ends meet. "Her employers didn't take good care of her," he says. "They demanded a lot and she didn't know her rights. But at that point, she just wanted a job." When Antal first began with the program, he says, "I came away thinking, this is fantastic. It's helping people just like my family improve their lives." ■

— Heather Salerno

Skills Building

Developing resilience is the best antidote to student stress



These days, everyone seems to be talking about stress, burnout, and wellness. Nowhere is this more a topic of conversation than in medical schools, and for good reason: medical students face unique stresses and suffer from higher rates of depression than their age-matched peers. For example, it's estimated that up to 27 percent of medical students experience clinically significant depression, compared to 9 percent among eighteen- to twenty-five-year-olds in the general population.

What makes medical school so stressful? To start, you have a group of very smart, high-achieving, idealistic young people who are accustomed to being at the top of their class, who soon discover that won't be possible for most of them in medical school. Then there is the sheer amount of information to learn, which can be overwhelming—to say nothing of the unique stress of learning to take care of patients and becoming a doctor. Next, most students have left their friends and family behind to come to medical school, so they experience a sudden loss of their supportive social network during a transition that is exciting yet stressful. And finally, these students are a medically healthy but psychiatrically at-risk group for the simple reason that three-quarters of all mental illnesses that we see in adults occur by the age of twenty-five. And depression and anxiety disorders typically have their onset in life during late adolescence and early adulthood.

Put all these factors together and it's easy to understand why medical school is stressful. But stress, especially the good type, can be healthy and promote psychological resilience—the ability to adapt to stress and adversity, and bounce back from it both psychologically and physically. It's bad stress that we want to avoid. What's the distinction?

Stress is the body's and brain's response to challenge. The key to good stress is that it is something you can manage and even master. We all have experienced the relationship between a challenge and the degree of stress we feel in response. It follows the famous "inverted U" function: as the pressure goes up, so does

PHOTOS: YOGA, STEPHANIE DIANI; FRIEDMAN, JOHN ABBOTT

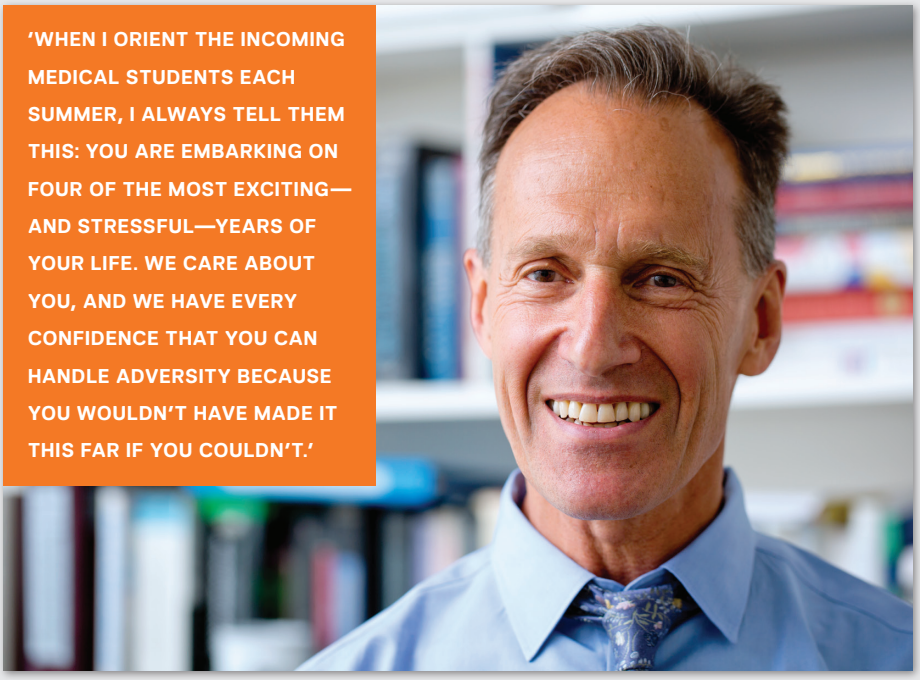
performance—but only to a certain point. Beyond that, anxiety rises and performance starts to drop. So there is a sweet spot for stress: too little and you are bored and under-stimulated, too much and you are anxious and overwhelmed.

When humans experience acute stress, we respond by secreting the hormones cortisol and adrenaline, which help us respond to the demands of the situation. A burst of cortisol mobilizes glucose for energy and enhances immune function, while adrenaline increases attention. But chronic stress—when adrenaline and cortisol levels are persistently elevated—is harmful and leads to serious medical problems like obesity, diabetes, and hypertension, while also impairing various cognitive functions. A brief pulse of cortisol can enhance neurogenesis (the growth of new neurons) in the hippocampus, which is critical to learning and memory. But chronically high cortisol levels have the opposite effect, causing those neurons to shrink and impair cognition. Also, chronic stress typically causes insomnia and sleep deprivation, which can disrupt the formation of new neurons in the hippocampus, a brain region that is critical to memory formation. So if you like to pull all-nighters to study, think again: your sleep-deprived brain is a poor learner.

I've seen all of this first hand over the eighteen years that I've been director of Weill Cornell Medicine's Student Mental Health Services. We are passionate about our mission to promote student mental health and focus on treating common psychiatric problems—like depression and anxiety—that are a source of pain and dysfunction in our students.

What about stress and burnout? It isn't possible—or even desirable—to protect students from normal everyday stress, like disappointing academic performance or social rejection. And everyday, good stress helps foster resilience. It shows students that they can deal successfully with difficult challenges, which enhances their self-esteem and sense of general fitness. There is also preclinical evidence that the neurotransmitters norepinephrine (which is released during acute stress) and serotonin play an important role in resilience.

'WHEN I ORIENT THE INCOMING MEDICAL STUDENTS EACH SUMMER, I ALWAYS TELL THEM THIS: YOU ARE EMBARKING ON FOUR OF THE MOST EXCITING—AND STRESSFUL—YEARS OF YOUR LIFE. WE CARE ABOUT YOU, AND WE HAVE EVERY CONFIDENCE THAT YOU CAN HANDLE ADVERSITY BECAUSE YOU WOULDN'T HAVE MADE IT THIS FAR IF YOU COULDN'T.'



Richard A. Friedman, MD

Of course, there are some unacceptable stresses—like bullying and sexual harassment—that have no place in the school or work environment and which all institutions must do all they can to eliminate. We want to help our students learn to distinguish healthy from unhealthy stress and develop various coping strategies to keep stress manageable, such as exercise, meditation, and healthy eating. That is one of the goals of wellness initiatives.

Another important role of wellness programs is to remind students of what most of them probably know, but forget when they feel overwhelmed by school: that you have to find a reasonable balance between work and life. You cannot study all the time, socially isolate yourself, neglect your hobbies, and expect to feel happy and well-adjusted. Exercise and social contacts don't just make people feel better; they contribute to resilience by raising the level of brain-derived neurotrophic factor (BDNF), which promotes neurogenesis. (We know BDNF has this effect in animals and may do the same in humans, too.)

When I orient the incoming medical students each summer, I always tell them this: you are embarking on four of the most exciting—and stressful—years of your life. We care about you, and we have every confidence that you can handle adversity because you wouldn't have made it this far if you couldn't. Will you feel stressed and overwhelmed at times? Of course; that's entirely normal. You have to find a way—and it takes some time to figure it out—to balance your work with the rest of your life. Don't forget your friends, families, and hobbies. They are important to keep in your life for many reasons, including the fact that they will help you adapt to stress and become more resilient. If, along the way, you are having difficulty that you can't handle, please come and talk with me and we'll help you.

So can medical school ever be stress-free? Of course not. But there is a lot we can do to promote mental health and resilience in all our students. ■

— Richard A. Friedman, MD

FRIEDMAN, A PROFESSOR OF CLINICAL PSYCHIATRY, IS DIRECTOR OF STUDENT MENTAL HEALTH SERVICES AT WCM AND A CONTRIBUTING OPINION WRITER FOR THE *NEW YORK TIMES*.

Closing the Gap

Weill Cornell Medicine researchers are working to combat the stark racial disparities in breast cancer outcomes

BY HEATHER SALERNO

In many ways, breast cancer doesn't discriminate. It strikes young and old, rich and poor, women and men—people from all walks of life. Yet for Lisa Newman, MD, it's long been clear that the disease isn't an equal-opportunity illness. When Newman was starting out as a general surgeon in Brooklyn in the Nineties, she started to notice something unusual among the African American women who were coming to her after being diagnosed. They were often younger than her white patients, and usually had tumors that were harder to treat.

This pattern of disparities inspired Newman to start looking into its causes, and since then she has become an internationally renowned surgical oncologist and breast cancer researcher who has spearheaded groundbreaking studies that strive to understand how the condition varies by race and ethnicity. ›

PHOTO: JOHN ABBOTT

Lisa Newman, MD

Melissa Davis, PhD

PHOTO: ABBOTT

She was appointed chief of the Section of Breast Surgery at NewYork-Presbyterian/Weill Cornell Medical Center and Weill Cornell Medicine in August 2018, having been recruited from the Henry Ford Health System in Detroit. In addition to her clinical work leading the Breast Surgical Oncology Programs for the NewYork-Presbyterian/Weill Cornell network, Newman is the founding medical director of the International Center for the Study of Breast Cancer Subtypes (ICSBCS), where she and other WCM researchers—like molecular geneticist Melissa Davis, PhD, an associate professor of cell and developmental biology research in surgery—are largely focused on investigating genetic links between African ancestry and a higher incidence of aggressive tumors in African American

women, including triple-negative breast cancer, a difficult to treat form of the disease that accounts for 15 to 20 percent of all breast cancer cases in the U.S.

It's an issue that hits home for both Newman and Davis, who are African American and among the few women of color working in this field. Davis says new therapies can't come soon enough for the black women in her life who she sees fighting the disease every day: a teacher at her child's school, other mothers in her neighborhood, fellow churchgoers. "One of my classmates from high school died of breast cancer, right after she had her first daughter," she says. "These women aren't grandmothers in their sixties—they're active women with young kids. These are tragic stories, and it's what compels me to continue doing what I'm doing."

An Unequal Burden

About one in eight U.S. women—or about 12 percent—will develop breast cancer in her lifetime, with an estimated 268,600 new cases expected to be diagnosed in 2019 alone. There's good news, though: according to the American Cancer Society, overall deaths from breast cancer have dropped significantly over the last thirty years, due to increased awareness, early diagnosis, and improved treatments. Its incidence has risen across all races and ethnicities since the Eighties—mostly because of increased detection by mammography—though the condition occurs less frequently in Asian, Hispanic, and Native American women than in white or African American women. Yet incidence rates have mostly stabilized for white women in recent years, while rates for African American women have continued to rise. And for women under forty-five, breast cancer is seen much more often in African Americans than in Caucasians.

Most significantly, black women have the highest breast cancer mortality of any racial or ethnic group in the country—shockingly, 42 percent higher compared to white women. That figure has so worried the medical community that the American College of Radiology and the Society of Breast Imaging updated its screening guidelines last year: for the first time, the organizations added black women to the list of groups considered to be high-risk. "All women, especially black women and those of Ashkenazi Jewish descent, should be evaluated for breast cancer risk no later than age thirty," the experts wrote, "so that those at higher risk can be identified and can benefit from supplemental screening."

Contributing to this gap are socioeconomic challenges faced by the African American community, such as higher poverty rates, a greater likelihood of being underinsured, and a lack of access to timely diagnostic tests, treatments, and other services. But doctors like Newman have long thought that genetic differences also play a role. She and her ICSBCS team have therefore developed a field of research they named "oncologic anthropology," which looks at genetic features associated with race/ethnicity and population migratory patterns that might predispose certain women to a higher or lower breast cancer risk. For example, Newman wondered why African American women are twice as likely as white women to have the disease's triple-negative form, so named because it lacks the three most common receptors known to fuel most breast cancer growth: estrogen, progesterone, and the HER2/neu gene. That means drugs aimed at those receptors, like hormone therapy, are less effective. "Unfortunately, we don't yet have targeted therapies for these triple-negative tumors," says Newman, "and they also tend to be more virulent." As a result, patients have a poorer prognosis, which could contribute to the disproportionate death rate among African Americans. ›

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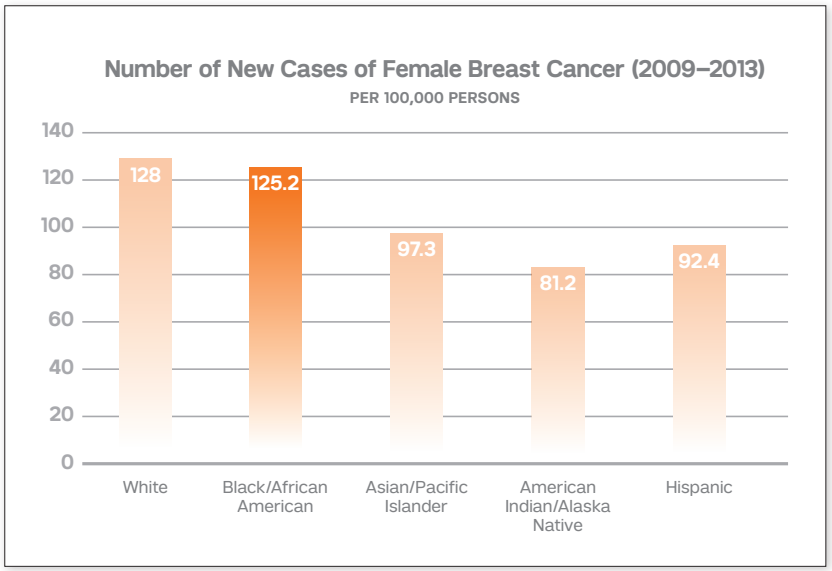


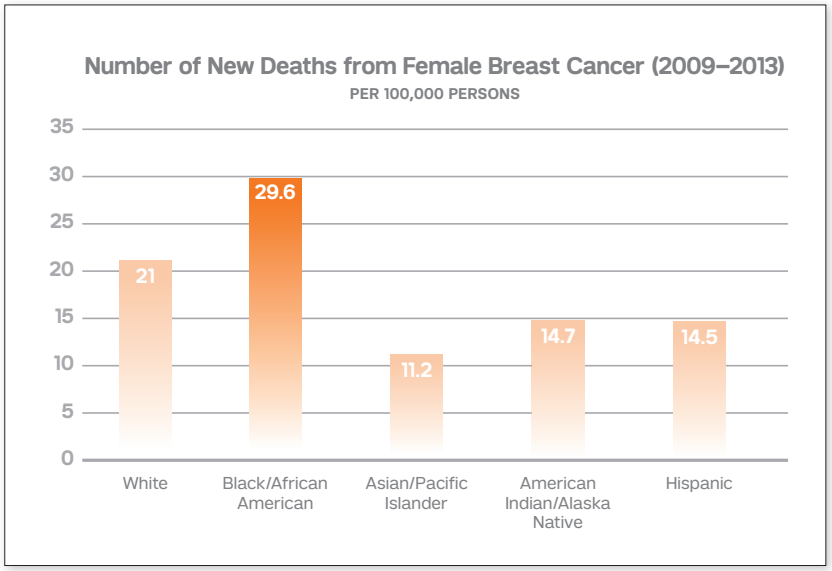


CHART: ORIGINAL BY AMERICAN CANCER SOCIETY ACTION NETWORK, ENHANCED BY JENNIFER KLOIBER INFANTE

Global Outreach

It bothered Newman that more hadn't been done to investigate racial disparities associated with triple-negative breast cancer, and she suspected the differences might have something to do with African ancestry. So in 2004, when she was head of the University of Michigan Breast Care Center, she reached out to the Komfo Anoyke Teaching Hospital in Kumasi, Ghana, a West African country where more than half of all breast cancers are triple negative. Newman offered mentorship and other resources to the medically underserved nation and began traveling to Ghana several times a year with medical students, trainees, and fellow physicians, bringing supplies and helping to evaluate and treat patients there—a collaboration that she continues through WCM in Ghana and other sites throughout Africa. She established a telemedicine service that allows African clinicians to confer with American colleagues, along with a core biopsy training program so breast cancers can be diagnosed more efficiently. She also set up opportunities for Ghanaian hospital staff to come to the U.S. for training in cutting-edge surgical and pathology techniques. As a result, Newman says, "I've been really happy to see that our international partnership has led to improved care for patients."

The ICSBCS features a biorepository for tissue and DNA samples gathered from Ghanaian breast cancer patients to be used in genetic studies. After comparing those specimens collected from African Americans and white Americans, Newman saw similar patterns of aggressive disease among the African Americans and Ghanaians, which suggested a strong hereditary component. Additional research backed up that theory: African Americans showed fewer similarities in breast cancer patterns when compared to women from the eastern African nation of Ethiopia, where the frequency of triple-negative breast cancer is relatively low. Newman believes this supports the idea that triple-negative status among African American breast cancer patients is strongly associated with hereditary susceptibility—with Western

INTERNATIONAL PARTNERSHIP: Newman (center) and Davis (third from right) in Ghana, where they've conducted research and Newman has done clinical work. Opposite page: Charts based on figures from the National Cancer Institute show the clear racial disparities between breast cancer diagnoses (top) and deaths.

PHOTO: PROVIDED

Sub-Saharan African ancestry appearing to be a crucial element. This makes sense, she adds, given the history of the global slave trade. Most black women born in the U.S. are likely descendants of West Africans who were enslaved and brought to North America and the Caribbean several centuries ago; East African slaves, on the other hand, were typically brought to the Middle East and Asia. "Contemporary African Americans therefore have more shared ancestry with Ghanaians than with East Africans," she explains.

Davis started collaborating with Newman on this part of her research in 2016, when she was recruited to join Newman's team in Detroit—though she'd known of her work for at least a decade before that. Now Davis, who joined the WCM faculty in fall 2018, serves as ICSBCS' scientific director. Most recently, the two co-authored a study that was published in April in *Cancer Epidemiology, Biomarkers & Prevention*, which examined a gene mutation that originated in Sub-Saharan Africa and may help explain why black women have worse breast cancer outcomes. This gene, DARC/ACKR1—also known as the Duffy gene—plays a pivotal role in immune regulation; when acting normally, it seems to control systemic or circulating signals of inflammation, which has long been connected to cancer growth. Over time, however, a mutation called "Duffy null" evolved in the West African population; it removes the expression of the gene in red blood cells and may alter expression in other tissues in the body. This gene alteration protects carriers against malaria, a life-threatening, mosquito-borne disease that is widespread in the Sub-Saharan region. Though it's helpful in staving off that illness, the mutation—which is present in nearly all West Africans and between 50 to 75 percent of African Americans—seems to have a detrimental effect when it comes to cancer.

> Newman saw similar patterns of aggressive disease among African Americans and Ghanaians, which suggested a strong hereditary component. Additional research backed up that theory.

For their study, Davis, Newman, and colleagues scrutinized tumor tissue and other genomics data from breast cancer patients from around the U.S. and found that tumors from African Americans on average had lower expression levels of the Duffy gene when compared to white patients. Lower levels were then linked to more aggressive tumor types,›

RAISING AWARENESS: Newman talking with attendees (above and right) at a June event at Riverside Church, co-hosted by Susan G Komen Greater New York City. Bottom: An attentive crowd listens to Newman's remarks.

while higher levels were associated with significantly longer survival. "For the first time," says Davis, "this shows a mechanism of why tumors are more aggressive or harder to treat in people of West African ancestry." She's continuing to build on these results, in the hope that it will lead to new ways to approach the disease. Ideally, she says, "I'd like doctors to be able to say to a patient, 'If you have this mutation and you develop a tumor, you will have a certain type of immune response. Therefore, here's what your first line of treatment should involve.' "

Targeted Approaches

For Olivier Elemento, PhD, director of the Caryl and Israel Englander Institute for Precision Medicine and associate program director of the Clinical and Translational Science Center—who is helping Newman, Davis, and their colleagues examine DNA samples from breast cancer survivors in the United States, Africa, and elsewhere—such efforts are an example of how analyzing cancer genomes can assist physicians in optimizing treatment for individual patients, something that is especially important for those who belong to an often-overlooked minority group. For instance, Newman's breast team works with the institute to interpret genetic tests performed on patients with metastatic breast cancer, the most advanced stage of the illness. Information gathered from such tests—such as whether a tumor will likely respond to chemotherapy or novel targeted treatments—helps guide doctors on the best course of action for individual patients. Elemento says research like Newman's may also help scientists discover more about the origins of breast cancer, leading to the advancement of new therapies that could aid a wider patient population.

Davis points out that part of the problem in addressing these disparities—and, in turn, finding more effective medications to improve outcomes—is that minorities haven't traditionally been included in adequate numbers in research studies or clinical trials. "A lot of breast cancer investigations that have resulted

PHOTOS: ENID ALVAREZ

in advances in treatment have overwhelmingly involved white women," she says. "So the treatments work better in those populations than in others. We're trying to change that." Elemento agrees, noting that recruiting a more diverse patient cohort for precision medicine studies and trials is a priority for the Englander Institute in the coming years. "We need to ensure that all patients benefit equally," he says.

Analyzing cancer genomes can assist physicians in optimizing treatment for individual patients, something that is especially important for those who belong to an often-overlooked minority group, says Elemento.

Breast cancer survivors like Mary Waters are trying to do their part as well. The sixty-three-year-old former Michigan state representative is a past president of the Detroit chapter of the Sisters Network, a national African American breast cancer survivor advocacy organization where Newman serves as chief medical adviser. Waters met Newman in 2009, not long after being diagnosed with Stage 2 breast cancer and joining the organization, and was immediately impressed with the physician's deep commitment to the cause. She helped recruit volunteers for Newman's research through network meetings and allowed her own DNA samples and medical records to be included in the ICSBCS registry. Waters says it can sometimes be difficult to convince African Americans to participate in such efforts; there is still a lingering mistrust of medical research among many that dates back to the Tuskegee study, as well as a cultural inclination to stay quiet about health problems. "But this is about staying alive," says Waters, "and we have to do whatever we can to help."

That also means increasing outreach so more black women know about their breast cancer risk and how to seek preventive care. In Detroit, Newman aided the Sisters Network chapter with its annual Gift of Life Block Walk, where members knock on doors in predominantly African American neighborhoods to talk to residents about breast cancer awareness. She's been involved with similar efforts since arriving in New York: in June, Newman spoke about her research at a senior center in Brooklyn, and later in the month at a brunch co-hosted by Susan G Komen Greater New York City. The goal of the community event, held at Riverside Church in Morningside Heights, was to motivate African American women to get screened. Addressing disparities among African Americans is a top priority for the Komen organization, which has funded some of Newman's research. (She is also an advisory board member for the group.) Komen NYC CEO Linda Tantawi says it's important for black women to see and hear an African American physician-scientist like Newman; it builds their trust in the healthcare system and urges them to do whatever they can to fight the disease. The strategy is working: Newman says that after her talks, women often tell her that she has inspired them to get their first mammogram or see a doctor about a potentially cancerous lump. "Hearing from someone like Dr. Newman, and seeing how much she cares, encourages these women to care about themselves and others in the community," says Tantawi. "And every person at that brunch probably told ten people about what they heard."

Moving forward, Newman, Davis, and the rest of her team will expand on their genetic studies of African Americans. They also plan to look at other minority groups: they want to learn why breast cancer incidence and mortality rates are lower for Latinas in the U.S. compared to African Americans and white Americans. Recent research—similar to the work that ICSBCS has been conducting related to African ancestry—has found that a higher proportion of indigenous American ancestry in Latinas tends to reduce their likelihood of developing breast cancer. The ICSBCS group is currently developing a partnership with a team of breast cancer specialists in Mexico to further explore the topic. "This type of research has broad implications," says Newman. "If we can figure out comprehensively how genetic factors are related to the causes of breast cancer, that will be useful information for everyone." ■

Elemento is the co-founder and equity holder for Volastra Therapeutics Inc. and OneThree Biotech LLC. Both companies focus on technologies related to precision medicine.

NEWS OF MEDICAL COLLEGE AND GRADUATE SCHOOL ALUMNI

Dear Alumni,

As a medical student, a member of the Weill Cornell Medical College Alumni Association board, and now Alumni Association president, I have always felt such pride in our institution. Every day in this position, I meet people who amaze me with what they do, and I am so grateful for the opportunity to be at the helm of this dynamic organization.

A recent event struck me as particularly symbolic of the Weill Cornell alumni commitment. As some of you may already know, we have decided to increase the number of seats on our Alumni Association board—and to give its most active members the option of renewing for a second four-year term—allowing it to grow and diversify. Like all organizational decisions, the reasons for this were complex. But one of our primary motivators was that our board members wanted to stay and do more! This passion for our mission is what fuels so much of what our board members do—and, in particular, it shapes our incredible roster of activities.

This past year is no exception. In the 2018–19 academic year, we ran nearly thirty programs throughout the country to foster the alumni community and provide ample support for current Weill Cornell students and recent graduates. Some highlights:

Student & Alumni Orientation Reception—We welcomed the Class of 2022 with a cocktail reception on the Starr-Greenberg Terrace.

Reunion 2018—Three hundred seventy-five alumni from around the world returned to 1300 York Avenue to celebrate their alma mater.

Student-Alumni Connections—We connected students who travel across the country for conferences, research opportunities, and other activities with alumni in those areas. Alumni provided insights on what it's like to work in their city or specialty, and helped with networking opportunities.

Funding Student Initiatives—We supported student-led initiatives that enrich the student experience, stimulate innovation, and improve human health.

Family Day 2019—We invited the families and friends of our students to campus to get a glimpse into what it's like to be a medical student.

Of particular note on our event schedule this year was the tenth anniversary of the Alumni-to-Student Knowledge (ASK) program. The Office of Alumni Relations launched ASK in February 2009 in response to the students' requests for more frequent and meaningful interactions with alumni. Since its inception in 2009, we have held more than thirty-six sessions, featured 109 alumni speakers, showcased twenty-three medical specialties, and hosted more than 681 students. By bringing students together with alumni and allowing them to ask questions about medicine in a casual environment, we have built an even stronger and more supportive alumni community.

As the Alumni Association grows—and our alumni, like our board members, continue to expand and deepen their involvement—our programming will follow suit. I look forward to sharing these developments with all of you—and I am excited to see what is on the horizon.

Natasha Leibel, MD '98
President, Weill Cornell Medical College Alumni Association
NL121@columbia.edu

RED SEA: Berobed graduates fill Carnegie Hall at Commencement 2019.

PHOTO: AMELIA PANICO

Medical College

1940s

Cedric C. Jimerson '40, MD '43, who recently turned 100, was honored along with other veterans at a ceremony in Harrisburg, PA, commemorating the 75th anniversary of D-Day. He served as a captain and battalion surgeon in the US Army Medical Corps in World War II; he spent a year and a half in Europe in the 663rd Medical Clearing Company, including six months in a combat zone in Germany, for which he won two Bronze Stars. He notes that he was well trained but that doctors often had to improvise to treat complex cases. He and other surgeons developed a method using tubing and condoms to stabilize gunshot wound patients and prevent collapsed lungs. After his military service, he was appointed chief of surgery at Community General Hospital in Reading, PA, in 1950, where he served until his retirement in 1986. He has written several books about his experiences.

1950s

Jack Richard '50, MD '53: "I retired fully in March 2018 and am enjoying life in New York City, especially theater, concerts, and museums. Through an acting course I am taking at the 92nd Street Y, I got a role in a movie, which was shot from October to January and is now being put in its final form. How's that for a new career at age 90? I would love to see any classmate who visits New York."

Herbert Vaughan Jr., MD '55, has been keeping up with the news and would like to hear from **Hiram Kendall, MD '55,** and any other classmates.

Stanley Landau '53, MD '56: "I have been retired almost 20 years from the practice of adult and pediatric urology. Still go to weekly Medical Grand Rounds. I travel abroad once a year and to Sarasota part of the winter. I'm still playing golf and duplicate bridge. Maxine and I have five children, nine grandchildren, and a great-grandchild on the way. Made the big move this year from Hewlett Harbor, Long Island, to the North Shore Towers. Life here is much easier and good. Onward and upward."

Kay Ehlers Gabler, MD '57: "Many of our classmates were deeply saddened by the recent death of **Jack Madaras, MD '57,** this spring. Jack was a successful thoracic and cardiovascular surgeon, an avid world traveler, and a longtime friend to many in our class. His personal outreach contributed enormously to the success of our 60th Reunion last fall, with a record class dinner attendance of 22 (12 alums and ten spouses or family members). For many years Jack pulled together classmates in South Florida, from Sarasota to Boca Raton, for a spring luncheon held on Sanibel or at Fort Myers, an occasion we all looked forward to and hopefully will continue. Jack will surely be missed for his friendship and goodwill, and respected for his loyalty to WCM."

WORDS OF WISDOM: Dean Augustine M.K. Choi, MD, addresses the graduates.

Bernie Siegel, MD '57: "I have a new book coming out in the next year via Hay House: *No Beginnings, No Endings*, about the true nature of life and what I have learned and experienced myself. Medical education needs to become a true education about life and not just information about physical facts."

James Hollister, MD '58: "Getting older and observing the problems of age, such as some memory lapses and impaired walking due to spinal stenosis—but it beats the alternative. Still married to my wonderful (former) student nurse Marjorie (Kuhn). Our four children are raising their families in various states. Condo living has been a blessing. My quadruple bypass coronary surgery seems to be holding up, so we take one day at a time."

1960s

Alvin F. Poussaint, MD '60: "I have been on the faculty at Harvard Medical School for 50 years. I am retiring from my positions as associate dean for student affairs and professor of psychiatry at Harvard Medical School, and will be designated a professor emeritus. My wife, Dr. Tina Young Poussaint, remains on the Harvard faculty as a professor of neuroradiology at Boston Children's Hospital."

Clay Alexander, MD '61: "I had a good long run with tennis: 70-plus years. I decided to quit after my fourth hamstring injury. You have to listen to your body when it waves the red flag. Still traveling a bit and continuing with art. Currently into stained glass to satisfy my curiosity about how it's done. My dad played the harmonica, and my brothers and I all followed his example. Music is supposed to be wonderful for older folks and might even help sustain our age group. Stay well and be happy."

Anthony Saidy, MD '62: "My only medicine-oriented news is the fruit of senile morbidity: the only primary physician who understands all the ramifications of my conditions is . . . me! Since my only high-functioning remaining organ is my brain, I like to run the show, like an extremely stable genius. A conundrum yet unsolved is that if I were to attempt to follow all the conflicting dietary injunctions of my various specialists, I might not eat at all. Yet I prefer my current situation to the alternative. As ever pursuing my first love, I have entered the National Chess Open in Las Vegas. The headline could be: Biological Phenomenon Still Pushing Pawns."

Don Catino, MD '64: "Now in my 81st year, I am retired from patient care but teaching at Dartmouth Medical School: first year physical diagnosis (à la Elliot Hockstein) and second year medical problem-solving. It is so interesting and so much fun. I do not regret giving up practice. I now have much more time for my wife, five kids, and ten grandchildren. I am re-reading all those 'classics' I did not fully understand, and those I never had time for, impeded by my premed science courses and the avalanche of scientific material in med school and beyond. What a joy, and how interesting, with more than 60 years of life experience to reflect on. We love to travel, and have a 'bike and barge' trip down the Danube

BIG DAY: Brandon Sumida, MD '19, waves to loved ones at Commencement.

River planned for this summer. Mindy and **Dave LaGasse, MD '64,** will visit this fall, and I stay in touch with **Dave Cappiello, MD '64,** and **John Ziegler, MD '64**. Life is good."

David Tucker, MD '66: "My wife, Lynda, and I are happy to report that we are both well. My memoir, *The Hard Bargain*, received an honorable mention for an Eric Hoffer Award in May 2019. Very proud and honored! My play, *Divo and Diavolo*, which I commissioned from playwright Adam Kraar, will be produced at the Ensemble Theatre in Cincinnati, OH, for its 2020–21 season. This dramatic comedy is based on my memoir, and I am thrilled to see it performed in the city where I practiced ophthalmology for 35 years. Hopefully it will make it to NYC in the future. Lynda, who has been a hospice nurse for over 35 years, has finally helped accomplish building a hospice residence, Fairfield County House, in Stamford, CT, for individuals who cannot get their end of life care at home. Such a special and needed place in the community. Best to all my fellow alumni."

Charlie Hennekens, MD '67: "A mighty oak fell when **Elizabeth Barrett-Connor, MD '60,** died. She was one of the last of the triple threats as a clinician, teacher, and researcher in women's health. She will be missed."

Ronald S. Rankin, MD '68: "My wife and I made a wonderful trip to Patagonia last January, and we plan to visit New Zealand next January. Retirement isn't all bad!"

Elaine Sarkin Jaffe, MD '69: "It has been a busy and productive year at the National Cancer Institute. I'm continuing my work on lymphoma diagnosis and pathogenesis, and receive many challenging cases in consultation at the NIH. It is rewarding to solve difficult diagnostic problems that have stumped others. This past year I received the Distinguished Pathologist Award from the United States and Canadian Academy of Pathology. On July 1, I completed my term as chair of the membership committee for the National Academy of Medicine for Section 4 (responsible for internal medicine, pathology, and dermatology)."

Alan Lockwood '65, MD '69: "I continue my activity with Physicians for Social Responsibility and have just completed a white paper on climate change and health, 'Heat, Fire, Water: How Climate Change Has Created a Public Health Emergency.' It is available free at psr.org."

1970s

Rich Hoppe, MD '71: "I continue to work full time as professor of radiation oncology at Stanford. In fall 2018 I was honored to receive the Karl Musshoff Prize for excellence in clinical research from the German Hodgkin

'My only medicine-oriented news is the fruit of senile morbidity: the only primary physician who understands all the ramifications of my conditions is . . . me!'

— Anthony Saidy, MD '62

PHOTOS: PANICO

ALL SMILES: Nicole Aguirre, MD '19 (center left), and Andre Belarmino, MD '19 (center right), line up to march.

'I have just retired from Memorial Sloan Kettering Cancer Center after 41 years as an attending radiologist and clinical professor of radiology at Weill Cornell Medicine. I am looking forward to spending time with my wife, four sons, and grandchildren (numbers 6 and 7 are on the way).'

— James F. Caravelli, MD '74

Lymphoma Study Group. This spring I was awarded the inaugural gold medal from the American Radium Society and received the Rodger Winn Award for commitment to the development of evidence-based guidelines for lymphoma from the National Comprehensive Cancer Network. My son, **Brad Hoppe, MD '03,** is an associate professor of radiation oncology at the University of Florida Proton Center in Jacksonville, FL."

James L. Bernat, MD '73: "Judy and I celebrated our 50th wedding anniversary this year. Two years ago, I retired following a 44-year career (including four years of residency) as a neurologist at Dartmouth-Hitchcock Medical Center and professor of neurology and medicine at Dartmouth Medical School, where I also held the Frank Chair of Neuroscience. As an active emeritus professor, I continue to consult in research ethics and teach and write about ethical issues in neurology, disorders of consciousness, and brain death. Although our children and grandchildren settled in Southern California, we happily remain in Norwich, VT."

John Quatromoni, MD '73: "My youngest son, Ben, crewed on the winning boat in the latest Block Island Race, a major annual sailboat racing event. My middle son, Jon, has entered his final year of vascular surgery training at UPenn, and Sam, the eldest, is an attorney in Manhattan."

James F. Caravelli, MD '74: "I have just retired from Memorial Sloan Kettering Cancer Center after 41 years as an attending radiologist and clinical professor of radiology at Weill Cornell Medicine. I am looking forward to spending time with my wife, four sons, and grandchildren (numbers 6 and 7 are on the way)."

Gene Resnick '70, MD '74: "At a ceremony before Commencement, **Alan Roper '70, MD '74,** received the Alumni Award of Distinction, recognizing his great achievements in neurology. He was introduced by **Steve Hoffman, MD '75** (whom we regard as a classmate), with classmates **George Ellis**, **Don Rubin**, **Bella Pace**, and me looking on. I've finished a nine-year term on the Cornell University Board of Trustees, where

there was much progress on research and student programs that bridge the Ithaca and Weill campuses. I am continuing as a WCM Overseer, so will be at 1300 York Avenue frequently. I'm mostly retired from the drug development services business we grew to 800 folks after acquisition a couple of years ago, though some consulting hours keep my hand in oncology. Otherwise, Susan and I travel a lot (Africa twice, Cuba, Galápagos, South America, Russia, Israel, Southeast Asia), do a lot of golf in the States and Europe, remain busy on some other nonprofit boards, and keep an eye on two grandsons in Nashville. We see **Peter Stone, MD '74,** and **David Fulton, MD '74,** in New England and California, where we spend some winter time away from the weather. Hope to see many of our classmates at Reunion 2020."

Suzanne M. de la Monte, MD '77: "I was appointed chief of pathology and laboratory medicine at the Providence VA Medical Center and vice chair of pathology at the Alpert Medical School of Brown University in July 2018."

Vincent "Vinny" de Luise, MD '77: "I have retired from active practice. I still teach in the Department of Ophthalmology at Yale University School of Medicine. I am currently researching and writing at the intersection of the humanities and medicine. I am program annotator for the superb Weill Cornell Music and Medicine Orchestra and a visiting scholar at Stony Brook University School of Medicine, and I will be a visiting professor at La Sapienza University in Rome, Italy."

Steven Schutzer, MD '79, and **Erol Fikrig, MD '85,** chaired the Cold Spring Harbor Laboratory Banbury Symposium on Protective Immunity and Vaccines for Lyme Disease. They are working on a novel anti-tick Lyme disease vaccine and diagnostics, and a paper is in progress. They recently published two papers, "Advances in Serodiagnostic Testing for Lyme Disease Are at Hand" and "Direct Diagnostic Tests for Lyme Disease."

Paul Skudder, MD '79: "Life is in transition to retirement, with part-time work at Southeastern Vascular Associates and in wound care settings. Hospital work, major procedures, and call are assumed by younger partners. My commitment to volunteer first responder work and teaching/training within

FAMILY AFFAIR: Edwin Zambrano-Acosta, MS '19, crosses the stage with his son to receive his degree in healthcare policy and research.

PHOTOS: PANICO

'At a conference in Augusta, ME, in April, I reconnected with Deb Hagler, MD '92. We have been living 30 miles apart, which is not far in Maine miles, yet did not connect until today. We took a selfie and will be sure to have coffee—we know many people in common!'

— Steven E. Diaz, MD '92

the National Ski Patrol continues to grow, as does other community involvement. Family life on Cape Cod offers wonderful opportunities, though grandchildren in Texas and Metro New York are too far away. I continue to see the wonderful gifts to Weill Cornell described in the frequent fundraising materials in the mail. I look forward to seeing Weill Cornell join NYU Langone and Kaiser in using these incredible resources to provide tuition-free undergraduate medical education."

1980s

Brad Radwaner, MD '80, writes that in addition to continuing his 27-year-old private cardiology practice in Manhattan (Cardiovascular Prevention PLLC), he has branched out into the treatment of varicose veins and chronic venous reflux disease, with the opening of Elite Veins NY. He notes that he even fits into his old cardiology fellowship scrubs!

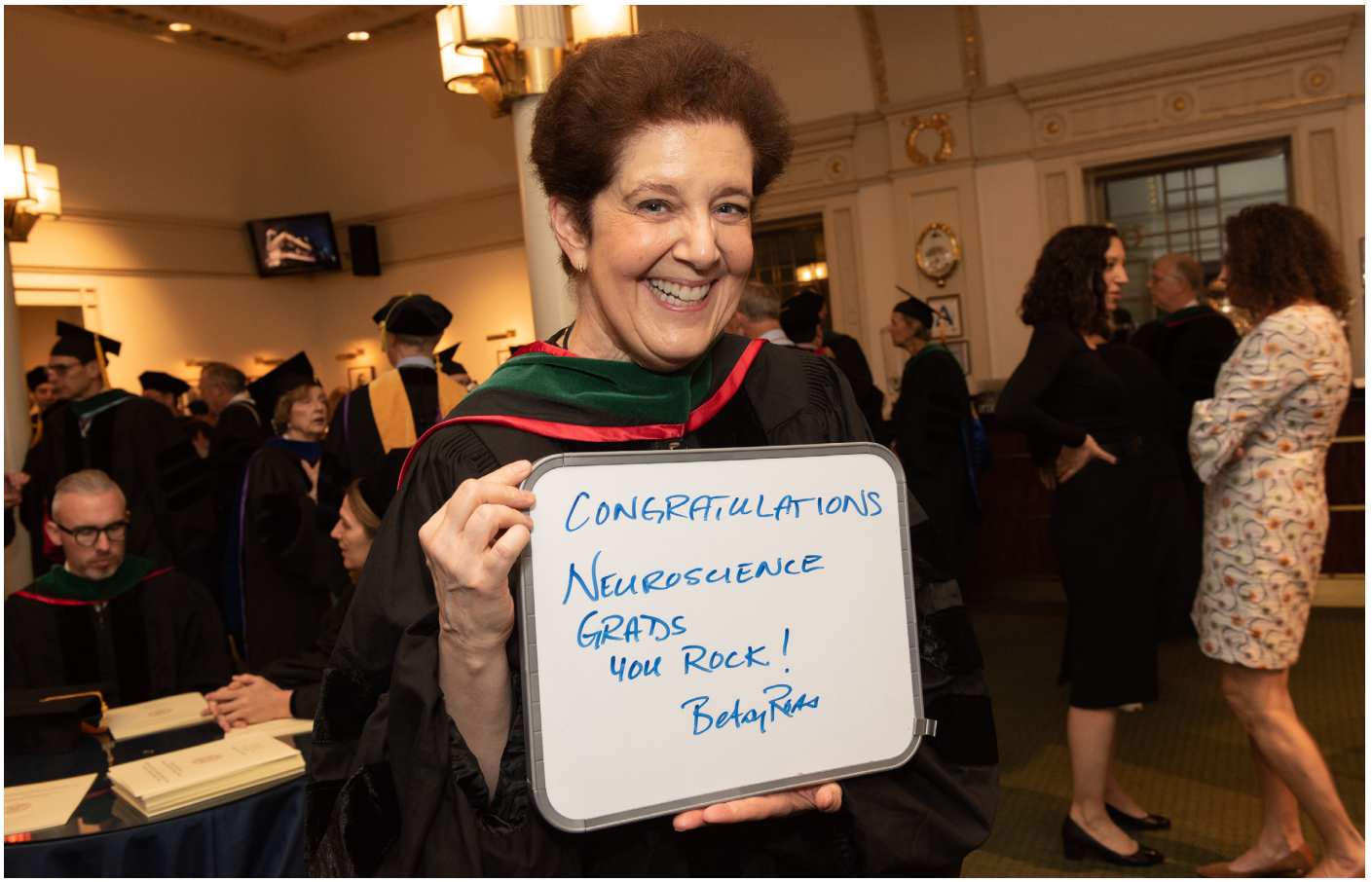
Scott D. Hayworth, MD '84, continues to serve as president and CEO of CareMount Medical PC (CMM), the largest independent multi-specialty medical group in the US. On January 1, the physicians and employees of the Murray Hill Medical Group joined CMM, establishing its presence in the NYC market. Dr. Hayworth is also CEO and board chairman of CareMount Health Solutions LLC (CMHS), a collaborative physician-owned management services organization launched by CMM in 2019. CMHS provides management services and expertise in population health for physicians, hospitals, and healthcare systems seeking to reduce costs, improve margins, and enhance the patient experience.

Roger Blumenthal, MD '85: "My wife, Wendy, and I became frequently traveling college lacrosse fans after our son, Ross, became the starting goalie at Drexel as a freshman. Among the most fun games was a one-goal win at Hofstra and 12 days later an upset win over top-seeded UMass in the CAA semifinals. It is very exciting but stressful to have a goaltender in the family with so many games decided by one or two goals."

Nan A. S. Hayworth, MD '85, a former US Congresswoman, is a strategic business development adviser for Pilot Growth Equity Partners and a frequent guest on television and radio providing commentary on government, healthcare, public policy, and politics. She has

MARCHING ON: Kuei-Chiu Chen, PhD (left), associate professor of biology, leads grads lined up for Commencement in Doha, Qatar.

PHOTO: JOHN SAMPLES



WAY TO GO: M. Elizabeth Ross, MD '79, PhD '82, the Nathan E. Cumming Professor of Neurology and Neuroscience and chair of the neuroscience graduate program, offers kudos to her former students.

PHOTO: PANICO

traveled the country to speak at forums including the r4 Leadership Council Conference and the 2019 John Breaux Symposium at Louisiana State University. She is board chair of ConservAmerica and a member of several other nonprofit boards, including the Independent Women's Forum, the Goodman Institute, Westchester County Health Care Corporation, and United Way of Westchester and Putnam, of which she is also a member of the Women's Leadership Council. She also serves on the advisory board of the politics department at Princeton.

Paul J. Hauptman, MD '87, is dean of the University of Tennessee Graduate School of Medicine in Knoxville (the main regional campus of the UT College of Medicine) and chief academic officer for University of Tennessee Medical Center.

Theresa Rohr-Kirchgraber, MD '88, and **Paul Kirchgraber, MD '88,** just became grandparents. Paul is traveling globally to help create new medicines through his work at Covance, and Theresa is practicing medicine at IU and treating eating disorders in adults with the Charis Center. Theresa remains in her role as chair of women's health.

Scott Rodeo, MD '89, and **Christine Frissora Rodeo '86, MD '90,** report that their son Scott has been accepted to Columbia University School of General Studies Postbaccalaureate Premedical Program; daughter Sarah is obtaining a degree from Yale Institute of Sacred Music, where her specialties include the organ; daughter Caitlyn is attending Millbrook School; and son Mark attends Cheshire Academy, where he is a major contributor to lacrosse and football.

1990s

Daniel B. Jones, MD '90, is a professor of surgery at Harvard Medical School and vice chair of surgery, technology, and innovation at Beth Israel Deaconess Medical Center, where he is also chief of the Division of Bariatric and Minimally Invasive Surgery. He recently co-edited a new textbook, *Operative Endoscopic & Minimally Invasive Surgery*, published by CRC Press.

Steven E. Diaz, MD '92: "At a conference in Augusta, ME, in April, I reconnected with **Deb Hagler, MD '92**. Deb is a pediatrician who moved to Maine about 25 years ago and is working out of the Brunswick area. I have been working out of the greater Augusta area for the last 26 years. We have been living 30 miles apart, which is not far in Maine miles, yet did not connect until today. We took a selfie and will be sure to have coffee—we know many people in common!"

Geetanjali Akerkar '88, MD '93: "Chairing Reunion with **Mia Talmor, MD '93,** allowed me to connect with so many classmates. We had a terrific turnout at our Class of '93 dinner: **Mike Johnson, Bob Cato, Lisa McCurry, Rob Shapiro, Mark Zoland, Maria Shiau, Jackie Ehrlich, Dave Cherry, Wendy Turchin, Miriam Bloom,** and **Liz Lazarus**. I'm excited to be back at 70th and York this summer as my son Neil will be working at WCM's Englander Institute for Precision Medicine. I am honored to be on the President's Council of Cornell Women (PCCW). My husband, Russ, and I are looking forward to traveling to Japan this summer and then Wyoming for a family vacation with our three sons.

Michael S. Irwig, MD '99, was promoted to professor of medicine at George Washington University.

GROUP SHOT: Dayyan Mohammed Adoor, MD '19, takes a selfie at the Qatar branch's Commencement.

PHOTO: SAMPLES

2000s

Piyush K. Agarwal, MD '00: "After finishing seven and a half years at the National Cancer Institute as the head of the Bladder Cancer Section in the Urologic Oncology Branch, I am moving to the University of Chicago to run one of the largest bladder cancer programs in the Midwest. I will be a full professor of urology/surgery, director of the Bladder Cancer Program, and director of the Urologic Oncology Fellowship."

Carin H. Gribetz, MD '00: "I am pleased to announce that I have moved my dermatology practice to 969 Park Avenue in New York City, where I continue to practice both medical and cosmetic dermatology."

Jian Shen, MD '02: "I continue to focus on the most advanced endoscopic surgeries of the cervical, lumbar, and thoracic spine. I have published six clinical study papers on endoscopic spine surgery in journals such as *World Neurosurgery*. I won the 2019 Parviz Kambin Award, the most prestigious international award in endoscopic spine surgery."

Rupa Krishnamurthy Wong, MD '02: "I co-founded the Association for Healthcare Social Media, the first nonprofit dedicated to positively influencing public health and healthcare through social media. We aim to accelerate the sharing of healthcare information over all platforms while advocating for the integrity of online medical information. Together with three other amazing female physicians, I also founded a conference for women physicians in private practice. In an era of continued gender pay disparity and workplace discrimination, the task of negotiating as a woman in the private practice sphere can be daunting. Our inaugural conference, Pinnacle, will be held December 6–8 at the Four Seasons in Dallas, TX. We seek to address the specific challenges that female physicians face by providing actionable information on tactics, tools, and strategies for running or joining a successful practice. Topics will include contract and salary negotiation, private practice management pearls, and branding and marketing. I hope some alumni will join me!"

Tali Lando, MD '04: I am a married mother of three girls, living in Westchester, NY, and a practicing pediatric otolaryngologist at ENT Faculty Practice in Ardsley, NY. After completing my residency in otolaryngology–head and neck surgery, I did a two-year fellowship in pediatric airway surgery at the Children's Hospital of Philadelphia. I started my current job straight out of fellowship. Last May, I published my first book: *Hell & Back: Wife and Mother, Doctor and Patient, Dragon Slayer.* It is available on Amazon and various other venues. Since then, I have written several articles and done various speaking engagements and podcasts related to the book. Check it out on my website, drtaliaronoff.com."

2010s

Stephanie Purisch, MD '12, completed her maternal fetal medicine fellowship at Columbia and will be joining its MFM faculty in September. She lives on the Upper West Side with her husband and their one-year-old son.

Neal S. Parikh, MD '13, became an assistant professor of neurology at Weill Cornell Medicine on July 1.

Kevin Johnson, MD '14: "I am the former head of Q! LGBTQ Students in Medicine at WCM. I finished my addiction psychiatry training this year and will be starting a transgender health clinic in Syracuse, NY. I have also been working as an editor for the second edition of *Trans Bodies, Trans Selves: A Resource for the Transgender Community.*"

Eda Dou, MD '16: "I'm a diagnostic radiology resident at NewYork-Presbyterian/Weill Cornell, currently finishing up my PGY-3 year. I was recently elected to the executive board of the New York Breast Imaging Society."

Graduate School of Medical Sciences

Bruce A. Sullenger, PhD '91, the Joseph and Dorothy Beard Professor in the Department of Surgery at Duke University Medical Center, was inducted as a fellow of the National Academy of Inventors last spring.

Maureen Gannon, PhD '96: "In recognition of the successful implementation of the Vanderbilt University Medical Center Mid-Career Leadership Development Program, I received an award at our end-of-year faculty assembly. I was honored to receive the Thomas A. Hazinski Award for Effectiveness in Monitoring Professional Development of Faculty, which is given every other year.

George T. Wu, PhD '07, joined the intellectual property group at the law firm of Lathrop Gage. He specializes in biomedical-related matters and cutting-edge technologies, and also counsels clients on patent applications and trademark and copyright registrations.

ALUMNI

'46 MD—Alexander R. Stevens Jr. of Seattle, WA, April 25, 2019; physician.

'49 MD—Harold W. Evans of Grand Forks, ND, October 29, 2018; internist, Grand Forks Clinic; worked with the University of North Dakota School of Medicine; Federal Aviation Agency medical examiner; Naval flight surgeon; veteran; enjoyed family genealogy, reading, golf, computer files, and ocean cruises; active in civic, community, and professional affairs.

'50 MD—Willard C. Thompson Jr. of Charlotte, NC, May 10, 2019; surgeon; chief of staff, Presbyterian Hospital; veteran; enjoyed classical music, astronomy, wilderness adventures, and woodworking.

'51 MD—E. William David Jr. of New York City, May 5, 2019; pioneer in the field of medical ethics; clinical professor of obstetrics and gynecology, Weill Cornell Medicine; first director of quality assurance and VP of medical affairs, New York Hospital; served in the OSS in World War II; active in community and professional affairs.

'54 MD—Walter L. Freedman of Tucson, AZ, December 3, 2018; former chief of ob/gyn at Denver Health; veteran.

'57 MD—John S. Madaras of Short Hills, NJ, April 9, 2019; thoracic and cardiovascular surgeon; veteran; enjoyed golf, sports, photography, ornithology, and travel.

'61 MD—James W. Ryan of Augusta, GA, May 4, 2019; professor emeritus, University of Miami; established the Lee Walter and Emma Elizabeth Haddox Ryan Memorial Endowed Scholarship Fund at WCM.

FACULTY

David A. Hamburg, MD, of Washington, DC, April 21, 2019; had a wide-ranging and distinguished career as a clinician, scientist, and public servant who advanced humanitarian programs; did early and seminal work on the impact of stress on the brain; awarded the Presidential Medal of Freedom in 1996 for his work toward understanding human behavior, preventing violent conflict, and improving the health and wellbeing of children; as chair of psychiatry at Stanford University in the early 1970s, created a multidisciplinary department that became a national model; served as president of the Institute of Medicine (now the National Academy of Medicine); directed the Division of Health Policy Research and Education at Harvard University; served as president of the Carnegie Corporation for nearly two decades, promoting peer counseling and after-school programs in the US and the development of policies and programs to prevent war and genocide across the globe; chaired commissions for the United Nations and European Union; since 2003, was a DeWitt Wallace Senior Scholar in the Department of Psychiatry at WCM, where he produced *Preventing Genocide: Practical Steps toward Early Detection and Effective Action* and *Learning to Live Together: Preventing Hatred and Violence in Child and Adolescent Development,* the latter co-authored with his late wife, Betty Hamburg, MD, who was affiliated with WCM's Department of Psychiatry.

We want to hear from you!

Share your news with your classmates

Email Chris Furst: cf33@cornell.edu

Send by mail to: Weill Cornell Medicine
401 East State Street, Suite 301
Ithaca, NY 14850

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Family Man

Fertility doctor Pak Chung, MD, gets a creative thank-you from some grateful patients

THE GREATEST GIFT: Pak Chung, MD (top right), was surprised with a book of patient portraits and (above) a gathering of some of the families he's helped create.

Earlier this year, some twenty families gathered in a conference room at the Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine. They kept their voices hushed as they waited for the arrival of the person they all had in common: Pak Chung, MD, an attending physician at the center and an associate professor of clinical obstetrics and gynecology. "When I walked in, for a second I didn't know what was going on," Chung recalls. "Then I took a closer look and realized that I knew them all—they were all my patients."

As a speechless Chung took in the crowd, he began to notice the many children, from infants to tweens—all of whom exist in large part because of his work. It was then that the group presented him with a second surprise: a custom-made hardcover book filled with black-and-white portraits of thirty-eight families whose children were conceived with Chung's help. Alongside each professional-quality photo is a personal message of gratitude from the parents. "When all seemed lost, we found you," reads one. Says another: "Every day, when we sit together at the dinner table, play together in the park, or read a story before bedtime, we think about how none of it would have been possible without your guidance . . . and emotional support." On the volume's last page, a blank space represents all of the "Chung babies" who are yet to be born.

"I could talk all day long about how wonderful Dr. Chung is," says Lindsay Cook, a children's photographer who spent months organizing both the book—she took most of the portraits in the Manhattan studio where she works—and the surprise party. Cook and her husband came to Chung in 2014; after undergoing several types of procedures, including in vitro fertilization, they are now the parents of healthy one-year-old twins, daughter Audrey and son Evan. "There's not a day that goes by that I don't think of him," says Cook. "I see him when I see my babies, and I always will."

After the birth of their twins, the Cooks were left with a daunting question: how does one thank the person who helped create their children? "I thought maybe I would send him a picture, but that just didn't do it justice," Cook says. "It finally struck me that if I feel this way about him, I'm sure other people do too." She took to social media, seeking fellow Chung patients through the UES (Upper East Side) Mommas Facebook group. "Within two hours, the post had 1,000 likes and people were commenting from all over the world about how amazing he was," she says. "People started calling the studio, and the rest is history."

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Chung, who joined the WCM faculty in 1996, says that the appreciation goes both ways. "I feel so honored and fortunate to be able to work with these patients, who gave their trust and faith in me and the center—however, what I can provide for patients is a collective effort under the visionary leadership of our mentor, Dr. Zev Rosenwaks," says Chung, who estimates that he has helped enable more than 4,000 births over the course of his career. As Cook adds with a laugh: "When my kids are old enough to ask where babies come from, I'm going to explain to them that they come from Dr. Chung." ■

— Alexandra Bond

PHOTOS: JASON PERALTA

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