weillcornellmedicine

THE MAGAZINE OF WEILL CORNELL MEDICAL COLLEGE AND WEILL CORNELL GRADUATE SCHOOL OF MEDICAL SCIENCES

VOL. 14, NO. 2

Personal Touch

New diagnostic methods are revolutionizing cancer treatment—and much more

Students in the audience at this year's Salute to Scholarship

Jeanne and Overseer Herbert Siegel with recipients of the Siegel Family Student Prizes

SALUTE TO **SCHOLARSHIP**

Members of Weill Cornell's Class of 2018

Dean Glimcher with the Salute to Scholarship panelists

Salute to Scholarship at Weill Cornell is always an exciting and special event for both donors and students, and this year was no exception. The event, which brings together donors, students, alumni and faculty to celebrate scholarship, was held on April 23 in Olin Hall.

Following opening remarks by recent MD/MBA graduate Zachary Strasser, MD '15, Dean Glimcher welcomed guests and moderated a panel discussion with Timothy Dutta, MD '99, Clinical Associate Professor of Medicine; Overseer Catherine Hart, MD, Clinical Associate Professor of Medicine; Richard Levine, MD '66, Professor of Obstetrics and Gynecology at Columbia University Medical Center; and Dr. Strasser on the important role of philanthropy in nurturing students' ambitions and maintaining the excellence of medical education at Weill Cornell.

The event culminated in the annual bestowing of the Siegel Family Student Prize to eight outstanding Medical College students, each of whom will receive a $25,000 scholarship. The Siegel Family prizes were established by longtime supporters Jeanne and Overseer Herbert Siegel.

This is an exciting time to support scholarship and education at Weill Cornell. In late 2014, the Medical College launched the $50 million Campaign for Education, which will bolster our new curriculum, increase our scholarship endowment, strengthen critical student resources, and support new and current faculty members. These efforts will continue to keep Weill Cornell at the vanguard of medical education.

2015

To learn more about giving to education, contact:

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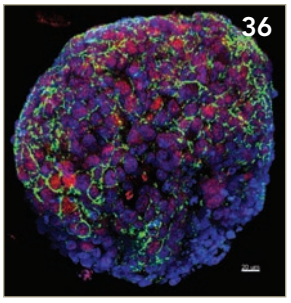

FEATURES

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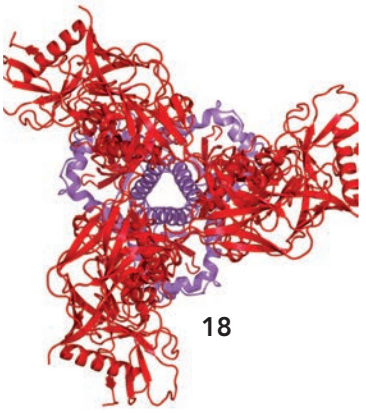

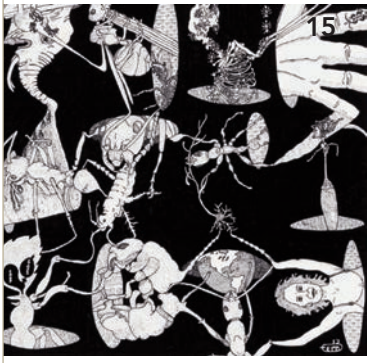

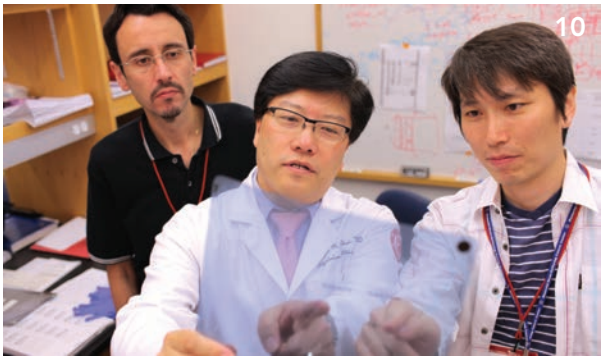

DEPARTMENTS

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The Promise of Early Discovery

Laurie H. Glimcher, MD,
Dean of the Medical College

LISA BERG

A few years ago, biochemist Frederick Maxfield, PhD '77, hit upon some promising results in the lab—a discovery that offered new hope for patients with Niemann-Pick Type C, a rare and fatal disease often called "childhood Alzheimer's." Then he was told something that's all too familiar to many medical researchers: his idea was considered too preliminary to attract interest from pharmaceutical companies or granting agencies. Without the funding to pursue it further, his work in this area stalled.

Then last year, Maxfield's project became one of seven accepted by the new Tri-Institutional Therapeutics Discovery Institute (Tri-I TDI). This nonprofit incubator—jointly run by Weill Cornell Medical College, Memorial Sloan Kettering Cancer Center, and The Rockefeller University—is changing the way therapies are brought to market by supporting early-stage drug development. Seeking to narrow the chasm that has traditionally separated academia and industry, the Institute allows scientists from each sector to work side by side, contributing their different strengths and ways of thinking. In doing so, the Institute will shepherd promising early discoveries through the proof-of-concept stage, presenting a more attractive opportunity for pharmaceutical company investment.

Tri-I TDI, which you'll read about in this issue, is an example of Weill Cornell's commitment to pioneering innovative, twenty-first century approaches to support basic science—something that's essential to the development of new and better therapies for patients with so many different diseases. Consider the success we have had in treating lymphoma, which is the focus of another story in this issue of Weill Cornell Medicine. Leandro Cerchietti, MD, has spent many years in the lab developing new ways to treat a highly aggressive form of lymphoma, one that's resistant to chemotherapy. By learning how epigenetic alterations switch off genes that normally trigger cell death, Cerchietti discovered a drug that reverses that process, essentially reprogramming the lymphoma into a less aggressive disease. That biochemical understanding of DNA led to a proof-of-concept trial in which eleven out of twelve patients achieved complete remission, proving that supporting basic science translates into saving lives.

Investing in early research is a key part of our mission to put the patient at the center of everything we do. Another Weill Cornell initiative—the Caryl and Israel Englander Institute for Precision Medicine, directed by Mark Rubin, MD, and also featured in this issue—is poised to lead the way in treating cancers and other diseases on the basis of an individual's genome and a molecular understanding of disease. Recent successes at the Institute, which opened nearly three years ago as one of the first of its kind, provide a glimpse of the future as data-driven technologies combine with our deepening understanding of human biology and chemistry to offer personalized and individually tailored therapies for especially intractable conditions. Precision medicine is already enabling a sea change in oncology, and innovations in the field are showing tremendous potential for the treatment of numerous other diseases.

These examples are just a few of many that demonstrate the promise and the payoff of early discoveries. They highlight the deep commitment we at Weill Cornell have to advancing human health by supporting foundational science as well as clinical care. And they illuminate the need for our society to make a renewed commitment through public funding for biomedical research at every stage. It is these commitments that will sustain and enhance patient care in the twenty-first century.

The Belfer Research Building: Unprecedented Growth

Just over a year since its ribbon-cutting, the Belfer Research Building is almost completely occupied

Richard Isaacson, MD, Director of the Alzheimer's Prevention Clinic, consults with Gregory Petsko, DPhil, Director of the Appel Alzheimer's Disease Research Institute, while new recruits Manu Sharma, PhD, and Jacqueline Burré, PhD, both Assistant Professors of Neuroscience at the Feil Family Brain and Mind Research Institute, work in a laboratory in the Belfer Research Building.

At the Belfer Research Building's ribbon-cutting ceremony in January 2014, the Weill Cornell community was abuzz, anticipating the potential for breakthroughs in research and patient care. Today, thanks to the continued dedication of numerous donors and the thoughtful planning and execution of the Medical College and University leadership, the building has already begun to fulfill the shared vision of physician-scientists working side-by-side to make groundbreaking medical discoveries that translate into better treatments, and even cures, for patients.

The 18-story building has 13 lab floors, each with 21,000 square feet of dedicated research space, and each laboratory, office and conference space was created with collaboration in mind. To date, in these laboratories and offices, 55 individual investigators and more than 300 junior scientists work together daily toward resolving today's most critical health concerns. The building now houses the Joan and Sanford I. Weill Center for Metabolic Health, the Sandra and Edward Meyer Cancer Center, the Helen and Robert Appel Alzheimer's Disease Research Institute, the Feil Family Brain and Mind Research Institute, the Gale and Ira Drukier Institute for Children's Health, the Jill Roberts Institute for Research in Inflammatory Bowel Disease, the Dalio Institute of Cardiovascular Imaging, the Tri-Institutional Therapeutics Discovery Institute, and more.

These multidisciplinary research powerhouses exist thanks, in part, to the generosity of the donors for which they're named, and the partnerships between these institutes and their clinical counterparts will spark innovations in research and patient care for generations to come.

To date, in these laboratories and offices, 55 individual investigators and more than 300 junior scientists **work together** daily toward resolving today's most critical health concerns.

To make an impact through giving at Weill Cornell, please contact:
Lucille Ferraro, Campaign Director, at (646) 317-7387 or luf2003@med.cornell.edu.

Gift Establishes Englander Institute for Precision Medicine

JASON ANDREW/GETTY IMAGES/WCMC

Precision team: (From left) Physician-scientist Jonathan Zippin, MD-PhD; Chair of Dermatology Richard Granstein, MD; Englander Institute Director Mark Rubin, MD; and physician-scientists Himisha Beltran, MD, and Olivier Elemento, PhD. The Englander Institute's expanded program will target additional areas of oncology including melanoma, a rare but serious form of skin cancer.

A significant investment in Weill Cornell's leading precision medicine program by Overseer Israel Englander and his wife, Caryl, will expand the scope of the institution's approach to understanding and treating disease through therapies customized to patients' unique genetic profiles.

The gift names the Caryl and Israel Englander Institute for Precision Medicine at Weill Cornell Medical College. The institute uses genomic sequencing to better understand the factors that drive disease development and progression and identify treatments that are most likely to be effective for each patient. The Englander Institute has focused on cancer since its inception in 2013 and this generous gift will widen its mission to emphasize dermatological malignancies as well as metabolic diseases, cardiovascular disease, genetic disorders, and respiratory diseases. The Institute plans to eventually offer precision medicine to as many as 6,000 cancer patients a year.

"We are deeply grateful to the Englanders for their visionary gift, which will enable Weill Cornell to transform the way we practice medicine," said Dr. Laurie H. Glimcher, the Stephen and Suzanne Weiss Dean of Weill Cornell Medical College. "Precision medicine offers great hope for understanding and treating some of the most formidable diseases of our time, and the Englanders' support will ensure that we can continue our work to enhance the care we provide our patients, both now and into the future."

For more on the Englander Institute and precision medicine, see "A Precise Approach" on page 36.

Grant Funds Stem Cell Work on Blood Disorders

A consortium of scientists and transplant clinicians from Weill Cornell and Memorial Sloan Kettering Cancer Center has been awarded a four-year, $15.7 million grant from the New York State Stem Cell Science Program (NYSTEM) to support research on new treatments for blood cancers and disorders such as sickle cell anemia. The consortium, comprising investigators from Weill Cornell's Ansary Stem Cell Institute and Sloan Kettering's Center for Cell Engineering, is conducting two clinical trials using an innovative method for nurturing hematopoietic stem cells outside the body. The first will use the approach on umbilical cord blood stem cells for transplantation in patients with blood cancers; the second aims to employ the method to cure sickle cell by correcting the disease's genetic abnormality in each patient's blood stem cells, then returning them to the body. The grant's principal investigator is Shahin Rafii, MD, director of the Ansary Stem Cell Institute and a professor of medicine, genetic medicine, and reproductive medicine.

New Cornell President Takes Office

Over the summer, Cornell University welcomed its thirteenth president. Elizabeth Garrett, the first woman to hold the office, began work in July. A prominent legal scholar, Garrett comes to Ithaca from the University of Southern California, where she served as provost. "With Beth joining the Cornell family as its first female president, we have forged a pioneering new chapter in our history," Dean Laurie H. Glimcher, MD, said at the time of Garrett's appointment, adding, "As a great research university, Cornell has the power to make a difference in the world, and I am thrilled to see what we can accomplish." Garrett succeeds cardiologist David Skorton, MD, now head of the Smithsonian Institution in Washington, DC.

ROBERT BARKER/UPHOTO

Elizabeth Garrett

LINDSAY FRANCE/UPHOTO

Nancy and Peter Meinig

$50 Million Gift for Biomedical Engineering

A $50 million gift has endowed a school of biomedical engineering on the Ithaca campus—strengthening collaborations with colleagues at the Medical College and enhancing the University's overall research and educational presence in the field. The gift comes from Cornell undergraduate alumni Nancy and Peter Meinig and their children. "Their new gift sets us on a course for increased impact in biomedical engineering and the convergent biosciences, an interdisciplinary effort that will drive advances in health and well-being over the next decades," says President Garrett. "The Meinig School will be a powerhouse of teaching and research with consequence for generations to come."

Surgeon Tapped as Giants Team Doc

Scott Rodeo, MD '89, a professor of orthopaedic surgery at Weill Cornell, has been named head team physician for the New York Giants. An associate team physician for the football squad since 2000, he has also treated American athletes at three summer Olympics. Rodeo is an attending surgeon at NYP/Weill Cornell and Hospital for Special Surgery.

TIP OF THE CAP TO...

Owen Davis, MD, professor of reproductive medicine, obstetrics, and gynecology, named president-elect of the American Society for Reproductive Medicine's board of directors.

Sabine Ehrt, PhD, professor of microbiology and immunology, elected a fellow of the American Academy of Microbiology.

Antonio Gotto Jr., MD, DPhil, dean emeritus, professor of medicine, and Weill Cornell overseer, winner of the Excellence in Academic Medicine Award from National Medical Fellowships, which lauded his work in establishing the Medical College's Office of Faculty Diversity in Medicine and Science.

O. Wayne Isom, MD, the Terry Allen Kramer Professor of Cardiothoracic Surgery, winner of a Lifetime Achievement Award from the American Heart Association.

Dattatreyudu Nori, MD, professor of clinical radiation oncology, awarded the Padma Shri from the Indian government—one of the nation's highest civil honors—for his contributions to cancer care.

Susan Pannullo, MD '87, associate professor of clinical neurological surgery, elected to a three-year term on the American Association of Neurological Surgeons' board of directors.

Peter Schlegel, MD, chairman of urology, the James J. Colt Professor of Urology, and a professor of reproductive medicine, named an honorary NYPD police surgeon.

Manikkam Suthanthiran, MD, the Stanton Griffis Distinguished Professor of Medicine, winner of the International Society of Nephrology's Jean Hamburger Award, which recognizes outstanding research with a clinical emphasis.

CHRISTOPHER LANE

Olga Boudker, PhD

Boudker Named Hughes Investigator

Olga Boudker, PhD, associate professor of physiology and biophysics, has been named a Howard Hughes Medical Institute Investigator. Out of some 900 applicants for the most recent round of awards, she was one of twenty-six scientists to receive the designation, which comes with unrestricted research support. Boudker's lab focuses on how glutamate pumps, which play an important role in brain function, work on the molecular level. The research could lead to new therapies for patients with brain disease and injury.

Biostatistics Names New Chief

A renowned biostatistician from the Mayo Clinic has joined the Weill Cornell faculty in a leadership role. Karla Ballman, PhD, is now chief of the Division of Biostatistics and Epidemiology in the Medical College's Department of Healthcare Policy and Research. A doctoral alumna of MIT, Ballman specializes in designing clinical trials, analyzing complex data, and developing molecular signatures that can help predict whether or not a cancer patient will respond to targeted therapies. Ballman is an associate editor for the *Journal of Clinical Oncology* and has published more than 130 peer-reviewed articles.

WCMC

Karla Ballman, PhD

Breakout Awards Honor Six Postdocs

The winners of the first round of Tri-Institutional Breakout Awards for Junior Investigators have been announced. The prizes, which each carry a $25,000 award, will be given annually to outstanding postdocs at Weill Cornell, Sloan Kettering, and the Rockefeller University. They were established with seed money from the three winners of the 2013 Breakthrough Prize in Life Sciences: Rockefeller's Cornelia Bargmann, PhD; Weill Cornell's Lewis Cantley, PhD '75; and Sloan Kettering's Charles Sawyers, MD. That award, which includes a $3 million cash prize for each winner, was established by several prominent tech entrepreneurs including Facebook's Mark Zuckerberg and Google's Sergey Brin.

The six inaugural winners of the Breakout Prize include two from Weill Cornell: Dilek Colak, PhD, who is investigating the mechanisms behind neurodevelopmental diseases in the lab of Samie Jaffrey, MD, PhD, professor of pharmacology; and Costas Lyssiotis, PhD, who recently joined the University of Michigan faculty after working in Cantley's lab on the biochemical pathways of pancreatic tumor growth.

Cantley Wins Ross Prize

WEST VIRGINIA WESLEYAN COLLEGE

Lewis Cantley, PhD '75

Lewis Cantley, PhD '75, the Meyer Director of the Sandra and Edward Meyer Cancer Center and the Margaret and Herman Sokol Professor in Oncology Research, has been awarded the Ross Prize in Molecular Medicine from the Feinstein Institute for Medical Research. The honor, which includes a $50,000 gift, recognizes scientists who have made distinguished contributions to understanding how human disease develops and might be best treated, and who show promise for future contributions to molecular medicine. Cantley was recognized for his groundbreaking discovery, more than two decades ago, of the enzyme PI3-kinase and the signaling pathway that it controls, which play key roles in most cancers and are now promising drug targets. In accepting the award, Cantley acknowledged the contributions of "an incredible group of brilliant students and postdoctoral fellows and collaborators."

Dean Glimcher Profiles WCMC Mentors

Dean Glimcher is hosting a Web video series that spotlights aspects of life at the Medical College. Entitled *Inside Medicine at Weill Cornell*, the show focused its first season on the vital role of mentorship. It showcased Glimcher's work with one of her own mentees, Sarah Bettigole, PhD, then a doctoral student in immunology; the relationship between Connor Liston, MD '08, PhD, assistant professor of neuroscience and psychiatry in the Feil Family Brain and Mind Research Institute, and his mentor, BJ Casey, PhD, the Sackler Professor of Developmental Psychobiology; and the guidance that students receive from patients who participate in the LEAP (Longitudinal Educational Experience Advancing Patient Partnerships) program.

"No one succeeds in medicine alone," Glimcher says. "Students become better doctors when they are inspired by the wisdom of their peers. Young scientists make the discoveries that transform patient care when senior faculty take an active and sustained interest in guiding them toward research they might not otherwise have had the confidence to pursue. And physicians are made better when they learn from their patients." The show can be viewed at inside.weill.cornell.edu.

WCMC

Words of wisdom: Dean Laurie H. Glimcher, MD, with one of her mentees, Sarah Bettigole, PhD

FROM THE BENCH

Food Order Found to Impact Blood Sugar


CARLOS RENE PEREZ

Louis Aronne, MD

A simple strategy may help people with type 2 diabetes control their blood sugar. According to a study in *Diabetes Care*, the order in which foods are consumed—specifically, eating protein and vegetables before carbohydrates—can lead to lower post-meal levels of glucose and insulin. "Carbohydrates raise blood sugar, but if you tell someone not to eat them, it's hard for them to comply," explains senior author Louis Aronne, MD, the Sanford I. Weill Professor of Metabolic Research. "Based on this finding, instead of saying, 'Don't eat that' to their patients, clinicians might say, 'Eat this before that.' "

Tracking Pancreatic Cancer's Spread


ABBOTT

David Lyden, MD, PhD

Nearly 40,000 Americans succumb to pancreatic cancer each year—but an international team led by Weill Cornell researchers is offering new hope by shedding light on the mechanics behind one of its direst outcomes. In *Nature Cell Biology*, David Lyden, MD, PhD, and colleagues describe the molecular process by which pancreatic cancer spreads to the liver, the most common reason why patients succumb. In the study, conducted in a mouse model, the team mapped the cancer's advance and attempted to block each stage. "Disrupting just one part of the process at any point of the circuit decreased metastasis, a discovery that could lead to the development of multi-targeted therapies that could prolong patients' lives," explains Lyden, the Stavros S. Niarchos Professor in Pediatric Cardiology and the study's senior author. The disease is one of cancer's most lethal forms, with just 6 percent of patients living five years after diagnosis.

Immune Cells Point to HIV Therapy

The body's own immune cells may be critical components in HIV therapy, reports an article in *Nature Communications*, with Dean Laurie Glimcher, MD, as senior author. "Our study has uncovered a potentially potent arsenal that patients have against the virus," says lead author Stanley Adoro, PhD, instructor of microbiology and immunology in medicine. The work, which could inform development of a vaccine against the virus, outlines a way to limit replication of HIV in the early stages of infection. It hinges on Interleukin-21 (IL-21), a substance produced by key immune cells, which not only jump-starts the immune system but hinders HIV from replicating. Unfortunately, though, the virus impairs its production. The team aims to better understand this process in the hope of harnessing IL-21's power to battle HIV.

Why Does the Gut Ignore Helpful Bacteria?

Until now, the body's method for maintaining a healthy gastrointestinal tract—treating the roughly 100 trillion beneficial bacteria that inhabit it as friends rather than enemies—has been a mystery. But a study published in *Science* sheds light on why the immune system doesn't attack these organisms—pointing the way toward new treatments for inflammatory bowel diseases, including Crohn's and ulcerative colitis. The work focuses on T cells, immune cells that can recognize, eliminate, and remember foreign microbes. The team's new understanding of how the cells learn to ignore microscopic helpers "demonstrates that there may be an efficient way to eliminate pro-inflammatory T cells in the intestine that attack beneficial bacteria," says senior author Gregory Sonnenberg, PhD, assistant professor of microbiology and immunology and a member of the Jill Roberts Institute for Research in Inflammatory Bowel Disease.

Gene Test Could Inform PTSD Treatment


ABBOTT

Francis Lee, MD, PhD

One-fifth of Americans have a genetic variation that affects how they process anxiety and fear, a Weill Cornell team reports. The discovery, described in *Nature Communications*, could lead to a genetic biomarker for which clinicians could test patients, to develop personalized therapies before prescribing medications or offering other interventions. "If a patient has PTSD, before coming up with a treatment plan, you could conduct a simple genetic test and determine who might respond better or worse to these drugs," says co-senior author Francis Lee, MD, PhD, the Mortimer D. Sackler, MD, Professor of Molecular Biology in Psychiatry.

Informal MD Networks Can Improve Outcomes

As doctors refer their patients to specialists they know and trust, they develop unofficial networks. In *Medical Care*, Lawrence Casalino, MD, PhD, the Livingston Farrand Professor of Public Health, and colleagues report that such networks can improve outcomes and lower costs—and suggest that other groups, such as hospitals and insurers, could learn from them. The study identified 417 informal physician networks and tracked their quality of care by identifying potentially preventable hospital admissions of patients with chronic conditions like congestive heart failure and asthma.

An Immune Defense Against Ovarian Cancer


PEREZ

Juan Cubillos-Ruiz, PhD

Ovarian cancer, which costs the lives of more than 14,000 American women each year, works by shutting down immune cells that would otherwise defend against the disease. But in *Cell*, researchers led by Dean Glimcher describe a discovery that she calls "a bright beacon of hope"—the identification of the gene that ovarian cancer switches on to prevent immune cells from fighting back. The team, which includes Juan Cubillos-Ruiz, PhD, assistant professor of microbiology and immunology in obstetrics and gynecology, is working to develop a therapy to inhibit that process. Says Glimcher: "Harnessing the natural ability of our immune system to eliminate malignant cells represents the most promising anti-ovarian cancer strategy since the development of chemotherapy."

Study Explores Obesity's Link to Breast Cancer

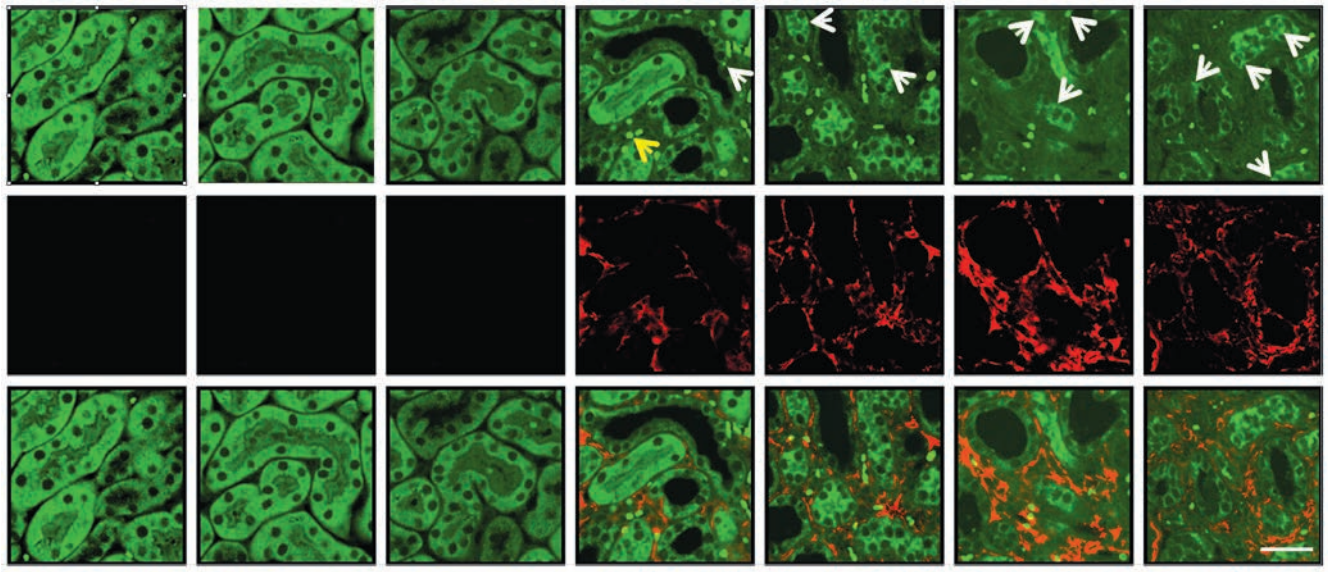

ABBOTT

Andrew Dannenberg, MD

A collaboration between Weill Cornell researchers and colleagues in Ithaca has helped explain why obese women have a higher risk of breast cancer. In work published in *Science Translational Medicine*, the investigators describe how obesity leads to a stiffening of the meshwork of material that surrounds fat cells in the breast—called the extracellular matrix—and that these changes create the right conditions for tumor growth. Due to this, the researchers say, clinicians may need to employ finer-scale mammography imaging, especially for obese women. Andrew Dannenberg, MD, the Henry R. Erle, MD-Roberts Family Professor of Medicine and associate director of cancer prevention in the Sandra and Edward Meyer Cancer Center at Weill Cornell, was the study's co-author.

The Autophagy Paradox

Could a process that's normally essential to life be a root cause of COPD?



Organ damage: In a mouse model of kidney fibrosis, epithelial cells show evidence of autophagy (the green spots marked by arrows), which was mounted as a defense against scarring (seen in red).

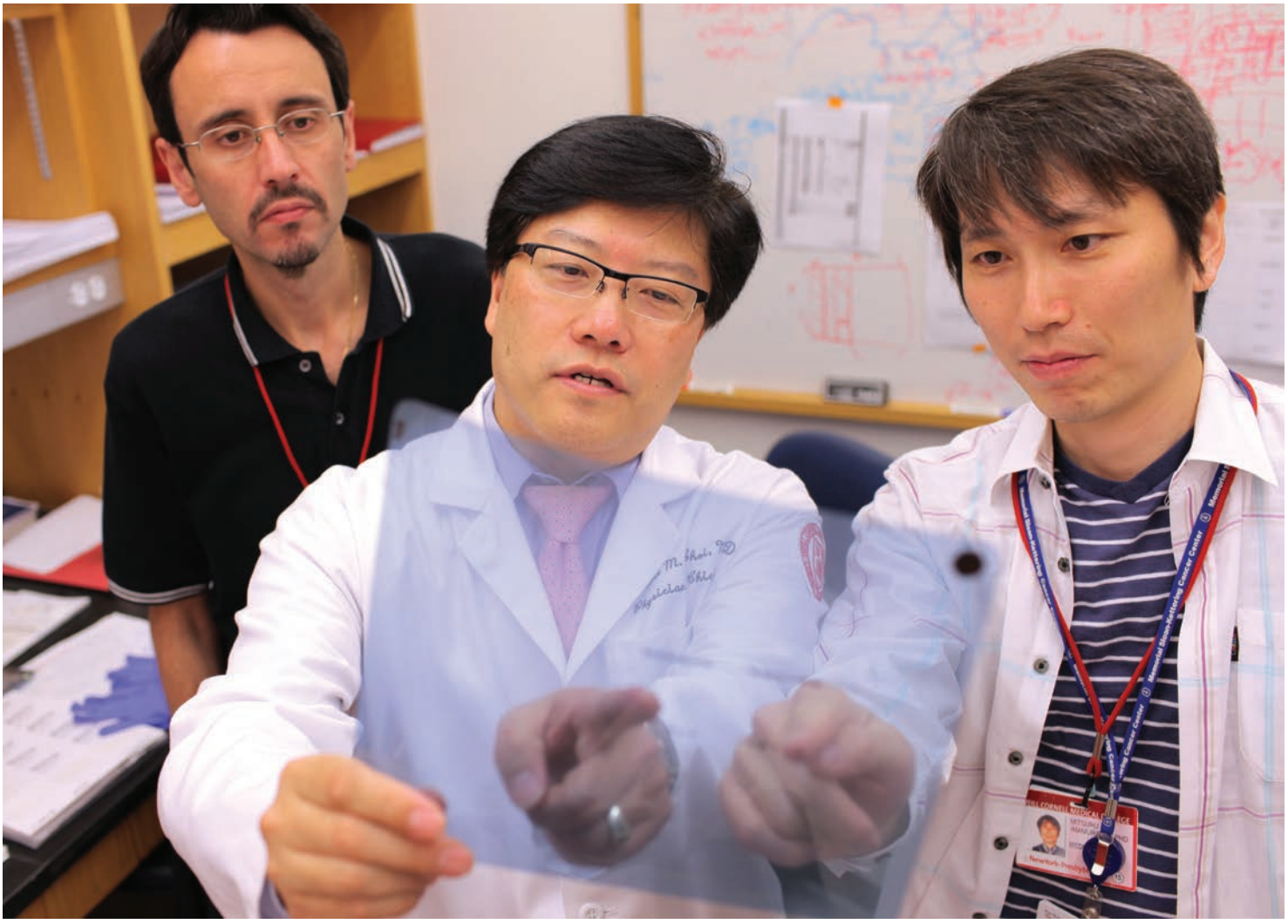
'We have to be cautious and systematic about how and when to target the autophagy in COPD.'

Chronic obstructive pulmonary disease (COPD) kills some 130,000 Americans every year—including, in February, the actor Leonard Nimoy, beloved by millions for playing Mr. Spock on TV's "Star Trek." While the disease—the third-leading cause of death in the U.S.—is strongly associated with smoking, its underlying causes have never been clear, and effective treatments have proven elusive. "Right now, all you can do is mitigate it," says Augustine Choi, MD, the Sanford I. Weill Chairman of the Weill Department of Medicine. "There's no cure." But Choi may have found an important clue to how COPD happens—and surprisingly, it's a process that is normally fundamental to our survival.

Known as autophagy, it's a mechanism in which cells conserve energy and nutrients by consuming damaged or unneeded organelles—the tiny structures that perform various functions within each cell. "When people are starving, autophagy is critical," Choi explains. "But it also regulates inflammation, cell growth, and many other processes." For example, in 2010 Choi and his team reported in *Nature Immunology* that autophagy confers a potent anti-inflammatory effect in acute inflammatory conditions. "The complexity of this," he notes, "is highlighted by the fact that in some other diseases of the lung, like pulmonary hypertension, autophagy is a good thing."

But that is not the case in COPD. Choi and his team had previously found higher rates of autophagy in the lungs of people with COPD, and they have demonstrated that this leads to cell death that ultimately affects pulmonary function. In a paper published last fall in the *Journal of Clinical Investigation*, they explained that when cigarette smoke enters the air sacs in a smoker's lungs, it harms their mitochondria, the organelles that serve as cellular power plants. The cells are prompted to destroy their damaged mitochondria, but then they become unstable and are killed off. "The obvious question then is, can we block autophagy with new chemical inhibitors or drugs?" Choi says. "This has significant therapeutic implications, for sure, but we have to be cautious and systematic about how and when to target the autophagy in COPD."

Autophagy was first described in the Sixties, and for the next few decades it was



JOHN ABBOTT

Autophagy investigators: Augustine Choi, MD (center), with research fellows (left) Ilias Siempos, MD, DSc, and Mitsuru Imamura, PhD

the province of cell biologists, who studied the process in yeast. It was only within the last ten to fifteen years, Choi says, that scientists began to investigate autophagy in humans. And since 2008, when his team first published findings about autophagy in lung tissue from COPD patients, other researchers have begun to investigate its role in a host of other human diseases. "We got into the game a bit earlier than most people," Choi says. "Now you can't pick up a journal without seeing a paper on autophagy. The cancer guys have been doing a lot of autophagy work. Alzheimer's, Parkinson's, infectious disease—I could go on and on." At Weill Cornell alone, researchers have found links between autophagy and gynecologic cancers, female genital tract infection, pancreatic cancer, metabolic diseases, and kidney failure.

Over the years, Choi has seen attitudes toward COPD shift significantly. It was once considered hopeless, he says, and research funding was limited in part because patients with diseases linked to smoking were not seen sympathetically. But while COPD patients may be haunted by the stereotype of the unrepentant lifelong smoker, the disease can develop decades after people quit, as in Nimoy's case. It can also strike non-smokers, for reasons that are still unknown. "The incidence of COPD not related to cigarette smoking is increasing," Choi says "Whether it's pollution, particulate matter in the environment, infections, or a virus—we don't know." And that's just one of the many questions Choi and his colleagues are working to answer. They are also looking into how protective mechanisms in the lungs could offset autophagy, and they're trying to find a way to detect COPD with a simple blood test rather than a CAT scan.

Among the Weill Cornell researchers working on autophagy is Choi's wife, Mary Choi, MD. An associate professor of medicine in the Division of Nephrology and Hypertension, she is leading investigations into its role in diseases of the kidney. She has found that impaired autophagy could lead to kidney fibrosis, a common feature in kidney failure and diabetic nephropathy—which means that therapies targeting autophagy could potentially restore kidney function. The couple came to Weill Cornell in 2013 from Boston, where both were on the faculty at Harvard Medical School and he was chief of pulmonary and critical care medicine at Brigham and Women's Hospital. There, as at Weill Cornell, patient care was a major aspect of his work. "Seeing patients gives you focus, and it helps you identify the questions that we need to address," Choi says. "Patients are what it's all about—you're trying to make an impact on human disease."

— Amy Crawford

Print It!

The library's new open-access 3D printer gets rave reviews

ABBOTT (LEFT AND BELOW)

Total fabrication: MD-PhD student Du Cheng with the 3D printer. Inset: A custom-made device attaches a smartphone to a microscope.

In the spring of 2014, first-year MD-PhD student Du Cheng brought a bone fragment from an anatomical model to Estomih Mtui, MD. Cheng told Mtui, professor of anatomy of radiology, that he'd found the fragment, part of a facsimile of the fourth lumbar vertebrae that had gone missing from the lab.

That was a fib: Cheng had actually created the piece using a 3D printer, a demo model he'd seen in a store. But he wanted to test the machine's prowess, so he passed it off to Mtui as the real thing. The professor slipped the bone model in place—and it fit. Only then did Cheng reveal that the crucial bit had been printed for mere pennies. As Cheng recalls it: "I said, 'Oh my God—you didn't realize that producing this only cost twenty-five cents!' "

In summer 2014—fueled in part by that success—Cheng convinced Weill Cornell to purchase a 3D printer for general use, and he has since formed a user's group that now includes more than 100 people. The printer is in the library—Cheng says he enjoys watching tour groups of prospective students stop and admire it—and is available to members of the Medical College community who complete a training class with the student group DimensionWorks for Biomedical Design, of which Cheng is president.

In 3D printing, a user designs an object using a computer program; the printer then creates it by extruding one thin layer of plastic on top of another, building it up into the desired shape. The technology is already having a positive impact on research, says Jonathan Witztum, a PhD candidate in physiology, biophysics, and systems biology. For example, Witztum recently needed a special kind of imaging chamber to study brain tissue for his thesis. "Having the printer on campus shortened the time it took to design and perfect the chambers we use," Witztum says. "Making it available to everyone has a great impact on people's work." The printer has fostered a number of other projects, Cheng says. It has been used to create a specialized platform for a microscope that would otherwise cost thousands of dollars; to make models of bone marrow for pediatric research; to create a fixation device for researchers imaging the brains of mice; and more.

As work at Weill Cornell and elsewhere has shown, 3D printing technology has the potential to revolutionize medicine, notes Francis Barany, PhD, professor of microbiology and immunology. In a collaboration between the Medical College and the Ithaca campus, for example, researchers are creating 3D printed ears made from living tissue that could be implanted in patients who lack them due to a congenital defect. "Every human is different, so the ability to print something that can be put into the body is very exciting," Barany says. "3D printing is a baby right now. Who knows how it's going to grow up?"

— Jeff Stein

Moral Compass

For one physician-scientist-lawyer, teaching bioethics is a calling

WCMC-Q

Pablo Rodriguez del Pozo, MD, JD, PhD

'I want the students to produce a new brand of medical ethics that belongs to them, that they understand, and they themselves contribute to defining.'

Pablo Rodriguez del Pozo, MD, JD, PhD, crisscrossed the globe en route to the Qatar campus, where he has taught bioethics for the past twelve years. After graduating from medical and law schools in his native Argentina, del Pozo earned a doctorate in bioethics in Spain. Now he works with students in the Arabian Gulf, exposing them to ethical questions that are intrinsic to the study and practice of medicine around the world. His curriculum for medical students parallels that of the New York campus, sensitively adapted to fit the society in which it's taught. "I'm trying to triangulate between cultures," he says. "I want to put students on the right footing to deal with medical ethics problems they may experience later on in their careers, but in a non-threatening way."

In his program, del Pozo imparts elements of medical ethics that are universal—the Hippocratic Oath; the patient always comes first; do no harm—while reflecting the local culture. He notes that healthcare in Qatar embraces two seemingly contradictory styles: a twenty-first century, hyper-specialized approach akin to that in the West, and a more traditional system where patients see a single doctor and don't necessarily play an active role in their own care. "The challenge is to show the students that medicine is universal, and that medical ethics has some universal elements," he said. "But the patient is always local, and we have to cater to the local patient and their culture, family, and environment."

Del Pozo infuses the humanities into medicine, so students learn to approach patient care by focusing on the whole person rather than just on his or her medical conditions. Pre-med students in his introductory ethics course analyze literary classics to gain insights into the patient experience. Franz Kafka's *The Metamorphosis* chronicles the life of a traveling salesman who transforms into a giant insect and sees how his new condition transforms him and the people around him. Leo Tolstoy's *The Death of Ivan Ilyich* depicts the often-disparate worlds that doctors and patients inhabit. Del Pozo hopes his students find in these stories and characters elements to which they can relate. "Fiction has a level of abstraction," he says. "This story represents all stories; this patient represents all patients; this situation represents all situations."

He takes a semester-long longitudinal approach with second-year medical students that weaves together a theoretical framework with real-world examples—clinical cases and patient interactions—to explore the ethics surrounding such issues as beginning- and end-of-life care, reproduction, and informed consent. At the end of the semester, they analyze bioethics in the context of a case they've witnessed while spending time at doctors' offices as part of other courses in the medical program. While the course is nearly identical to the one taken by students in New York, del Pozo tailors the subject matter to accommodate cultural differences. In the Middle East, he notes, individuals consider themselves extensions of their families, and are diligent to represent them and their mores respectfully. And importantly, much of Middle Eastern culture—and the ethics that go with it—are deeply rooted in religion. Del Pozo doesn't seek to indoctrinate his students or to change their values and culture, but rather help them develop a brand of ethics that reflects their own beliefs. "I want the students to produce a new breed of medical ethics that belongs to them, that they understand, and they themselves contribute to defining," he says. "That would be the real success."

In the third year, del Pozo contributes to an exercise on medical ethics during the medicine clerkship; in the fourth, he oversees a two-week clerkship that happens to be the students' last requirement before graduation. For the soon-to-be MDs, it's something of a capstone experience on the issues del Pozo has discussed with them throughout their Weill Cornell careers. With no specific clinical responsibilities, they are tasked with interacting with patients in chronic care settings—learning about them, their values, and what they expect from their care. Such concepts, he says, are too often overlooked. "We usually do fast-paced medicine," del Pozo says. "But I think as a doctor you will be a lot happier—and feel truly fulfilled—if you always keep in the back of your mind that

every patient has a personal history, not just a clinical history."

Del Pozo took a circuitous journey to his calling. After earning his MD and JD degrees, he began a residency in forensic medicine in a coroner's office in Argentina. He knew that it was important work, but he wasn't passionate about it and couldn't envision doing it for his whole career. Then, while taking a course on health legislation at the Universidad Complutense in Madrid, where he was doing specialty training in legal and forensic medicine, he had an epiphany during an animated discussion about patients' rights. "I realized, this is what I want to do," del Pozo recalls. "This is why I studied medicine and law—I just combined them in the wrong way with forensic medicine."

He completed his residency, went back to school for a doctorate in law with a focus on bioethics, and never looked back. In the years since, he has published thirty-two articles in peer-reviewed journals in English and Spanish, co-authored a book, and written twenty-four book chapters and essays. He is a founding member of the Spanish Bioethics Association in Madrid, serves as a senior advisor to the Institute for Argentine Social Development, and is a member of the American Society for Bioethics and Humanities. He also routinely receives teaching awards from his students. "Pablo Rodriguez del Pozo is one of the leading bioethicists in our generation," says Joseph Fins, MD '86, chief of the Division of Medical Ethics and the E. William Davis, Jr., MD, Professor of Medical Ethics at Weill Cornell. "He's a great fount of scholarship, and he has enhanced the experience of our students. I have had the pleasure of meeting many of them in New York, and they always have a smile on their face when they talk about Pablo."

— Alyssa Sunkin-Strube

Seen It, Done It

Med students mentor Cornell undergrads aiming for an MD

Cornell junior Robyn Anderson faced a major decision: should she take a gap year and travel the world after graduation, or go directly to medical school?

Luckily, a program linking undergraduates on the Ithaca campus to medical students at Weill Cornell provided some valuable perspective. Dubbed the Weill-Ithaca Network (WIN), it helps aspiring doctors get first-hand advice from older peers who've already gone through the medical school application process.

Through the program, Anderson was matched with a mentor, Nick Maston of Weill Cornell's Class of 2016. In a conversation over Skype, Maston helped her assess the pros and cons of taking a gap year. "He reminded me that interviews take place in the fall, and thus it would be very difficult to be abroad during that time," says Anderson, who ultimately decided to forgo a gap year and instead aims to travel during the summer before med school.

Launched in fall 2014, WIN is the brainchild of James Wang '16, who graduated from the Ithaca campus in 2012. He recalls that as an undergraduate, he wrestled with conundrums such as how to get clinical experience or gain insight into doctors' working lives. "I decided to pursue medicine at the end of my sophomore year, but I didn't have any physicians in my family," Wang explains. "I kind of just stumbled through the process and got help where I could."

Part of the challenge, Wang realized, is that Cornell's medical school is located more than 200 miles from its undergraduate campus. After talking with some Weill Cornell classmates who'd attended other undergraduate institutions—and hearing how they'd had much easier access to their respective medical schools, some of which were literally across the street—he decided to try to bridge the distance. Wang and Cornell undergrad Catherine He put together a proposal, garnered funding, and recruited mentors and mentees.

PROVIDED

Everybody WINs: Cornell University undergrads in the Weill-Ithaca Network learn about life at the Medical College.

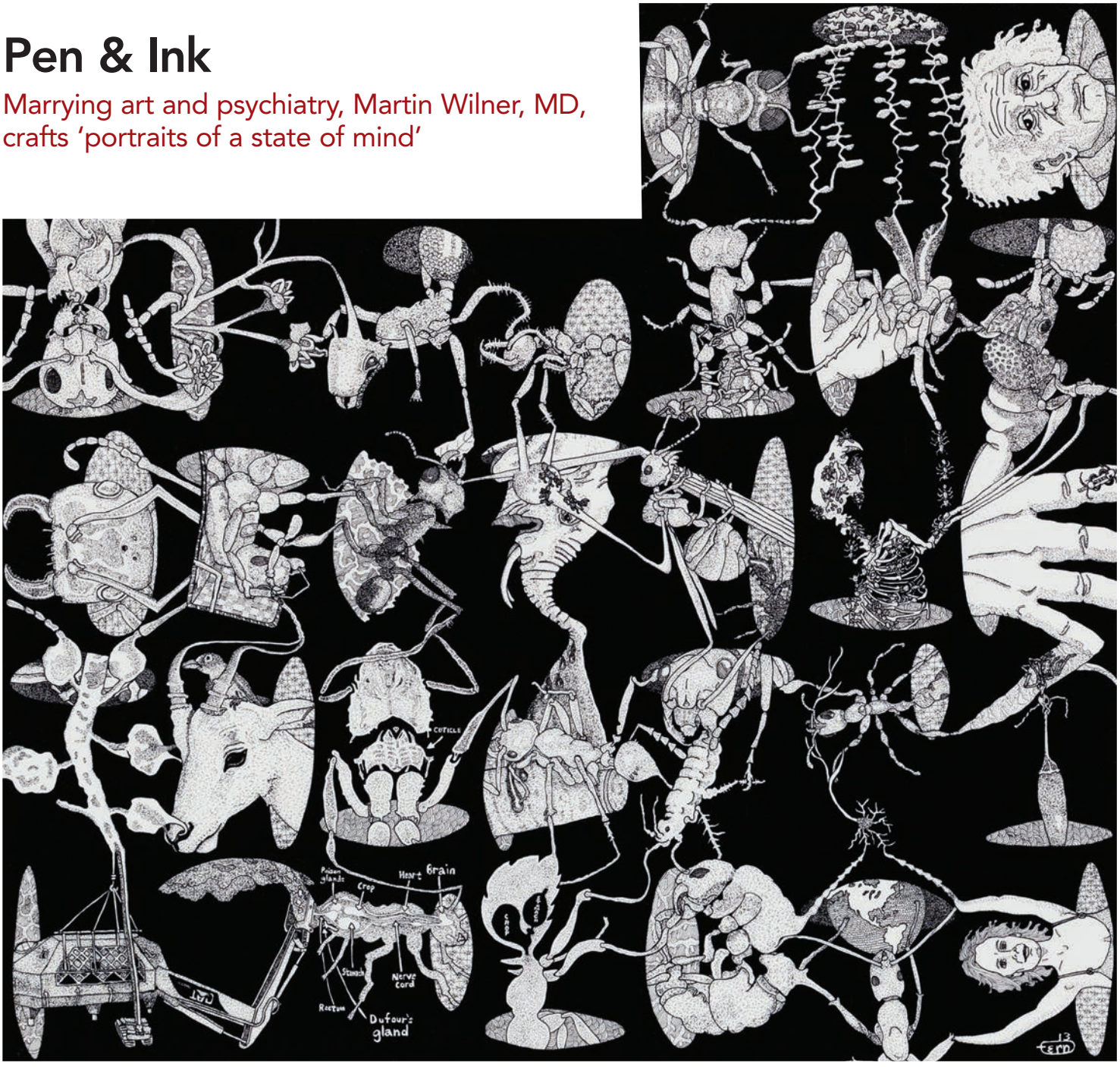
There are currently about two dozen mentors; the number of mentees, who were chosen through an application process that drew 140 hopefuls, is capped at about seventy—a figure dictated by space on the two buses that WIN charters from Ithaca to the city for visits during the school year. Last September, WIN hosted a day trip that included a tour of NewYork-Presbyterian Hospital, informal chats with faculty members, and meetings with mentors. Later in the semester, the undergrads returned as part of a regional premed conference, where they learned more about financial aid and the application process.

In mid-April, WIN hosted its first event in Ithaca, an hour-long panel discussion featuring five mentors and a student representative from the WCMC physician assistant program. They talked about the pros and cons of a gap year, how to study for the MCATs, coping with the application and interview processes, and what medical students' daily lives are like, among other topics. The event was open to all Cornell undergrads, not just those enrolled in WIN, and about fifty attended. "It was good for students to get different perspectives," says Wendy Aquadro, senior associate director of advising in the Ithaca campus's Office of Undergraduate Biology. "Nobody can provide better information than the people who are in the thick of it."

— Jim Catalano

Pen & Ink

Marrying art and psychiatry, Martin Wilner, MD, crafts 'portraits of a state of mind'



COURTESY OF MARTIN WILNER, MD

Mind's eye: *August 2013: Catherine Chalmers* is part of the *Case Histories* series by Martin Wilner, MD

Every day, people tell Martin Wilner, MD, about their lives. Many are patients whom the clinical assistant professor of psychiatry sees in his practice. But each month, Wilner also invites someone—a friend, an acquaintance, even people he hasn't met in person—to communicate with him once a day via text, phone, or e-mail about their thoughts and experiences. And then the self-taught artist, whose work has been exhibited in New York and London, picks up his pen and begins to draw.

The result is *Case Histories*, a series of drawings Wilner began in 2012. Through a process of free association, Wilner creates visual responses that interpret the subjects' input and integrate his own reactions and reflections. "My job is to accept whatever someone sends to me," says Wilner. "If what they send is, 'I had an amazing sandwich today,' I might

draw a sandwich, but I probably wouldn't. I would ask myself questions. Are they making light of this process? Are they being serious and saying, 'You're not nurturing me, I have to feed myself'? Is this about who's feeding whom?"

Wilner describes *Case Histories* as "portraits of a state of mind." He organizes the images within the structure of a monthly calendar, one day's drawing connected to the next; each work in the series is named for that month's collaborator—for example, *January 2014: Alexander Adler*. "Over time, my work as an artist has absorbed much of what I do as a psychiatrist, particularly in psychoanalysis," he says. "My relationship with the subjects parallels the kind that one has with a patient—but for the purpose of making art, not for treating illness."

Case Histories evolved from an ongoing project, *Making History*, which Wilner began in the aftermath of 9/11: over the course of a decade, he did a drawing a day in response to a news event. Wilner's work has been featured in the magazines *Art in America* and *BOMB*, and an artist's print portfolio edition of *Case Histories 2012* was recently produced with the Drawing Center, a SoHo museum devoted to the medium. (Additional details are available on his website, martinwilner.com.) "I was always the student in the back of the class, drawing in my notebooks," he explains. "Since I had a dozen years of post-graduate education to become a psychiatrist, I had lots of time to refine my skills."

Wilner's fans include his colleagues in the Department of Psychiatry—ranked the best in the nation by *U.S. News & World Report*—where his brother, Philip Wilner, MD, is also on the faculty. Chairman Jack Barchas, MD, the Barklie McKee Henry Professor of Psychiatry, calls him "a modern Renaissance man who is able to think across disciplinary lines. As both an artist and a psychoanalyst, he recognizes the difficulty and the dignity of human efforts to be in the world." And in other worlds, too: for 2015–16, Wilner is serving as a virtual-artist-in-residence with the Search for Extraterrestrial Intelligence Institute (SETI), whose scientists are the subjects for his current drawings. "I find that this opportunity allows for me to expand the range of my creative inquiry," Wilner says, "which can only enrich me as an artist—and as a psychiatrist."

— C. A. Carlson

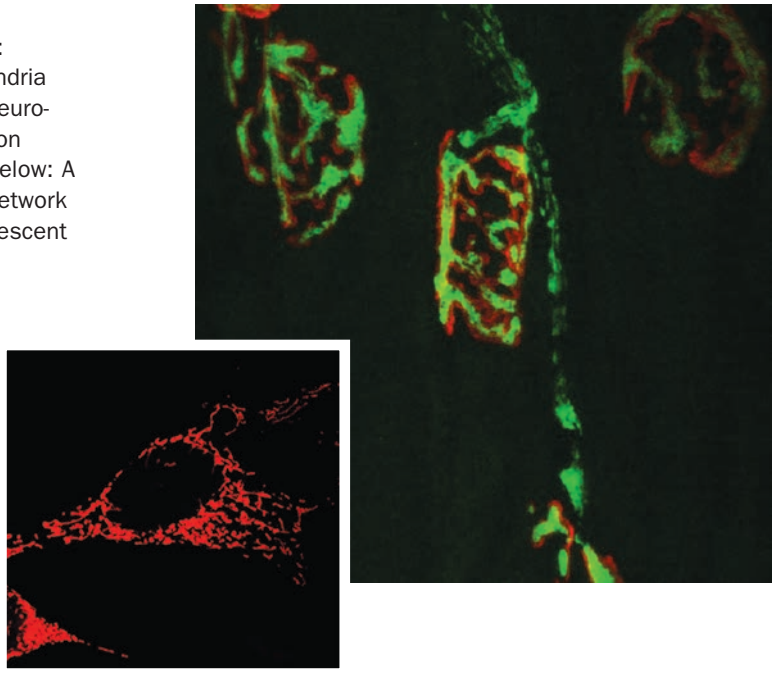
Power Failure

Giovanni Manfredi, MD, PhD, traces the link between mitochondrial disruption and diseases like ALS

Behind the mechanics of every step we take, cellular powerhouses called mitochondria are hard at work, enabling us to walk and talk with relative ease. These fascinating metabolic hubs convert food into energy. Brain cells depend on this energy to interact with each other and to make muscles contract; muscle cells, in turn, use this power source to move and maintain posture.

Since 1999, researchers at Weill Cornell have been exploring why this apparently seamless process sometimes goes awry, causing motor neurons—the muscle-controlling nerve cells—to begin withering away, resulting in conditions such as amyotrophic lateral sclerosis (ALS). A team led by Giovanni Manfredi, MD, PhD, professor of neuroscience in the Feil Family Brain and Mind Research Institute, has pioneered research illuminating how impaired mitochondria play a pivotal role in the development of ALS, the rapidly progressive and fatal neurodegenerative affliction commonly known as Lou Gehrig's disease. "Mitochondria are terribly important for the understanding of neurological disorders, being the final common pathway in which many of these diseases—Alzheimer's, Parkinson's, ALS, and others—converge," says Institute Director Costantino Iadecola, MD, the Anne Parrish Titzell Professor of Neurology. "Even stroke and trauma converge in mitochondria as a major mechanism of disease."

By better understanding the molecular mechanisms underlying mitochondrial changes, Manfredi and his colleagues hope to spur the development of targeted therapeutics for neurodegenerative conditions. For instance, researchers already know that abnormal protein deposits accumulate in the motor neurons of many people with ALS. Normal protein molecules are folded nearly flawlessly in a three-dimensional



Metabolic hubs: (Right) Mitochondria (green) in the neuromuscular junction (red) of mice. Below: A mitochondrial network labeled by fluorescent protein.

Giovanni Manfredi, MD, PhD

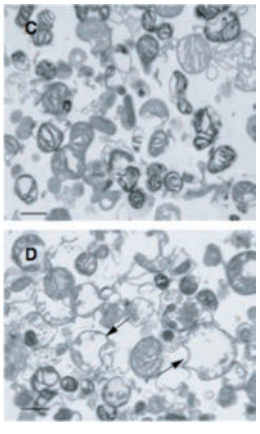
ABBOTT

configuration. If disruption occurs, proteins can form aggregates—clumps in the cells. Using mouse models, Manfredi's lab demonstrated that aggregates of misfolded proteins manifest within the mitochondria of the mutant enzyme SOD1, resulting in one of the most common causes of inherited ALS. His laboratory also pioneered work highlighting how faulty calcium regulation in mitochondria and secretion of toxic molecules by supportive cells in the brain, known as astrocytes, result in the death of motor neurons.

Because many neurological conditions involve mitochondrial dysfunction, symptoms can overlap and appear similar, even if the diseases are distinctly different. For instance, some genetic forms of ALS may occur in families with a prevalence of dementia. Contrary to the frequent misperception that the mind remains fully intact in people with ALS, cognitive dysfunction often ensues after paralysis and interferes with memory and behavior. It's also common for dementia to develop in people with Parkinson's disease. "The same person can have both diseases," says Manfredi, who directs the graduate program in neuroscience, "or different individuals in the same family may have one or the other."

By interfering with the disease pathways that damage mitochondria, Manfredi aims to stabilize these cellular powerhouses against stress and halt further damage. His team has begun searching for approaches to unravel the mystery surrounding the causes of sporadic ALS, which arises without any known genetic link or family history, and accounts for about 80 percent of all cases. "Sporadic ALS is probably a combination of diseases," he says, with paralysis being the main unifying symptom. His research focuses on genetically altering proteins in human cells and mice—work that could pave the way for promising drugs.

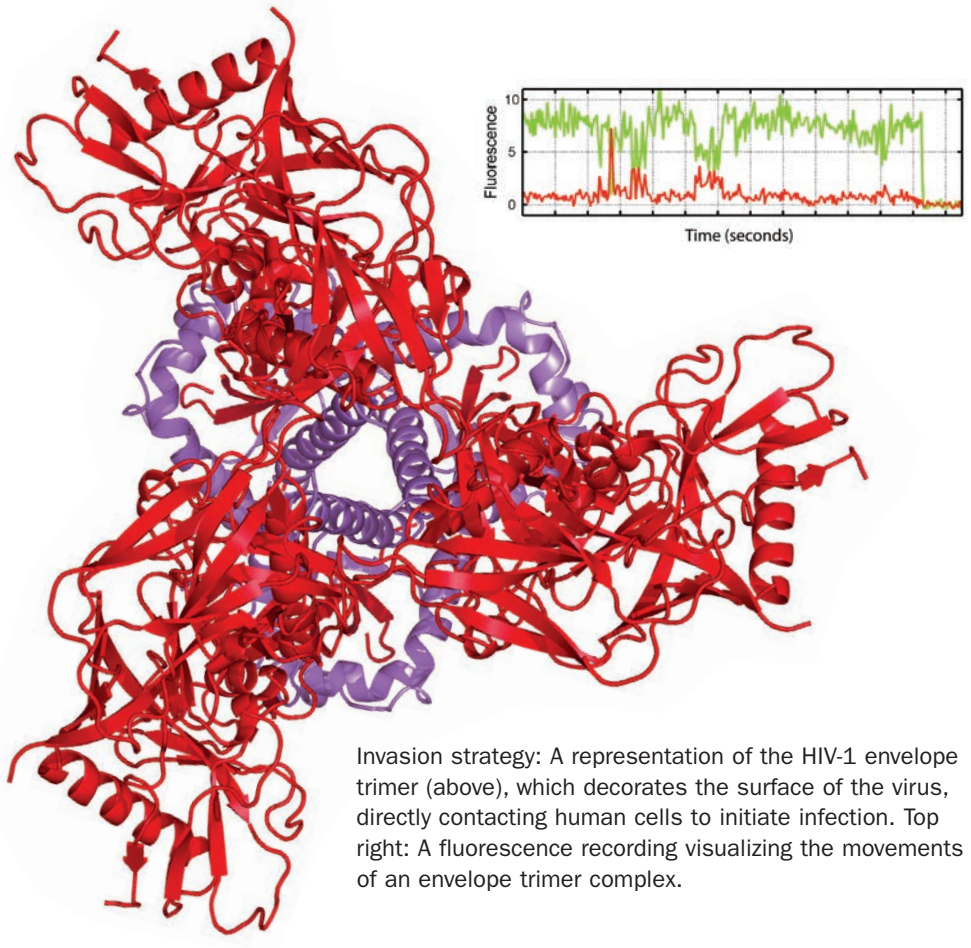
— Susan Kreimer



Disease process: Electron microscopy shows mitochondria in a normal mouse brain (top) and one damaged by ALS.

Double Vision

A two-pronged approach offers new insights into HIV



Invasion strategy: A representation of the HIV-1 envelope trimer (above), which decorates the surface of the virus, directly contacting human cells to initiate infection. Top right: A fluorescence recording visualizing the movements of an envelope trimer complex.

It's been dubbed the "super-resolution revolution": the development of biomedical imaging tools strong enough to see individual molecules—units so miniscule, they're smaller than the wavelength of light. Such technologies are transforming the way scientists look at living cells, examining the tiniest molecular details in the search for new disease-fighting treatments.

Among the researchers contributing to the revolution is Scott Blanchard, PhD, associate director of the Tri-Institutional Chemical Biology Program, whose lab utilizes such single-molecule imaging techniques to gain further insight into complex, ever-changing biological processes. "It's much easier to simplify your understanding of a system when you watch one molecule at a time, rather than billions at a time," explains Blanchard, associate professor of physiology and biophysics. "If you're looking at many of them, it's like trying to listen to a conversation with a billion people talking at once."

In two parallel studies published last fall in *Science* and *Nature*, Blanchard and his colleagues revealed how they modified this super-resolution technology to track—for the first time—the precise movements of proteins on the surface of the human immunodeficiency virus (HIV). They were also able to use a method known as X-ray crystallography to determine the 3D structure of one of those proteins. Together, these discoveries could help researchers find a way to prevent HIV infection, stemming an epidemic that the WHO estimated has affected 78 million people worldwide.

For the *Science* study, Blanchard's group adapted single-molecule fluorescence resonance energy transfer (smFRET) imaging—an approach that uses fluorescence to measure distance on an atomic scale—to analyze the behavior of HIV. The team designed special long-lasting fluorescent molecules, or fluorophores, which were inserted into proteins on the virus's outer coating, known as envelope proteins. These glowing beacons, in conjunction with the imaging system, allowed them to visualize how the molecules moved over time, as the virus proteins changed shape.

This was important because the envelope consists of multiple proteins, referred to as trimers, that blossom like a flower when HIV comes in contact with immune cells carrying CD4 receptors, which the virus uses to enter the cell. There are ten to twenty trimers on the surface of each HIV particle, which quickly mutate, making it hard for the body to combat the disease—and challenging researchers working to develop a vaccine. "One of the problems with HIV," says Blanchard, "is that the rate of infection and mutation is faster than your immune system can keep up."

Scientists long thought that the trimers remain passive when CD4 isn't present. But Blanchard's group found that the envelope proteins constantly shape shift, or "dance"—even without CD4. Even more striking, he and his colleagues showed that the introduction of certain antibodies stopped the envelope from opening, thereby lowering the infection rate. Tests with a small-molecule drug under development by Bristol-Meyers Squibb to prevent HIV produced similar results. "Now we know the rule—or at least, we have a hint of the rule—on how to inhibit the virus," Blanchard says. In other words, these findings could aid pharmaceutical companies in screening for more effective medications in the future, by providing a better "road map" of the virus. "If you're driving cross-country in a car but you don't have a compass or any understanding of which way is west or east, it's really difficult," he says. "We think that our approach is going to make the search for therapeutic interventions more directed."

In the other study, outlined in *Nature*, researchers turned to X-ray crystallography in an attempt to take a high-resolution picture of an HIV protein, with the goal of obtaining additional data about the virus's biological makeup. However, the procedure couldn't work if the molecule remained dynamic; as Blanchard puts it, "The nemesis of crystallography is movement." To freeze that molecule's actions, the team employed the same antibodies that were used in the *Science* study to keep the

envelope protein closed.

To Harel Weinstein, DSc—the Maxwell M. Upson Professor of Physiology, chair of the Department of Physiology and Biophysics, and director of the Prince Alwaleed Bin Talal Bin Abdulaziz Alsaud Institute for Computational Biomedicine—the combination of these two technologies is what makes Blanchard's endeavors extraordinary. Not only do scientists now have concrete information about the structure of HIV molecules, he notes, they know exactly how they change when different proteins in the virus interact. And that knowledge could have benefits beyond HIV, pointing the way toward improved therapies for cancer and other illnesses. "The idea," says Weinstein, "is that it's only at this detailed level that we can hope to get cures."

— Heather Salerno

Thought Pieces

Psychiatrist Richard A. Friedman, MD is a fixture on the *New York Times* op-ed page

In May 2014, a disturbed young man named Elliot Rodger murdered six people in a killing spree in Isla Vista, California, before committing suicide. Rodger—who'd penned a lengthy online manifesto blaming his actions on social alienation and sexual frustration—had a history of mental health problems and off-putting behavior, including posting unsettling YouTube videos that prompted his mother to notify the police. They visited Rodger, but didn't detain him.

A few days after the murders, as the barrage of media coverage continued, the *New York Times* ran an op-ed whose headline posed a question on the minds of many Americans: Why can't doctors identify killers? "One of the biggest misconceptions, pushed by our commentators and politicians, is that we can prevent these tragedies if we improve our mental health care system," the piece said. "It is a comforting notion, but nothing could be further from the truth."

The author of the op-ed was Richard A. Friedman, MD—a byline long familiar to *Times* readers. A professor of clinical psychiatry and director of the Psychopharmacology Clinic at Weill Cornell, Friedman is a regular contributor to the paper's opinion and science sections, having published roughly a hundred pieces since 2002. "It's a different mental activity from writing for a journal," observes Friedman, who specializes in the treatment of anxiety and mood disorders and is active in clinical research on depression. "The mindset is more playful. You have much less space to make an argument; you have to get to the point quickly, and do it in a way that's fun and interesting."

> 'People are fascinated by stories that explain their own behavior to them.'

The evolutionary advantages of ADHD. The overprescription of psychoactive drugs in the military. Divorcing your "toxic parents" or your "bad seed" child. Adolescent risk taking (which ran under the headline "Why Teenagers Act Crazy"). The shrinking psychoanalytic hour. Therapists' temptation to play matchmaker for their single patients. The mood benefits of Botox. Friedman has weighed in on those subjects and many others, with his pieces often topping the *Times*' list of most e-mailed articles. "People are fascinated by stories that explain their own behavior to them," Friedman says. "They're so interested in why they do things and what makes them tick."

ABBOTT

Richard Friedman, MD

Friedman's op-ed career began with a dog. In 2002, with animal cloning in the headlines, Friedman's father asked if he would consider having a genetic copy made of his beloved canine, Homer, who was dying of bone cancer. His musings on the subject formed the basis for his first piece published in the *Times*, in which he admitted that he'd investigated pet cloning but decided against it. "Homer's clone would look like Homer and possibly even act like him, but he would not be Homer," Friedman wrote. "Homer was in essence the relationship, built over many years, of shared and unrepeatable experiences. Cloning could not recreate the most precious thing about him—our bond."

These days, Friedman publishes in the *Times* roughly once a month. If a topic is particularly *au courant*, the turnaround time can be just a matter of days from pitch to publication—as with the Elliot Rodger piece, or a similar one that Friedman did following the massacre in Newtown, Connecticut. "The level of scrutiny and detail from the *New York Times* is unlike anything I've ever seen," notes Friedman, who holds the coveted title of "contributing writer" for the paper's Op-Ed section. "Every single fact is checked. Sometimes they call the primary authors on papers that I've referenced to better understand the arguments, so they know I'm representing the science accurately."

Pondering the reasons for his foray into the news cycle—in the midst of a packed professional schedule—Friedman says he often writes as a way to understand his own opinions about a subject. He also feels it has helped him become a better, more sensitive psychiatrist. "Writing has made me much more observant," he says. "It increases your curiosity and focus, makes you more aware of things." Another strong motivator, he says, is a desire to accurately represent his specialty. "So much is written about us and our field," he says. "We psychiatrists have always been bad about communicating to the public; we tend to be in our offices and in our heads. But if we don't tell the public who we are, what we think, and what we do, others will do it for us."

— Beth Saulnier

ISTOCK

Smoke & Fire

With 'vaping' on the rise, a health economist explores e-cigarette use

In mid-April, the Centers for Disease Control and Prevention reported a startling statistic: in just a single year, the use of electronic cigarettes among middle and high school students more than tripled. The numbers, from the 2014 National Youth Tobacco Survey, mean that some 2.5 million teens nationwide are using the devices, which turn liquid nicotine into an aerosol that's inhaled—a process commonly known as "vaping." "This is the first time since the survey started collecting data on e-cigarettes in 2011 that current e-cigarette use has surpassed current use of every other tobacco product overall," the agency noted in its *Morbidity and Mortality Weekly Report*, "including conventional cigarettes." Among high schoolers, the vaping rate was 13.4 percent; by contrast, 9.2 percent reported smoking cigarettes and 5.5 percent used smokeless tobacco.

The increasing popularity of e-cigarettes—known in academic parlance as ENDS, for electronic nicotine delivery systems—has policymakers in something of a quandary, as they struggle to understand the products' pros and cons. That debate, as the World Health Organization noted in a report to an international tobacco control convention in September 2014, has become increasingly divisive. One underlying challenge is that, with e-cigarettes invented only about a decade ago, their long-term health implications remain unclear—compared with vast amounts of research on the dangers of conventional smoking. For example, while some

studies have found that the devices deliver just a tenth of the carcinogenic compounds of regular cigarettes, others have found them to contain higher levels of potentially harmful metals such as nickel and chromium. "Whereas some experts welcome ENDS as a pathway to the reduction of tobacco smoking, others characterize them as products that could undermine efforts to denormalize tobacco use," the WHO stated, adding that e-cigarettes "represent an evolving frontier, filled with promise and threat for tobacco control."

Health economist Michael Pesko, PhD, has long focused his research on tobacco use. He has investigated such topics as how smokers stymie public health efforts by dodging higher cigarette prices, and documented a costly rise in smoking rates in response to the psychosocial stresses of 9/11—work that earned him a spot on *Forbes*'s 2014 list of "30 Under 30 Who are Changing the World in Science and Healthcare."

Increasingly, Pesko is turning his attention to e-cigarettes, with a variety of research projects exploring how and why people use them. "There are a lot of interesting questions relating to e-cigarettes in terms of their impact on overall public health," says Pesko, an assistant professor of healthcare policy and research and the Walsh McDermott Scholar in Public Health. "On one hand, there's legitimate concern that the devices themselves are harmful, or that they can be a gateway into regular cigarette use for adolescents. But on the other hand—within an adult smoking population, for example—there is evidence that they're risk-modifying products. If a smoker is going to use one or the other, you'd rather have them use the e-cigarettes, because while they're not harmless, they're less harmful and potentially could be used for smoking cessation."

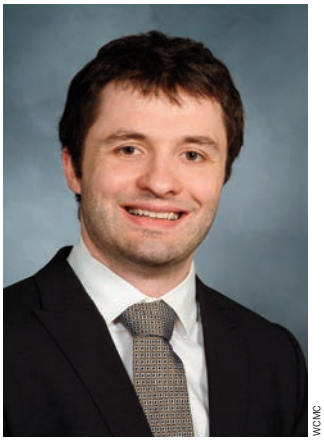
In a study that's under journal review, Pesko is exploring how age restrictions on ENDS purchases affect tobacco use. Currently, he notes, forty states prohibit anyone under eighteen from buying vaping products. "Surprisingly, there are still ten states where a twelve-year-old can legally walk into a 7-Eleven and buy an e-cigarette," Pesko says, "but the FDA has proposed a law that would apply that under-eighteen purchasing restriction nationwide."

However, such rules could have unintended consequences, by driving youths to regular cigarettes when they can't obtain the electronic version. That's what Pesko has found, at least among high schoolers who describe themselves as infrequent smokers. "When the restriction is the same as accessing traditional cigarettes in terms of age, it can cause a substitution effect," Pesko says. "If e-cigarettes are equally hard to get, some people on the margins will use a regular cigarette—whereas before, maybe they wanted a regular cigarette, but an e-cigarette was so easy to buy, why jump through all the hoops?"

In another study under review, Pesko and colleagues conducted a national survey of 1,200 adult smokers, presenting them with hypothetical purchasing options: either their regular cigarettes, a vaping device (with a variety of prices, flavors, and health warnings), or nicotine replacement therapy. They conducted half the research in late 2014 and half in early 2015, to capture the effect of New Year's resolutions to stop smoking. "If adult smokers are trying to quit, what are they reaching for—nicotine replacement or e-cigarettes?" Pesko wonders. "We found some evidence that they're reaching for the e-cigarette as a quitting device more frequently."

Still another project is focusing on teens. In a collaboration with adolescent medicine specialist Lisa Ipp, MD '96, Pesko is surveying patients in NYP/Weill Cornell's Adolescent Medicine Program about their vaping habits. The team began collecting data in January; participants will be rescreened at six months and one year. While preliminary numbers indicate that use of ENDS is "quite a bit lower" among the program's patients than the national average—for reasons that aren't entirely clear—Ipp is still concerned. Like many anti-smoking advocates, she points out that vaping products don't have the same rigorous regulation as traditional cigarettes, can be advertised on television and radio, and are available in a variety of kid-friendly flavors that the government bans from conventional tobacco products. "We're basically making nicotine an attractive, appealing option for teenagers who are particularly impressionable," says Ipp, an associate professor of clinical pediatrics. "I worry greatly that they're going to be addicted to tobacco down the road."

— Beth Saulnier



WCMC

Michael Pesko, PhD

'There are a lot of interesting questions relating to e-cigarettes in terms of their impact on overall public health.'

Breath of Fresh Air

GHESKIO opens new tuberculosis and cholera hospitals that embrace Haiti's abundant sunlight and tropical breezes

When a major earthquake devastated Haiti in 2010, it not only took the lives of 220,000 people, but severely damaged the impoverished nation's medical infrastructure. Among the buildings lost in the 7.0-magnitude quake were the five major tuberculosis hospitals in the capital city of Port-au-Prince. "Patients with TB were on the streets," recalls Warren Johnson, MD, the B. H. Kean Professor of Tropical Medicine. "They didn't have access to meds. They didn't have a roof over their heads. They were living in tents, which is the worst conceivable environment."

One of the destroyed TB hospitals was run by GHESKIO, a Weill Cornell-affiliated medical organization founded by Jean Pape, MD '75, the Howard and Carol Holtzman Professor in Clinical Medicine. Established in 1982, the institution was the first in the world dedicated to the fight against HIV/AIDS—its name is the French acronym for "Haitian Group for the Study of Kaposi Sarcoma and Opportunistic Infections"—but it has since expanded to treat other infectious diseases and offer primary care services.

In the earthquake's aftermath, GHESKIO opened a tent hospital for patients with the worst form of tuberculosis, multi-drug resistant TB. Then, within ten months of the disaster—and with some 1.5 million people still without permanent homes—Haiti faced the world's worst outbreak of cholera in recent history. So, in response to that ongoing epidemic—which has affected 800,000 people and claimed 8,500 lives over the last four and a half years—GHESKIO opened a second tent facility, this one dedicated to cholera.

Out of these temporary fixes grew awareness of a need for a research-based, long-term care facility. People with multi-drug resistant TB, for example, require lengthy hospital stays, with treatment lasting from eighteen months to two years. "We required a place where we could provide quality care in a dignified environment for patients," Johnson says, "and where we could conduct studies to improve therapy, find new drugs, and evaluate new regimens."

As a result, GHESKIO has built new hospitals in Port-au-Prince dedicated to TB and cholera—facilities whose designs have been lauded by patients, medical professionals, and architectural critics alike. Established through collaborative efforts by Weill Cornell, GHESKIO, the Haitian and U.S. governments, the CDC, USAID, and medical technology firm Becton Dickinson, the centers officially opened in March with a ceremony at the new TB hospital, known as the Ludwig Pavilion. Located at GHESKIO's newest site near Haiti's main airport, the facility is named in honor of benefactor Ed Ludwig, former CEO of the global medical technology firm Becton-Dickinson, and his wife, Kathy; the company gave $1 million toward the project, and the Ludwigs made a personal contribution as well.

Boston-based MASS Design Group created the facilities, partnering with two Haitian engineering firms. The buildings have numerous features that advance GHESKIO's medical and social missions. For example, their furniture was designed and constructed by participants in a vocational training program that GHESKIO opened in 2013 to improve economic opportunities for women at risk for HIV.

Two stories high, the TB hospital has private rooms for thirty-two patients configured around an open-air garden courtyard; the cholera facility is a one-story pavilion at GHESKIO's original site downtown. Both are innovative spaces that aim to set a new standard in design, development, and patient care. *New York Times* architecture critic Michael Kimmelman wrote that the buildings "could serve as relatively light-footed models for other struggling countries that lack resources for high-end Western-style hospitals." He added that they could even "nudge hospitals in the United States away from the mid-century model of sealed buildings that rely on imperfect mechanical systems costing a king's ransom and gobbling up energy."

PHOTOS PROVIDED

Healthy atmosphere: The new TB hospital (above and far left) features a comfortable courtyard and natural ventilation. Left: Warren Johnson, MD, and Jean Pape, MD '75, at the dedication ceremony.

'We worked on every detail, on every single space that was going to be built.'

Understanding of disease transmission dictated design. While the architects had experience in building healthcare facilities, they also collaborated closely with Pape. "We worked on every detail, on every single space that was going to be built," Pape says. "We reviewed carefully how our staff would come to examine patients." Tuberculosis, for example, is a highly communicable, airborne disease that's transmitted in enclosed spaces—so the hospital's designers sought to maximize sunlight, which kills the bacteria that causes the disease, and to enhance passive ventilation through open-air spaces. Physicians and nurses have areas for treating patients outside of their rooms, at the edge of a courtyard; janitorial staff also have special means of egress to clean patient bathrooms without entering adjacent bedrooms. As Pape told the *New York Times*: "Architecture and health are inseparable. A building that is ugly, with no fresh air, no dignity or common sense, is a place people will avoid, and this encourages epidemics."

Cholera spreads through contaminated water, so that facility's designers faced the challenge of how to improve a wastewater system in a city that doesn't yet have the capacity to do it itself; while Port-au-Prince plans to build underground wastewater infrastructure, it likely will be at least twenty years before the system is fully implemented. Currently, two-thirds of residents lack access to a clean, private toilet and more than one-third lack access to clean drinking water. (The city is not alone in this: one billion people around the world live in informal urban settlements lacking in civic infrastructure and regulation.) In Haiti, diarrheal disease is the second-leading cause of death for children under five; globally, such diseases cause one in every five child deaths each year.

The cholera facility features a dedicated wastewater treatment system designed to prevent recontamination of the water table and thus limit spread of the disease. Deep basins limit spillage of wastewater, which then passes through vertical chambers over the course of five days, as anaerobic bacteria breaks down the hazardous waste. The interior is designed for ease of cleaning, which occurs four times a day.

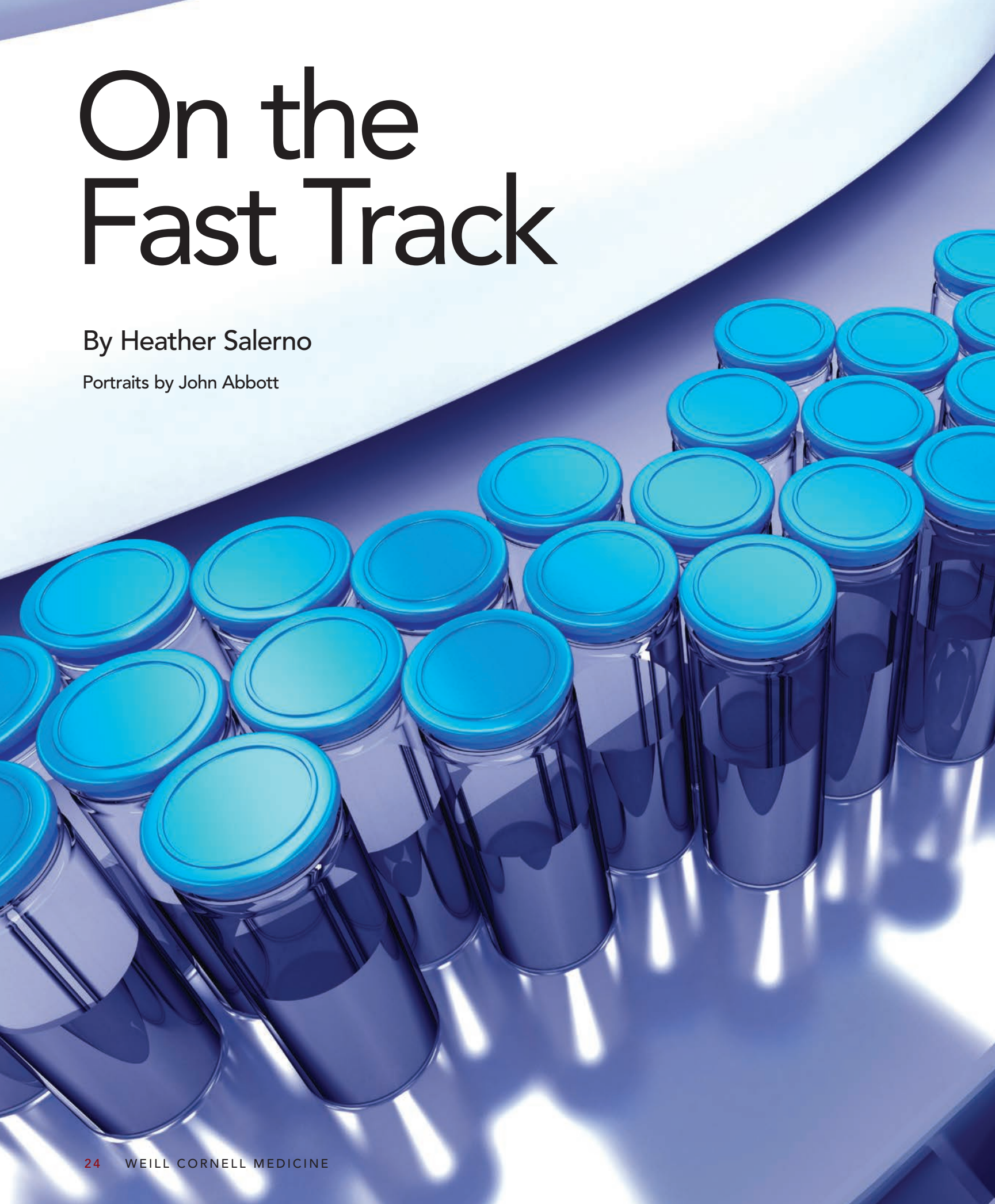
All these features help keep diseases from spreading—but a key part of the designers' vision was to improve the day-to-day lives of the patients themselves. People who are sick and suffering need to be in a pleasant atmosphere, Pape emphasizes, in comfort and surrounded by beauty. As Haitians with TB and cholera began moving from tents into the new facilities in May, he says, he saw looks of astonishment on their faces. As he recalls: "They told me, 'We're just surprised that it is so nice.' "

— Andrea Crawford

On the Fast Track

By Heather Salerno

Portraits by John Abbott



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It's a rare, heartbreaking disease. Niemann-Pick Type C—which is often called "childhood Alzheimer's" because its adolescent victims deteriorate mentally as well as physically—lacks a cure or even a treatment. Patients most severely affected by the rare, hereditary, neurodegenerative disorder generally don't live beyond age twenty. "We're also starting to realize that it's usually misdiagnosed," notes Frederick Maxfield, PhD '77, chair of biochemistry and the Vladimir Horowitz and Wanda Toscanini Horowitz Distinguished Professor in Neuroscience. "In the United States and Western Europe, it takes an average of five years from the first doctor visit to a correct diagnosis."

In 2009, Maxfield—who has been investigating the disease for more than a decade—developed some theories about how to enhance an existing experimental therapy for Niemann-Pick, which strikes just one in 150,000 people. Tests in his lab showed promise, but when Maxfield sought funding for further exploration, he was told that his ideas were too preliminary to attract much interest from pharmaceutical companies or granting agencies. Without the money to cover the next stages of analysis, he couldn't move the project forward.

It's a paradox that many researchers are all too familiar with—a form of scientific limbo known as the "valley of death." "The attitude was, 'This is interesting academic science, but you'll never be able to take it to the next level,' " Maxfield recalls. "So for three years it just sat there. It was frustrating, because I did think it had potential."

Then, in fall 2013, Weill Cornell joined Memorial Sloan Kettering Cancer Center and The Rockefeller University to form the Tri-Institutional Therapeutics Discovery Institute (Tri-I TDI), a nonprofit devoted to fast-tracking early stage drug development. Founded by two major gifts from Weill Cornell overseers—$15 million from Lewis and Ali Sanders and $5 million from Howard and Abby Milstein—Tri-I TDI is a kind of incubator whose goal is to transform fledgling discoveries into promising treatments for some of the world's deadliest diseases, bringing them to the proof-of-concept stage where drug companies might invest in them for further development. At the time of its founding, the Institute announced that it had formed an alliance with an industry leader: Japan's largest pharmaceutical firm, Takeda Pharmaceutical Company Ltd.

Last year, Maxfield's project was one of seven the Institute accepted—out of four dozen applicants from the three institutions—for additional financing and support. As with Niemann-

Pick, "In some cases we were looking at significant unmet medical needs," Gregory Petsko, DPhil, the Arthur J. Mahon Professor of Neurology and Neuroscience at Weill Cornell and a member of the Institute's scientific advisory board, says of the first round of projects. "That means if anything comes of this, it would really help people. That's really exciting." The Institute's director, Michael Foley, PhD, assistant professor of biochemistry—who has worked at Harvard, MIT, Bristol-Myers Squibb, and GlaxoSmithKline—is equally enthusiastic. "As far as I'm concerned," says Foley, "there's unlimited opportunity here."

Traditionally, drug development has been a complex, costly, and disjointed process, with a wide chasm separating academia and industry. For corporations, it's usually not practical to hire squads of researchers to work at the early stages of drug discovery. And most academic scientists aren't experts in medicinal chemistry, a specific skill set needed to bring a drug to the marketplace. "To approve one drug, it typically takes thirteen and a half years and costs approximately $1.8 billion," Foley says, then adds: "That's billion, with a 'b.'"

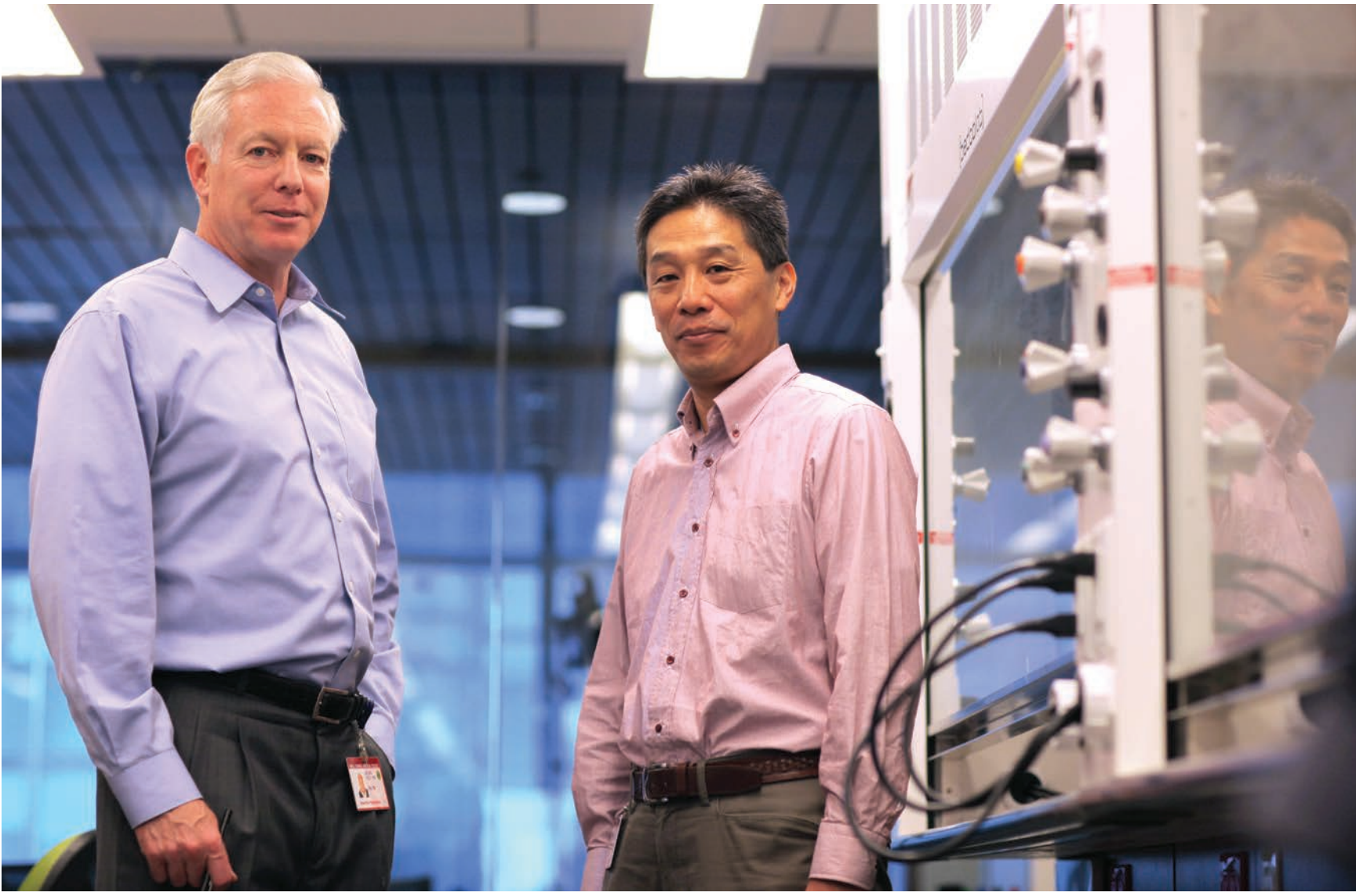
'Academics are good at thinking about problems in new ways,' says Carl Nathan, MD. 'We develop new technologies that may break open a problem, but we're not so good at the rest of it. The things we need from each other are complementary.'

Under the old system, researchers with fresh insights into a disease might identify and create an innovative compound with great therapeutic potential. After showing so-called "proof of principle"—meaning that the drug would likely have real-world applications—they'd hand it off to an interested company. But there would be little interaction between the two sides after that, even as a firm's own scientists worked to smooth the compound's flaws. In recent years, though, there has been a growing recognition of the need to bridge this gap, with many pharmaceutical companies trying to strike up relationships with academia earlier on. "The new idea is that you work together as partners," says Carl Nathan, MD, chairman of the Department of Microbiology and Immunology and one of Tri-I TDI's board members. "Academics are good at thinking about problems in new ways. We develop new technologies that may break open a problem, but we're not so good at the rest of it. The things we need from each other are complementary."

The Power of Three

Among the more unique aspects of the Tri-I TDI partnership is the collaboration among three renowned institutions, all located in the same Upper East Side neighborhood. Not only does the joint effort allow them to share the cost of salaries, equipment, and other operating expenses, it offers valuable economies of scale. "You just widen the funnel for great ideas," Foley says. "Setting up three of these—having three CEOs and three directors working with three different companies—would be tripling the expense with no improvement in efficiency." And while similar efforts generally target one specific illness, Tri-I TDI can address a variety of maladies, from widespread health challenges like cancer and malaria to conditions such as Niemann-Pick, which affect only a small number of people. Research proposals are chosen based on scientific potential, not future profitability. "I could have a great idea for a drug for tuberculosis—which almost 1.5 million people a year are dying from—and a company might say, 'Yes, but they're all poor, so we don't see a market for that,' " Nathan says. "At this Institute, we don't have those kinds of conversations. That's why this is so different."

As Tri-I TDI's industry partner, Takeda—which has assigned fifteen full-time medicinal chemists to the effort—embraces every project that the Institute takes on. The Takeda scientists become part of a principal investigator's research team, in the belief that close collaboration will accelerate discovery. And indeed, if Maxfield is stuck on a problem and feels like brainstorming, he only has to walk across the street from his Weill Cornell office and go to the top floor of the Belfer Research Building, where the Tri-I TDI lab is housed. There, he can meet face-to-face with the Takeda chemists, which he says has pushed his research along faster than he and his academic collaborators could have achieved alone. "Every two weeks or so, we have a meeting and we get anywhere from three to ten new compounds to test," he says. "It's incredible."



Academia and industry: Tri-I TDI director Michael Foley, PhD (left), with Kazuyoshi Aso, PhD, vice president of medicinal chemistry

One recent morning, Maxfield stopped by to check in with Yoshiyuki Fukase, PhD, his project's lead chemist and Tri-I TDI's director of medicinal chemistry. In the pristine, all-white-and-glass lab, he watches one scientist input data about their latest compound on a laptop. Another hunches under a fume hood, wearing protective goggles to carefully mix a cocktail of chemicals.

Maxfield's group is attempting to modify cyclodextrin, a sugar-based substance that the NIH is studying as a remedy for Niemann-Pick. Those with the disease can't properly process cholesterol, which eventually accumulates to toxic levels. Cyclodextrin seems to reduce the cholesterol and prolong survival—but in the form now being tested on young patients, it must be given in high doses, which can trigger devastating side effects like hearing loss. Plus, the blood-brain barrier prevents the medication from reaching the most-affected cells—the neurons—so it must be injected directly into the brain. "We're trying to see if we can link something to the cyclodextrin that will allow it to get shuttled from the peripheral blood into the cerebrospinal fluid," Maxfield explains. "By doing that, you could hopefully get enough into the brain to be effective." Aiming to improve upon the results of their first round of tests, his team is tinkering with their initial compounds in the hope that new formulations will bind more tightly to cells. Says Nathan: "The close interaction with the TDI chemists lets us make improvements on the fly."

Yariv Houvras, MD, PhD (right), with Ritu Kumar, PhD, assistant research professor of cell and developmental biology in surgery

A 'Stunning Commitment'

According to Kazuyoshi Aso, PhD, Tri-I TDI's vice president of medicinal chemistry, the Institute is giving Takeda scientists experience unlike anything they'd encountered in a corporate environment. The principal investigators and their lab members, Aso notes, have different perspectives on drug discovery research from their counterparts at pharmaceutical companies. "We can learn a lot of cutting-edge science from these academic institutions," Aso says. "And on the other hand, our role is to teach both the drug discovery process and the concepts of drug design." The effort is a stunning commitment by the Takeda scientists: all moved from Japan to New York, where they'll spend from one to three years. In some cases, workers left spouses and children behind to pursue the opportunity.

For Weill Cornell, Sloan Kettering, and Rockefeller, a major advantage of the arrangement is that intellectual property rights remain with the institution whose faculty originated the proposal. In return, Takeda gets inside knowledge about the targets and drugs in Tri-I TDI's pipeline, along with first crack at negotiating licenses—though there is no obligation to accept Takeda's offer. Either way, Nathan believes the institutions will likely receive a higher royalty rate than usual, since a company would be buying a compound with fewer liabilities. "We'll be adding enormous value to the project," he says. "We'll already have shown that it seems to work."

One Tri-I TDI drug that seems particularly promising is being studied by Enrique Rodriguez-Boulan, MD, the Charles and

Margaret Dyson Professor of Ophthalmic Research. As it happens, some of the same compounds that Maxfield is using in his Niemann-Pick project have been shown by Rodriguez-Boulan and his team to be promising therapeutic agents for Stargardt Disease (SD), an incurable type of juvenile blindness that affects about one in 10,000 children in the U.S. Rodriguez-Boulan's rationale was akin to Maxfield's: he wondered if cyclodextrin could heal SD, after discovering that the substance also removes a toxic waste product that collects in patients' retinas.

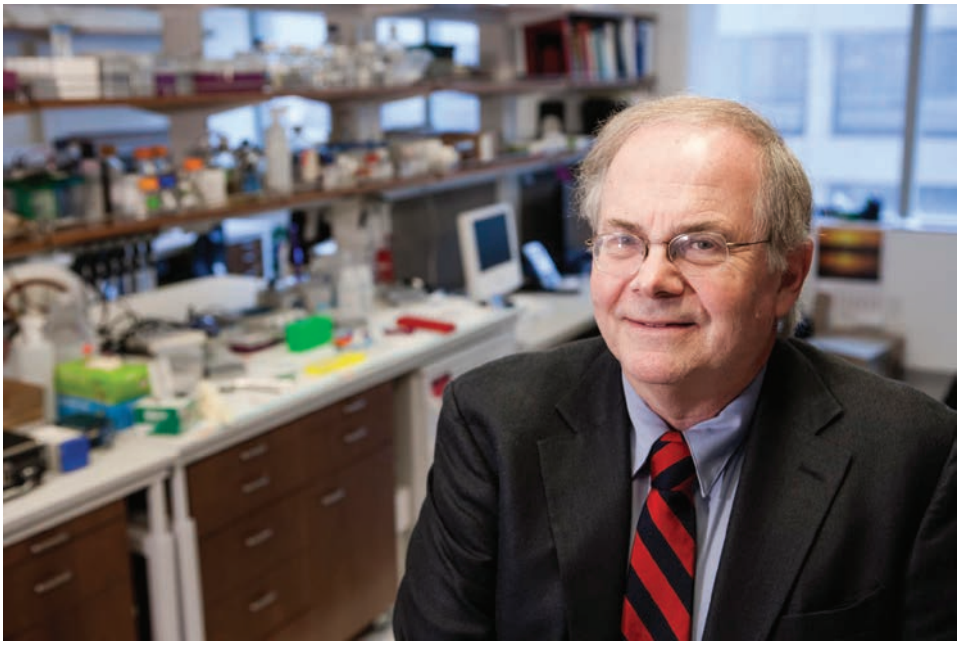
Working with Rodriguez-Boulan's team, the Tri-I TDI-sponsored chemists have already created and tested derivatives that are several times more efficient than current cyclodextrins in clearing the toxic lipid from cultured retinal cells. He's now doing experiments in model SD mice to gather evidence of whether these enhanced cyclodextrins can prevent vision loss and promote vision recovery after clearing the toxin from the retina. "If we can show we can protect them from blindness," he says, "then we're set to go on to humans." Rodriguez-Boulan adds that these drugs might also help with a more far-reaching condition: age-related macular degeneration (AMD), the leading cause of blindness in older Americans. "No one knows the exact cause, but as we get older, we accumulate this toxic lipid," he says. "So there's a good chance that at least some forms of AMD may be sensitive to this as well."

For medical oncologist Yariv Houvras, MD, PhD, assistant professor of medicine, funding from Tri-I TDI came at the perfect time. His lab uses zebrafish as a model organism to study cancer; working with Minkui Luo, PhD, a Weill Cornell associate professor of pharmacology who leads a lab at Sloan Kettering, Houvras is targeting an enzyme called SET8, which is associated with the proliferation of cancer cells. After putting a small-molecule inhibitor of SET8 on zebrafish embryos, Houvras and his team saw a specific effect on melanocytes, the pigment cells that give rise to melanoma. "We believe that if we can interfere with that biochemical activity," he says, "we can stop cancer cells from growing." Yet the project faltered once the group got to the point of developing a preliminary chemical compound, prompting him to seek out Tri-I TDI—without whose intervention, Houvras believes, the research would still be at a standstill. "Compounds that work in cells, or will work in animals like zebrafish, usually don't have drug-like properties that would make them appropriate for treating humans," he says. "That's where the partnership with Takeda comes in. They can help turn compounds into actual drugs. That's an important goal, because ultimately we want to treat patients."

'Compounds that work in cells, or will work in animals like zebrafish, usually don't have drug-like properties for treating humans,' says Yariv Houvras, MD, PhD. 'That's where the partnership with Takeda comes in.'

While the length of funding for a Tri-I TDI project is determined on a case by case basis, Foley believes that for most, two years should be sufficient to determine whether continued investment is warranted. As projects exit the program—whether it's because a drug company licenses the technology or because investigators are unable to make progress—they will be replaced by another from the same institution, insuring that all three academic centers get an equal shot. The total number of ongoing projects will likely remain the same, between six and eight at a time. Petsko, for one, is astounded by how quickly the Institute has generated interest among talented researchers. "We really expected this to take a while to ramp up," he says. "Nothing could be further from the truth."

Gregory Petsko, DPhil




Richard Furman, MD

Improving the Odds

For decades, Weill Cornell has been a leader in the research revolution that's making lymphoma a survivable disease

By Amy Crawford

Portraits by John Abbott

When Bob Azopardi arrived for his first appointment at the Sandra and Edward Meyer Cancer Center at Weill Cornell Medical College and NewYork-Presbyterian Hospital in October 2010, he was desperately ill. It had been ten years and many rounds of chemotherapy since he was first diagnosed with chronic lymphocytic leukemia, a type of non-Hodgkin's lymphoma. His oncologist had told him that he'd done all he could. "My doctor had gone through his whole bag of tricks," recalls Azopardi, who'd been forced to give up his X-ray repair business as his health declined. "I was told to put my house in order, because this was it."

With swollen lymph nodes the size of oranges in his neck, under his arms, and pressing on his sciatic nerve, Azopardi was in constant pain and could walk only with difficulty. At the age of sixty, he was preparing to say goodbye to his wife of two years—high school sweethearts, they'd rekindled a romance at their thirty-fifth reunion—when a colleague of his oncologist suggested he see Richard Furman, MD, director of Weill Cornell's Chronic Lymphocytic Leukemia Research Center. "It took three people to get me on the table,"

New lease on life: Bob Azopardi with his oncologist, Richard Furman, MD

Azopardi recalls. "Dr. Furman looked at me and said, 'You're a very sick man, but I do have a clinical trial, and if it works for you, you'll be dancing in six weeks.' I said, 'Dr. Furman, have you ever thought about seeking psychiatric care?' He said, 'Trust me.' "

It turned out that Furman's promise was nearly correct: a little more than four weeks after starting on a new, once-daily pill called ibrutinib, Azopardi walked unassisted for the first time in nearly two years. The 2010 trial he participated in was just one of dozens that have taken place at Weill Cornell's Center for Lymphoma and Myeloma over the past two decades. Still thriving more than four years later, Azopardi is just one of countless patients whose lives have been saved.

Physicians diagnosed about 80,000 new cases of lymphoma in the U.S. in 2014, attributing 20,000 deaths to the disease. On the upside, five-year survival rates have been rising steadily. In the more common non-Hodgkin varieties, for example, survivability has risen from less than 50 percent in 1990 to more than 70 percent in 2011. That's the last year for which statistics are available, but lymphoma specialists say that rates have improved even more in just the past few years, thanks in large part to drugs like ibrutinib, which saved Azopardi's life. Now marketed under the trade name Imbruvica, it was approved by the FDA in 2013. "There have been several major breakthroughs, and what excites me is that we're actually turning them into new treatments for patients," says John Leonard, MD, associate dean for clinical research, the Richard T. Silver Distinguished Professor of Hematology and Medical Oncology, and chair of the Lymphoma Committee of the National Cancer Institute's Alliance for Clinical Trials in Oncology, which helps set the national agenda for cancer research. Plus, he notes, because lymphoma is principally treatable with drugs—not surgery—research on the disease often leads to discoveries that spur progress in the fight against other cancers.

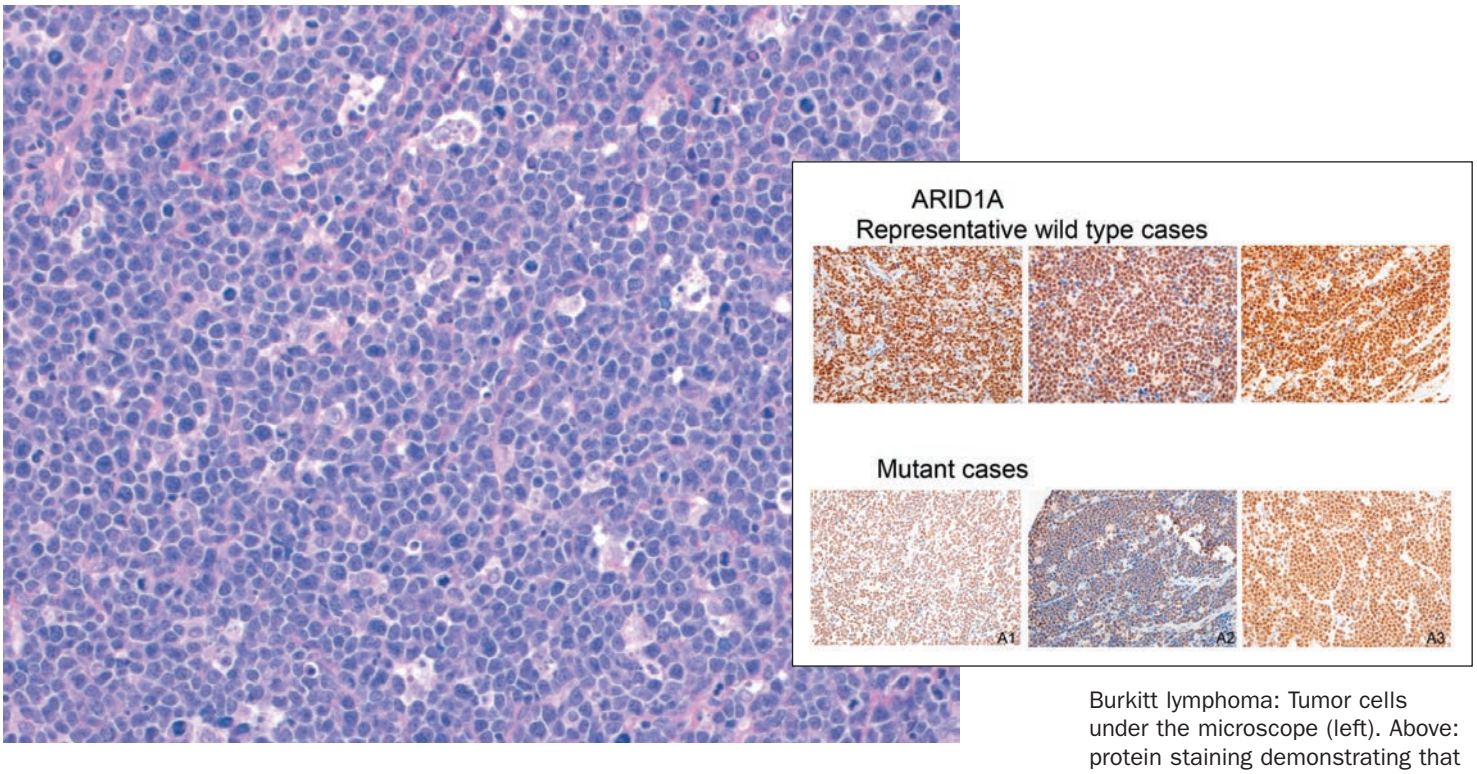
'There have been several major breakthroughs, and what excites me is that we're actually turning them into new treatments for patients,' says John Leonard, MD.

Leonard—along with Furman and Morton Coleman, MD, a clinical professor of medicine and the center's former director—was among the first Weill Cornell physicians to get involved in trials of lymphoma drugs, back in 1997. Since then, Weill Cornell has helped to develop a series of breakthrough treatments, including nearly every lymphoma drug that the FDA has approved in the past fifteen years. It's a track record that Leonard chalks up to the Medical College's ability to attract the best doctors and researchers in the field, and encourage them to work together to tackle what was historically one of the toughest problems in oncology. Among the core group of veterans, Leonard says, are Coleman (who remains an active member of the voluntary faculty) and Furman, who has been at Weill Cornell for twenty years. "There have been some key clinical faculty who have been here awhile, and we've trained or recruited some additional ones," he says. "We've got a critical mass of people who are involved, and I think it feeds on itself. You get more opportunities, people know you, they approach you, you build collaborations. This has led to partnerships with a number of talented laboratory researchers, and even greater progress."

Lymphoma's Long History

Lymphoma is cancer of the lymphatic tissue, part of the body's immune system that includes the lymph nodes, spleen, thymus gland, and bone marrow. It originates from abnormal lymphocytes, a type of immune cell, and it can spread throughout the body or remain, in so-called indolent form, in the lymphatic system. It was known in the early nineteenth century; in 1823, the English physician Thomas Hodgkin described the class of lymphomas that would bear his name. By the 1960s, lymphoma was routinely treated with chemotherapy and radiation, but these therapies could have devastating side effects that in some cases were worse than the disease. Beginning in the Nineties, medicine began to make serious headway, improving understanding of the myriad types of lymphomas and how they differ, and then developing therapies precisely targeted to each disease.

First came monoclonal antibodies, artificial versions of immune system proteins that



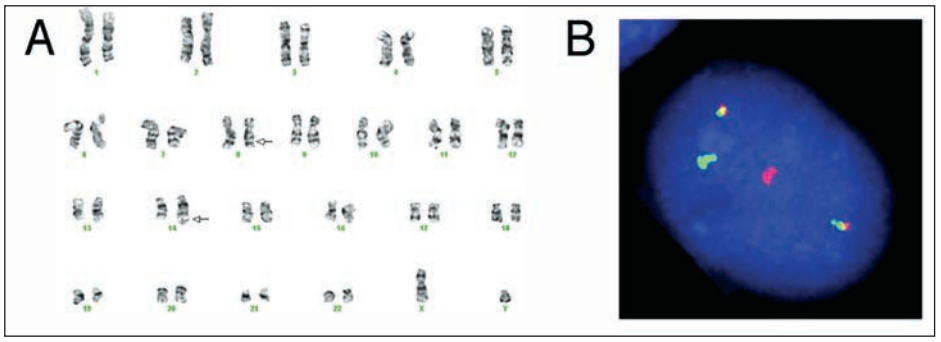
Burkitt lymphoma: Tumor cells under the microscope (left). Above: protein staining demonstrating that some Burkitt tumors lack the ARID1A protein, which may help explain why they're more aggressive and resistant to chemotherapy.

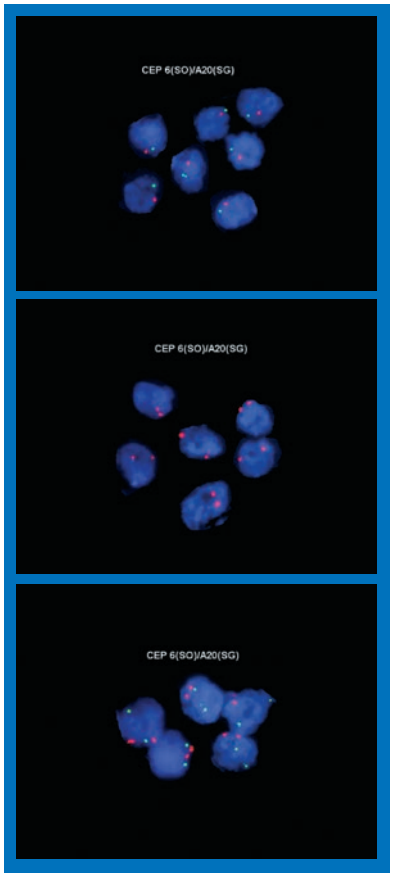
bind chemically to surface markers on specific types of cells. The technology, in development since the Seventies, had helped refine the classification of lymphomas during the Eighties and early Nineties, leading to its therapeutic use to tag cancer cells and recruit the body's own immune system to eradicate tumors. In 1997, when the FDA approved a monoclonal antibody called rituximab for B-cell non-Hodgkin lymphoma and chronic lymphocytic leukemia, the new drug offered the first proof that immunotherapy could be an effective cancer treatment. "That was the thing that heralded the move beyond standard chemotherapy," says Peter Martin, MD, the Charles, Lillian, and Betty Neuwirth Clinical Scholar in Oncology and director of the Clinical Research Program in Lymphoma. "Oncology was entering a new era."

Monoclonal antibodies have been followed by other classes of targeted therapies, including immunomodulatory drugs (IMiDs) like lenalidomide and thalidomide—although the latter causes birth defects in pregnant women, it's an effective treatment for certain cancers—and small-molecule kinase inhibitors, which block chemical signaling to interfere with lymphoma cells' ability to survive and grow. Because they are so precisely targeted, these new drugs have far fewer side effects than either chemo or radiation, which kill healthy cells along with cancerous ones.

One kinase inhibitor, ibrutinib, is the drug Furman used to treat Azopardi. It blocks an enzyme called Bruton's tyrosine kinase, which is necessary for the maturation of B-cells, part of the immune system that becomes cancerous in most non-Hodgkin lymphomas. In 2013, the results of clinical trials at Weill Cornell and elsewhere—including the one for which Azopardi volunteered—showed that patients with mantle cell lymphoma and chronic lymphocytic leukemia, both incurable, responded remarkably well to ibrutinib. The FDA labeled it a "breakthrough drug" and accelerated its approval for patients who had had at least one prior therapy. But even as the lymphoma community celebrated, a team of Weill Cornell researchers led by Furman made a troubling discovery: lymphoma cells could eventually mutate and become resistant to the drug. Those findings led them to embark on new clinical trials to look at a second-generation version of ibrutinib and to study how it performs in combination with other drugs. Leonard, Coleman, Furman, and Martin have been intimately involved in the development of some of the most promising molecules of the past decade—ibrutinib included—as have colleagues Lisa Roth, MD, assistant professor of pediatrics, and Jia Ruan, PhD '98, MD '99, associate professor of clinical medicine.

Furman adds that it appears patients are less likely to become resistant when they have not previously been exposed to chemotherapy, which means that the standard of care for





All aglow: Fluorescent probes (above) staining a newly described gene, A20, important in Burkitt lymphoma. Top: Chromosomes of a Burkitt tumor (A) and fluorescent probes (B) showing its classic chromosomal change.

certain lymphomas might one day leave out chemo entirely—an exciting prospect not only because it has devastating side effects but also because the cancers quickly develop resistance to it. "Patients die from their disease becoming refractory to treatment, or due to the toxicities of the treatments themselves," explains Furman, the Morton Coleman, MD, Distinguished Associate Professor of Medicine, adding that life expectancy was once ten years after the start of treatment. "We still need long-term data, but these new agents even work in chemotherapy refractory disease. The ability to work when chemotherapy does not, and without toxicities, indicates the tremendous potential that exists for these new agents. I have patients who came to me at death's door five years ago who are alive and well and have wonderful quality of life. Now, I can honestly say I hardly ever lose a patient. It's certainly very nice for an oncologist to be in that position."

Rewriting Faulty Instructions

As good news continues to come from the front lines, researchers at the Meyer Cancer Center and elsewhere at Weill Cornell are also at work in the lab, trying to improve understanding of the disease and searching for even safer and more effective treatments. Roth, head of the newly created Adolescent and Young Adult Lymphoma Program, notes that lymphoma is the most common cancer among people between the ages of eighteen and thirty. While current therapies are often very effective for this population, young adults also have different needs—preserving their fertility, for example—so the potential for better treatments is exciting. "In the laboratory, we're looking at a large panel of drugs that haven't made their way to clinical trials yet," says Roth, the Charles, Lillian, and Betty Neuwirth Clinical Scholar in Pediatric Oncology. "What is most radical and new is how we screen these drugs."

In the past, lymphoma has been modeled in the lab using mice that have been injected with lines of human lymphoma cells. These cell lines were derived from patients as far back as the Fifties and maintained in the lab, but because of their age they no longer replicate in the same way that lymphoma grows in people. "That's why a lot of these drugs make it to clinical trial and fail," Roth explains. But Weill Cornell researchers now maintain a bank of lymphoma samples from recent patients, which can be injected directly into mice. "We have these systems up and running now to mimic, in a much more accurate manner, what would likely happen in a patient," Roth says. "We can take a patient's tumor and put it into a mouse and then evaluate these new drugs to see which one is most effective."

The most promising direction for drug development may lie with the epigenome, the set of chemical switches that modify how cells read their genetic codes. "You can think of the genome of DNA as being like the computer hardware," explains Ari Melnick, MD, the Gebroe Professor of Hematology-Oncology and director of the Raymond and Beverly Sackler Center for Biomedical and Physical Sciences. "Computer hardware is kind of inert on its own, but epigenetics is the cell software, the instructions that control how cells behave."

Sometimes, this software contains errors that cause cells to proliferate out of control: they become cancerous. That's especially likely to happen in B-cells, Melnick says. "B-cells are our defense mechanism—they can't fool around," he says. "So in order for normal B-cells to make antibodies to the bugs that infect us, they undergo radical and rapid changes. That's all controlled epigenetically." But sometimes, instead of helping B-cells adapt to fight new pathogens, these changes switch on instructions that tell cells to proliferate or that keep them from dying when they're no longer needed. Such errors may mean the patient develops lymphoma. But drugs could rewrite these faulty instructions.

Epigenetics are coordinated by regulatory proteins—including, in B-cells, a molecule called BCL6. Normally, when the immune system is fighting a pathogen, this protein coordinates key sets of genes to increase B-cell production. However, growing B-cells have a tendency to develop mutations that maintain BCL6; the end result is that B-cells grow out of control and transform into lymphomas. Melnick and his team are designing drugs that inhibit BCL6 without harming the immune system, and they hope to have a new therapy ready for clinical trials within a year

or two. “All those instructions that are required for lymphoma disappear when we target BCL6 with our inhibitors,” Melnick says. “Without BCL6, the lymphoma cells can’t survive; they just dissolve.”

Other Weill Cornell and Meyer Cancer Center labs are working different epigenetic angles. Leandro Cerchietti, MD, the Raymond and Beverly Sackler Research Scholar and an assistant professor of medicine, has spent many years developing a new protocol for treating diffuse large B-cell lymphoma, a common but highly aggressive subtype. In chemotherapy-resistant forms of the disease, epigenetic alterations switch off genes that normally trigger cell death, effectively silencing them by adding chemicals called methyl groups to the DNA. But Cerchietti and colleagues discovered that a drug called azacitidine could remove these methyl groups and switch the genes back on, making subsequent chemo more effective. It took five years to figure out how to make this work in humans, but eventually they settled on a five-day regimen that led to complete remission in eleven out of twelve patients in a 2013 proof-of-concept trial.

John Leonard, MD (left), and Leandro Cerchietti, MD

The drug, Cerchietti explains, reprograms the lymphoma into a less aggressive disease—a technique that could prove effective in many different cancers. “Over the past years there has been an increasing understanding of the molecular basis of lymphomas that fueled an explosion of therapeutic opportunities,” Cerchietti says. “The biggest challenge we face nowadays is how to rationally translate them to cure more patients.” To that end, Cerchietti and his colleagues are developing strategies against lymphomas based on characteristics that extend to the molecular level. In addition to testing these new targeted therapies in lab mice, they are working with the College of Veterinary Medicine on the Ithaca campus, looking at how new drugs might help fight spontaneous lymphomas in pet dogs; investigators include research oncologist Kristy Richards, MD, PhD, who has a joint appointment at both institutions. “This is an incredibly challenging endeavor, but it is also extremely rewarding,” Cerchietti says, “and it’s made possible by a highly motivated and collaborative team of scientists and physicians.”

‘This is an incredibly challenging endeavor, but it is also extremely rewarding,’ says Leandro Cerchietti, MD, ‘and it’s made possible by a highly motivated and collaborative team of scientists and physicians.’

Although more breakthroughs may be on the horizon, lymphoma remains a challenging disease. For Martin, the story of a patient he treated several years ago sums up both the excitement and the frustration of working in the field today. His patient, an older man with mantle cell lymphoma, had come to Weill Cornell to participate in a clinical trial of ibrutinib after his disease had failed to respond to the standard treatments. “He was starting to become quite sick, losing a lot of weight,” recalls Martin. “He had a lot of lymphoma in his lungs, and his breathing was getting worse quickly. The day that he was due to start the clinical trial, he had to be hospitalized.”

A few doses into his treatment, the patient choked on a pill because tumors were compressing his airway and affecting his ability to swallow. He stopped breathing, and after doctors resuscitated him he wound up intubated in the ICU. “It was a real challenge, because the lymphoma was the reason he was so sick—and the only means for treating it was with the ibrutinib, but there was no way we could give him an oral therapy while he was intubated,” Martin remembers. “We spent a day really not knowing what was going to happen. Then in a moment of delirium the patient pulled the tube out, and, surprisingly, his breathing was okay. He was able to swallow the pills and, in a very short period of time, improved dramatically, so that six months later the lymphoma was mostly gone. Nine months later he was hiking in the mountains. This was a man who had literally almost died in the hospital—unbelievable.”

Two years later, the patient’s lymphoma returned, and this time he succumbed. “That story really sticks with me for a couple of reasons,” Martin explains. “One, because of all of the work that people did to develop this drug, this guy had two years that would have been taken away from him. You have this incredible celebration of life, a victory.” Martin pauses, smiles, and shakes his head. “But then, on the other hand, there’s still so much work left to do.”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A Precise Approach

Precision medicine nets early results—with the promise of more to come

By Anne Machalinski
Portraits by John Abbott

In December 2013, right before she had her bladder removed, Irene Price heard the term "precision medicine" for the first time. She'd been diagnosed with cancer about five years earlier, and in the interim had exhausted the standard treatments—chemotherapy and a bladder-cancer-specific immunotherapy—both of which had shown early promise. But the once-contained cancer continued to spread, and she was running out of time. Then her doctors told her they planned to analyze her tumor using next-generation DNA-sequencing technology to look for genetic alterations that might point to new treatment options. "I was excited," says Price, a seventy-seven-year-old from Livingston, New Jersey, "and also anxious to see the results."

When the tests came back, they revealed something unexpected: multiple copies, or amplification, of a gene typically associated with breast cancer growth. Based on these results, Price's medical team targeted the alteration using an approach not FDA-approved for her type of disease—chemotherapy with Taxol and Herceptin, drugs frequently used in breast cancer—and it worked. As of June 2015, the date of her most recent CAT scan, she has shown no evidence of cancer. "I don't think I'd be here without that test," Price says. Her oncologist agrees. "The genomic testing was extremely informative," says David Nanus, MD, chief of the Division of Hematology and Medical Oncology. "I would never have used Herceptin without the precision medicine data."

Caring relationship: David Nanus, MD, with patient Irene Price


Mark Rubin, MD

While Price represents an early ideal of this approach, patient success stories are expected to multiply as clinicians increasingly target the genomic characteristics of a disease rather than its site of origin. Having already performed comprehensive genomic testing on about 300 patients with advanced cancers over more than two years, the Caryl and Israel Englander Institute for Precision Medicine at Weill Cornell is poised to lead the charge toward making this personalized approach the standard of care. The Institute received a generous gift from the Englander family this month to widen its mission to emphasize dermatological malignancies as well as metabolic diseases, cardiovascular disease, genetic disorders, and respiratory diseases and eventually offer precision medicine to as many as 6,000 cancer patients a year. (For additional information, see "Scope" on page 6.) "There's no playbook. We need to establish our own guidelines in real time," says the Institute's founding director, Mark Rubin, MD, the Homer T. Hirst III Professor of Oncology in Pathology. "Our goal is simply to direct the patient to the right care. It's really out-of-the-box thinking, and we're innovating and figuring out what to do all the time."

While the Englander Institute—comprising a growing team of about fifty—offers advanced-stage cancer patients access to the most powerful genomic test in New York State, three years ago the organization didn't even exist. Rubin is a renowned pathologist and expert in genomics research who has dedicated his career to understanding and combating prostate cancer; he came to Weill Cornell seven years ago to develop a genomics center. Since the early days of his career—which has included work at a number of prestigious institutions like NYP/Columbia, the University of Michigan, and Harvard Medical School—he has always believed in the concept that doctors are "clever detectives," making discoveries about their patients based on direct observations and clinical data. "Adding genomics to the toolbox means having thousands of additional pieces of information that can help you make discoveries and answer questions," he says. "That's the genius of medicine."

Guided by his vision, the Institute for Precision Medicine opened in January 2013 as one of the first entities of its kind. Rubin's first order of business was to gather a dream team of clinicians, researchers, data experts, and others. Its leadership includes Himisha Beltran, MD, a medical oncologist and physician-scientist who serves as the Englander Institute's director of clinical activities, and Olivier Elemento, PhD, who joined the team from the HRH Prince Alwaleed Bin Talal Bin Abdulaziz Alsaud Institute for Computational Biomedicine (ICB) at Weill Cornell, where he heads the Laboratory for Cancer Systems Biology.

Although Rubin's team has advocated for precision medicine's potential for years, the approach got widespread attention in January when President Obama used his State of the Union address to announce a national initiative, which earmarked $215 million from the proposed 2016 budget for expanded clinical and research development in the field. More recently, the National Cancer Institute launched a nationwide precision medicine research study that will sort patients into treatment groups based on genomic alterations in their tumors, representing a sea change in oncology. "All of a sudden, there's an environment where people want to know what precision medicine is and what's going on," says Rubin, who was invited to the Obama initiative's announcement at the White House. "The fact that we are already doing it allows us to drive the conversation and innovation in this field."

A Key Test

To pinpoint individualized therapies, a number of clinicians offer patients a simple genomic test that canvasses a tumor tissue sample for mutations on fifty to 400 genes that can be targeted with proven therapies. This process is called "focused" or "panel" sequencing. But there's a second, more comprehensive type of test that reviews up to a hundred times more genes to uncover alterations basic tests can

miss. Called "whole exome" sequencing, this process looks where DNA is transcribed into RNA—a region of the gene called the exome—and helps researchers find new therapeutic pathways for patients who have exhausted standard protocols. While some area medical centers offer the first kind of test, Weill Cornell is the only institution in New York State to offer the second.

The Englander Institute-developed test, called EXaCT-1 (for EXome Cancer Test-1) was recently described in *JAMA Oncology* by Beltran and colleagues; it looks for any and all mutations across more than 21,000 genes. Because it doesn't focus on expected mutations or those tied to a specific treatment protocol (what physicians call "actionable"), it's especially effective in pinpointing previously undetected alterations in patients' tumors. (As Elemento notes: "The advantage of sequencing the entire tumor genome is that we're not going to miss anything.")

> 'All of a sudden, there's an environment where people want to know what precision medicine is and what's going on. The fact that we are already doing it allows us to drive the conversation and innovation in this field.'

Early on, the team decided to focus on patients with advanced-stage cancers. "The typical approach in cancer treatment is that you first start with the most advanced disease, because those patients are out of options," Rubin explains. "The discovery of an effective drug in this advanced setting paves the way for using it earlier and earlier with the hope that it will prevent the tumor from progressing. That's where we can have a cure."

Rubin and his team emphasize that the test is not just about sequencing a tumor's DNA. It's about gathering that data—enough to fill a 100-gigabyte hard drive—and then synthesizing it and delivering the results in a way that's easy for the physician to access, read, understand, and share. "How the clinician interacts with the data and communicates the findings back to their patient is the most important thing," Rubin says.

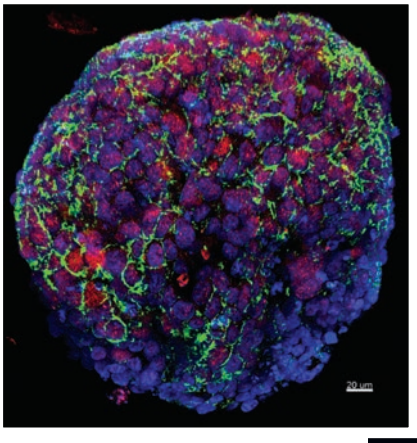
The process—which requires extensive teamwork between surgeons, medical oncologists, and radiation therapy experts—starts with the samples: the patient's blood (the control) and tumor tissue, ideally with a large percentage of abnormal cells. DNA sequencing takes about two days, after which the raw data is sent to a supercomputer for additional, automated analysis. At the end of this process, an easy-to-read report—including clinical information, images of the tumor, and a summary of discovered mutations—is generated. Someday soon, Rubin hopes to benefit patients by seamlessly delivering such reports directly to a clinician's iPad, Android device, or Apple Watch—"the simplest solution in an elegant, easy way"—but today, it's e-mailed as a PDF file. On it, the list of mutations is grouped into three categories. At the top are mutations that drive cancer growth and are connected to a known treatment protocol; the middle have been previously observed in other tumors and may very well drive the disease but are not well understood and not therapeutically targetable; and the bottom are of unknown significance, and not yet connected to cancer.

On Fridays, the precision medicine team meets in a tumor board to review the results of one to five patients to discuss available treatment options and next steps. From start to finish, the process of running the sequencing test, generating the report, reviewing the findings, and pursuing new treatments currently takes four to six weeks—slower than a focused test that looks at only a few hundred genes, but still fast enough to influence outcome if there's a new therapeutic option available. Rubin, though, hopes to speed up that timeline to two weeks from the start of the test to the treatment recommendation.

Big Promise, Mixed Results

For Irene Price, the standard treatment—flushing out her bladder with a weakened form of a tuberculosis vaccine pathogen, called BCG therapy, and monitoring her disease—was enough to keep the cancer contained within her bladder for years. After it spread to her lymph nodes, Price underwent chemotherapy, and in October 2013 she was given a clean bill of health. But the cancer returned within weeks. That December, she had her bladder removed.

Early in 2014, tumor tissue from that surgery was sequenced and the precision medicine report came back with a targetable alteration: over-expression of a gene called HER2. Amplification of this gene is known to drive cancer growth, and it is frequently detected in breast cancer patients, says Nanus, who is also the Mark W. Pasmantier Professor of Hematology and Oncology in Medicine and the associate director of clinical services at the Sandra and Edward Meyer Cancer Center at Weill Cornell and NYP. An antibody-based therapy that targets that alteration has saved many lives, but it is not normally used in a patient like Price, who had bladder—not breast—cancer. But because Price had run out of options, and her cancer had spread to her liver—giving her, statistically, about a year to live—they gave it a try. And it worked. "I can tell you very clearly that we would not have been able to find that mutation using a fifty-gene panel," says Elemento, noting that commonly used



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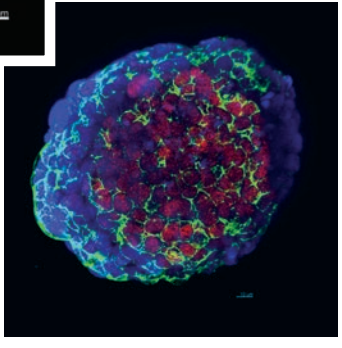

Genomic testing: Tumor cells from a biopsy of a patient enrolled in a trial evaluating the efficacy of whole exome sequencing.

focused panels do not look for gene amplifications or deletions.

But not all precision medicine results are as straightforward as Price's. While her report included a known alteration that had a highly proven and available therapy connected to it, many patients' reports don't reveal mutations that can be tackled with readily accessible treatments. New research that Beltran, Elemento, Rubin, and colleagues recently published in *JAMA Oncology* detailed the Englander Institute's work with its first ninety-seven patients. They explained how they were able to pinpoint previously unknown mutations and recommend new therapeutic options 92 percent of the time—but only 5 percent of those patients actually gained access to the recommended treatment. In some cases there wasn't a clinical trial being offered nearby. In others, clinicians couldn't access the proposed drugs, or they were too expensive. "As trials are developing and the medications become more accessible, I think that success rate will change in the coming years," Beltran says. But for now, she says, accessibility of therapies is one of precision medicine's major limitations.

Even in Price's case, once the clinicians found a target, the recommended treatment wasn't FDA-approved for bladder cancer, so Nanus and others from the team had to petition her insurance company to pay for it. They gained that approval, but advocating for each and every precision medicine patient—or starting single-subject clinical trials to get them the drugs that they need—is time-consuming and unsustainable. "We need to figure out a process to quickly and seamlessly get FDA approval and move past this bottleneck," Rubin says.

'We're learning from each individual patient,' says Himisha Beltran, MD. 'By studying the extremes—people who respond really well and people who don't respond at all when they should—we are learning more about which molecular alterations are important in predicting response to treatment.'

Another challenge of using the EXaCT-1 test—which reviews genes without looking for specific mutations, like panel tests do—is that the majority of alterations fall into the category of "unknown significance." This is why research is so important, Beltran says. Some of those alterations are likely driving cancer growth and spread—and by identifying these key drivers and understanding how they work, scientists can develop new therapeutic options—but many others are likely inconsequential to the disease. "We're learning from each individual patient," Beltran says. "By studying the extremes—people who respond really well and people who don't respond at all when they should—we are learning more about which molecular alterations are important in predicting response to treatment."

To learn more about mutations, the precision medicine team often splits the biopsied tumor tissue in half. (Indeed, a patient can only benefit from precision medicine when his or her cancerous tissue is made available for analysis.) While one part goes toward DNA sequencing, the other is used in the lab to grow mini-tumors (also called organoids) or implanted into mice. These tumors can be propagated indefinitely and treated with various drug combinations in a search for the most effective treatment strategy. In time, the team hopes to identify new targetable mutations and develop treatment protocols based on this bench work.

The Case for Data

While gathering genomic information can help clinicians determine the right treatment for each patient, the development of robust, searchable databases (a process that received early attention from the ICB) is also vital to precision medicine's success. Currently, the Englander Institute has its own internal database, which it updates with information on genetic mutations, associated drug trials, and patient outcomes. But that data set, while growing, is relatively small. Creating databases that incorporate clinical information from patients at institutions across the country and around the world is essential, Elemento says. "Individual institutions just can't keep up," he says, "and it doesn't make sense for everyone to have their own database." Rubin agrees. "With vast clinical data, if we have a patient sitting in front of us who has a mutation that we've never seen before, we can ask the question, 'Has anyone ever seen it before?' " he says. "One of the biggest hurdles within precision medicine is to marry clinical and genomic data and also have a way to share that data. Our dream is to find a way to do this."

The New York City Clinical Data Research Network (NYC-CDRN), launched in January 2014, is an early example of effective clinical data sharing to support research. Notable for its breadth and scope, it includes the largest and most diverse collection of patient records in the country, connecting more than 40 million encounters from the medical records of a growing pool of more than 4 million individual patients records from six healthcare systems in New York City. "For common conditions, getting broad data like this is phenomenal," says the project's principal investigator, Rainu Kaushal, MD, MPH, chair of the Department of Healthcare Policy and Research and a national leader in developing medical data systems. "For rare diseases or mutations, it's even more valuable because you can get a significant sample size to study them."

Investigators working on a wide variety of diseases and conditions are already requesting access to the network's data, which could eventually include everything from the results of an annual physical to those of a genomic test, Kaushal says. Doctors, too, will be able to gain valuable insights from it; for instance, by tracking how cancer patients with a rare mutation have responded to a certain treatment, they can make more informed decisions in treating people with that same genetic make-up.

Beltran notes that while the identity of individual patients is scrubbed from these databases, it's important that there be a way to re-identify them, if necessary. "I think in the next five years we're going to be able to present patients who have genomic information in their medical records with new findings and treatment options," she says. "If a mutation moves from the 'unknown' to the 'actionable' category, there would be good reason to follow up with patients who have it."

Looking Ahead

While at present the precision medicine approach is primarily used in cancer diagnosis and care, experts agree that in the future it will have

Precious time: Price at home with her grandchildren

wider clinical relevance. As our understanding of human biology improves, Elemento says, doctors will increasingly look to analyses of "germline"—or heritable—DNA, for alterations that predispose people to Alzheimer's, schizophrenia, pulmonary disease, or other conditions. BRCA1 and BRCA2 mutations—germline DNA variations connected to an increased risk of developing breast or ovarian cancer—are the most prominent examples of how this type of test is used to date.

Increased use of sequencing tests in cancer is likely in the future, too, Rubin says, especially earlier or more often in the diagnosis and treatment stages. The results may dictate not only how a patient is treated, but also what approaches are used early on, like whether to try the latest immunologic therapies. "I think a year or two from now—but not five—insurance companies will be advocating for patients to have some sort of genomic test before they're approved for treatment," he says.

But to make this type of test more accessible, its costs will have to decrease. While EXaCT-1, which is currently being reviewed by the New York State Department of Health for clinical use, currently costs a few thousand dollars per patient on paper, it's likely closer to $30,000 if everyone's time and effort is taken into account, Rubin says. But that doesn't mean the test—or approach—should be abandoned. "It's like if you were building a prototype car," he says. "The first car might cost $3 million; you would never sell it. But you can't get to the final car that costs $15,000 or $20,000 until you've done all the testing and established a production line. Soon, all of these worries about the turnaround time and cost are going to be trivial." Nanus agrees, comparing genomic testing's rise in technological sophistication and drop in cost to cell phones, which were once expensive but are now affordable and ubiquitous. "Someday, it will be the standard of care," he says. "Everybody will get their tumor sequenced."

Despite the high cost and mixed results, Rubin says, there's substantial value in charting new territory in this field. By being in the vanguard, he says, the Englander Institute for Precision Medicine can build things like the EXaCT-1 test from the ground up to its own specifications. He compares the Englander Institute to a start-up company that helps define an industry. "We could wait and then re-enter this arena when there's a kit and the test will be done in an hour," Rubin says. "But with contributions from pathology, oncology, urology, and computational biology, we're gaining expertise, we're honing our communication platform so that the results make sense to the patient, and we're conducting meaningful research that's going to have a long-lasting impact."

For Price—who still has CAT scans and heart tests every few months, and regularly checks herself for new lumps in her groin, where they appeared in the past—the glass is more than half full. Precision medicine and her Weill Cornell team have bought her more time with her family—allowing her to see the birth of her second great-grandchild, Hailey, in March; to help move her granddaughter to a town just thirty-five minutes away; and to gather with her extended family to celebrate her grandson's kindergarten graduation this summer. Despite being on maintenance chemotherapy—a Herceptin drip every three weeks for thirty minutes—she's feeling good. "I'm just so thankful," Price says. "I'm not ready to go."

Notebook

News of Medical College and Graduate School Alumni

PROVIDED

Spencer Kubo, MD ’80

Dear Alumni,

Graduation season is always a special time for the Alumni Association. On May 5 and 6, I had the pleasure of attending Convocation and Commencement ceremonies for forty-two new graduates of the Doha campus. On May 27 and 28, I had the same privilege for the ninety-six from the New York campus.

I enthusiastically welcomed the graduates into our Alumni Association and encouraged them to become active members. We are a very select organization: there are approximately eight million physicians in the world, but only 5,700 can claim membership in our association. We now have 138 new members, representing some of the brightest and best-trained physicians anywhere.

From the Commencement stages, I had panoramic views of the graduates and their families who were sitting in the audience beaming with a sense of accomplishment and pride. I reflected on memories of my own graduation thirty-five years ago and felt an overwhelming sense of gratitude and appreciation for a fulfilling and rewarding career in medicine.

During the festivities, a central theme repeated by several speakers was the importance of mentorship, as students and faculty expressed their appreciation of its vital role and how it shaped their lives. Alumni, too, expressed that same sentiment countless times during Reunion 2014 last October. Undoubtedly, there is an enduring tradition of mentorship at Weill Cornell. In fact, in my opinion, the tradition of mentorship is what makes it the very special institution it is today.

Another recent highlight was the Award of Distinction Dinner, where we honored Steven Gabbe, MD ’69. An internationally acclaimed expert in obstetrics and gynecology, Dr. Gabbe has held leadership positions at six prestigious institutions, including as dean of Vanderbilt University and senior vice president and CEO of Ohio State University’s Wexner Medical Center. The event was a double celebration for me, since Dr. Gabbe was nominated by my friend and classmate Mark Landon, MD ’80, chief of obstetrics and gynecology at Ohio State.

The criteria for the Award of Distinction has remained the same since the first was given to William Sharp McCann in 1949: it goes to an individual “who demonstrates exceptional achievement in the areas of education, research, or patient care and who has brought honor and acclaim to the Medical College.” The next time you’re on campus, be sure to check out the plaque, in the corridor leading to Griffis Faculty Club, listing all sixty-seven honorees—certainly a great source of pride for Weill Cornell.

I hope you enjoyed your summer. The Alumni Association was thrilled to welcome the Class of 2019 in August!

Warm regards,

Spencer Kubo, MD ’80
President, WCMC Alumni Association
spencer.h.kubo@gmail.com

1950s

Charles Santos-Buch, MD '57: "Our entering class was blessed to 'walk among giants'; they were accessible and so personal and helpful to us. I had the privilege to be a member of the Department of Pathology for many years. My research interests, like those of Ben Kean, were in tropical diseases and the autoimmunity they provoke, and like those of George Murphy in myocarditis and the subsequent cardiomyopathy they induce. I published avidly on research of hypertensive disease-induced strokes. Associate Dean Jim Curtis and I administered and ran the very successful integration of minority disadvantaged candidates into our student body and opened up the admission requirements to women. I was the first Hispanic full professor in the Medical College's history. I also developed modern techniques for the Papanicolaou Cytology Laboratory and gained the trust of a great many of our clinical faculty over the years. My retirement is at Key Biscayne, FL, and we have endeavored to explore the Bahamas and enjoy the enormity of the archipelago and its beauty with friends there. We have traveled widely in Asia, principally Hong Kong and Phuket, Thailand. We have taken a boat, a Baby Bertram, along the Malacca Straits and avoided pirates along the way. Carol, my beautiful wife, is at my side always, and right now I am writing a book tracing my family's journey from 16th-century Spanish colonialism in Cuba to American modernity. Rogues and heroes alike. I hope my writings are exacting and humorous, interesting and contributory. We shall see. My three boys are successful in business, and two of them are near in South Florida with their children. A third regrettably is far away in Seattle. Here is a toast with aged Bacardi rum to my entire Class of '57: may we live long and significantly."

Howard R. Francis, MD '58: "I'm retired from a very busy ob/gyn practice and am currently delivering lambs and calves out on the ranch in Nevada. I snowmobile in Wyoming and mule-ride in Utah. I go fishing with some of my 29 grandchildren, welcome the great-grandchildren one by one, and travel in the camper with my wife of 54 years. I will be 86 this year. I want you all to know, retirement is seriously underrated!"

Martin W. Korn '55, MD '58: "Phyllis and I summited Mt. Kilimanjaro in 2009, transited Southeast China's Tiger Leaping Gorge (gorgeous!) in 2012, and spent six weeks this past winter meandering south by car visiting family and friends. We left Rochester, NY, and explored Key West and the Everglades, and many stops with wonderful people in between. It was a perfect winter not to be in the North with its brutal cold! I'm developing a new internal fixation system with some unique features, with biomedical engineers at the University of Rochester, for a different technique for high tibial osteotomy. I also do some orthopaedic independent medical exams. Our summer home in the Adirondacks town of Schroon Lake, and its Seagle Music Colony (this is the centennial year!), occupy much of our attention. And then there's tennis, sailing, music, theatre, family, and friends: a full life for which we are grateful."

WCMC

Perfect fit: Faculty help first-years don their white coats at the traditional ceremony in August.

Michael H. Stone '54, MD '58: "During the past year I have lectured on personality disorders and forensic topics in Milan, Vienna, Mexico City, and Guatemala City. I became an associate editor of a new journal, *Violence & Gender*, and wrote articles there on mass murder, men who kill policemen, and varieties of murder committed by men. In other journals I have published articles recently on the neurophysiology of borderline personality disorder and on the adverse effects of marijuana in adolescents. My wife and I are patrons of the Metropolitan Opera and are members of the Reform Club in London."

Edward Wallach, MD '58, and his co-authors, Esther Eisenberg, Isabel Greene, and Stacey A. Scheib, explain all aspects of hysterectomies in an updated edition of *Hysterectomy: Exploring Your Options*. Hysterectomy is the second most common major surgical procedure performed on women in the U.S. For some women, the decision to have the procedure is an easy one; for others, it is a difficult choice associated with concerns about risks, discomfort, and female identity. Yet many disorders of the uterus—fibroid tumors, uterine and cervical cancer, pelvic inflammatory disease, endometriosis, adenomyosis, and uterine prolapse—may require surgical treatment.

> 'I am writing a book tracing my family's journey from 16th-century Spanish colonialism in Cuba to American modernity.'
>
> — Charles Santos-Buch, MD '57

'I am grateful to the thousands of patients who have touched my life over the past 40 years, and forever grateful to the Medical College family for the opportunity it has given me.'

— George Popel, MD '69

1960s

Robert Pezzulich '61, MD '65: "My late wife, Helen, passed away in 2013. On February 28 of this year I married Alice C. Goodman, a nurse practitioner. One of her sons is a thoracic surgeon, so she figured, having raised one, she could handle an OCD, left-brained retired surgeon. So far, so good."

Sam Greenblatt '61, MD '66: "In December my wife, Judy, and I blew our wad on a trip to Antarctica. The scenery is so constantly spectacular that the spectacular becomes mundane. I can still hear the honking of thousands of penguins, but fortunately I don't smell them anymore."

Glenn A. Meltzer, MD '66: "Although I have survived too many medical problems, I continue to improve my painting skills; my acrylic of a barkeep chasing a dog away from his establishment will be shown at the Massachusetts Medical Society annual meeting. I've participated in this doctors' show for 30 years. Hobbies are as important as work. You can't play golf forever."

Edward Goodman '64, MD '68: "I recently received the Max Cole Leadership Award from the Dallas County Medical Society for service to the medical community. I also received the Texas Medical Association's Presidential Citation for my service during the Ebola event at our hospital in Dallas. I was the spokesman for Texas Health Dallas Hospital on three nationally broadcast news conferences when the first U.S. case of Ebola was diagnosed at our hospital in September 2014."

WCMC

Future doctors: Members of the Class of 2019 with their new white coats and stethoscopes

Steve Pieczenik '64, MD '68, has recently published two more *New York Times* best sellers, *Out Of The Ashes* and *Into The Fire* (St. Martin's Press). He has had more than 37 *Times* best sellers including *Tom Clancy's Net Force* and *Tom Clancy's Op Center*. Dr. Pieczenik continues to serve as a senior consultant to the Department of Defense on recent regional issues and conflicts concerning the Iran Treaty, ISIS, Ukraine, the Russia Annexation of Crimea, Hamas, Iraq, Low Intensity Conflict, and China. He has also been involved in voting for the Academy Awards for the past ten years as a member of the Academy of Arts and Sciences and the Writers Guild Of America. He has written and produced TV miniseries and been a judge for the Emmys. After having started 28 new companies over the past twenty years, he is proud to commit most of his entrepreneurial talents to growing his NBI Companies located in Montana. He was fortunate in receiving over 15 Orphan Drug designations for his proprietary products. He has a new grandson named Alexander Marango, who will become a physician like both his parents—extending the Pieczenik dynasty of physicians that started in Toulouse, France, over 100 years ago.

Steven Gabbe, MD '69: "I recently stepped down after nearly seven years of service as the CEO of the Ohio State University Wexner Medical Center. I am proud that during my tenure it became one of the highest-rated academic medical centers for quality and safety and completed a $1.1 billion expansion, including the new 348-bed James Cancer Hospital and Solove Research Institute and Critical Care Center. I'll be spending more time seeing patients in our diabetes and pregnancy clinic, collaborating with my wife, Dr. Pat Gabbe, to reduce infant mortality in Ohio, and working on the 7th edition of our obstetrics textbook. At the end of May, I was honored to receive Weill Cornell's Award of Distinction."

George Popel, MD '69: "I retired from ophthalmology in 2011. Over the years I have pioneered cataract, advanced intraocular lens, and combined glaucoma and cataract surgery. I was the first to pioneer multifocal intraocular lens implants in the Delaware and Pennsylvania area in the 1990s. Also, I was a pioneer in the use of topical drops for cataract surgery, eliminating retrobulbar injections and using no sutures for cataract surgery in the 1990s. This was a huge advance in eliminating sutures and reducing cataract surgery from 1 hour to 10 to 15 minutes and at the same time reducing the risks and complications tremendously. I am grateful to the thousands of patients who have touched my life over the past 40 years, and forever grateful to the Medical College family for the opportunity it has given me. I came to this wonderful USA as an

immigrant from Ukraine at age 8, and Weill Cornell has given me an opportunity to pay back this great country."

1970s

Jeffrey Eckardt, MD '71, accepted a faculty position at UCLA in 1980. Specializing in orthopaedic oncology, he was named the Helga and Walter Oppenheimer Chair of Orthopaedic Oncology in 2001. In 2010, he became chair of the Department of Orthopaedic Surgery at UCLA, and in 2015 he was promoted to distinguished professor. Continuing as chair for five years now, he has no plans to retire and looks forward to a bright future for the department.

John Nees '70, MD '74: "In July 2014, I started working for SonoBello doing liposuction. In January 2015, I played the piano with the West Valley College Orchestra in Saratoga, California, and I continue to participate in the Piano Texas Amateur Program in Fort Worth. My wife and I also continue to travel each year to our ocean home at Playa Blanca, near Lima, Peru."

Milagros Gonzalez, MD '75: "My husband, Keith Bracht, and I traveled to South America in January. We visited Rio de Janeiro and the beautiful and magnificent *Cristo Redentor* (Christ the Redeemer) as well as Sugarloaf Mountain. We loved Buenos Aires, an example of a European city. We learned how to tango in Buenos Aires as well as ride horses in the Pampas. The best part of the trip to South America was in Peru. We climbed to Machu Picchu, situated 7,970 feet above sea level. It's truly one of the wonders of the world. We loved Cuzco, with its Incan ancestry, as well as modern Lima. We spent 15 days and had a wonderful time."

Paul Miskovitz, MD '75, clinical professor of medicine in Weill Cornell's Division of Gastroenterology and Hepatology and the Department of Medicine, was featured in a CBS Cares public service announcement televised nationwide and watched by some 75 million viewers during March, Colorectal Cancer Awareness Month. Dr. Miskovitz is a long-standing consultant on health topics to CBS Cares and editor of the book *Colonoscopy*, published in 2011. His appearance follows previous successful televised public awareness programs such as the "Colonoscopy Sweepstakes," where winners were given a free vacation in New York City along with a screening colonoscopy. The TV spot can be found at cbs.com/cbs_cares.

Sheldon Eisenberg, MD '76: "Still going strong. I'm currently the chairman of the Department of Cardiology at Hackensack UMC at Pascack Valley. I'm expecting my third grandchild any day now."

Paul F. Lachiewicz, MD '77, completed his term as president of the North American Hip Society this year. He continues in part-time private practice in orthopaedic surgery (hip and knee replacements) in Chapel Hill, NC, and teaching at Duke University. He and his wife, Dr. Ave Lachiewicz, have five children and five grandchildren.

Paul Skudder, MD '79: "I was elected to the board of directors of Cape Cod Preferred Physicians, the physician organization representing all physicians on Cape Cod. I'm looking forward to another summer on the seashore, and hoping that work responsibilities don't eat up all my time this year."

1980s

Robert Naparstek, MD '80: "I've been named the president-elect and chair of the Rhode Island Philharmonic Orchestra and Music School. It demonstrates the link between music education, performance, and public health."

David Haughton, MD '84, sent news about his art show, "Nocturnes III—New Paintings of the Georgia Strait and Vancouver Harbour," exhibited in May. "It featured acrylic paintings of the Burrard Inlet, including views of the working harbor, freighters in the bay, the mountains, and dramatic evening and early morning skies. I find these paintings are particularly poignant in light of the recent oil leak in English Bay, and the possibility of additional oil tanker traffic. Vancouver's enchanting and fragile way of life, our beaches overlooking the sea, unencumbered views of a few scattered and benign ships surrounded by myriad sailboats, paddleboards and windsurfers, may soon be dramatically altered. We are privileged to live in such a place of natural beauty and I certainly enjoy painting it."

Brian Aboff, MD '85: "I completed a master's degree in medical management from Carnegie Mellon University last year, and in June I wrapped up a three-year term as chair of the ACGME's Transitional Year Residency Review Committee. I'm very excited to be president-elect of the Association of Program Directors in Internal Medicine (APDIM); I'll have the honor of becoming president in July 2016. I'm perhaps most enthused about my youngest son's graduation from college and being done paying tuition."

Joseph J. Fins, MD '86: "I was inducted as an Academico de Honor of the Royal National Academy of Medicine in Spain in November 2014. My new book, *Rights Come to Mind: Brain Injury, Ethics and the Struggle for Consciousness*, was recently published by Cambridge University Press."

Christopher V. Plowe '82, MD '86: "I have recently been named founding director of a new Institute for Global Health at the University of Maryland School of Medicine in Baltimore, and am directing a new Center for Malaria Research within the Institute."

Steven M. Erde, MD '87: "I'm happy to be back in academia at one of my alma maters, as the chief information officer at the College of Dental Medicine at Columbia University. In addition to my computer work, I've been teaching gross anatomy to the medical and dental students at Columbia with my wife, Dr. Paulette Bernd, professor of pathology, who is the course director. I've been actively working on my glassblowing hobby and just had the opportunity to blow glass in Sweden at Kosta Boda, as well as in Istanbul last summer. I am proud that the last of our three children finished college in May."

Frances Farley, MD '87: "I am excited to be sending my daughter, Anne, to Cornell this fall. Four years ago I had colon cancer, which was caught early thanks to the gastroenterologists, and I am fine. I'm very grateful to the GI docs and a big advocate for colonoscopy. My best to all."

Peter Stein, MD '87, is busy practicing hand surgery on Long Island. He is now the second most senior partner in a 13-member orthopaedic surgery group. In addition to his private practice, he teaches residents and medical students at the new Hofstra North Shore-LIJ School of Medicine. Dr. Stein and his wife have three children, ages 16, 13, and 10. He will serve as the president of the New York Society for Surgery of the Hand for 2015-16.

Abigail Falk, MD '89: "I am back in New York City practicing interventional radiology. I am still very active in my professional society and have maintained my academics throughout my career. When I am not working I am introducing my 6-year-old daughter (yes, that is right) to the adventures the city has to offer."

Charles Flowers, MD '89: "After barely surviving the economic downturn of 2008,

Photo op: Grads capture the moment backstage in Carnegie Hall at Commencement 2015.

WCMC

I eventually sold my LASIK practice in San Diego in 2012 and took a consulting position to set up a LASIK center in Guam. After completing that assignment in late 2014, I joined the faculty at the USC Eye Institute, Keck School of Medicine of the University of Southern California, and I am currently an associate professor of clinical ophthalmology at USC in the Department of Ophthalmology."

Jeff Webber, MD '89, reports that it's been a busy year for the Webber family: he and Paula are new grandparents. One grandson was born in October and a granddaughter was born in November, both healthy and prospering. Another granddaughter, born in June 2015, rounds out a prolific year for the three oldest Webber children: Chase, Brooke, and Wade. The fourth and youngest Webber, Clay, got married in August. Jeff joined a new cardiology group in June: Centennial Heart, located at Centennial Medical Center in Nashville, TN.

1990s

Daniel B. Jones '86, MD '90, professor of surgery at Harvard Medical School, and his co-authors recently published *Minimally Invasive Surgery: Laparoscopy, Therapeutic Endoscopy, and NOTES* (JP Medical Publishers). The book provides a comprehensive review of the latest advances in minimally invasive surgery, including the latest NOTES-based procedures that allow the surgeon to pass an endoscope through a natural orifice thereby avoiding external incisions or scars.

Abraham C. F. Leung, MD '91, is executive director and Distinguished Scientist, Oncology and Clinical Development and Research, at Merck.

David S. Levine '88, MD '92: "After completing my general surgery internship at UCSD Medical Center, I returned to New York and completed my orthopaedic surgery residency at Hospital for Special Surgery in 1997. I then had a foot and ankle fellowship at Harborview Medical Center in Seattle. I returned to New York and remain on staff at HSS, where I'm currently the fellowship director of the Foot & Ankle Service. Outside of the hospital, I am proud of my daughter, Sophia, who graduated from Cornell's College of Agriculture and Life Sciences (CALS) in May. My son, Payton, will begin his studies as a freshman in the undergraduate business school (Dyson) this fall. I remain more active than ever on the Ithaca campus as a member of the Dean's Advisory Board at CALS. Finally, my wife, Davena, and I have started the Dyson Business Minor for Life Sciences Majors. This popular program provides the core business education so important in the ever-changing and complex world of modern healthcare. We are looking forward to creating an endowment so the program may continue to educate future physicians in perpetuity."

Matthew Brengman, MD '93: "Currently I'm the medical director for bariatric surgery at Parham Doctors Hospital in Richmond, VA, and chair of the insurance committee of the American Society of Metabolic and Bariatric Surgeons. I'm married to **Jane Cecil '89, MD '93**."

Jeffrey Kauffman, MD '93: "I've moved from Sacramento, CA, to Franconia, NH, where I joined the Alpine Clinic as an orthopaedic surgeon specializing in sports medicine."

Kent V. Hasen, MD '95: "After 13 years in practice in Naples, FL, I will be moving to a 7,600-square-foot building with two fully accredited operating rooms and a full service medical spa."

'When we left [Ethiopia], we graduated the first three pediatricians trained in Gondar and put ourselves out of a job, a global health sustainability dream.'

— Elizabeth Triche, MD '09

2000s

Daniel Yadegar, MD '04, is a clinical instructor in medicine at Weill Cornell, where he teaches medical students, residents, and cardiology fellows. When he is not teaching, he is practicing cardiology and integrative medicine. You can see him on CBS News, where he contributes regularly as a medical correspondent.

Emily Arch, MD '05: "After my dermatology residency in 2009, my husband and I moved to Chicago, IL, where I am currently practicing medical dermatology in a private practice in Wicker Park. I'm also affiliated with Northwestern University Feinberg School of Medicine, where I enjoy participating in monthly Grand Rounds and giving board review lectures to the dermatology residents. A few months after moving to Chicago we welcomed our first daughter, Lillian ('Lila'), who was joined by sister Amelia two years later and then by our third daughter, Elisabeth, six months ago. While I still miss New York, Chicago has been wonderful—there is an incredible medical community here, and my family and I have found great friends, schools, parks, restaurants, museums, and activities in the city. As our oldest daughter starts kindergarten in the fall, we are getting ready to start the next phase of our lives."

Elizabeth Triche, MD '09: "I'm originally from the Class of 2008, but took a year off to get a

Master of International Public Health at the University of Sydney in 2007–08, so I graduated with the Class of 2009 (I still think of myself as a 2008er). Since finishing my pediatrics residency at UCSF in 2012 in the Pediatric Leadership for the Underserved track, I worked for a year and a half with the Baylor Global Health Corps in an academic hospital in Gondar, Ethiopia. Ethiopia has one of the highest rates of 'brain drain' with more Ethiopian MDs on the East Coast of the U.S. than in Ethiopia. I trained Ethiopian medical students and residents in pediatrics alongside local pediatricians and helped care for children in the general pediatrics, malnutrition, and oncology wards. When we left, we graduated the first three pediatricians trained in Gondar and put ourselves out of a job, a global health sustainability dream. Then in February 2014, I signed up with the National Health Service Corps and moved to Saipan, an underserved Pacific island paradise that is a U.S. Commonwealth. Here I work as a pediatrician in the only hospital on the island, providing outpatient, inpatient, NICU, and PICU services as well as outreach to neighboring islands. I'm thankful for all of the support I received at Weill Cornell for my interest in global health; the many electives I was able to do abroad (even paid for by Cornell!) as a budding physician fanned the flame of my interest and continue to push me to have some truly remarkable experiences as a pediatrician."

2010s

Peter Coombs, MD '11: "I stayed on at WCMC as an ophthalmology resident and am finishing this June. I have matched for a retina fellowship for two more years at Weill Cornell. My wife, **Hediyeh Baradaran, MD '11**, and I had a baby girl, Mina Baradaran Coombs, on September 19, 2014. My wife has one more year of radiology residency at NYP/Weill Cornell."

We want to hear from you!

Keep in touch with your classmates.

Send your news to Chris Furst:
cf33@cornell.edu

or by mail:
Weill Cornell Medicine
401 East State Street,
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In Memoriam

ALUMNI

'45 MD—Emily Townsend Crane of Plymouth, NH, July 4, 2013; physician; retired administrator of the New Hampshire Alpine Racing Association; site supervisor for local Red Cross blood drives; Girl Scout troop leader; bridge player.

'55 MD—Richard C. Lippincott of Little Rock, AR, March 10, 2015; psychiatrist; professor, University of Arkansas for Medical Sciences; directed mental health programs for the states of New Hampshire, Louisiana, and Oregon; also taught at the University of Vermont Medical School, Tulane School of Medicine, and Louisiana State University; advocated for the inclusion of mental healthcare coverage in state and federal health insurance programs and testified before Congress and state legislatures.

'61 MD—John Kuiper of Los Angeles, CA, April 27, 2015; led the nephrology service at UCLA for three decades; active in bioethics, wilderness medicine, and the Sierra Club; avid mountaineer and bicyclist who cycled cross-country in 2003; endowed professorships at Weill Cornell (the John J. Kuiper Professorship of Medicine) as well as at UCLA and the University of Rochester; established the John J. Kuiper Scholarship at Weill Cornell to support students who pursue careers in general internal medicine, family practice, and geriatrics.

'88 MD—Mitchell Newmark of New York City, April 4, 2015; psychiatrist; specialist in depressive disorders and addiction treatment; active in religious affairs.

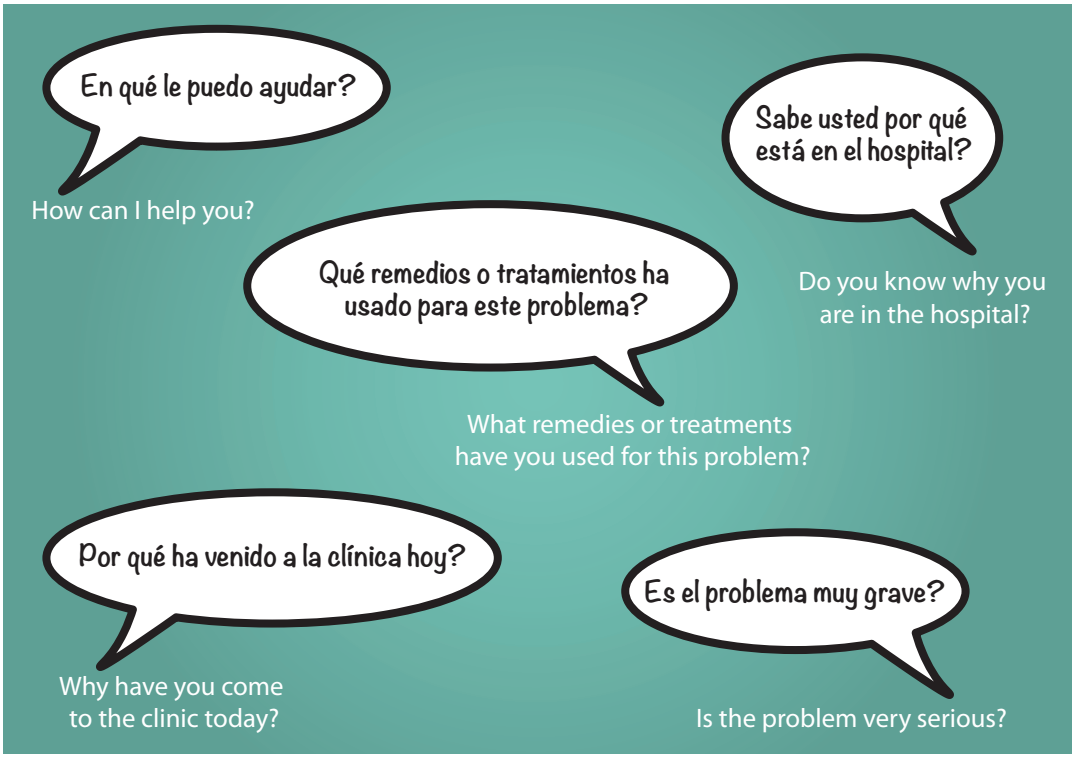
FACULTY

Menard M. Gertler, MD, of New York City, May 6, 2015; physician, researcher, and professor of cardiology; professor emeritus at Weill Cornell; also taught at McGill, Harvard, NYU, and Columbia; assisted in the construction of a plastic model of the human brain and helped develop a major heart surgery technique; collaborated on *Coronary Heart Disease in Young Adults: A Multi-Disciplinary Study* and *You Can Predict Your Heart Attack and Prevent It*; conducted research on conge stive heart failure that led to the introduction of the drug Inocor.

Aaron J. Marcus, MD, of Scarsdale, NY, May 6, 2015; pioneering scientist in hemostasis, coagulation, thrombosis, and vascular biology; professor of medicine at Weill Cornell; isolated and characterized the lipids of human platelets; conducted studies of the role of eicosanoids in hemostasis and thrombosis that led to the concepts of cell-to-cell interactions and transcellular metabolism; helped discover AIDS in the form of Kaposi's sarcoma; spent more than fifty years at the Veterans Administration Harbor Healthcare System; co-wrote *The Physiology of Blood Platelets*; was a fan of opera, Thomas Mann, fountain pens, fine leather shoes, audio equipment, photography, the Beatles, chocolate, and the Chrysler Building.

Talk Therapy

With medical Spanish lessons, future clinicians can ask, *"¿Cómo está?"*



During a hospital preceptorship his first year at Weill Cornell, Patrick DeGregorio '18 got a glimmer of how a language barrier can impede a doctor's work. After a Spanish speaker, patched in by telephone, helped an attending communicate during an exam, the patient thanked the interpreter—but not the doctor. For DeGregorio, that small moment underscored the distance that the inability to speak directly can create between patient and physician, and he found the implications worrisome. "It might preclude you from asking the question you need to ask," he says, "and getting a candid answer from your patient about their history."

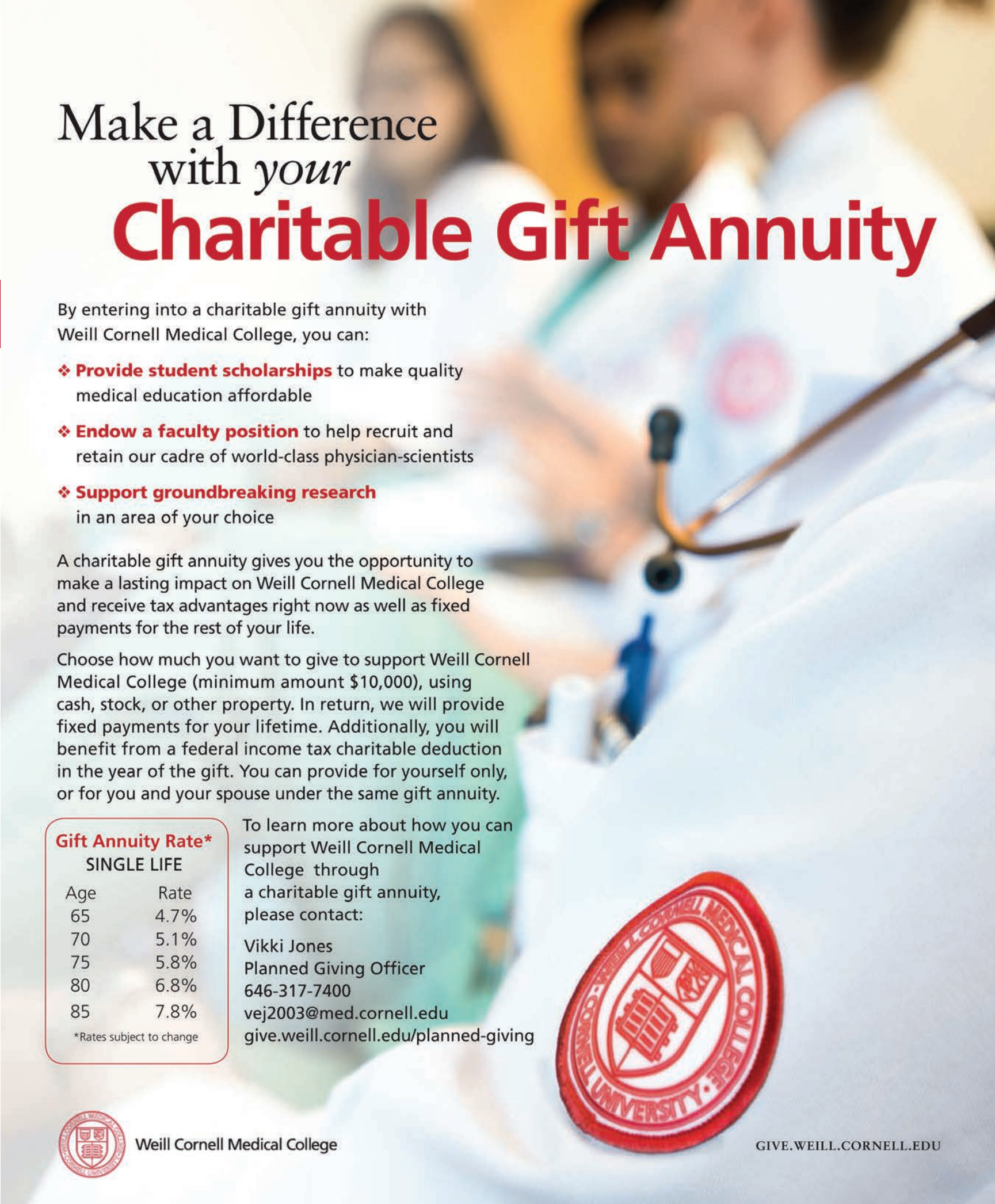
That's why DeGregorio, along with about fifty other students in the MD and physician assistant programs, took medical Spanish last semester. The nine-week courses—divided into beginning, intermediate, and advanced sections—have been offered since 1998. In the introductory group, students learn the terms for many body parts, plus key phrases and common verbs needed for taking histories. In probing cardiovascular issues, for instance, they learn how to ask whether the patient is experiencing shortness of breath (*"falta de aire con actividad"*) or whether they suffer from sleep apnea (*"despertarse durante el sueño con falta de aire"*).

The ability to speak medical Spanish is in high demand in New York City, where Hispanics make up more than a quarter of the population. And as instructor Michael Shane tells his students, a little conversation can go a long way. "I've never heard of anybody saying a patient got angry because their doctor tried to speak Spanish," says Shane, a medical Spanish specialist who also teaches at Columbia and New York Medical College. "They might giggle, but they are more likely to try to teach you."

A few weeks into the intro Spanish course, which was held on Wednesday evenings in spring 2015, students sit at desks arranged in a horseshoe shape, trying to reply to Shane's conversational prompts. The atmosphere is designed to be relaxed and nonjudgmental, says course organizer Luis Romero '18. "To learn a language you have to stop being so nervous about making yourself look foolish," says Romero, a Cuban native eager to expand his grasp of colloquial variations among Hispanophones. "Here, we all make ourselves look like fools from time to time. If you don't, it means you aren't pushing yourself hard enough."

At the course's intermediate and advanced levels, students not only delve more deeply into the language, but talk about cultural norms. Establishing rapport with patients, they learn, can often be a matter of small courtesies, like asking where someone comes from. (*"¿De dónde es usted?"*) And with more and more students interested in language proficiency, such offerings may someday be expanded to include other tongues such as French and Mandarin, says faculty advisor Madelon Finkel, PhD, professor of clinical healthcare policy and research. "Anything that will help patients feel comfortable is a good thing, so even with pathetic Spanish you're showing that you're trying to speak," says Paul McClelland '18. "As a medical professional, obviously you're competent at what you do—but even super-smart doctors can't speak every language."

— Ken Stier



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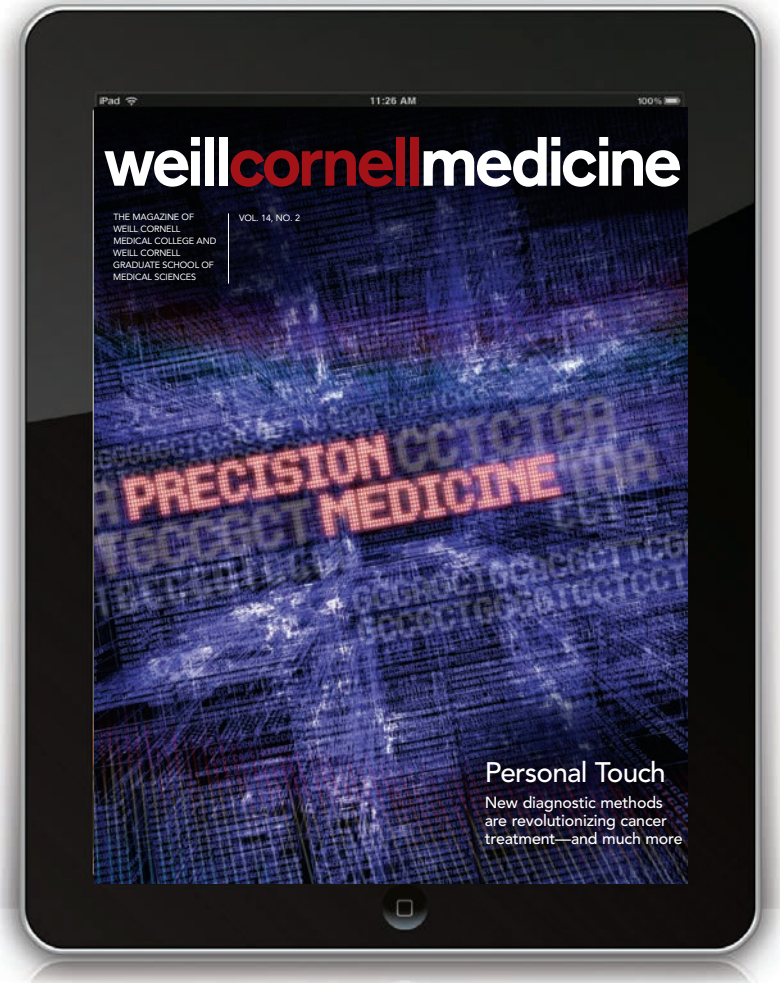

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