

THE EVOLUTION OF MEDICAL EDUCATION, OCTOBER 10-11

Hosted by the Weill Cornell Medical College Alumni Association, Reunion will take place from Friday, October 10, to Saturday, October 11, offering engaging guest speakers, institutional updates and tours, class get-togethers, a gala dinner dance, and opportunities to mingle and network with old friends.

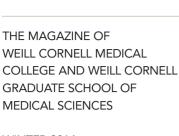
This year's theme will explore the myriad ways advancements in medical science have altered the way we educate medical students. Alumni will also have the opportunity to learn about the reformed curriculum we're launching this year, which complements the most recent innovations in technology and medicine.

Class years ending in '3, '4, '8, and '9 are celebrating milestone reunions, and, as always, all alumni are invited back to campus to commemorate another year since graduation.

The accomplishments of alumni are a point of pride for the Weill Cornell community. This is an opportunity to not only thank alumni for all that they do for the Medical College, but also for alumni to stay informed on the newest developments while meeting with old friends and making new contacts. This keystone event is an opportunity to stay connected to Weill Cornell and to each other!

Visit www.weill.cornell.edu/alumni/reunion for updates.





WINTER 2014



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BETH SAULNIER

Formally opened in late January, the \$650 million, eighteen-story Belfer Research Building is the crown jewel of Weill Cornell's scientific enterprise. Nearly doubling the Medical College's research space, the 480,000-square-foot facility will bring together investigators in a light-filled, collaborative environment—symbolized by such design elements as glass walls and open staircases that connect each pair of floors. "This is an era when we pick collaborators globally, but it still matters a great deal who you're close to," says Carl Nathan, MD, the R. A. Rees Pritchett Professor of Microbiology and chairman of the Department of Microbiology and Immunology. "It's a very human thing, but who you bump into—the evolving informality of relationships builds trust and leads to unexpected synergies."

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NEW LEASE ON LIFE ANDREA CRAWFORD

A quarter century ago, HIV was a grim diagnosis. It was in those dark days that Weill Cornell's HIV/AIDS clinic, the Center for Special Studies, was founded. Today—thanks in large part to drugs tested in clinical trials at Weill Cornell and elsewhere—HIV has become a chronic, manageable disease. But the Center remains a mecca for comprehensive patient care—and two of its founding doctors are still on staff. "I started my medical career in the depths of the worst part of the HIV epidemic," notes Samuel Merrick, MD, associate professor of clinical medicine, "and now there's a growing sense of optimism that there may someday be a cure."

36 TURNING THE 'TIDE **BETH SAULNIER**

Peptides make bad drugs—or so the assumption went. But with a novel peptide in clinical trials and a promising start-up company based on it, pharmacology professor Hazel Szeto, MD '77, PhD '77, is challenging that long-held notion. Szeto and her collaborators are investigating the socalled Szeto-Schiller peptides as possible treatments for a whole host of conditions—from Alzheimer's and Parkinson's to genetic disorders, liver and kidney failure, heart disease, transplant rejection, macular degeneration, diabetes, and more.

On the cover: Detail of the Belfer Research Building's digital artwork. Photograph by John Abbott. For more, see page 6.

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weillcornellmedicine

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

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Creative Solutions

reative translation" is a phrase that we often use at Weill Cornell to define our approach to bringing research from bench to bedside and back again. As technological advances drive the pace of scientific discovery ever faster, we are seeking more innovative ways to ensure that

> these advances ultimately lead to improved patient care.

> But while the technologies may be novel and the pace of discovery certainly unprecedented, that creative work—the breaking down of barriers in order to make research relevant to patients' liveshas a long, robust, and diverse tradition on our campus.

> A quarter-century ago, our clinicians and researchers did just that when New York City's HIV epidemic required urgent care for a stigmatized patient population at a time when treatment efficacy was still unproven—as you'll read in our feature story on the Center for Special Studies and the Cornell Clinical Trials Unit. Our faculty do it every day as they seek innovative funding sources to counteract decreasing government support for basic science—a can-do attitude exemplified by pharmacologist Hazel Szeto, MD '77, PhD

'77. Szeto made the structure of a novel peptide she created openly available to fellow researchers and used an academic-industry hybrid model to found her biopharmaceutical start-up, Stealth Peptides, which is developing targeted therapies for a wide range of diseases.

Our students, too, are taking creative approaches to fusing research with patient care. In this issue, you'll meet one such individual: David Saunders '14, who is bringing together Eastern and Western healing practices as he simultaneously works toward an MD at Weill Cornell and a PhD in Buddhist studies at Emory University.

But perhaps the most vivid example of our commitment to creative translation is the com-

pletion of the long-awaited Belfer Research Building. The facility, which opened in January, is designed both physically and conceptually to break down research silos and to foster crossdisciplinary collaborations as well as privatepublic partnerships. For example, it houses the Sandra and Edward Meyer Cancer Center, directed by Lewis Cantley, PhD '75, which will expand Weill Cornell's world-class enterprise in cancer research and clinical care. The Mever Cancer Center, like others housed in the new building, allows disparate specialists to work together toward a common, ambitious goal. Researchers will find new ways to use the tremendous advances in technology—precision medicine, improved molecular imaging, computational biology, and more—to turn scientific breakthroughs into cutting-edge therapies for the patients who need them.

The Belfer Research Building also serves as the headquarters for the Tri-Institutional Therapeutics Discovery Institute, an innovative public-private partnership among Weill Cornell, Rockefeller University, and Memorial Sloan-Kettering. In this effort, we have also allied with Takeda Pharmaceutical Company, which is placing eighteen of its medicinal chemists to work alongside our biologists. This type of partnership is crucial if we are to turn early-stage scientific discoveries into effective medications. Academic scientists can aid their pharmaceutical counterparts in identifying drug targets and generating small molecules that show therapeutic promise in tissue cultures and animal models. The companies, in turn, have strengths in transforming such compounds into human therapies through their expertise in medicinal chemistry, toxicity testing, pharmacokinetics, and more.

These examples are as diverse as the historical contexts that shape them. But they have a common goal: to improve the lives of patients and their families. That's why-in the face of a changing scientific, medical, and cultural landscape—our work at Weill Cornell must advance with urgency, resourcefulness, and creativity.



The Belfer Research **Building:** oised for Success

The Belfer Research Building stands tall on 69th Street.

Weill Cornell Medical College

New York City has a brand new, state-of-the-art research hub: the Belfer Research Building.

The Belfer Research Building is preparing to house groundbreaking research in priority areas such as:

- Cancer
- Cardiovascular disease
- Neurodegenerative diseases
- Children's health
- Global health
- Infectious diseases

Recruitment of leading physicianscientists in each of these areas will be a major force behind our *Driving Discoveries, Changing Lives* Campaign. With new technology, the potential to make major advancements in therapies has never been higher. Our acclaimed researchers working side-by-side in the top notch laboratories of this building will be in a position to lead the way in breakthrough discoveries, affecting human health in New York City and around the world.



The laboratories in the Belfer Research Building are filled with the most cutting-edge and advanced equipment available today.

"This building allows us to take advantage of the enormous scientific advances that have been made and translate them into therapies

Laurie Glimcher, MDStephen and Suzanne Weiss Dean
Provost for Medical Affairs

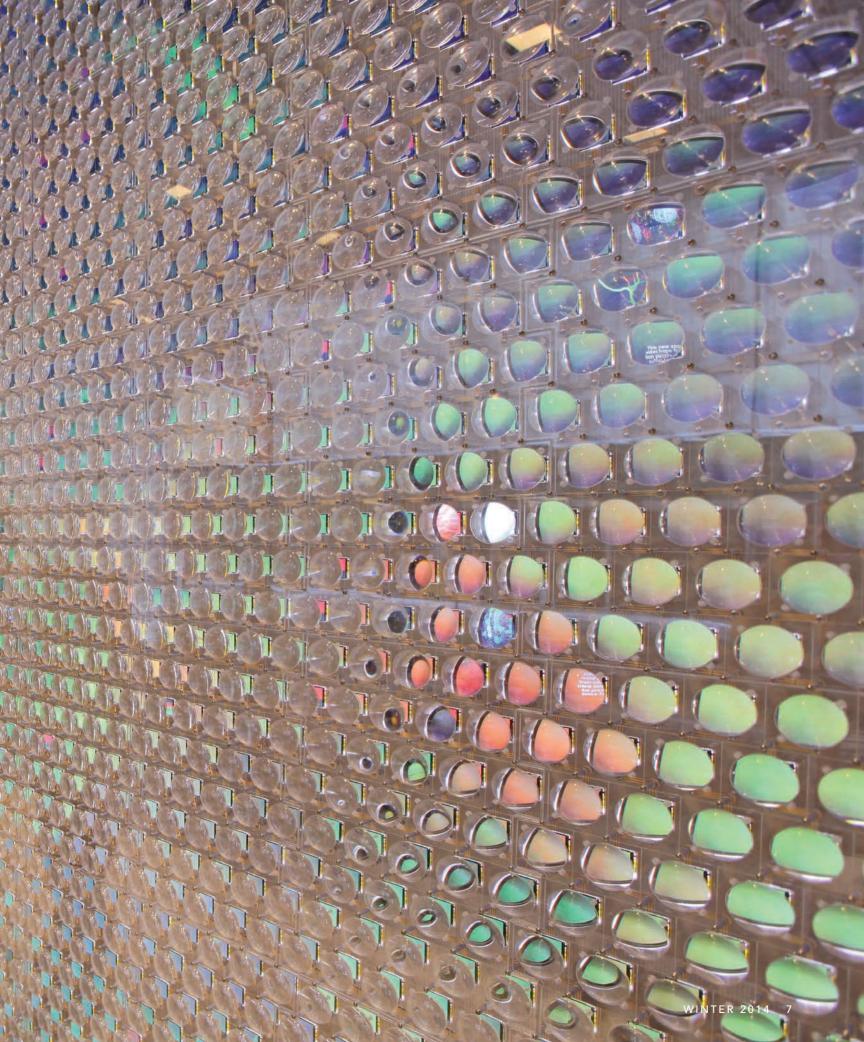
for patients."

Take a Look Inside...

Floor 16	TRI-INSTITUTIONAL THERAPEUTICS DISCOVERY INSTITUTE Abby and Howard P. Milstein Program in Medicinal Chemistry Sanders Innovation and Education Initiative
Floor 15	Laboratories for Molecular Imaging and Physiology
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Floor 9	FEIL FAMILY BRAIN AND MIND RESEARCH INSTITUTE (Opening Summer 2015)
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Floor 4	HUNTER COLLEGE, CITY UNIVERSITY OF NEW YORK
Floor 3	THE STARR FOUNDATION-MAURICE R. GREENBERG CONFERENCE CENTER Ruben Family Conference Center
Floor 2	THE STARR FOUNDATION-MAURICE R. GREENBERG CONFERENCE CENTER AND TERRACE Friends Donor Wall Mahon Family Conference Rooms
Floor 1	Principal Benefactor Wall Daisy and Paul Soros Student Meeting Room Centers and Institutes Wall Time capsule

We are grateful to all of our donors for their continued support. For more information on making a gift to the *Driving Discoveries, Changing Lives* Campaign, please contact Lucille Ferraro, Campaign Director, 646-317-7387 or luf2003@med.cornell.edu.







ROGER TULLY

Dream team: Celebrating the establishment of the Meyer Cancer Center are (from left) Dean Laurie Glimcher, MD, Sandra Meyer, Edward Meyer, Lewis Cantley, PhD '75, the Meyer Director of the Center, and Anthony Meyer.

Meyer Cancer Center Founded with \$75 Million Gift

\$75 million gift from Sandra and Edward Meyer and their foundation has established a state-of-the-art cancer center at Weill Cornell. The Sandra and Edward Meyer Cancer Center is dedicated to using precision medicine and other advanced biomedical approaches to facilitate research breakthroughs and translate them to the bedside. "Cancer is a disease that touches everyone's lives," says Dean Laurie Glimcher, MD, "and with Ed and Sandy's generous support, we will be able to rapidly accelerate our pursuit of groundbreaking treatments and therapies for our patients."

With a home in the Belfer Research Building, the center is led by Lewis Cantley, PhD '75, the Meyer Director of the Meyer Cancer Center and the Margaret and Herman Sokol Professor in Oncology Research. In honor of the Meyers' gift, Weill Cornell has named its flagship building on 1300 York Avenue the Sandra and Edward Meyer Research and Education Building. "Their generosity will enable us to realize our goal of developing cancer treatments that capitalize on precision medicine, offering targeted, individualized care based on each patient's tumor," Cantley says. "This gift will make it possible for us to be at the forefront of cancer research, to purchase the necessary technology, and recruit the very best talent to carry out this vital work."

Comprising scientists, pathologists, bioinformaticians, surgeons, radiation oncologists, and radiologists, the Meyer Cancer Center will unify cancer research activities throughout Weill Cornell and enhance three core areas: a centralized biobank, cancer genomics, and computational biology. In addition to using the latest technolo-

gies for basic, clinical, and translational research, it will offer support for initiating and conducting novel clinical trials. "Sandy, our children, Meg and Tony, and I gave careful consideration to which New York institution was best poised to produce breakthroughs in cancer, and Weill Cornell was the obvious choice due to its exceptional roster of translational, cutting-edge scientists and commitment to building its oncology research enterprise," says Edward Meyer, a Cornell University alumnus and former CEO of Grey Global Group, one of the world's largest advertising, marketing, and communications firms. "We can think of no better investment that will make as big a difference in the world, and we know that together we can do great things for cancer patients and their families."

Department of Medicine Named for Weills

In gratitude for Joan and Sanford Weill's long-standing support, the Medical College has named its Department of Medicine in their honor. The naming recognizes the Weills' recent \$100 million gift—which also established the Joan and Sanford I. Weill Center for Metabolic Health—as well as their landmark \$250 million gift to the *Discoveries that Make a Difference* campaign. "This is a tremendous moment for Weill Cornell and for its largest department—a moment that will allow us to continue delivering innovative treatments and cures to patients in New York City and throughout the world—and we are grateful to Joan and Sandy for making this possible," says Dean Glimcher. The Weill Department of Medicine comprises more than 1,700 faculty members, clinicians, and researchers.

Kaushal Heads New Department of Healthcare Policy and Research

Rainu Kaushal, MD, an expert in healthcare quality, patient safety, and information technology, has been named chair of the Department of Healthcare Policy and Research. Formerly the Department of Public Health, its new name reflects current challenges in health care. It will analyze health-care delivery and find innovative ways to optimize the value and quality of patient care, exploring such issues as unsustainably rising costs and spending, uneven access, variable quality, and socioeconomic disparities. Faculty will use data-driven approaches



Rainu Kaushal, MD

to evaluate the efficacy and cost-effectiveness of various health-care interventions and delivery models, and develop new technologies designed to improve care. Eventually, it will offer doctoral and master's degrees in health-care policy and research.

The Frances and John L. Loeb Professor of Medical Informatics and a professor of pediatrics, medicine, and public health, Kaushal is executive director of Weill Cornell's interdepartmental Center for Healthcare Informatics and Policy. In December, the Patient-Centered

Outcomes Research Institute announced that it had awarded \$7 million to a consortium, led by Kaushal and involving nearly two dozen New York City health-care systems and organizations, to develop a city-wide research data infrastructure that will securely collect, store, and share comprehensive medical histories for as many as 6 million consenting patients. Known as the New York City Clinical Data Research Network, it includes six Clinical and Translational Science Award Centers, the new Cornell Tech campus, and other institutions.

Regional Stroke Center Established

Investigators from Weill Cornell and Columbia have teamed up to create a new regional stroke center. One of twenty-five such centers nationwide, the New York Stroke Trials Network of Columbia and Cornell will run clinical trials in stroke prevention, treatment, and recovery. It has been funded for the next five years by the NIH Health Stroke Trials Network (NIH StrokeNet), beginning with \$250,000 annually for the first three years. "This grant will allow us to provide our stroke patients with the most up-to-date, cutting-edge treatments available through high-quality clinical trials," says co-principal investigator Dana Leifer, MD, associate professor of neurology. Other coprincipal investigators include Matthew Fink, MD, chairman of the Department of Neurology and the Louis and Gertrude Feil Professor of Clinical Neurology, and Philip Stieg, MD, PhD, professor and chairman of the Department of Neurological Surgery.

TIP OF THE CAP TO...

Robin Davisson, PhD, the Andrew Dickson White Professor of Molecular Physiology, elected a fellow of the American Association for the Advancement of Science for her contributions to understanding how hypertension develops.

Joseph Fins, MD '86, the E. William Davis Jr., MD, Professor of Medical Ethics and chief of the division, elected a distinguished member of the Royal National Academy of Medicine of Spain.

Marc Goldstein, MD, the Matthew P. Hardy, PhD, Distinguished Professor of Reproductive Medicine and Urology, winner the 2013 Star Award from the American Society of Reproductive Medicine.

Antonio Gotto Jr., MD, DPhil, dean emeritus and co-chairman of the Board of Overseers, recipient of the Texas Chapter Laureate Award from the American College of Physicians, which honors fellows and masters of the college who have demonstrated a commitment to excellence in medical care, education, research, and service.

Katherine Hajjar, MD, the Brine Family Professor of Cell and Developmental Biology and chair of the department, elected to the American Clinical and Climatological Association.

Janey Peterson, EdD, MS '07, assistant professor of clinical epidemiology in medicine, winner of the Paul B. Beeson Career Development Award in Aging Research from the National Institute on Aging and the American Federation for Aging Research. She will receive a four-year grant of about \$720,000 to develop a physical activity intervention for older adults with multiple high-risk chronic diseases.

Mark Rubin, MD, director of the Institute for Precision Medicine and the Homer T. Hirst III Professor of Oncology in Pathology, winner of the Prostate Cancer Foundation's 2013 Mentor of Excellence Award, given to individuals who have impacted the careers of the foundation's young investigators.

Theodore Schwartz, MD, professor of neurological surgery, winner of the Gentle Giant Award from the Pituitary Network Association, its highest honor. Schwartz was recognized for his work with Vijay Anand, MD, clinical professor of otolaryngology, in advancing the use of endoscopy in pituitary surgery.

Lee Shearer, MD, assistant professor of medicine and of medicine in pediatrics, winner of the James Horowitz Award for Chief Resident. The award, now in its second year, is given to one NYP chief resident for outstanding resident advocacy.

Jason Spector, MD, associate professor of surgery, whose bioengineered ears—a collaborative effort with Lawrence Bonassar, PhD, a professor of biomedical engineering on the Ithaca campus—took first place at the World Technology Summit.

Luise Weinstein, MD, assistant professor of clinical medicine, winner of NYP's Physician of the Year Award, which recognizes physicians, fellows, house staff, and medical students who show competence and caring in the clinical setting and work together with nurses to attain the highest standards of patient care.

Fink Named First Dean of Clinical Affairs

Matthew Fink, MD, chairman of the Department of Neurology and the Louis and Gertrude Feil Professor of Clinical Neurology, has been appointed to the new position of assistant dean of clinical affairs. In this role, Fink will help lead the clinical enterprise at NYP/Lower Manhattan, the NewYork-Presbyterian campus that was established last summer in a merger with the former New York Downtown Hospital. He will also work with the Weill Cornell Physician Organization to recruit doctors in



Matthew Fink, MD

the area. Prior to joining the Weill Cornell faculty, Fink was president and CEO of Beth Israel Medical Center in Lower Manhattan.

New Board of Overseers Members Appointed

Weill Cornell has welcomed four new members to its Board of Overseers. Physician-scientist Stanley Prusiner, MD, is director of the Institute for Neurodegenerative Diseases at the University of California, San Francisco. He won a 1997 Nobel Prize for his discovery of prions, which are implicated in such diseases as Creutzfeldt-Jakob—the human equivalent of "mad cow" disease. Edward Meyer, a 1948 alumnus of the Ithaca campus, is an advertising industry legend; his wife, Sandra, is active in philanthropic causes. Their recent \$75 million gift created a cancer center in their name at Weill Cornell. Internist and cardiologist Thomas Lee, MD '79, is chief medical officer for Press Ganey Associates, a patient experience improvement firm.

NFL Grant Supports Head Injury Research

A team led by radiologist P. David Mozley, MD, is among the sixteen winners—out of more than 400 applicants—of challenge grants funded by the NFL and General Electric. The investigators have been using nuclear medicine and advanced MRI techniques to diagnose head injuries in athletes immediately after they occur—even before brain damage is detected. The Weill Cornell team will compare scans from former professional boxers with known, long-term head injuries against those of NFL players in whom a concussion is suspected. If the technique works, it could change the way concussions are diagnosed. "The idea is really simple," says Mozley, chief of the Division of Nuclear Medicine, "but it's never been done before."

Foley to Serve as Director of Tri-I TDI

A chemist and entrepreneur with more than twenty-five years of industry and academic experience has been tapped to lead the Tri-Institutional Therapeutics Discovery Institute (Tri-I TDI). Michael Foley, PhD, was most recently director of the Chemical Biology Platform at the Broad Institute of Harvard and MIT. Located in the Belfer Research Building, Tri-I TDI is a collaboration by Weill Cornell, Rockefeller University, and Sloan-Kettering to expedite early-stage drug discovery into novel treatments. Says Dean Glimcher: "Dr. Foley's



Michael Foley, PhD

experience in academia and industry and distinguished track record of moving early-stage compounds through drug development are a



Body image: "Reflect 3" by Ali Mendelson, MD '13, is among the artwork in the latest issue of the student journal *Ascensus*.

perfect match for the Tri-I TDI's ambitions of accelerating bench discoveries into effective therapies for patients."

The scientific co-founder of four companies and an academic institute, Foley has placed twelve single-agent or combination drugs into clinical development. In recognition of the \$15 million gift from Lewis and Ali Sanders to help establish the Institute, his title is the Sanders Director of Tri-I TDI and director of its Sanders Innovation and Education Initiative. "The structure of the Tri-I TDI has enormous potential to not only bridge the gap between academia and the pharmaceutical industry, but to take burgeoning ideas and rapidly adapt them into real, tangible treatments that can benefit patients now," says Foley, who previously worked at Bristol-Myers Squibb and GlaxoSmithKline.

Cardiovascular Imaging Institute Founded

Raymond Dalio, a life trustee of NewYork-Presbyterian Hospital, has made a gift of \$20 million to create a cardiovascular imaging institute at NYP/Weill Cornell. It will take a multidisciplinary approach to the detection and treatment of heart disease, with a focus on prevention in at-risk patients. The Dalio Institute of Cardiovascular Imaging will be led by James Min, MD, an expert in the field and a physician-scientist who has led several large, multicenter clinical trials.

Focusing on the central role of imaging in diagnosing cardiovascular disease, the Institute will not only use tools such as MRI, CT, and PET scanners, but will also develop new technologies and diagnostics. Its primary research initiative is to identify "vulnerable plaque," or the specific coronary artery lesion responsible for a future heart attack or sudden cardiac death. Its clinical program, serving both outpatients and inpatients, comprises initiatives for early detection in women, minorities, and young people with a family history of premature heart disease. "More than half of the people who die from sudden heart attacks never knew they were at risk because their underlying heart conditions had never been diagnosed," notes Min, a professor of radiology. "Many heart attacks can be prevented if people know of the extent and severity of their asymptomatic heart disease and are properly treated."

FROM THE BENCH

Half of Psychiatrists Reject Insurance, Study Finds

A study led by Tara Bishop, MD '02, the Nanette Laitman Clinical Scholar in Public Health-Clinical Investigation, has found that psychiatrists are increasingly refusing to accept private and public insurance, requiring patients to pay out of pocket. In a paper published in JAMA Psychiatry, Bishop and colleagues also reported that the number of practitioners is falling. From 2000 to 2008, they found, there was a 14 percent drop in psychiatrists nationwide; many are retiring, while fewer medical students are entering the field. "In the current climate, where the need for increased mental health services is now recognized, I suspect our study conclusions will be an eye opener for both the public and the medical community," Bishop notes. "I must say we were surprised by the findings. No prior studies have documented such striking differences in insurance acceptance rates by psychiatrists and physicians of other specialties—primarily because no one has looked closely at the issue."

Snapshot of AIDS Protein Is Progress Toward Vaccine

In a potentially promising step toward an AIDS vaccine, virologist and immunologist John Moore, PhD, and colleagues at the Scripps Research Institute have determined the first atomic-level structure of the three-part HIV envelope protein. In work published in Science Express, they describe the mushroom-shaped "trimer" protein, known as Env, as being made up of three identical, loosely connected structures. Its form, the researchers say, both makes it difficult to study and enhances its ability to latch on to susceptible human cells. Says Moore: "Now we all need to harness this new knowledge to design and test next-generation trimers and see if we can introduce the broadly active neutralizing antibodies that an effective vaccine is going to need."

Pill Could Treat Form of Leukemia Without Chemo

A twice-daily pill could transform chronic lymphocytic leukemia (CLL), a deadly blood cancer, into a highly treatable disease. Known as idelalisib, the drug "melts away" the cancer, says lead investigator Richard Furman, MD. Findings suggest that it may even allow patients to avoid

chemotherapy and its inherent side effects. "Even if this cancer remains incurable," says Furman, the Richard A. Stratton Associate Professor in Hematology and Oncology, "it now can be treated as if it was a chronic disease, with a pill, in the same way that high blood pressure is treated." In a randomized, doubleblind study, nineteen medical centers tested idelalisib in combination with another drug in 220 CLL patients who could no longer receive chemotherapy. Six months later, 93 percent of the drug recipients' symptoms had not worsened, compared to 46 percent in the control group. The work was published in the New England Journal of Medicine.

Exploring How Ambien Increases Brain Activity

In a very small number of severely braininjured patients, the sleep aid Ambien has led to an increase in awareness. Now, neurologist Nicholas Schiff, MD, and colleagues have discovered the possible mechanism behind the phenomenon.



Nicholas Schiff, MD

After using an EEG to monitor the idling brain, they posit that Ambien works like anesthesia briefly triggering excitement in the cells before putting the patient to sleep, a state known as paradoxical excitation. "What we think is happening in these patients is that the initial excitation produced by Ambien turns on a specific circuit," says Schiff, the Jerold B. Katz Professor of Neurology and Neuroscience and the study's senior investigator. "The drug creates the opportunity for the brain to effectively catch a ride on this initial wave of excitation, and turn itself back on."

'Rare' Gene Tied to **Increased Triglycerides**

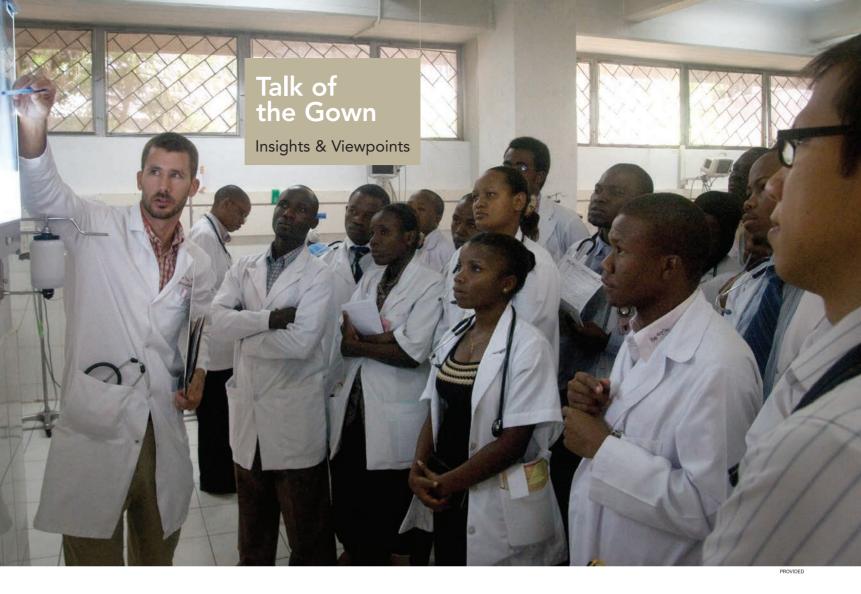
A genetic variation previously believed to be rare has been linked to increased triglyceride levels, particularly in people of African ancestry. Ronald Crystal, MD, professor and chairman of genetic medicine, found that African Americans with the variant—known as ApoE—had, on average, 52 percent higher triglyceride levels compared with those in the study who did not have the variant. "The prevalence of the ApoE mutation may put large numbers of Africans and African descendants worldwide at risk for a triglyceride-linked disorder," says Crystal, the Bruce Webster Professor of Internal Medicine. "But we don't vet know the extent of that risk or its health consequences." The mutation was studied in Arab, Persian, and sub-Saharan African populations; 17 percent of the African subgroup had the ApoE gene, while no members of the other groups had it.

Prostate Cancer Risk Linked to Specific Protein

The presence of a particular protein in biopsied prostate tissue seems to indicate an increased risk of cancer. The finding offers a potentially valuable tool in deciding which men would most benefit from future biopsy screenings, reports Mark Rubin, MD, the Homer T. Hirst Professor of Oncology in Pathology and director of the Institute for Precision Medicine. His team found that biopsies classified as having high-grade prostatic intraepithelial neoplasia (HGPIN), which are lesions that may morph into cancer. tested positive for the protein ERG. "This study is the largest ever conducted that focuses on looking at HGPIN and ERG in a systematic way." says Rubin, whose findings were published in the Journal of Clinical Oncology. "We found that more than half of patients with these biomarkers go on to develop prostate cancer, and that is a significant finding that we now want to test in a prospective clinical trial."

Harnessing the 'Guardian of the Genome'

A multi-institutional research team led by Lewis Cantley, PhD '75, has identified a family of enzymes crucial to the growth of cancers associated with aberrations in the most frequently mutated gene in tumors. While it has previously been difficult to target the p53 mutations with drugs, the enzymes offer a new front on which to stymie the growth of p53 mutant cancers, which include those of the breast, ovary, lung, colon, and brain. In Cell, the investigators describe two enzymes—known as Type 2 PIP kinases—essential for cancer growth when cells have lost p53, the powerful tumor-suppressor gene dubbed the "quardian of the genome." Cantley, the Margaret and Herman Sokol Professor in Oncology Research and director of the Meyer Cancer Center, is leading an effort to develop drugs to shut down these kinases. "Well-designed Type 2 PIP kinase inhibitors," he says, "may turn the tide on p53 mutant cancer."



Crisis team: Assistant professor of medicine Rob Peck, MD (left), is educating staff and patients at Weill Bugando about the rising dangers of high blood pressure. Opposite: Peck uses a portable ultrasound to confirm hypertensive heart disease.

High Alert

Sounding the alarm on Africa's unlikely epidemic

ob Peck, MD, was ten when his grandmother took him to Kenya, a trip that set the course of his professional life. "I came home saying, 'When I grow up, I want to be a doctor in Africa,' " Peck recalls. "No one believed me."

More than two decades later, Peck is an assistant professor of medicine at Weill Bugando Medical Centre in Mwanza, Tanzania. Last fall, another African experience prompted a startling pronouncement—but this time, he's finding a receptive audience.

In work published in the *Journal of Hypertension*, Peck reported that high blood pressure and related conditions like stroke and heart disease have grown to epidemic levels in the East African nation. While people in the developing world have long been considered most at risk from infectious diseases like malaria and TB. Peck

noted, noncommunicable diseases—primarily related to hypertension—accounted for nearly half the deaths and admissions at Weill Bugando over a three-year period. As a cause of mortality and morbidity, it was second only to HIV/AIDS. "When I went to Africa, this is not what I thought I'd be studying," says Peck, whose previous research was in HIV and tropical diseases like anthrax. "But my experience in Tanzania has convinced me that hypertension is a growing problem, and it's an area where not many people are working."

Although Peck has an appointment at Weill Cornell, he is based at Weill Bugando, located in northwestern Tanzania on the southern shore of Lake Victoria. (Affiliated with the Medical College, the institution is also named for its first major benefactor, Board of Overseers Chairman Sanford Weill.) Tanzania is home to Peck and his

family; he and his wife, a nurse practitioner, have five children, two adopted from Tanzania. Parsing the causes of the steep rise in hypertensive illness over the past generation or two, he points to societal changes. "In Africa, urbanization and industrialization are occurring rapidly," he says. "Fifty years ago, less than 10 percent of the population of sub-Saharan Africa lived in cities; now more than 50 percent do. And as people move into cities, there's decreased exercise related to work and increasing rates of obesity. Clearly, that's taking a toll. And it's happening much faster than it did in the West."

While fast food chains are not yet ubiquitous, the Western diet is becoming more widespread, nurturing a taste for foods that are fatty, fried, and salty. "If you think about African populations fifty or 100 years ago, the only way you'd get salt in rural Africa would be to go to the salt lick and cart it off," he says. "Now you can buy it in a store." But Peck notes that two major causes of noncommunicable diseases (NCDs) elsewhere in the world—obesity and smoking—aren't as much of a culprit, simply because many people can't afford these excesses. "We think there might also be other factors at work," Peck says. "Chronic infections, like schistosomiasis or malaria, could be contributing. We also think there could be kidney disease occurring at young ages that predisposes young adults to hypertension. There might also be a genetic predisposition in this population, just as we see in African Americans in the U.S."

Dan Fitzgerald, MD, co-director of Weill Cornell's Center for Global Health and one of Peck's mentors, notes that the emergence of NCDs can be seen as a "third wave" of mortality in the developing world. "The first wave is in early childhood, with diseases like acute diarrhea and respiratory infections," says Fitzgerald, associate professor of medicine. "The second wave is in young adulthood, with HIV and tuberculosis. And then in the thirties and forties, we're seeing this third wave of noncommunicable, chronic diseases like hypertension and diabetes hitting the adult population. So if someone survives childhood, survives the infections in their twenties and thirties—and if women survive maternal mortality—then they're hit by this third epidemic. It's tragic."

On the upside, Fitzgerald and Peck say, the global health community is taking notice. In spring 2011, the WHO held a

conference in Moscow on healthy lifestyles and NCD control; that fall, the U.N. convened a summit on the subject in New York. NCDs figure prominently in the National Heart, Lung, and Blood Institute's global health strategic plan for 2012–17, and nonprofits like the Young Professionals Chronic Disease Network (founded by Weill Cornell MD-PhD student Sandip Kishore) seek to raise awareness and shape policy. "When I've shared the findings of this paper with people, they've been shocked," says Fitzgerald. "The donor community is fortunately beginning to address this as a major epidemic and a major problem."

Fitzgerald notes that a model for curbing NCDs could be drawn from successes in HIV treatment, which also requires community outreach, a system for testing and diagnosis, and life-long care. "We might do the same thing with hypertension, diabetes, and cardiovascular disease." he says. "We can learn from that experience and build on it." But Peck warns that since local health systems have long been geared toward combating infectious disease, establishing workable protocols for NCDs—including supplying affordable medicines—will be a major undertaking. "Clinics in sub-Saharan Africa are set up to provide vaccines, to treat malaria and worms; they don't have the human or physical resources to provide chronic care for diseases such as hypertension," he says. "Strengthening those health systems, particularly at the primary care level, will be an important part of the strategy."

Peck recalls one patient, a man in his mid-forties with undiagnosed hypertension, who lost consciousness and developed weakness on his right side—the result of a stroke caused by "tremendously high" blood pressure of nearly 260 over 140. "We put him on antihypertensives and physical therapy, and he improved dramatically," he says. "A year later he walked in to the hospital without a limp. He continues to follow up every month, and his blood pressure is well controlled." A more tragic outcome befell a hospital worker in her sixties, who'd been diagnosed with hypertension but failed to follow up regularly. "She didn't seem to understand that she had to take her medications daily," Peck says. "One day at work, she suddenly lost consciousness. She was found to have had a massive hemorrhagic stroke and died within twenty-four hours in the ICU."

Such cases, Peck says, underscore the importance—and efficacy—of proper treatment. While the logistics may be daunting, the methods for controlling hypertension are tried and true. "The answers are relatively simple," he says. "That's why I get excited about this research—because these things can be prevented."

— Beth Saulnier





JOHN ABBOTT

Life Lessons

In the LEAP program, patients are the professors

f all the teachers that Sarah Littlehale '17 and Jacqueline Romero '16 have in medical school, one of the most important may be a young woman who's still a student herself. Her name is Sequoia Worrell, and she's a twentythree-year-old New Yorker who has battled pulmonary fibrosis since she was fifteen. Every few weeks or so, Littlehale and Romero touch base with Worrell-accompanying her to medical visits, meeting for coffee, or just saying hi via text. "I don't look sick, so people from the outside wouldn't know that anything is wrong with me," says Worrell, a Harlem resident who's studying at CUNY schools, with an interest in community health and social work. "I don't like sympathy. I tell Sarah and Jacqui, 'Empathize, don't sympathize.'"

Worrell is among the first volunteers in Weill Cornell's LEAP program, which pairs medical students with patients who have chronic illnesses. Now in its second year, the effort—whose acronym stands for Longitudinal Educational Experience Advancing Patient Partnerships—currently comprises some 130 patients matched with half of the first- and second-year classes, plus twenty third-year medical students. Ultimately, it's planned to include the entire student body with students participating as their schedules allow. "Being a doctor is about being around patients," says the program's director, Keith LaScalea, MD, associate professor of clinical medicine, "and the earlier and more longitudinal, the better."

LEAP was inspired in part by a finding of the 2010 Flexner 2.0 report, which examined the state of medical education. It noted that due to shortened hospital stays and an overall trend toward outpatient care, medical students weren't getting enough long-term exposure to patients. As

LaScalea points out, there was a time when routine gallbladder surgery meant a two-week stay; now it's an overnight, if that. "Even patients with complex illness are in the hospital for much shorter periods of time," he says. "So unless you follow them longitudinally as an outpatient, you're going to miss a lot of critical elements."

In the LEAP program, teams of two students are generally assigned to follow two patients throughout their Weill Cornell careers—going to doctor's appointments or procedures, stopping by to see them if they're hospitalized, making home visits, or simply checking in. "We stress to the patients that they're the teachers," says the program's coordinator, Susan Kane. "They're there to teach the students about what it is to be a patient."

A few LEAP patients are pediatric; others are expectant mothers; some require recurring care like dialysis or chemotherapy. "When you're a doctor, it's critical that you understand not just the technicalities of a medical condition, but also what it's like to actually live with it," says Charlotte Roy '16. "LEAP is a great way to develop some perspective on what people with chronic conditions go through and how it

Patient as mentor: Sequoia Worrell (center) helps medical students Jacqueline Romero (left) and Sarah Littlehale understand what it's like to cope with chronic illness.

affects their lives." Through the program, Roy has already faced a difficult reality of doctoring: one of her patients, a middle-aged woman battling end-stage cancer, died. "Once, I went over while she was having chemo," Roy recalls. "She was upset, talking about her family. A lot of her concerns were not about herself-they were more about everyone around her, not being able to take care of them like she wanted to. I kept thinking, What can I do? And I realized: you listen and give your input where it's useful, but a lot of the therapeutic value is in just letting patients talk and get those issues off their chest."

One of Larry Wineland's patients is a woman in her eighties who's coping with high blood pressure, respiratory problems, and cardiovascular disease. LEAP has given Wineland, a thirdyear student, the chance to observe the lengthy process of finding the right medications to manage her conditions. "It's important to stop and think how a patient's chronic illness affects them psychologically." he muses. "We're so preoccupied with trying to figure out the clinical reason for what's going on—the patho-physiological mechanism of their disease—and so focused on the treatment. But they're living it. You need to ask, 'How are they doing as a person?' You can't think of them as just a set of lab results."

For Romero and Littlehale, working with Worrell has offered a novel perspective—that of a peer coping with a chronic, life-altering illness. For instance: like many young people, Worrell is an avid texter—but not just for the usual reasons. "Sometimes I'm out of breath, so I don't want to talk," Worrell explains. "And I cough a lot, so I'll just text." LEAP students also get insights into practical matters like the logistics of waiting for appointments, interacting with different specialists, or simply getting to the doctor's office—not always easy for older patients with limited mobility. "It not only lets us form long-term relationships with patients, but we're seeing their care from a completely different perspective," says Littlehale, a Harvard grad from South Carolina. "We're not the doctor and we're not the patient, but we're kind of along for the ride. It's been really eye-opening. It gives us a better concept of how patients exist outside of the exam room."

Among the challenges for LEAP is recruiting enough patients to expand the program. To that end, LaScalea met with Medical College faculty last spring to explain the criteria. Worrell, for her part, was eager to participate. "I feel like I'm getting my story out, what I go through," she says. "When I was first diagnosed, I ran into a lot of doctors that I felt didn't have the right interpersonal skills. LEAP is an opportunity to teach future doctors how I feel as a patient, and maybe they'll take that with them."

- Beth Saulnier

Circuit Breaker

Is 'faulty wiring' to blame for disorders like autism and epilepsy?



Samie Jaffrey, MD, PhD

espite years of research, autism still has no known cure, and interventional therapies—physical, occupational, speech, or a combination thereof—remain the standard of care. That can be a time-consuming and costly proposition, sometimes requiring one parent to leave the workplace and for families to foot the bill for treatment sessions not covered by insurance. And with autism spectrum disorders now affecting one out of every eighty-eight American children—as the CDC has reported—it's a national concern.

But there is renewed hope that effective autism drugs may someday be within reach. Because the brain is so plastic in the first few years of life, says Samie Jaffrey, MD, PhD, professor of pharmacology, understanding the roots of autism could offer the opportunity to repair its circuitry. As Jaffrey and his team reported last summer in Cell, a type of faulty wiring among nerve cells can lead to developmental disorders. And it's not just autism, he notes—other conditions such as intellectual disability, epilepsy, and schizophrenia may also be linked to these wiring issues. "The idea that faulty wiring can lead to these neurodevelopment disorders is not new," Jaffrey says. "But the question that has been around for a while is: what pathways lead to the altered wiring?"

The root of the matter might lie with RNA molecules—specifically, when the RNAs within a growing axon (nerve fiber) fail to degrade properly. As the brain is developing, neurons extend axons in order to make connections with one another and create the neural circuits that form the basis of learning and behavior. At the tips of axons are structures known as growth cones, which function as antenna. These cones sense where the target cells are and enable the axon to travel toward them. In their findings, Jaffrey and his team discovered that RNA molecules within the growth cones encode instructions that dictate which direction the axon finally takes.

Within a growth cone, Jaffrey explains, RNAs are translated and ultimately produce proteins, which steer the axon. However, Jaffrey found that growth cones also contain proteins that degrade RNAs. Degrading the RNAs "fine tunes" the amount of axon-steering proteins that are made. When RNA degradation does not occur, a person's brain circuitry can completely change. "It's known that mutations in RNAdegrading proteins are one cause of autism and childhood schizophrenia syndrome," says Jaffrey. "Our studies raise the possibility that when you don't properly degrade your RNA, or you don't degrade it at the right time, you get the wiring that ultimately can contribute to autism. It points to the importance of this pathway in brain circuitry and raises the possibility that by altering its activity we could potentially work toward rewiring the brain."

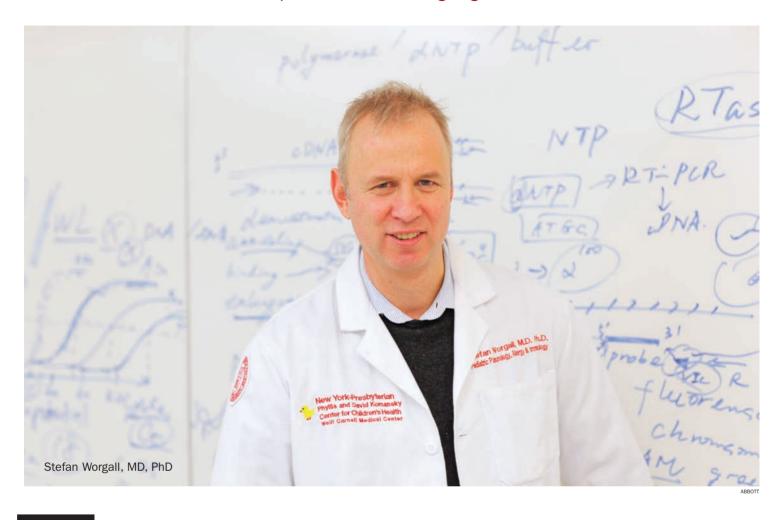
Jaffrey has long tried to understand the connection between RNA molecules and brain disorders. One of the first projects his lab undertook after he joined the faculty in 2001 was on how brain wiring occurs, and over the years he has published studies on such topics as the role of RNA interference in developing axons and growth cones.

The field's future looks bright. Jaffrey and his team are particularly excited about the potential of using miniature brain "cortexes" that can be formed from human stem cells rather than mouse tissue, to better understand human brain abnormalities. "We can now prepare stem cells from the skin of autism patients. We can then coax the stem cells to form a miniature cortex so that we can re-create the connectivity abnormalities in a dish," he says. "And then we can evaluate whether manipulating RNA pathways can potentially restore the connectivity."

- Andrew Clark

Breathing Easier

Research holds promise for treating a genetic form of childhood asthma



o see the urgency of his work, pediatric pulmonologist Stefan Worgall, MD, PhD, has to look no further than the residency clinic he leads every Tuesday afternoon. Each week, some two-thirds of the children in the waiting room are wheezing from the same disease. "Asthma is our biggest problem," says Worgall, who is chief of the Division of Pediatric Pulmonology, Allergy, and Immunology and Distinguished Professor of Pediatric Pulmonology. A cystic fibrosis expert, he became interested in asthma because of its relationship to infections. "It's a huge problem for kids, it's a huge problem for New Yorkers, and nobody knows how asthma really works. We don't have drugs to get rid of asthma. We can only change the symptoms."

But perhaps not for much longer.

Two years ago, Worgall and his collaborators set out to investigate the role that a small group of lipid molecules, tasked with signaling between cells and holding them together, played in a form

of childhood asthma. Previous studies had found that an overactive gene was linked to 20 to 30 percent of patients with the disease—and that the gene's related protein had something to do with this group of lipids, known as sphingolipids. But the connection between sphingolipids and asthma was far from clear.

Today, not only have they found the connection, but their discovery opens the door to new treatments that could end children's suffering from this genetic form of asthma—which, unlike most, is not characterized by inflammation.

About 7 million children in the United States—nearly 10 percent of Americans under eighteen and some 177,000 in New York City—have asthma, making it the most common serious respiratory disease of childhood. Asthma presents in many forms—the most common are triggered by allergens, infections, or exercise—but is not well understood. With only one-size-fits-all treatments available, physician-scientists like Worgall are looking for specific thera-

pies tailored to a child's individual form, including this genetic iteration.

In a study published last spring in Science Translational Medicine, Worgall and his team found that the overactive gene, known as ORMDL3, interrupts a crucial pathway that enables new synthesis of sphingolipids, and that the dysfunction of this process can create the genetic form of asthma. "I was most skeptical in the beginning," says Worgall. "I thought, Let's try it—but I didn't think it would work because it's too far from what we know."

As it happens, sphingolipids are an area of expertise for his wife, Columbia pathologist Tilla Worgall, MD. With their combined knowledge, they set out to study the connection between sphingolipids and asthma. Using two mouse models, they showed how weakening the pathway that produces new sphingolipids causes the disease. In one, they gave the mice an inhibitor that slows down new sphingolipid production; in the other, they produced a model that mimicked the overactive genetic defect in ORMDL3 found in humans. The animals became asthmatic in both cases.

Then Worgall and his team became particularly curious. How does limited production of sphingolipids produce asthma? Using samples of human bronchi, they found that reduced sphingolipids in the body cause the muscles around the airway to contract, closing off the windpipe to oxygen—the very conditions of asthma. "We knew the genetic change was there, but nobody knew what it meant," he says. "Now we understand the function, that it's related to a completely new pathway. And now we see the potential for new drugs."

Today, there are only two verified treatments for asthma: steroids and the bronchodilator albuterol. A third, magnesium, has shown mixed results in clinical settings. Worgall is now testing the efficacy of drugs previously approved for other conditions that can target this pathway and speed up production of sphingolipids. Ultimately, he envisions a day when doctors can use a child's individual genetic profile to determine if he or she is affected by the ORMDL3 form of asthma and prescribe proper medications to control it. Such precision medicine could also clarify why certain treatments are effective in some children and not in others. Worgall surmises that the patients who do respond have the genetic mutation.

But to get there, Worgall and his collaborators first have to see if what he found in mice is true in children. Using blood samples collected from patients, they will use mass spectrometry to gauge changes in sphingolipid production. Worgall hopes the study, the first of its kind, will be completed in the next year.

- Alyssa Sunkin

'This House Believes...'

That the WCMC-O debate club likes a good argument

n addition to chemistry and biology, some students at WCMC-O have had other things on their minds. Such as: military intervention in Syria, over-the-counter dispensing of psychotropic drugs, disarmament of military drones, conditions for migrant workers, Islamophobia, and cheating in professional soccer.

Those and many other topics have been argued by the Qatar branch's debate club, a successful squad that has won the state's universitylevel national championships four years out of



the past six (and been a finalist the other two). "Debating for me is about giving voice to an opinion that's not heard," says Khalid Ahmed, a second-year premed student from Egypt. "It's about looking at all sides of arguments, talking about things you don't regularly get a chance to talk about. I just love it."

The first official debate society in Doha's Education City, the WCMC-Q team has competed as far away as Ithaca (where they held their own against the Cornell squad, says their coach, Rodney Sharkey, PhD), Vermont, Botswana, and Manila; they aim to compete in Vienna this spring. Debate is a thriving art in Qatar; according to Sharkey, an Irish-born associate professor of English in the premedical program, a recent Qatar University Debate League day drew three dozen War of words: Team member Lama Obeid '16 at a debate competition

teams to the WCMC-Q campus—a six-fold increase in the past six years. "You see developments in the students' interpersonal skills that they don't necessarily recognize themselves," says Sharkey, a self-confessed "frustrated debater" who still laments his loss at the Irish national competition in 1981. "You could have moderate public speakers take up debate in Premed 1, and by the time they get to Med 2 or 3, they've taken on a confidence in their ability to communicate that doubtless will be useful to them as doctors."

Rebal Turjoman, a second-year medical student from Syria who competed in Manila, calls debating a "productive hobby." "It forces you to look at things from many sides," says Turjoman, who credits his training with helping him win the student council presidency last year. "Sometimes you end up making arguments you wouldn't vouch for in life, and other times you end up being convinced by an argument you'd never have accepted in other settings. It lets you exercise your mental strengths and see where you stand on issues. It helps you be more aware of why you think a certain way."

In addition to frequent practice sessions, Sharkey says, the team does community service like coaching high schoolers, serving as volunteer judges, and teaching English to expatriate workers. Says Sharkey: "They do a lot of socially conscious things that reflect well on the fact that they're debaters." And debating has practical benefits for future physicians and researchers, including training them to think on their feet. They get the position to be argued for or against—typically beginning with the statement "This house believes..."—just fifteen minutes in advance. Says Sharkey: "I'm constantly telling them that debate sharpens the mind in a way that should improve their reasoning skills when it comes to creating scientific hypotheses."

Second-year medical student Lama Obeid sees debating as a vital part of her WCMC-Q education. "Debating is one of the best ways to figure out if what you're thinking is right, and what path you want to go down," she says. "It forces you to keep up to date on what's going on in the world, to read about things you might miss out on when you're so busy. Right before you enter a debate tournament, you sort of cram life."

- Beth Saulnier

Put to the Test

After two decades of research, a better way to predict kidney rejection is within reach

or transplant patients, receiving a kidney often represents the granting of their fondest wish. But as physicians and patients well know, this happy ending is also the beginning of a life-long effort to ensure that the body accepts the organ. In addition to taking anti-rejection drugs, recipients must be closely monitored with



Manikkam Suthanthiran, MD

regular checkups and diagnostic tests, including blood work and biopsies.

For the past two decades, researchers at Weill Cornell have been working to develop a way to make that essential process easier, less invasive, and more precise. Now, they seem on the cusp of success. In work whose progress has been reported in the *New England Journal of Medicine* several times since 2001, a team led by Manikkam Suthanthiran, MD, has designed a urine test that can predict incipient kidney rejection with about 85 percent accuracy. "There is tremendous excitement in the transplant community about this study," says Suthanthiran, the Stanton Griffis Distinguished Professor of Medicine at Weill Cornell Medical College and chief of transplantation medicine, nephrology, and hypertension at NYP/Weill Cornell. "For the first time, we think we have something like a blood pressure cuff for the immune system of the transplant recipient. This has never been done in the history of transplantation. And should we be successful in preventing rejection, it has enormous consequences for patients."

The test, a PCR assay, measures what Suthanthiran calls a "three-gene signature"—elevated levels of three types of messenger RNA indicating that the body is marshaling its immune cells against the transplanted organ, which it sees as foreign tissue. In a five-center trial launched in 2006—sites included Weill Cornell and Columbia—researchers collected 4,300 urine specimens from 485 patients, starting on the third day after kidney transplantation. They found that the test accurately predicted rejection, as confirmed by a kidney biopsy in patients whose clinical signs warranted it. "We had an easy time recruiting patients, because they see the potential benefit of being able to monitor the possibility of rejection at any given time post-transplant without having to undergo a biopsy," says the study's principal clinical investigator at Weill Cornell, Darshana Dadhania, MD, MS '09, associate professor of medicine. "This test will make it easier for patients to be monitored more frequently and allow you to get results with a quicker turnaround time."

Suthanthiran says the test is much more specific than the current method, which evaluates kidney function by measuring creatinine in the blood. And while it isn't meant to replace all biopsies (which are performed when creatinine levels suggest possible rejection), it could make them much less common—good news both for patients and the health-care system. A biopsy, after all, is an invasive and uncomfortable procedure with inherent risks—including graft rejection or even death—that takes up a patient's entire day and costs some \$3,000. Plus,

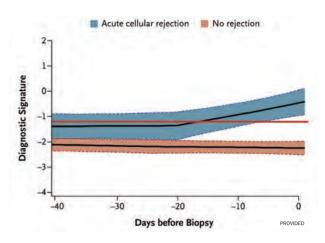
Suthanthiran says, urine gives a fuller picture of the organ's function. "There are one million nephrons"—the kidney's functional units—"and when you do a biopsy, you get only about fifteen to twenty," he says. "But urine comes from the entire kidney, so it gives us very good data. We think it's a brilliant window into what's going on."

The NIH-funded trial was observational: individual test results didn't influence treatment and weren't used to evaluate the need for a biopsy. In the next phase, Suthanthiran and colleagues aim to refine the test—potentially increasing its accuracy through further genetic studies-and gauge its efficacy in helping doctors finetune levels of anti-rejection drugs. "This is like a surveillance program," he says. "It's not just to predict rejection or make a diagnosis. We want to use this test to titrate how much immunosuppressant to give. Right now, we have one size fits all: we give it by milligram per kilogram of body weight." He posits that about a third of patients are under-medicated, increasing risk of rejection; another third are overmedicated, raising the specter of known complications like infections and cancer.

When the New England Journal published the team's most recent paper last summer, it ran an accompanying editorial entitled "One Step Closer to 'Rejectostix' "—referring to the longed-for ability to predict rejection with dipsticks like those used in routine urinalysis. While that may be far off, Suthanthiran estimates that the three-gene signature will go into widespread clinical use within five years. Currently, his team is streamlining the testing

process by training patients to collect and filter their own samples. Ultimately, a blood-based version may be used to detect rejection in patients who have received hearts, lungs, or other organs. "Transplants are very successful at one year, but over time they fail," Suthanthiran observes. "So we have fairly ambitious goals about making them last a lifetime."

— Beth Saulnier



Rising danger: A graph published in the New England Journal of Medicine shows that the three-gene signature test indicated incipient kidney rejection, with levels rising in the twenty days before biopsy. Patients whose biopsies revealed acute cellular rejection are in blue, while those whose did not are in red.

Good Rhythms

To soothe the tiniest patients, NICU head prescribes Mozart

he neonatal intensive care unit, home to a hospital's youngest and most fragile patients, is hardly a restful environment—and Jeffrey Perlman, MD, has the acoustical measurements to prove it. Perlman, professor of pediatrics, has long been concerned about sound levels in the NICU. He reports that the humming of an isolette is typically 50 to 60 decibels, roughly equivalent to light traffic. Closing an incubator door (80 decibels) is about as annoying as a ringing telephone. A crying baby reaches as high as 100 dB, akin to a revving motor. Add in the beeping of multiple monitors, physicians conferring on rounds, or the sound of a vacuum cleaner down the hall, and the decibels rise to near that of a rock concert, which Perlman notes clocks in at around 120 dB. "The intensive care unit is a very noisy place," he says, "and there's clear evidence that can affect the babies in an adverse manner."

Perlman, director of newborn medicine at NYP/Weill Cornell's Phyllis and David Komansky Center for Children's Health, advocates a simple but elegant remedy: music. In work that he has presented at research meetings, Perlman studies the beneficial effects of instrumental pieces on infants in the NICU. It's not just a question of creating a more calming mood; the right music, he says, can have measurable physiological benefits including slower heart rates, higher oxygen saturation, more restful sleep, and improved feeding.



Those gains, in turn, can mean higher weights, faster recoveries, and shorter hospitalizations. "It really does help," says Rebecca Loveszy, DA, the NICU's music therapist. "It helps them sleep more deeply and calms them when they've had something stressful like a procedure or a diaper change."

The idea that music can have physiological benefits is hardly a new concept. A century ago, surgeon Evan O'Neill Kane, MD, published in JAMA on the use of a phonograph to calm patients and improve tolerance of anesthesia. In 1960, an article in Science described how music could reduce the perception of pain during dental work. And the so-called "Mozart effect," described in Nature in 1993, holds that spatial reasoning can be temporarily improved by listening to the composer's works. Last May, a study based at Beth Israel and reported in the Journal of the American Academy of Pediatrics found that music—specifically, lullabies sung live can improve vital signs, feeding, and sleep. As William Congreve put it more than 200 years ago: "Music hath charms to soothe a savage breast, to soften rocks, or bend a knotted oak."

When it comes to soothing premature infants, Perlman recommends playing

music three times a day, twenty minutes at a time; benefits emerge after the babies become acclimated to the sounds, in about a week. And not just any music will do: Perlman uses single-instrument works, more complex pieces being harder to process neurologically. At the cribside, Loveszy performs childhood standards like "Row, Row, Row Your Boat" on acoustic guitar, using nylon strings for a softer, warmer tone; she also plays during "kangaroo care," when parents hold their infants against their chests for therapeutic and bonding purposes. At discharge, families receive MP3s of NICU songs, including custom tunes that Loveszy creates for each patient. "We're born into a musical environment—the sounds of the womb, the mother's heartbeat, the father's voice, the things that happen during the day," says Loveszy, who often tries to match the key of a beeping monitor in the hope of blocking it out. "There's a lot of rhythm in it, a lot of tone."

For preemies, Perlman notes, good sleep is a vital—but often elusive—part of the healing process. While full-term newborns get thirty to forty minutes of quality sleep at a stretch, he says, for preemies it's just two to three minutes. And while music helps, Perlman has found that it works only when

preemies are lying on their stomachs—the preferred position, since their underdeveloped airways make it harder for them to breathe when on their backs. Why would lying supine negate the music's effects? When you're gasping for air, he explains, music is just an annoying distraction. He compares the situation to driving on city streets at rush hour. "If you've got music on—but the traffic is bad, people are cutting in front of you, and you're worried about having an accident—are you listening to it?" he muses. "No, you're not. Whereas, if you're at home and the time is right, it's beautiful."

While Perlman is particularly partial to Mozart's piano compositions for soothing NICU patients, he and Loveszy stress that preferences can be intensely personal. (Loveszy recalls one premature twin who, unlike her sibling, would immediately start wailing at the sound of "Twinkle, Twinkle, Little Star.") A baby's tastes might well be influenced by what the mother listened to during pregnancy; while practicing in Texas, Perlman had one tiny patient who was partial to country tunes. "To me, it's the tempo that seems to suit the baby," Perlman says. "Miles Davis's Sketches of Spain is one of my favorites, and babies chill to that."

- Beth Saulnier

Right Under Our Noses

Does our olfactory organ hold the secrets of gene regulation?

ur nose doesn't just deliver the aroma of freshbaked bread, the heady bouquet of roses, or less pleasant scents to our consciousness. Recent studies at WCMC-Q show that the organ may be a gateway to understanding how humans, through random gene regulation, become engines of biological complexity beyond the sum of our parts.

Benjamin Shykind, PhD, and his team are studying odorant receptors (ORs), a group of 1,000 genes that comprise the largest family in the genome and give us our sense of smell, known as olfaction. These receptors are located

on the olfactory receptor cells, which occupy a small area in the upper part of the nasal epithelium—the sinuses—and detect inhaled odorant molecules. Shykind's research probes the remarkable processes through which these nasal cells use ORs to regulate their genes. Their genetic talents are a paradigm of gene regulation that has fascinated molecular biologists and neurobiologists alike, says Shykind, assistant professor of cell and developmental biology and of biochemistry.

At the core of his research is the enduring question of how we develop from a single cell, the fertilized egg, into complex creatures. Humans have more than 100 billion nerve cells in our brains that make 1,000 times that many

contacts, or synapses, among one another. This extreme complexity far outstrips the comparatively meager number of genes we possess—roughly 23,000.

What does the nose know about this process? In that organ, each nerve cell picks just one OR gene out of the 1,000 found in the genome, from one of the two copies we inherit from our parents. That's a choice of 1 in 2,000, meaning there are that many different types of olfactory neurons in our nose. "It appears that these nerve cells are using a tricky sort of regulation of gene expression to get this done," says Shykind. "When the need for diversity outpaces the usual genetic mechanisms, cells turn to 'stochastic' processes, mechanisms that can generate random outcomes and then use them."

These neurons, Shykind notes, lead a pretty rough life. They're the first responders to everything we inhale, and they don't live long—perhaps two months at most. But they regenerate throughout our lives; most other nerve tissue dies and is not reborn. Understanding how the nose regenerates its nerve cells may unlock treatments for repair and regeneration of damage elsewhere in the nervous system.

In addition to employing standard mechanisms to control genes, the nose uses a yet-to-be-understood process to roll the dice and choose a different receptor gene for each nerve cell. When a neuron regenerates, it will again become dedicated to a specific gene, rarely the same one—but how that happens exactly is still unknown. Shykind believes that OR neurons in the human nose are harnessing randomness "to basically roll a 2,000-sided die to come up with an enormous variety of cell fates. So we have a compelling model for how cells can use their genes to create biological diversity."

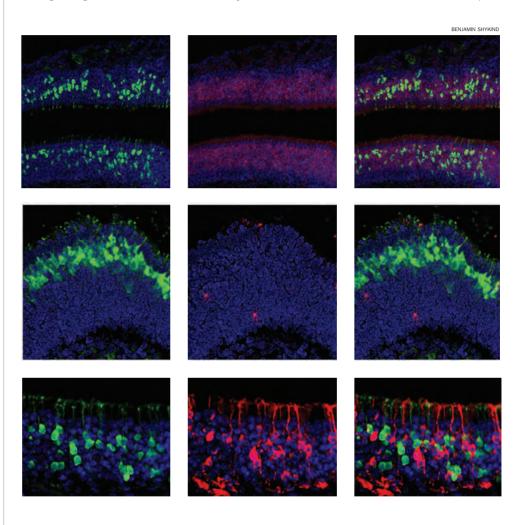
The underlying mechanisms of this process take Shykind's research into the emerging field of epigenetics. If the sequencing of the human genome told us how our genes are arranged, he explains, the epigenome "will tell us how they are actually used by our cells—how they are turned on and off-and when." His team's latest paper, published in PLOS Biology in May, is one of the first to directly explore the epigenetic state of a gene in a living cell. Using genetically engineered mice, they demonstrated that OR genes undergo transitional states, periods when the nerve cell may possibly turn them "on"-followed by a longer period during which

these genes are inaccessible and permanently "off." That kind of rarified data is, well...nothing to sneeze at. "If we can understand how a gene that needs to be on to prevent unregulated cell growth becomes repressed or turned off, then we have a jump on diseases of deregulation like cancer," Shykind says. "You might be able to reactivate a tumor-suppressor gene that's been turned off, or turn off certain oncogenic genes that are on when they

should be off. These are all basic biological questions about gene regulation."

Shykind likens the human genome to a piano with its eighty-eight keys. We know their number and sequence—but there's a big difference between playing "Chopsticks" and performing a Chopin étude. The ultimate job, he says, is to discover the mechanisms that allow our genetic piano to be played so masterfully.

- Franklin Crawford



Smell test: Work by Qatar-based researcher Benjamin Shykind, PhD, includes (top row) visualizing olfactory sensory neurons in genetically modified mouse lines; (middle) visualizing such neurons expressing different receptor genes; and (bottom) an experiment to determine the onset of olfactory receptor genes in the mouse nose.



David Saunders '14

cores of MD-PhDs have trained at Weill Cornell over the years. But David Saunders may be the only one whose doctoral work involves not microscopes and test tubes, but silence and a cushion.

A fourth-year medical student, Saunders is simultaneously working toward his MD at Weill Cornell and a PhD in Buddhist studies at Atlanta's Emory University. Ultimately, he plans to specialize in psychiatry and use his knowledge of Tibetan Buddhist practice to treat patients suffering from anxiety, depression, and other ailments. It's an unusual path—but one that makes him uniquely qualified to incorpo-

Doctor of Divinity

David Saunders '14 took a hiatus from medical school to pursue a PhD in Buddhist studies

rate meditation and mindfulness into medical treatment, a trend that's on the rise as alternative therapies gain acceptance. "Many people involved in the field know quite a lot about the science but not a lot about the Buddhism, or they know a lot about the Buddhism but not much about the science," says Saunders's thesis adviser, Emory religion professor John Dunne, PhD. "That has always been an obstacle in mov-

ing the field forward—having people who have a good understanding of both and can bridge the two. So I thought this was a wonderful idea, although I had my doubts about whether someone could really do it. But David has alleviated all of them. He's quite remarkable."

Juggling medical studies in New York with doctoral work in the humanities some 800 miles away has taken dedication,

organization, self-discipline—and the kind of goal-oriented focus that recently had Saunders, an avid distance runner, pushing through a race despite the severe pain of what proved to be a stress fracture. (He wound up spending weeks on crutches, still moving faster and more nimbly on one leg than most people do on two.) Saunders entered Emory after two years at the Medical College, which granted him a leave of absence. "I can't overstate how grateful I've been to Weill Cornell for letting me pursue this unorthodox path," says Saunders, sitting in a favorite Upper East Side café with his crutches stowed against the wall and his leg stretched out, ever solicitous of other patrons trying to navigate the closely packed tables. He chuckles as he recalls leaving a Basis of Disease lecture to do his graduate school interview over Skype with what he thought would be two or three faculty but proved to be a panel of eight. Because he'd put on a dress shirt and tie but left on his blue jeans, he notes, "I was hyper-conscious not to stand up."

In addition to his graduate coursework, Saunders trained as a teacher of compassionbased meditation, taught mindfulness to Emory psychiatry residents, and studied how meditation can reduce stress in foster children. He also maintained his own work-life balance: throughout his time there, he and his then-girlfriend, Tri-Institutional MD-PhD student Jennifer Small, kept up a long-distance relationship, with one or the other flying to visit every third weekend. (The couple married last summer.) After they graduate this spring, she'll go into residency and he'll spend a year writing his dissertation—on mindfulness and meditative practice in Western psychotherapy in psychiatric settings, with a discussion of how Buddhism has grown in America since the Transcendentalist age—before matching in psychiatry. "David is the model student," says Dimitry François, MD, assistant professor of psychiatry, who oversees the psychiatry clerkship and was an attending on Saunders's rotation. "He's extremely engaged and reliable; he reads a lot; he wants to know more. He's the student you dream of having."

The sixth of nine children from a small town in Minnesota—his father is a school principal, his mother an arts administrator—Saunders grew up in an observant Roman Catholic household. But as he describes it, several factors combined to alter his relationship with the church, pushing him away from the strict devotional Catholicism he grew up with and toward a more intellectual one. His mother earned a master's degree in theology, adding a historical, scholarly dimension to his understanding of the faith. He grew increasingly unhappy with the church's treatment of women and homosexuals-especially as two family members came out as gay-and by its lack of compassion for sexual abuse victims, decrying its "dogmatic, antiquated views on contemporary sociopolitical issues."

In the midst of this turmoil, Saunders took an undergraduate course at Boston College on interfaith dialogue between Buddhism and Christianity—his first exposure to non-Catholic religious teachings. He went on to spend half his junior year in a community of Tibetan refugees in Nepal, double majored in theology and premed, and wrote a senior thesis on how Buddhist practice can aid physicians suffering from burnout. After being accepted to Weill Cornell, he deferred for a year to return to Nepal on a Fulbright, studying Buddhist cultural perceptions of tuberculosis. When it came time to matriculate, he made a deal with himself: if he still felt drawn to study Buddhism after his first year of medical school, he'd apply to graduate programs and somehow make it work.

"David is an incredibly intelligent person," says Dunne. "He has a tremendous amount of energy and a wonderful, infectious enthusiasm coupled with a sunny demeanor. Some people with that energy level could burn out, but I'm not concerned that David will, because he understands the importance of balance—between working hard and finding time for yourself and your family, and also between intellectual effort and the type of learning that occurs when you sit back and let things stew a bit."

When Saunders returned to medical school. he aimed to practice meditation for ten to fifteen minutes a day. It didn't quite happen. "Third year is rigorous, and I probably sat formally on a cushion three to five times a week," he admits. "But even though I wasn't practicing as much as I wanted to, I was trying to incorporate moments of mindfulness throughout the day." Such a moment could come, for example, while observing a long surgery. "Rather than thinking about the test you're going to take next week or what you said to the attending a few minutes ago," he says, "maybe as you're standing there above the patient you're feeling your feet grounded, experiencing the in-breath and the out-breath to bring you to the present moment."

This academic year, Saunders is passing on his meditation skills to fellow students. Under a grant from the Gold Foundation, he's teaching compassion-based techniques for burnout reduction to second-years and conducting a study of the results. "By teaching students, residents, and physicians how to avoid burnout, you reach so many patients," he says. "If physicians are more empathic and compassionate—and less burned out, depressed, and anxious—the consequences for patients are almost incalculable."

- Beth Saulnier

'Third year is rigorous, and I probably sat formally on a cushion three to five times a week. But even though I wasn't practicing as much as I wanted to, I was trying to incorporate moments of mindfulness throughout the day.'



Without Walls

Ell Comellan

By Beth Saulnier Photographs by John Abbott

Designed to break down barriers, foster collaboration, and spur translational science, the Belfer Research Building opens for discoveries

or Carl Nathan, MD, the new Belfer Research Building's form and function are intimately intertwined. "I feel a lot of echoes in this building in how it was designed, what it's for, and what will happen here," says Nathan, the R. A. Rees Pritchett Professor of Microbiology and chairman of the Department of Microbiology and Immunology. For one thing, he says, "the act of building it was an interdisciplinary event of enormous complexity, and the building is designed to support interdisciplinary work." Among the many other analogies that Nathan draws between Belfer's design and its mission are its myriad thoughtful details—from highly flexible lab infrastructure to built-in mechanisms for conserving energy. "You look at them and say, 'That's clever. That's so well thought out," " Nathan says. "I hope that influence will be felt by the people working here, because that's what's expected of us."

Architectural marvel: (Clockwise from top)
The building's exterior, a bird's-eye view from the second floor, the lobby, and one of the staircases that connect each pair of floors







Formally opened in late January, the \$650 million, eighteen-story Belfer Building is the crown jewel of Weill Cornell's scientific enterprise. Nearly doubling the Medical College's research space, the 480,000-square-foot facility will bring together investigators in an open, collaborative environment. "Today marks an extraordinary milestone for Weill Cornell," Dean Laurie Glimcher, MD, said at the building's dedication, attended by such dignitaries as U. S. Senator Charles Schumer and U.S. Representative Carolyn Maloney. "Our new Belfer Research Building is an inspiring symbol of scientific breakthroughs that can advance patient care, enhance health, and change lives."

The Belfer Building is a stylistic cousin to the nearby Weill Greenberg Center: an airy, modern space with ample daylight and state-of-the-art features. While the Weill Greenberg Center is a locus for patient care, the Belfer Building will be its partner in the translational mission; if Weill Greenberg is the metaphorical bedside, Belfer is the bench. "I think it's spectacular," says Vice Dean Michael Stewart, MD, chairman of otolaryngology and the E. Darracott Vaughan Jr. Senior Associate Dean for Clinical Affairs. "This is going to enable us to grow our research specifically in ways that target translation to the bedside. It's a beautiful space—it fits into the neighborhood, it's very large, and it's right on campus—so it's a great addition."

Named for Renée and Robert Belfer, who gave \$100 million to fund its construction, the Belfer Building was supported by numerous other gifts, including ones from Joan and Sanford Weill, who



gave \$250 million, and Maurice and Corinne Greenberg and the Starr Foundation, who gave \$100 million. Located on East 69th Street between First and York avenues, the facility was designed by Ennead Architects, who also created the Weill Greenberg Center. Its investigations will be centered around themes representing some of society's greatest medical challenges including cancer; cardiovascular, metabolic, and neurodegenerative diseases; children's health; and global health and infectious disease. It will host the Sandra and



Edward Meyer Cancer Center, founded in January with a \$75 million gift from the Meyers and their foundation, as well as the Tri-Institutional Therapeutics Discovery Institute (Tri-I TDI), which will facilitate translating early-stage drug discovery into treatments. "We can go to their team and say, 'We have a validated target; can this be made into something that can be used in the clinic?'" says Lewis Cantley, PhD '75, the Meyer Director of the Meyer Cancer Center and the Margaret and Herman Sokol Professor in Oncology Research. "That step is rarely taken in academia, but here we'll be set up to allow that to happen. So that's very exciting."

n addition to the medicinal chemistry labs, the top floors of the Belfer Building will house state-of-the art facilities for imaging and mass spectrometry; the Meyer Cancer Center will be on the two floors immediately below. In an innovative partnership, the fourth floor was purchased by CUNY's Hunter College, which will conduct translational research there. "This is a physical expression of a long-standing relationship between two institutions that will advance scientific study and train the next generation of scientists," says Hunter's president, Jennifer J. Raab. "We are incredibly fortunate to have this first-class space to work side by side with Weill Cornell."

Communication and collaboration were the watchwords for the building's design, which is marked by an open, airy feel. "Opening the new building is a phenomenal event for the Weill Cornell Graduate School of Medical Sciences," says its dean, Gary Koretzky, MD, PhD. "There will be easy communication and interaction

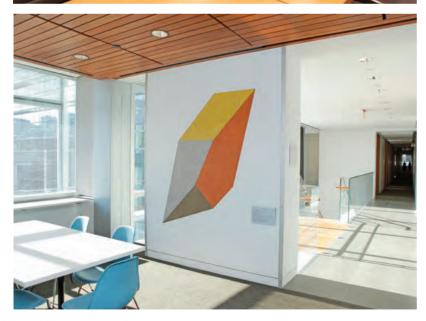
among research groups, so students doing their training in the building will have the advantage of working not only with their major sponsor, but will have many opportunities for interaction with other investigators."

In addition to the large exterior windows—which offer a sweeping view that comprises the spire of World Trade Center One, the Ed Koch Queensboro Bridge, and Midtown skyscrapers-most of the interior walls are made of glass. The labs, which are located on the north side, are separated from the southern-facing offices by such walls, offering light without direct sun. Just outside the labs are lounge areas—particularly important since no food or drink is allowed inside. "It's well designed to give a sense of light without impairing laboratory research," says Cantley. "I love the openness, the fact that it's glass all the way through, so you can be sitting in the eating area, which is facing south, and see all the way through the lab to the north side." Each pair of floors is connected by a glasswalled staircase, reinforcing the expansive feel while connecting groups of researchers; Nathan calls that particular design element "a terrific idea." "This is an era when we pick collaborators globally, but it still matters a great deal who you're close to," he says. "It's a very human thing, but who you bump into—the evolving informality of relationships—builds trust and leads to unexpected synergies. Ideas at their most fertile point are still closely guarded for fear of being wrong. In what circle can you risk sharing ideas that are as likely to be wrong as right? It's the people you interact with, your neighbors."

Each of the thirteen laboratory floors has space for five or six lab groups comprising a total of eighty bench scientists. Unlike in most research facilities, the groups will share spaces like those for tissue cul-







Just right for research: (Clockwise from far left) Scientists in one of the building's first occupied laboratories, a lounge area with a view of the lab, a conference center space, and a Sol LeWitt artwork

ture, darkrooms, and more. "There's one set of scientific glassware for everybody on the floor," notes campus architect Bill Cunningham. "Again, it's those silos getting broken down." The lab spaces—which are accented in anigre, a warmly toned, sustainable tropical hardwood—are designed for maximum flexibility, with mobile benches and detachable ceiling valves for resources like water, gases, and vacuum. "Where one lab ends and the next begins is pretty much arbitrary," Cantley says. "There may be a bench where half the people are from one lab and the other half are from another. I like the concept of having that sort of elasticity as scientists move through their careers."

Cantley's lab, the first to move into the building, is located on the thirteenth floor. When it comes to allocating space, Koretzky says, a key issue is grouping researchers according to the building's themed areas of interest. Nathan, for example, will be on the eleventh floor with some longtime collaborators—including microbiology and immunology colleagues Sabine Ehrt, PhD, Dan Fitzgerald, MD, Kyu Rhee, MD, PhD, and Dirk Schnappinger, PhD—who work on overlapping topics on the biology of tuberculosis, but had previously been spread throughout campus. "This will bring us together physically for the first time," Nathan says. "It's a thrill to get a group of people together who range from the atomic to the clinical."

From its earliest planning stages, the aim of the Belfer project has been to aid in the recruitment of top-tier scientists and to empower faculty who are already at the Medical College, thus strengthening the overall research effort. The bottom floors of the Belfer Building are devoted to conference and meeting space available to the entire campus, including a flexible room that can seat 225. Off the second floor, adjacent to Lasdon House, is something that Weill Cornell has long lacked: an outdoor "quad." The space will have benches, picnic tables, plantings even a small grove of trees. The building's other amenities include a coffee bar—a prime locale for those "creative collisions" among researchers—and an art collection featuring several works by famed conceptual artist Sol LeWitt, whose father, Abraham, graduated from the Medical College in 1900. The lobby, with walls of French limestone and a terrazzo floor with cherrywood accents, greets visitors with a digital art installation—made up of thousands of tiny video screens—that's also visible to passers-by on East 69th Street.

The building's many energy-efficient elements include its double-glass curtain wall on the south façade—the outer one shades the inner—as well as automatic systems for controlling window shades, lights, HVAC, and more. According to Cunningham, Weill Cornell is aiming for LEED Gold certification—a rare designation for a research facility. As faculty, graduate students, and support staff move in, work on several floors of the building continues. Stewart notes that it was purposely built with more space than is currently needed, with the aim of growing into it as the research enterprise expands. "Any space would have been helpful," Stewart muses, noting the former crunch for square footage. "But the Belfer space is extraordinarily helpful, because it's so well designed, so large, and so flexible. It will enable us to do science in a new way." •





Founded in the darkest days of the epidemic, Weill Cornell's treatment center and clinical trials unit have seen HIV/AIDS become something previously unimaginable: a chronic illness

By Andrea Crawford Photographs by John Abbott

lthough Berlin ranks among the world's most vibrant cultural centers, the city still carries dark resonances. The most obvious, of course, is its legacy of Nazi atrocities and Communist oppression. But for HIV specialists Jonathan Jacobs, MD, and Samuel Merrick, MD, and many of their colleagues, Berlin is the nexus of another painful memory: the International AIDS Conference of 1993.

There, researchers presented results from several large studies showing that Zidovudine alone—more commonly called AZT, the first drug approved for treatment of HIV infection—had no medium- or long-term benefit. Jacobs and Merrick remember walking around that city stunned, having just been told, basically, that what they had been doing to treat patients had accomplished nothing. "Even today when I think of Berlin," says Merrick, associate professor of clinical medicine, "I think of depression."

At that moment twenty years ago, the NewYork-Presbyterian Center for Special Studies (CSS)—the AIDS treatment and research center that Jacobs had helped found—was just five years old. Merrick was fresh out of residency, thinking he might work in AIDS care for a year or two. And HIV was a virtual death sentence.

In 2013, CSS celebrated its twenty-fifth anniversary. Jacobs and Merrick are still there, as executive director and medical director, respectively. And HIV has

Taking care: HIV patient Clark Shannon (left) with his longtime doctor, Jonathan Jacobs, MD, professor of clinical medicine



Treatment team: Jacobs (right) and Center co-founder Samuel Merrick, MD, associate professor of clinical medicine

become a chronic disease. "I started my medical career in the depths of the worst part of the HIV epidemic and now there's a growing sense of optimism that there may someday be a cure," says Merrick. Moreover, much of the research behind that transformation has occurred next door to CSS, at the Weill Cornell Clinical Trials Unit (CCTU), which opened in 1986 and just received renewed NIH funding through 2020. Says Roy Gulick, MD, chief of the Division of Infectious Diseases: "These two groups have synergized over the years to make great progress." It was there in the aftermath of Berlin, he notes, that the first research appeared that truly changed the way people thought about the disease, and that some of the first patients began to respond to therapy.

The founding of CSS and of CCTU followed closely upon the appearance of AIDS in 1981. New York State leaders realized the potential impact of an epidemic that, in disproportionately affecting young people, was rendering some of the most productive members of society too sick to work. To promote better patient care, the Department of Health offered enhanced Medicaid reimbursement rates to officially designated AIDS centers. In 1984, the same year the human immunodeficiency virus was proven to be the cause of AIDS, the state released requests for proposals for new centers. Jacobs was finishing an infectious diseases fellowship in WCMC's Department

of Medicine and contemplating the next phase of his career.

To create an outpatient center, Jacobs and his colleagues asked patients what they would like in an HIV clinic. "We had the great benefit of not knowing anything about hospital organization," says Jacobs, professor of clinical medicine, "so we just put together a list of services." The vision was one of integrated care, comprising not only nursing staff and physicians but social workers, psychiatrists, nutritionists, chaplains, and even legal aid volunteers. Over the years, other services, such as gynecology and dentistry, were added; now the Center is seen as a model for patient-centered medical homes, encouraged by the Affordable Care Act.

"Dr. Jacobs recognized the tremendous need for multidisciplinary comprehensive care for patients with HIV—and that was important, but it was not unparalleled," says Merrick, who joined the Center in the early Nineties. "What is unique is that he worked to provide that high quality of care to underserved patients marginalized in society." The Center would have a horizontal administrative structure—because, Jacobs says, "frankly, I could often do less for these patients than their social worker could."

Selected by the state as one of the first centers, CSS opened in August 1988. "At that time, AIDS care was end-of-life care, and there was a strong need for research to provide anything effective to treat

the illness," says Gulick. "The Clinical Trials Unit was able to recruit patients right from the clinic, and the patients had access to the latest strategies and investigational drugs."

In the late Eighties, Jacobs was introduced to the prominent New York socialite Judy Peabody, who had volunteered for the Gay Men's Health Crisis after the death of a friend. As a "care partner," Peabody took responsibility for

dozens of men with AIDS—literally holding their hands, notes Jacobs, as they died in dire circumstances and social isolation, "something critically important at this time, when other people were afraid to touch them."

Peabody wanted to do more, and within a couple of months after CSS opened, she brought a few of her philanthropist friends to visit the fledgling Center's offices. These friends—the designer Bill Blass; Glenn Bernbaum, owner of Mortimer's restaurant; Nancy Kissinger, wife of former Secretary of State Henry Kissinger; Casey Ribicoff, widow of Connecticut Senator and Governor Abraham Ribicoff—and Peabody formed a lasting partnership with CSS, helping to create an endowment that still funds a portion of the Center's staff. Their support also enabled the purchase of fine furnishings that make the Center feel more like a well-appointed home than a clinic; Blass's gift of a weekly delivery of fresh flowers continues to this day. Ultimately, Blass left half his estate to CSS. "That money gave us true flexibility to address patient needs," says Jacobs. "As the dynamic of the epidemic changed, we were able to change the services we offered."

At its inception, the Center had more in common with hospice care than a typical health center, as it was designed to help people feel better despite the fact that every patient was expected to die. Marianne Johnson certainly expected to die when she was diagnosed in December 1988 at age forty-three. Johnson (not her real name) had noticed she was losing weight, feeling nauseated, and breaking out with small blisters, but she didn't pay much attention to her symptoms until one evening when her husband's doctor called their home and said he needed to speak with him about his blood test. He was HIV positive—and, as Johnson would learn, so was she. "As far as I was concerned, it was a death sentence," she recalls. "I thought, A few months, and I'll be gone."

Those early days were bleak for both patients and physicians. Some of the first studies showed median survival rates from three to thirteen months. "It was brutal, sad, emotionally draining," Merrick recalls. "Every patient who walked into my office and sat in that chair, I knew was going to die; I just didn't know exactly when. And they knew—not only that they were going to die, but that they would die from difficult and disfiguring illnesses," he says. He remembers the names of several hundred patients, many of whom died young; he recalls their T-cell counts and the opportunistic infections that killed them. "I had one week when three patients died while I was physically in contact with them, conducting an examination," he says, admitting that he's not sure he could have stayed in the field if prognoses had not improved. But HIV/AIDS medicine was also intensely rewarding work because of the bond that formed between caregivers and patients and their families. Says Jacobs: "It was instructive to me-although I'm sure this is something that's long been known to oncologists—that you can help a person feel better even if you don't ultimately save them."

'We went from a situation where we saved no one to one where, if their immune systems weren't too damaged, we could offer people what is now a normal lifespan.'

By 1994, AIDS had become the number one killer of Americans—both men and women—aged twenty-five to forty-four. The appearance of AZT brought the first measure of hope—only to be dashed in Berlin. But soon after, in work done by Gulick and other researchers at CCTU, clinicians learned that a combination of three drugs—known first as HAART (highly active anti-retroviral therapy), now called ART—could keep HIV at bay over the long term. "So we went from a situation where we saved no one," says Jacobs, "to one where, at least if their immune systems weren't too damaged, we could offer people what is now a normal lifespan."

Finding effective treatment for HIV was one of the most significant advances in medicine in our lifetime, says Gulick. After the discovery of ART, the death rate for young Americans dropped two-thirds in two years. It was life-saving therapy, but it required patients to take some twenty pills a day in precise eight-hour increments. Over the next several years, CCTU researchers tested regimens that were easier to adhere to; today, three different one-pill-a-day therapies are available.

ven after the discovery of effective treatment, patients and researchers continue to navigate uncharted territory, just as they have throughout the history of the epidemic. They now confront the long-term implications of living with HIV. As the New York Times recently noted, HIV has become something unthinkable: "a disease of the middle-aged." Whereas the typical patient used to be a young gay man with Pneumocystis pneumonia who would be dead in two years, today the Center's typical patient is a fifty-year-old whose HIV may be controlled but who also has diabetes and heart disease. So CSS has transitioned, essentially, from specialty to primary care. A lifetime of medications often triggers side effects that can cause complications such as decreased bone density and increased levels of cholesterol and triglycerides. Says Marshall Glesby, MD, PhD, professor of medicine and medical director of CCTU: "A lot of our work is now aimed at understanding, preventing, and managing some of the other infections that people with HIV are at risk for." These include hepatitis C and human papillomavirus, which causes cervical and anal dysplasia and cancer.

Even with a viral load that's low to undetectable, replication continues, causing inflammation—so patients with HIV have higher rates of heart disease and other conditions associated with inflammation. They have higher rates of dementia as the virus replicates in the brain. And they have higher rates of cancer than the population at large—the result, perhaps, of inflammation or of weaker immune systems in general. So CCTU researchers study ways to dampen the inflammation and immune-cell activation that occur even when HIV is well controlled and could contribute to chronic, aging-

related complications. And they have NIH funding for a large study looking at the optimal timing for initiating ART therapy—which could play a role in limiting some inflammatory conditions.

t some point in the Nineties—Marianne
Johnson does not remember exactly
when—the medications started working, she began to feel better, and she realized she
might even see her fiftieth birthday. "No one expected it to be a dis-

might even see her fiftieth birthday. "No one expected it to be a disease that you could live with for so long," she says. Now sixty-eight, she is contending with heart disease and a hip that needs to be replaced. "I know the medication does a whole lot of things to your body," she says, "but I don't let it bother me anymore." She comes to CSS every twelve weeks and over the years has used its full range of services.

At the beginning of the epidemic, stigma was endemic and even some physicians did not want to treat HIV-positive patients. While such stigma had antecedents in the history of medicine—with the plague, influenza, and polio, to name a few—discrimination made HIV different, Jacobs notes. "It's one thing to be fearful for your life, and I fully get that," he says. "But by 1984 we knew this was caused by a virus that was transmitted sexually and through blood, yet there were still medical professionals who said it was better not to treat these patients so as not to perpetuate the epidemic."

Johnson recalls that the first doctor she saw after her diagnosis said he would try to help her—but only if she "stopped doing what she was doing." Johnson didn't understand what the physician was talking about, having lived so sheltered a life that she'd never even tasted alcohol. She asked him to explain, and he said: "Are you going to stop doing drugs?" To this day, the memory of his remark stings.

Attitudes toward the disease have improved dramatically, but patients today can still feel a stigma. Even after living with the disease for twenty-five years, Johnson has told only a few of her closest relatives and friends. When she's hospitalized or when others wonder why she long ago left her job, they assume she has some kind of cancer. Jacobs says this is quite common. "There is still a tremendous psychological burden tied to this virus," he says. "Even our training doctors sometimes ask about patients, 'How did they get it?' That, in my mind, is not the most important question."

Sixty-one-year-old Clark Shannon never told his parents, who are now deceased, and he has still never told his siblings—even though today, ten years after his diagnosis, he works for an HIV/AIDS organization. "I talk about HIV and AIDS every single day of my life," he says, but "I've chosen not to speak about my personal experience of it."

On the tenth anniversary of his diagnosis and the twenty-fifth anniversary of CSS/CCTU, Shannon decided to speak openly. When he was diagnosed in August 2003, HIV was no longer an automatic death sentence, but he didn't know that. In the aftermath of 9/11, Shannon had lost his job and his health insurance. When an unusual sinus infection would not clear and his HIV test came back positive, his doctor sent him straight to CSS. "I was extremely nervous and frightened about what was going to happen to me," says Shannon. "I was so unprepared for the diagnosis. It was a very scary, desperate time."

To begin treatment, CSS social workers helped him get coverage through Medicaid. Then he joined CCTU and was given access to

'Frankly, one of the great failures in the United States is that the infection rates have remained stable for the last fifteen years.'

cutting-edge therapies. "I was so fortunate," says Shannon, "not only to have my doctor's visits taken care of, but also to get all the medication that I needed to get stable and stay well." (In gratitude, he says, he has enrolled in several clinical trials, including the first human trial that tested the safety of the human papillomavirus vaccine.) In the years since, Shannon regained insurance coverage and started a new career as director of operations for a nonprofit social services organization in New Jersey.

At the time of his diagnosis, Shannon thought he would be single for the rest of his life. But six years ago, when he met someone who was—and still is—HIV negative, the staff at CSS told him there was no reason he couldn't have a healthy sex life and provided counseling to him and his partner. Such support is an essential part of the Center's mission. For example, Merrick recently helped a patient and his wife who wanted to conceive a child. "Although we're at a point where his virus is undetectable, she understands the risk is probably not zero," he says. Willing to take that risk for herself, by going on pre-exposure prophylaxis (PrEP) to prevent HIV infection, the patient's wife was able to conceive naturally and remain HIV negative. (At the CCTU, Gulick and Timothy Wilkin, MD, associate professor of medicine, are leading a new, large NIH-sponsored study on HIV prevention with PrEP.)

Despite the dramatic advances in HIV/AIDS care over the past quarter-century, many challenges remain. In 2010, 15,000 people in the U.S. died of the disease, according to the CDC. More than 1.1 million people are HIV-positive, with almost a fifth of them unaware of their infection. Little progress has been made in lowering rates of new infection: each year, 50,000 Americans are newly infected with HIV—10 percent of those in New York City. "Frankly," says Merrick, "one of the great failures in the United States is that the infection rates have remained stable for the last fifteen years."

And while the number of patients has risen—in large part because people have stopped dying from the disease—funding for research and treatment has ebbed. Some commentators have noted a growing sense of complacency, both in terms of prevention as a new generation comes of age and in the activist passion the disease once inspired. "A lot of people who brought this sense of urgency—those people are all dead," says Jacobs. Official sources for funding, like those from the U.S. Government's Ryan White HIV/AIDS Program, have shrunk. "People have gone on to other things," he says.

Today, the Center cares for 2,500 patients at its two clinics, one at NYP/Weill Cornell and one in the Chelsea neighborhood of Manhattan. Weill Cornell has had a presence in Chelsea since it won a competition in 1997 to provide health-care services in conjunction with the Gay Men's Health Crisis; its lease there ended in 2010, and last summer CSS opened a new facility on 23rd Street. "Chelsea continues to be one of the epicenters of the epidemic in this country," says Jacobs. "And with the loss of St. Vincent's downtown, there is a need for care."



Drug development: Roy Gulick, MD, chief of the Division of Infection Diseases, stresses the important role that clinical trials have played in creating more effective—and manageable—therapies for HIV.

As CSS marks these milestones and moves into its next chapter, Jacobs would like to see the Center increase the number of people it cares for while enhancing its services. He would like to bring a neurologist and oncologist onto the staff, and he would like to expand occupational support, to help keep chronically ill people in the workforce. The brightly colored lobby on the twenty-third floor, designed to cheer pediatric patients, now needs to be redone—for the best of reasons. "Fortunately," says Jacobs, "the problem of HIV-infected children has been almost eliminated in this country."

The Center's holistic administrative structure continues as designed. It is still the case, Merrick notes, "that physicians cannot even begin to hope to deliver to our patients any kind of medical care without also addressing their substance use, mental illness, poverty, and homelessness." The staff meets for an hour each day to discuss treatment for every patient, just as it has for a quarter-century. Likewise, it retains its continuity of care model, so that the first physician, psychiatrist, or social worker a patient sees remains that person's provider throughout the course of treatment. This means that the caregivers often follow patients over decades—Merrick has treated Johnson since he arrived—a situation that's rare these days, even among the well-insured.

One day, after discussing a particularly demanding patient, a vis-

iting physician said to Merrick: "They need to understand that it's a privilege for them to be here." Merrick replied: "No. What you need to understand is that it's a privilege for *us* to be here." The staff at CSS feels fortunate: they have emerged from the darkest days of an epidemic into a time when it's possible to build long-term relationships with patients and provide the highest quality of care to anyone with HIV, no matter their ability to pay. And CCTU researchers are proud to serve a group of people who are underrepresented in clinical trials generally, with women making up 30 percent of their study subjects and people of color 60 percent.

All of these physicians also feel privileged to be on the cusp of something previously inconceivable. When an American man living in Berlin—the city so many people working in HIV/AIDS care associate with the nadir of their history—received a bone marrow transplant that knocked out his virus, he was the first person certified as cured. "There was a time," says Gulick, "when you wouldn't even say the word 'cure.' " And indeed, Merrick admits, until that news broke in 2006—followed more recently by another case—"none of us believed, in our heart of hearts, that a cure might be possible." Adds Gulick: "The really great news today is that someone with HIV who is diagnosed and successfully treated has a life expectancy that's almost that of the general population."

With a potentially revolutionary drug heading into Phase 3 trials, Hazel Szeto, MD '77, PhD '77, aims to prove the promise of peptides

By Beth Saulnier

hen a certain pharmacology professor was a twelve-year-old growing up in Hong Kong, she made an announcement to her mother. "I'm tired of being introduced as Mr. Szeto's daughter," she said. "I'm going to do something totally different, so *he* is Hazel Szeto's father."

Szeto's dad was a prominent architect and engineer; her three younger siblings all went into architecture. And Szeto has indeed charted her own course—not only earning undergraduate, doctoral, and medical degrees in a span of just eight years, but discovering an unorthodox family of drugs whose potential seems dizzying in the depth and breadth of their possible applications.

They're known as the Szeto-Schiller (SS) peptides, named for Szeto and her collaborator at the University of Montreal, Peter Schiller, PhD. Szeto, MD '77, PhD '77, discovered them a decade ago, when a search for new opioid analgesics—work that involved small, brightly colored frogs from South America—unexpectedly upended the conventional wisdom of peptides as poor drug candidates.

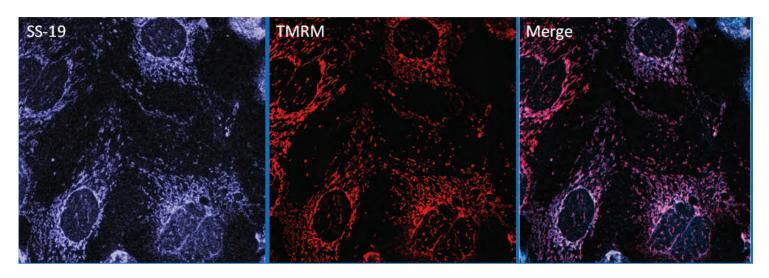
In the intervening decade, Szeto and collaborators around the U.S. and abroad have investigated the peptides as possible treatments for conditions ranging from Alzheimer's and Parkinson's to genetic disorders, liver and kidney failure, heart disease, transplant rejection, age-related muscle loss, macular degeneration, diabetes, and more. Cosmetic companies have even come calling, drawn by the peptides' antioxidant—and potentially age-defying—properties. "SS peptides can thus

Hazel Szeto, MD '77, PhD '77

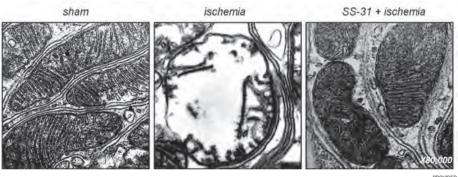


JOHN ABBOT

Turning the 'Tide



In living color: Microscopic images of a cell (above) show the SS peptide in blue (at left) and mitochondria in red (center). When they were overlaid (top right), it sparked Szeto's "eureka" moment. Right: An electron microscope reveals how SS-31 protects kidney mitochondria from ischemia, or lack of blood flow.



now be added to the long list of useful drugs stumbled on by serendipity," an editorial writer in the *Journal of the American Society of Nephrology* enthused last August, "which already includes penicillin, lithium, cisplatin, sildenafil, and many others—without which modern medicine would be much the poorer."

While Szeto and her collaborators are still working to understand the peptides' mechanism, the crux of the matter is that they seem to repair mitochondria—the power plants that produce the cellular fuel ATP. When she gives talks, she often opens with a slide of the Weill Cornell campus at night, noting that it takes a ConEd plant to keep the lights on. As she tells her audiences: there are "blackout" diseases like heart attack and stroke, where tissue essentially dies because the power switches off. But in "brownout" diseases, she says, "the mitochon-

dria are there, but they're not working efficiently." So organs and tissues become weak and dysfunctional, like a toy with a fading battery. "Liver failure, kidney failure, diabetes, even cancer—they all develop when the powerhouse isn't working well," Szeto says. "The idea is this: If I can restore mitochondrial energetics, would it be beneficial for these complex diseases with unmet needs? This would be a huge claim to make. But if only one little part of my dream comes true, we could help a large number of people."

In 2006, Szeto started a company to develop drugs based on her work. Its marquee compound, SS-31, has been dubbed Bendavia—in part to honor microbiologist Carl Benda, who identified mitochondria in 1898. The company is currently wrapping up a four-country, multi-site Phase 2 clinical trial of intravenous Bendavia as a preventive for reperfusion injury—the cellular damage

caused by restored blood flow—after cardiac stenting, with Phase 3 trials in the works. This year, another trial will be conducted on an oral version to treat heart failure; its efficacy has already been demonstrated in animal studies. "When the energy supply is not enough to satisfy demands, that's heart failure," Szeto explains. "So you have to balance the equation. If energy production is too low or demand is too high, you can either drop one or raise the other. Currently, all treatments go to reducing demand by lowering heart rate or blood pressure. There are no good drugs for the problem of generating enough ATP to contract properly. Bendavia is the first compound that can raise energy production."

On a Monday in late November, Szeto is hosting a meeting in her office on the eighth floor of 1300 York Avenue. When one of her collaborators, renal pathologist Surya Seshan, MD, stops by the open door, a visitor asks her how she feels about Bendavia's potential applications in the kidney, which include preventing reperfusion injury and reducing delayed graft rejection following transplantion; a trial at the Mayo Clinic is exploring its efficacy in repairing damage caused by hardening of the renal arteries. "I'm super excited," Seshan says. "If there's a panacea of a drug, that's what this is." Another collaborator— Glen Prusky, PhD, a professor of physiology and biophysics—chimes in: "That's exactly how I feel about its applications for the retina."

Based at the Weill Cornell-affiliated Burke Medical Research Institute, Prusky's lab develops methods for measuring vision in rodents. This year, an ophthalmic formulation of Bendavia, based on his work with Szeto that resulted in several successful rounds of animal studies, will go into clinical trials for use in diabetic retinopathy. "You give this drug, and it's not just that it changes the trajectory a little bit," he says. "It not only stops the visual decline but actually restores vision." Once the eyedrops are shown to be safe and effective in humans, they will be tested as a treatment for macular degeneration, a condition that now requires injections by an ophthalmologist. "It's all very honest and straightforward science," Prusky says of the Bendavia research. "I wouldn't call myself a curmudgeon, but I'm certainly a skeptic-and I'm a card-carrying member of the SS-31 family. It has earned its way into our hearts because it works like nothing we've ever seen before. It drew me in completely from the outside, and it has turned out to be gold."

Among the many apparent benefits of the peptides, Szeto says, is their ability to do no harm—to, essentially, restore balance. "There are no adverse effects," she says. "In young, healthy animals, these compounds seem to do nothing. But in old animals, or ones who are compro-

mised, they normalize." For example, a paper published in 2013 with a collaborator in Seattle noted that while SS-31 helped restore thigh muscle in geriatric mice, healthy adults were unaffected; the drug, in other words, wouldn't tempt a Tour de France rider seeking enhanced performance. "You don't go beyond," Szeto stresses. "You just normalize."

ducated in the British system when Hong Kong was still under colonial rule, Szeto attended an English boarding school before matriculating at Indiana University. She started off majoring in physics, then switched to math, then chemistry. "I never thought about medicine," she muses. "I was always one of these kids who would study, get bored, and move on to something else." She finished college in three years, graduating at twenty. In New York for her graduate school interview, she met with legendary pharmacology chairman Walter "Wally" Riker, MD '43, who led the department for nearly

'If only one little part of my dream comes true,' Szeto says, 'we could help a large number of people.'

three decades. "He asked me, 'Have you ever thought of medical school?' "Szeto recalls. "He said he wanted a couple of people to go to med school, get a PhD, do research, and be good teachers. He was worried that medical students would be taught only by PhDs."

Szeto said no. Riker kept asking. Szeto kept turning him down. She protested that she hadn't even taken the MCATs. Riker said it didn't matter, since at the time the first two years of the MD and PhD programs were essentially the same, with the exception of gross anatomy. "It took until August; just before school started, he was still calling me," Szeto says with a rueful head-shake. "I was so stupid. I owe my whole career to Dr. Riker, because he knew better than I did." After earning an MD-PhD in just five years, she faced another crossroads: whether to do a residency or immediately devote herself to research. Again, she turned to Riker. "He said, 'Hazel, your most creative years are between twenty-five and thirty-five," she recalls, " 'and

you don't need to be creative to be an intern.'" After Szeto completed a postdoc at the University of Vermont, Riker asked her to join the Weill Cornell faculty.

While Szeto's research was going well, she missed doctoring; the idea of doing a residency still tugged at her. "Every year I agonized over it," she admits. "I always said, 'If I run out of research money, I'll go back to medicine.' But the money never ran out." Working in an ovine model, she became an expert in maternal-fetal pharmacology —exploring how drugs are distributed to the fetus, how they affect fetal brain activity, and how sleep-wake behavior develops before birth. Back then, she notes, animal-handling procedures were decidedly more informal. "I'd walk the sheep down York Avenue," she recalls, "and bring them in through the front door."

After a while, though, her restless intellect—the one that had cycled her through three undergraduate majors—demanded fresh challenges. "I thought, I'm not coming up with any new understandings," she says, "so it's time to quit." She switched to searching for new compounds to target opioid receptors—work that led her to study peptides found on the skin of frogs from the genus *Phyllomedusa*. With the frog as a basis, her lab eventually created a peptide, just

'I want to make aging a better experience, to improve quality of life. I want to be that ninety-year-old who's still got my marbles and can move around and do things.'

four amino acids long, that she tested in a rodent model. Since it was so water soluble, Szeto figured that it would have to be injected directly into the brain or spinal cord to have any hope of efficacy. After all, she was well aware that peptides—being easily broken down by the body's enzymes—had long been dismissed as drug candidates.

Then, in a bit of serendipity, a fellow in her lab injected the drug into a rodent subcutaneously. "We got terrific results for analgesia," she says. "I thought, Whoa—how could I be so wrong? How could this cross a membrane, especially the blood-brain barrier?" That, Szeto says, "was the beginning of the journey that peptides could actually get into cells, get through cells. And then I thought, Where does it go *inside* the

cells?" Szeto asked Schiller for a fluorescent label to track the peptide; it showed that it only appeared in certain specific streaks inside the cell. And that reminded her of a lesson from medical school.

Szeto applied a fluorescent label that tracks mitochondria in red. The peptide tracker was blue. Laid atop each other, they overlapped into perfect streaks of purple: the peptide was targeting mitochondria. "And that," she says, "was the eureka moment."

hile Szeto initially feared the peptide might be toxic to mitochondria, further work showed the opposite: it had a protective, even reparative effect. Since then, her lab has continued to develop new SS incarnations—for example, flipping the positions of the amino acids to create a version that wouldn't target opiate receptors.

Almost ten years after the accidental discovery of these peptides, Alexander Birk, PhD '00, in Szeto's lab discovered the specific target for these SS peptides and revealed their mechanism of action. It turns out that the peptides target cardiolipin, a phospholipid on the inner mitochondrial membrane that is important for the assembly of the electron transport chain. By improving the efficiency of the electron transport chain, these peptides promote ATP synthesis and reduce the production of reactive oxygen species.

The work has been primarily supported by private funding, in the form of an investor in the Boston tech corridor. Szeto dubbed her start-up Stealth Peptides, comparing the compounds to the military aircraft: "They're invisible, cloaked, and completely targeted." Szeto's firm licenses SS-31 from Cornell University, which holds the patents on her work. "Hazel's the best teacher," says Travis Wilson, the firm's president and CEO. "What she's been able to do out of a small lab at the University is a tremendous feat."

One group avidly following Szeto's work is parents of children with genetic mitochondrial diseases such as Leigh syndrome, a neurodegenerative disorder, and Barth syndrome, whose symptoms include heart ailments and stunted growth. "The United Mitochondrial Disease Foundation is urging us to try SS-31 on their kids," she says. "I get requests every day, and it's hard to have to turn them away." Szeto is less conflicted about fending off requests from cosmetic companies eager to market Bendavia as a fountain of youth in a jar. "My investor and I don't want to mess with that," she says. "Antiaging and wrinkles kind of cheapens the whole



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Eager mentor: Szeto in the lab with graduate students (from left) Bonnie Quach, Wesley Chao, and Bill Mills

thing. I've got bigger things to do. I want to make aging a better experience, to improve quality of life. I want to be that ninety-year-old who's still got my marbles and can move around and do things."

Stealth Peptides doesn't have its own research space; its investigations are mainly done in Szeto's lab, which has three full-time employees and three graduate students. Rather than holding regular lab meetings, members share results with Szeto informally or present findings to Stealth staff and consultants. "It's cool that we get to work with this company," says third-year PhD student Bill Mills, a 2011 alumnus of the Ithaca campus. "A lot of

researchers are stuck in an academic bubble, and it's great to interact with the outside world. It has helped me understand the whole health-care landscape, where our research applies, and how we're making a difference. That's a unique place for a graduate student to be."

Around the time that Szeto had her peptide breakthrough, she was planning to scale back her workload; she and her husband, an engineer, had just adopted a daughter from China. She never suspected that, contrary to her mentor's belief, her biggest discoveries lay ahead. "I think Dr. Riker was wrong," she says with a smile. "The last few years have been the best of my life, and the most creative."

Notebook

News of Medical College and Graduate School Alumni



PROVIDED

R. Ernest Sosa, MD '78

Dear fellow alumni:

The 2013–14 academic year has been about transformation and innovation. Dean Laurie Glimcher has done an outstanding job furthering Weill Cornell's reputation as a premier medical research institution. Over the past two years, she has been actively working to recruit top-notch physicians and scientists to fill the Belfer Research Building. Not only is this facility one of New York's most environmentally friendly buildings, it nearly doubles WCMC's research space. If you haven't had a chance to see it yet, be sure to stop

by during your next visit to campus.

Additionally, an updated curriculum is being designed and implemented. As we all know, the practice of medicine has changed significantly over the last decade. The new curriculum will help bring the latest innovations into our classrooms to ensure that Weill Cornell continues to produce some of our nation's top doctors. It has been exciting to see all of the changes to medical education since my time there.

In early November I traveled with Dean Glimcher and Lewis Drusin, MD '64, to Philadelphia for our annual AAMC alumni and friends reception. More than sixty guests joined us to make the evening a great success. It was a pleasure for us to meet so many alumni. Dean Glimcher and I also had the opportunity to share many of the exciting initiatives and developments that are happening at the Medical College.

Susan Solomon, in the Office of Alumni Relations, will continue traveling to different cities to host regional dinners. Over the past few months she spent time in Los Angeles, Providence, Baltimore, Washington, and Chapel Hill, as well as Great Neck, New York, and Stamford, Connecticut. These intimate gatherings are a great opportunity to learn more about what's going on at the Medical College and to connect with alumni in your area. For more information, please contact Susan at sus2033@med. cornell.edu or (646) 317-7414.

We have started planning for Reunion 2014, which will take place October 10–11. The theme is "The Evolution of Medical Education," which coincides perfectly with the curriculum redesign. The weekend promises to be a great one and I look forward to seeing the extended Weill Cornell family, so be sure to save the date!

We are especially passionate about our work to support current students. In November, we held the first Alumni-to-Student Knowledge (ASK) session of the academic year, featuring speakers who practice in pediatrics and subspecialties. The program complements the academic experience by providing an informal venue for students to ask candid questions in a relaxed environment. As in past years, the Alumni Association will once again put approved funds toward student programming organized by the Medical Student Executive Committee, most recently to support their annual December Decadence event.

As always, thank you for your continued support of the Alumni Association, the Medical College, and our students.

Best and warmest wishes,

R. Ernest Sosa, MD '78
President, WCMC Alumni Association
drsosa@nyurological.com

1940s

William C. Robbins, MD '45: "Danny and I have moved to a retirement center called Waterman Village in Mt. Dora, FL. We hear occasionally from Gerry Klingon, MD '45, and Rudy Jones, MD '45, and would enjoy hearing from other classmates or seeing them on a visit."

Lester J. Schnell Jr., MD '47, is enjoying retirement and still living in Garden City on Long Island, NY.

1950s

Richard T. Silver '50, MD '53, received an honorary award in appreciation of active participation and outstanding contributions to the annual conference of the Israeli Society of Hematology and Blood Transfusion and for lifetime achievement in the field of hematology. Dr. Silver received the award during the MD Anderson–Israel Hematologic Malignancies meeting held last October in Jerusalem.

William H. Gordon Jr., MD '54: "I'm living in Upland, CA, with my wife, Jean, and surrounded with family. I retired from Kaiser Permanente after 44 years. I founded the Department of Nuclear Medicine in Fontana and Riverside, CA."

Sherburne M. MacFarlan, MD '56: "I'm alive and well and retired since age 76. My wife, Susan, BS Nurs '55, passed away in 2011."

Donald B. Lathrop, MD '57: "My wife, Jackie, and I are thriving, although some of our joints are wearing out. I keep busy with golf at the Stanford University golf course, reading, bridge, playing the piano, and doing volunteer pediatric work at a local free medical clinic. That, along with 22 grandchildren in our combined families, leads to a busy retirement."

Robert A. Levine, MD '58: "I am currently a professor of medicine at Boston University School of Medicine, Boston Medical Center, in the section of gastroenterology."

John T. Queenan, MD '58: "I attended a celebratory ceremony at Johns Hopkins University honoring the meritorious service of Edward Wallach, MD '58. Ed has trained more than 40 physicians in reproductive medicine and ten physicians who became chairs of ob/gyn. They announced the Edward Wallach Fellowship in Reproductive Medicine. Bravo, Ed!"

L. Davis D. Arbuckle Jr., MD '59: "I recently returned to Florida from Vancouver, where I spent the summer. Unfortunately, I broke my wrist before returning—no golf for two to three months."

1960s

Stebbins B. Chandor, MD '60: "Mary Carolyn and I moved into a retirement facility near our



former house last September. We're still near friends and activities such as golf and tennis, just less cooking and traveling."

Elinor Miller '59, MD '63: "God willing, I will be in Ithaca in June."

Michael Lesser, MD '64, published the article "Seeing Schizophrenia Through a Personalized Medicine Prism" and completed a monograph entitled *Nutrition and Vitamin Therapy and Cystic Fibrosis*.

Orlo H. Clark '63, MD '67: "I retired from

Welcome mat: The Belfer Research Building's main entrance on East 69th Street is an inviting, airy space. 'The changes in medicine in 45 years have been breathtaking, but the principles I learned in medical school remain.'

Allen A. Nimetz '64, MD '68 clinical practice as an endocrine surgeon at the University of California, San Francisco. I'm still teaching and doing research. My wife and I published a book entitled *The Remarkables: Endocrine Abnormalities in Art*, which has been well received. My colleagues and I are also editing the third edition of our *Textbook of Endocrine Surgery*, which should be published in 2014. Retirement is great."

Allen A. Nimetz '64, MD '68: "Carol and I live in Bethesda, MD. I continue to practice general and interventional cardiology full-time in Chevy Chase, MD. The changes in medicine in 45 years have been breathtaking, but the principles I learned in medical school and at Mt. Sinai remain. I enjoy teaching George Washington medical students and try to impart these principles. I'm looking forward to Reunion."

N. Reed Dunnick, MD '69, was named president of the Radiological Society of North America on December 4, 2013. He is the Fred Jenner Hodges Professor and chair of the Department of Radiology at the University of Michigan Health System in Ann Arbor, MI, where he has been since 1992. Dr. Dunnick began his academic appointments at Stanford as an assistant professor in 1976. Later that year, he moved to the Diagnostic Radiology Department at the National Institutes of Health. At Duke University Medical Center, he held many posts from 1980 to 1992, including professor of radiology, chief of uroradiology, and director of the Division of Diagnostic Imaging. He has authored or co-authored more than 250 peer-reviewed scientific articles, 62 book chapters, and ten books. He has served on the editorial boards of 14 journals, including Radiology, American Journal of Roentgenology, Academic Radiology, and Journal of the American College of Radiology.

Michael Schwartz, MD '69: "Anyone else with a new job? Less than a year ago, I was charged with creating the Humanities in Medicine Department at our new regional medical school campus near Austin in Round Rock, TX, at the Texas A&M Health Science Center College of Medicine. Austin is a wonderful town to live and work in. Y'all come on down."

1970s

Peter W. Blumencranz, MD '70: "In September 2013, I lectured on 'The Dilemma of Occult Metastases in Sentinel Nodes' at the Fourth China Breast Disease Symposium in Beijing, China, and at the Asian Breast Cancer Academic Exchange Forum in Taipei."

Gerard V. LaSalle, MD '73: "After practicing emergency medicine since 1974, and working as a co-founder and senior executive of TeamHealth, effective July 2014, I plan to retire from my cur-

rent positions as its national chief medical officer (since 2001) and also the president and executive director of the TeamHealth Patient Safety Organization (since 2009) to pursue my writing career. Widow Walk, my first historical novel, has won the 2013 USA Best Books Award for Best New Novel and is selling well. I'm working on the sequels in a series and developing options for screen adaptation (www.widow-walk.com). I live in Seattle now, but continue to maintain my sculpture studio on Vashon Island."

Dennis Lutz, MD '73: "Forty years after graduation I continue to chair the Department of Ob/Gyn at the University of North Dakota School of Medicine. Meryl and I enjoy five grandchildren ranging from age 9 to 4-year-old twins. The North Dakota energy economy is booming, so state legislature funding has been generous."

George Ellis, MD '74: "I joined MD2, a small medical concierge company and opened their NYC office in February 2013. It's a dream job. Shari Midoneck, MD '89, joined the practice in July 2013. Nancy and I enjoy being with family and our occasional travels. We had a great trip to Chile in November. Fortunately, both of our daughters are in NYC. What I remember most is hanging out with friends in Olin Hall."

Michael A. Weitz, MD '74, is president of the Florida Society of Rheumatology and program chairman of their yearly educational meeting. He is medical director of the Center for Arthritis Thematic diseases in Miami, FL.

Paul Skudder, MD '79: "I was inspired by the experience of my father, Paul Skudder '53, to participate in a volunteer commitment. I served for two weeks as a 'Distinguished Visiting Surgeon' in the trauma program at Landstuhl Regional Medical Center. This program is underwritten by the Society for Vascular Surgery, the American Red Cross, and the U.S. Army. Landstuhl, the largest American hospital outside of the USA, is located adjacent to Ramstein Air Force Base in southwestern Germany. It serves as a tertiary care facility providing care to injured soldiers from the war in Afghanistan, as well as providing tertiary care services to the 250,000 or so American military personnel and their families. This proved to be a humbling commitment. I was impressed beyond measure by the bravery of the injured soldiers we cared for and by the dedication of the surgeons caring for them.

"My father did his surgical residency at NYH-CUMC and spent his entire professional career on the surgical attending staff and faculty at Cornell. I clearly 'inherited' my surgical career from him. His commitment to surgery was born in the Army, as an enlisted man who had signed on in 1942, without finishing high school. He spent the war in Europe, assigned to the 16th

General Hospital. He was overcome with admiration for the surgeons caring for the injured soldiers during the war, including the Battle of the Bulge. He returned, completed high school in his twenties, attended college with help from the GI Bill, and enrolled at the Medical College in 1949. I guess that he and I both owe our careers to Army surgery, so it seemed totally reasonable to go back to Germany and care for the injured troops."

1980s

Barnaby F. Starr, MD '82: "HMOs, electronic medical records, now Obamacare—they can throw everything at us including the kitchen sink, but medicine is still about helping people and making a living while doing that. You can't beat it!"

Michael M. Ziegelbaum, MD '82: "I am president-elect of Nassau County Medical College. I'm involved in medical work in Cap Haitien, Haiti, as well as forming the first American Haitian Urology Conference to develop strategies to improve medical/ urological care in that country."

Arthur V. Moore, MD '83: "I retired from internal medicine practice nearly three years ago. I was 38 when I graduated, so this was not an early retirement. My wife, Susan Turner Moore, and I have traveled to Italy and Croatia, and we are off to Africa for a photo safari this year. Our first grandchild, Maggie, arrived early last year. We are enjoying New Hampshire's natural beauty."

David Haughton, MD '84: "My September 'flash' exhibit at the Visual Space Gallery was a successful and enjoyable event. The exhibit format—three days only—was so much fun that I plan to repeat it. You may view my latest post at haughton-art.ca/upcoming-exhibit-nocturnes."

Beth P. Abrams '81, MD '85: "After 25 years as a community public psychiatrist, I am now on staff at the Albany VA and Albany Medical School, working to bring integrative/complementary medicine practices to the VA. It's exciting, meaningful work. The veterans I am privileged to work with are inspiring in the face of substantial challenges. I'm blessed to still love my work as a physician."

Roger S. Blumenthal, MD '85: "In June 2013, I received an endowed professorship at Johns Hopkins School of Medicine. I am now the inaugural Kenneth Jay Pullin Professor of Cardiology and director of the Johns Hopkins Ciccarone Center for the Prevention of Heart Disease. I greatly

enjoyed seeing **Steve Berger**, **MD '85**, and Linda; **David Blaustein**, **MD '85**, and Jill; and **Troy Elander**, **MD '85**, and Diane over the summer."

Edward Chaum, PhD '86, MD '87, continues an active academic career as the Plough Foundation Professor and director of the retina service at the

active board member of the Juvenile Diabetes Research Foundation. I teach internationally via interactive webinars for Johnson & Johnson Diabetes Institute. I'd love to retire from delivering babies and am hoping to be able to dedicate more time to my extracurricular activities, primarily my work with the JDRF (on an international



ABBOT

Bright and cheery: The Belfer Research Building features colorful furniture, expansive south-facing windows, and open staircases.

University of Tennessee Hamilton Eve Institute. His research over the past decade has focused on translating biomedical engineering concepts into clinical medicine and maturing these programs into commercial opportunities. He is the founder and CMO of three start-up companies based in Tennessee: Hubble Telemedical (telemedicine), Nanophthalmics (surgical devices), and Infusense (biomedical sensors). He was named an inaugural 2013 Innovation Award Winner by Memphis Business Quarterly and awarded the 2013 B. Otto and Kathleen Wheeley Award for Excellence in Technology Transfer by the University of Tennessee.

Margarita de Veciana Haugh, MD '88: "I'm a professor in the ob/gyn department, maternal-fetal medicine, at Eastern Virginia Medical School. I'm involved with Physicians for Peace working to improve maternal-child health conditions in the Dominican Republic and an

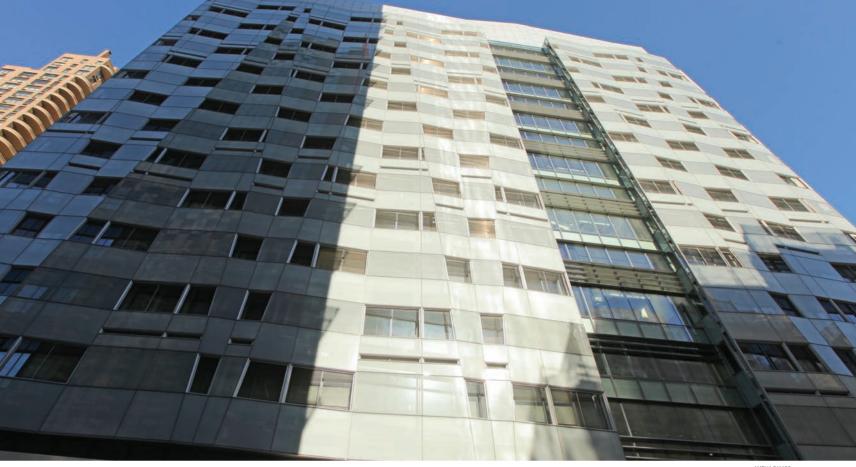
level) and with Physicians for Peace. What do I remember most? The awesome shows our class put on and the great takeout food in Manhattan. I'd love to hear from Answorth Allen, MD '88, and Judith Tanenbaum, MD '88. Keeping busy raising two teenage girls and caring for my almost 90-year-old mom. I can't imagine doing this without my incredible husband, Barry."

Kenneth Vega, MD '88: "I was recently promoted to professor in the Division of Digestive Diseases at the University of Oklahoma Health Sciences Center."

1990s

Tammy Gruenberg, MD '94, is currently the medical director at Women's Health/ Morris Heights Health Center. In October 2013, she received an MPH in health-care management from the Columbia Mailman School of Public Health.

Piers C. Baker, MD '95: "I'm enjoying living in North Carolina. I was just promot-



AMELIA PANICO

Blue skies: A view of the Belfer Research Building's facade on a sunny winter day ed to professor of pediatrics and obstetrics/ gynecology at Duke University, where I direct the pediatric cardiac non-invasive imaging program."

Seth M. Manoach '88, MD '95: "After practicing academic emergency medicine for ten years and becoming assistant chief medical officer at Downstate, I decided to 'go to graduate school.' I did anesthesia critical care and internal medicine critical care fellowships. I got boarded in medical critical care and neurocritical care. Back at Weill Cornell, I'm an assistant professor of medicine in the Division of Pulmonary and Critical Care Medicine in the ICU at NYP/LMH. I'm trying not to

miss my kids growing up—that is the other biggie."

Peter K. Kim, MD '97: "I was promoted to associate professor of clinical surgery at Albert Einstein College of Medicine. I will complete a Master of Medical Management from the University of Southern California, Marshall School of Business, in May 2014."

Mary Beth Lewis-Boardman, MD '98: "I relocated to the Orlando, FL, area nine years ago and am enjoying a rapidly growing ob/gyn private practice. I recently reconnected with Bonnie Bidinger, MD '98, and we're looking forward to getting together in the Sunshine State."

Suzanne Magherini-Rothe, MD '98, is the director of the Women's Clinical Service at the Women's Wellness Center of Monmouth Family Health Center, Long Branch, NJ.

2000s

Kathleen D. Keeffe Hough, MD '00: "I am currently an attending physician in emergency medicine in Maryland. I also work with the Maryland Medical Society (MedChi), where I am on the Legislative Council and am chair of the Disaster Preparedness Committee. I live in an Annapolis suburb with my husband and two children."

Jillian M. Ciocchetti, MD '05, is in her third year of practice in general surgery in North Denver. She and her husband, Corey, are expecting their first child.

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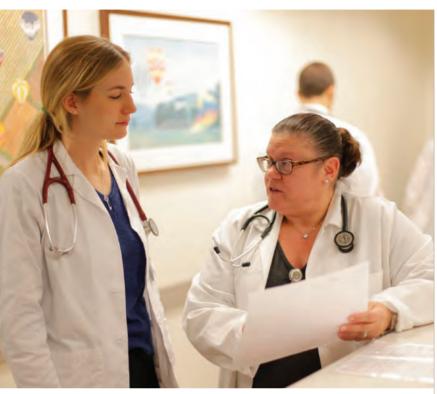
- **'36, '40 MD—Elizabeth Spaulding Scharff** of Sun City West, AZ, June 1, 2011; missionary doctor in Mexico and Ethiopia; active in religious affairs.
- **'43 MD—Harry T. Powers** of Satellite Beach, FL, August 18, 2013; ob/gyn; veteran; golfer; active in community and professional affairs.
- **'43 MD—David R. Tomlinson** of Troy, NY, November 22, 2013; ob/gyn, Family Birth Center at Samaritan Hospital; chairman of obstetrics and gynecology and president of the medical staff, Samaritan Hospital; one of the first physicians to use hypnosis in baby delivery; first recipient of the Northeast Health Founder's Award; co-founder, Northeast New York Orchid Society; veteran; active in civic, community, professional, and religious affairs.
- **'44 MD—James L. Tucker** of Lake Forest Park, WA, August 17, 2012; pediatrician; adjunct professor in pediatrics at the University of Washington; board member, Slingerland Society, Dyslexia Society, Overlake School, and Hamlin Robinson School.
- **'47 MD—Frances Thomsen Nye** of Norwich, VT, November 23, 2013; psychiatrist; worked at the VA Hospital in White River Junction, VT, and Mary Hitchcock Memorial Hospital; advocate for Vietnam veterans, community mental health, and alcoholism treatment; peace and social justice advocate; member, Iona Community; volunteer, Witness for Peace; active in civic, community, and religious affairs.
- **'49 MD—David Sonabend** of Palm Beach Gardens, FL, November 22, 2011; physician; philanthropist; active in Jewish causes.
- **'49 MD—Clinton G. Weiman** of Greenwich, CT, January 7, 2014; physician; senior VP for medical affairs, CitiBank; established an electronic medical record system.
- **'47, '50 MD—Leopoldo E. Margarida** of Abington, PA, September 23, 2013; radiologist; Korean War veteran; enjoyed sports, skiing, and camping; active in alumni affairs.
- **'52 MD—William N. Hill Jr.** of Springfield, MA, October 1, 2013; ob/gyn; delivered more than 2,000 babies; veteran; active in professional and religious affairs.
- **'54 MD—Wilmot C. Ball** Jr. of Baltimore, MD, October 12, 2013; did pioneering work in lung physiology, inflammatory lung diseases, and lung cancer screening; professor emeritus of medicine, Johns Hopkins School of Medicine; former head of the Division of Respiratory Diseases and director of clinical record systems, Johns Hopkins Hospital; director of pulmonary medicine, Good Samaritan Hospital; author; woodworker; volunteered with the Baltimore Symphony Orchestra; active in professional affairs.
- **'50, '55 MD—Kenneth M. Jensen** of Houston, TX, December 27, 2013; radiologist, St. Joseph Hospital; veteran.
- **'56, '60 MD—Martin J. Edelman** of New York City, December 24, 2013; diagnostic radiologist at Memorial Sloan-Kettering Cancer Center; veteran. Sigma Alpha Mu.
- **'60 MD—John H. Gould** of Turner, ME, October 14, 2013; child psychiatrist, New England Memorial Hospital, Northern Essex Mental Health Center, and in private practice; also worked at St. Mary's Hospital, Tri-County Mental Health Services, Jackson Brook Institute, Sweetser Children's Services, and Kennebec Behavioral Health; pediatrician; veteran.
- '62 MD—Edward J. Fredericks of Bradenton, FL, formerly of Avon, CT, January 3, 2014; neurologist; director of neurologic education, medical director of the rehabilitation unit, and electromyographist at Hartford Hospital; consultant, Newington Children's Hospital Muscle Disease Clinic; clinical professor of neurology, University of Connecticut; fellow of the American Board of Psychiatry and Neurology and the American Board of Electrodiagnostic Medicine; served on the Connecticut Medical Examining Board; received several teacher of the year awards.
 - '71 MD—Florence G. Crawford of New York City, October 3, 2012; pediatrician.

We want to hear from you! Keep in touch with your classmates. Send your news to Chris Furst: cf33@cornell.eduor by mail: Weill Cornell Medicine 401 East State Street, Suite 301 Ithaca, NY 14850 friend us on facebook.com/wcmcalumni Weill cornell Medical college alumni Association for the latest information and news... twitter.com/wcmcalumni Weill cornell Medical college alumni Association

Post Doc

Physician 101

Medicine, Patients, and Society teaches first-year students the art of doctoring



JOHN ABBOTT

On-the-job training: Amanda Kahn '17 with her preceptor, Debra Taubel, MD, associate professor of clinical ob/gyn

he cases on the hospital drama "Grey's Anatomy" are often outlandish and melodramatic, but one serves as a real-world teaching tool for first-year medical students. Carla Boutin-Foster, MD, MS '99, associate professor of medicine, stands before a full lecture hall and introduces an episode in which a young Hmong woman urgently needs surgery for a spinal tumor, but her father insists that a shaman must first perform a healing ritual to restore her soul. With only hours until the patient is paralyzed for life, the physicians offer a compromise: the ceremony, complete with open flames, can be performed at the bedside.

Boutin-Foster, assistant dean for faculty diversity, screens the clip during a fall semester talk on cultural competency. She goes on to discuss the importance of recognizing one's own unconscious biases, and the assumptions that physicians can make based on a patient's race, ethnicity, culture, or language. Then she puts a slide up on the screen and has a student translate its medical jargon into everyday English. "Sometimes," Boutin-Foster muses, "I think we use 'doctor talk' because we have no idea how to state things plainly."

Welcome to Medicine, Patients, and Society I—the course that introduces new students to the art and culture of being a physician. Founded in 1996 after the last round of curriculum reform, MPS I covers such essentials as doctor-patient communication, health-care disparities, epidemiology, evidence-based medicine, and much more. "The way I describe the course is that it's the doctoring piece of the curriculum in the first year; it's everything that's not biochemistry and anatomy," says director Keith LaScalea, MD, associate professor of clinical medicine. "The purpose is to expose students to the sociocultural elements that are important to being a physician."

A Weill Cornell rite of passage for the past decade and a half, MPS I is held each Thursday. In the morning, students attend a lecture, then meet for small, faculty-led group sessions. In the afternoon, they shadow their preceptors—physicians practicing throughout the city, who offer firsthand experience in taking histories and other aspects of patient care. "It was really valuable, because it gave us a big-picture view of how to think about our patients and their problems," says Larry Wineland '15, a Bennington College graduate contemplating a specialty in anesthesiology. "It's more a social skills class than a technical medicine class, and that's important for every physician, because you need your patients to trust you and be comfortable talking to you."

In the fall of 2012, Charlotte Roy '16 shadowed a family medicine doctor in Greenpoint, Brooklyn; the following spring, she worked at an HIV/AIDS clinic in Chelsea. "It was a nice break from the science," says the Vassar alumna. "MPS is the one day where you address other aspects of medicine. It was good to step outside the basic sciences and nitty-gritty details of those courses and take a broader look at what it means to be a doctor and a patient."

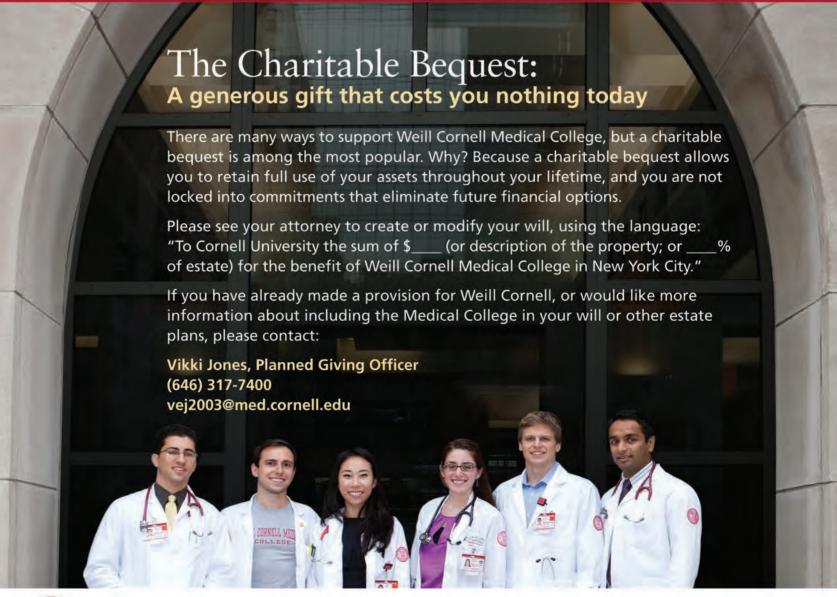
After Boutin-Foster's talk—on a day that happens to be Halloween—the students break into groups to continue the cultural competency discussion. In one session, led by Adam Stracher, MD, associate professor of clinical medicine, and Peter Wilson, MD, professor of clinical psychiatry, one student shares her discomfort with the fact that her preceptor alters his approach according to a patient's educational and socioeconomic status. "We all treat patients differently depending on what we believe they want, based on our knowledge and what we hear from them," Stracher tells the students. "The art of medicine, and the skill, is that not everybody wants the same information from you. It's a balance that you have to strike. But to go into an encounter, or to treat people differently, based on a bias that may not necessarily be true—that's the whole point of this discussion."

— Beth Saulnier

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