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VOLUME 15, NUMBER 2

The Immunotherapy Revolution

Weill Cornell Medicine investigators aim to make cancer a chronic rather than deadly—disease Silvia C. Formenti, MD Professor and Chairman Radiation Oncology



Weill Cornell Medicine

Alumni Reunion

Save the date for **Reunion 2016,** hosted by the Weill Cornell Medical College Alumni Association!

Reunion will take place from Friday, September 23 – Saturday, September 24, once again offering engaging guest speakers, institutional updates and tours, class get-togethers, a gala dinner dance, and opportunities to mingle and network with old friends.

Class years ending in '0, '1, '5 and '6 are celebrating milestone reunions, and, as always, all alumni, spouses, and guests are invited back to campus to commemorate another year since graduation.

Special highlight:

Our keynote speaker for this event will be **Dr. Anthony Fauci**, Class of 1966, director of the National Institute of Allergy and Infectious Diseases. Dr. Fauci is an immunologist who is nationally renowned for his contributions to HIV/AIDS research and his research on other immunological diseases. He will be interviewed on stage by Michael Specter of the *New Yorker* about his life and career.



Sept 23-24 2016

Class Booklets:

There will be class booklets for each anniversary class available at Reunion. Every class member, regardless of whether or not he/she is able to attend Reunion, is encouraged to submit photographs and complete an anniversary class questionnaire. The photograph and questionnaire reply form should have arrived in March. Please forward your photographs and anniversary class questionnaire to the Office of Alumni Relations no later than **Friday, August 26, 2016**.

We hope to see you there! Visit www.weill.cornell.edu/alumni/reunion for updates.







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THE MAGAZINE OF WEILL CORNELL MEDICINE

VOL. 15, NO. 2



FEATURES

28 TRANSFORMING CANCER CARE

ANNE MACHALINSKI

Cancer immunotherapy traces its roots to the early 1890s, when a surgeon infected patients with strep bacteria in the hope that they'd have a strong response that might eradicate their tumors. Over the years, scientists pursued aspects of this approach, with little success; it wasn't until they better understood how the immune system functions that they could begin to harness it to fight malignancies. Now, researchers at WCM and elsewhere are making significant advances—with the ultimate aim of transforming cancer into a disease that's more chronic than terminal. "Now that we have better surgery, less severe and more targeted radiation and chemotherapy, plus immune therapies, we are beginning to attack cancer in a scientific way rather than an empirical way," says Lewis Cantley, PhD '75, the Meyer Director of the Meyer Cancer Center and a professor of cancer biology in medicine. "Our goal is to figure out how to combine these therapies for each and every patient so that we can control their disease and help them live a healthy, normal life."

36 RESISTANCE MOVEMENT

BETH SAULNIER

For more than a decade, Carl Nathan, MD, has devoted a great deal of energy to publicizing and combatting what he calls a universal threat: antibiotic resistance. The R.A. Rees Pritchett Professor of Microbiology ardently advocates the development of new antibiotics, as well as measures to curb the over-use that drives evolution of drug-resistant strains. One of the world's leading authorities on tuberculosis, Nathan has written numerous academic articles on the topic and been a global thought leader in the research community and beyond. But he notes that understanding patients' real-life struggles—like that of a New York Giants player who recently battled a potentially career-ending MRSA infection—is essential to making both average Americans and government officials appreciate the issue's urgency. "It makes no impact to talk about the threat numerically and statistically, with epidemiologic arguments," says Nathan. "What gets people is the individuals: the face, the name, the personal story."

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Cover portrait of Lewis Cantley, PhD '75, and Silvia Formenti, MD, by Tiffany Walling/Getty Images for WCM

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Making the match

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The Future of Cancer Immunotherapy Is Now



ore than twenty-five years ago, when I was still in the early phases of my career, my team discovered a protein with an important role in a number of immune functions. I've continued to study this protein over the years, as well as the gene that encodes it, and recently uncovered the role of the gene, called XBP1, in allowing deadly types of breast and ovarian cancer to grow and thrive after shutting down the immune system. If a drug was developed to silence XBP1, the protein might then serve as an Achilles' heel of sorts-letting a cancer patient's immune system vanguish each and every tumor cell in the body.

This has been incredibly gratifying work, and while our research must still be translated into the clinical setting, other therapies like this, which harness the body's ability to fight cancer from within, are already being used-in some cases with astounding success. Some of these immune-based drugs have recently been FDA-approved for treating cancers of the skin, lung, bladder, and blood, as well as other disease types; others are currently being tested as part of promising clinical trials; and others still are in early phases of development. This concept is known as immunotherapy, and today, after more than a century of false starts, it's finally joined surgery, chemotherapy, radiation, and precision-targeted therapeutics as the fifth pillar of cancer care.

We're in the midst of a revolution in cancer immunology—a time when fundamental research that's been pursued for decades is finally resulting in groundbreaking discoveries and therapies. In combination with our ability to map the human genome and analyze big data, these advances mean profound improvements in cancer patients' lives. Thanks to immunotherapy, people whom doctors thought were in the final stages of their disease have experienced complete and durable remissions, while others have lived much longer than many thought possible, and with fewer and less toxic side effects.

This is an extraordinary time, and there is undoubtedly a lot to be excited about. But while two ambitious cancer "moonshot" projects are in the works—one led by Vice President Joe Biden, whose expert advisory panel I sit on—my hope is that we reach a place where cancer is more chronic than deadly.

Consider HIV/AIDS: In the Eighties, an HIV or AIDS diagnosis meant an almost certain and untimely death. But today, thanks to decades of fundamental research that led to the development of targeted therapies that were quickly translated into the clinical setting, an HIV diagnosis is usually manageable. A combination of antiretroviral drugs can keep the virus under control, and in most cases keep patients healthy and stable for a very long time.

In cancer, getting to that same placewhere the disease is chronic and controllable rather than deadly-is now a reality for certain patients, thanks in part to the amazing discoveries in the immunotherapy field. But there is still a lot of important biomedical and clinical research needed to bring those benefits to more people, which, as you'll read in these pages, is what a host of Weill Cornell Medicine scientists and physicians-many of them at the Sandra and Edward Meyer Cancer Center-are pursuing with laser focus. With additional advances, plus a continued investment in precision medicine that will help physicians determine how to best treat each individual based on characteristics and mutations specific to their disease, we'll be able to provide many more patients with-if not a cure-a way to live with their illness.

After decades of painstaking work, what could be more gratifying for all of the physician-scientists invested in these efforts than to witness immunotherapy's transformative effects on patients' lives?



Discovering New Therapeutics through the Power of Philanthropy

The Tri-Institutional Therapeutics Discovery Institute (Tri-I TDI), a novel collaboration between Weill Cornell Medicine, The Rockefeller University, and Memorial Sloan Kettering Cancer Center, arms the most talented researchers with the tools, technology, and expertise to remove the barriers that impede drug discovery in academic settings. Thanks to support from generous donors like Overseer Lewis Sanders and his wife, Ali, who have recently bolstered this exciting initiative with a new \$15 million gift split between the three institutions, the Tri-I TDI has entered a period of exciting growth, moving promising discoveries to the next phase of drug development.

Mr. Sanders notes three words that capture the heart of the institute: empower; encourage; and leverage.

"To empower is to bring to investigators the know-how to optimize their intellectual property. To encourage is to incentivize investigators to translate, to commercialize their work. And as a philanthropist, you leverage your gift toward innovation that benefits the many." "You have a chance to advance the standard of care in a very significant way, and **save or improve tens of thousands, if not millions, of lives**. If a philanthropist is thinking about how they can impact the lives of the many, investing in healthcare research in academia is a compelling route."



Dr. Michael Foley (left) and Overseer Lewis Sanders

In this unique alliance, the scientists who discover therapeutics work side by side with medicinal chemists, speeding the conversion of therapies from the laboratory to effective treatments for patients.

"We wouldn't have infrastructure or be able to do what we do if it weren't for philanthropy," says Dr. Michael Foley, Sanders Director of the Tri-I TDI and director of its Sanders Innovation and Education Initiative. "The National Institutes of Health doesn't routinely fund medicinal chemistry for academic drug discovery, and pharmaceutical companies cannot do all the basic biology within their walls."

"You have a chance to advance the standard of care in a very significant way, and save or improve tens of thousands, if not millions, of lives," says Mr. Sanders. "If a philanthropist is thinking about how they can impact the lives of the many, investing in healthcare research in academia is a compelling route."

To support the Tri-Institutional Therapeutics Discovery Institute or other critical research initiatives at Weill Cornell Medicine, please contact: Lucille Ferraro, Campaign Director, 646-317-7387 or luf2003@med.cornell.edu

Cornell Community Mourns Death of Elizabeth Garrett



ornell University is mourning the loss of President Elizabeth Garrett, who passed away in early March after battling colon cancer, just eight months after taking office. Garrett, fifty-two, was Cornell's thirteenth president, and the first to die while in office. "Not only was she one of the great leaders in Cornell history," said Jessica Bibliowicz, chair of the WCM Board of Overseers and a 1981 alumna of the Ithaca campus, "but I'm quite confident that if she had more time she would have been one of the great leaders in university history."

Garrett—a legal scholar whose distinguished résumé included clerking for Supreme Court Justice Thurgood Marshall—was remembered in a packed memorial service on the Ithaca campus, which was live-streamed online. Nearly 200 Cornellians in New York City joined in the celebration of her life and legacy with a gathering, hosted by Bibliowicz, in WCM's Uris Auditorium. In her remarks, Bibliowicz noted

that despite Garrett's brief tenure, she made tremendous strides toward connecting the Ithaca and New York campuses. And she made a lasting impact on Bibliowicz, who recalled their many long conversations about everything from University initiatives to social culture. "At the end of the day, that's why I say Cornell University lost its thirteenth president," she said, "but like so many of you in this room, I lost a friend."

Among the dignitaries in attendance at the ceremony in Ithaca's Bailey Hall were Dean Laurie Glimcher, MD; New York State Lieutenant Governor Kathleen Hochul; and Cornell President Emeritus Hunter Rawlings, PhD, who will serve as interim president while the University conducts its search for Garrett's successor. The speakers who eulogized Garrett included one of the WCM physicians who attended her during her illness-Orli Etingin, MD, the Lisa and Stanford B. Ehrenkranz Professor in Women's Health-who called the late president "an awesome woman, a scholar, a true leader, and a visionary." She brought the attendees to tears when she described Garrett's final hours, but also sparked smiles by talking about the president's upbeat attitude and indefatigable sense of humor. "On the day she went home from the hospital, after five weeks, which turned out to be her last day, I asked Beth what she wanted to do most when she got home," Etingin recalled. "Would she want to sit in her sunny spot in the living room or do something special? She replied to me, she wanted to do her taxes. And she said with her great, dazzling, big grin: 'Orli, you've forgotten; I'm a tax attorney.' "

'Cornell University lost its thirteenth president,' said Jessica Bibliowicz, chair of the WCM Board of Overseers, 'but like so many of you in this room, Host a friend.'

Glimcher to Head Dana-Farber; Choi Serves as Interim Dean



Dean Laurie Glimcher, MD, has been tapped to be the next president and CEO of the Dana-Farber Cancer Institute. Augustine Choi, MD, the Sanford I. Weill Chairman of the Weill Department of Medicine, will assume the post of interim dean on June 1; Glimcher will serve as an adviser through the end of August. A search

Augustine Choi, MD

committee has been formed to find her successor. "I am grateful for Laurie's many efforts on behalf of Weill Cornell Medicine, and wish her all the best," says Jessica Bibliowicz, chair of the Board of Overseers. "Thanks to her leadership and the dedicated support of our overseers, faculty, and staff, Weill Cornell Medicine is positioned on an impressive trajectory of growth in care, discovery, and education."

Cantley Wins 'Israel's Nobel'

Lewis Cantley, PhD '75, the Meyer Director of the Sandra and Edward Meyer Cancer Center and a professor of cancer biology in medicine, has won the Wolf Prize in Medicine for his discovery of a family of enzymes, known as PI3-kinase, fundamental to understanding diabetes and cancer. The prizes, considered "Israel's Nobel," are given to researchers who have made seminal achievements in their fields.

Pitt To Lead Cardio Research Institute

After a national search, Geoffrey Stuart Pitt, MD, PhD, has been appointed director of the Cardiovascular Research Institute at WCM. Pitt, who will also be the Ida and Theo Rossi Distinguished Professor of Medicine, will lead basic and translational research programs focused on cardiovascular disease. An internationally recognized authority on calcium signaling and ion channels, he comes to WCM from Duke University.

Fellowship Will Train Bioethics Leaders

WCM, NewYork-Presbyterian, and Houston Methodist have established a fellowship to train bioethicists who will serve as leaders in the field—improving care by providing guidance to clinicians navigating ethically difficult situations. "It's essential that an activity with so much consequence for patient welfare is well regulated and that the people carrying out clinical ethics have the proper training," says Joseph Fins, MD '86, chief of the Division of Medical Ethics at WCM, director of the new fellowship program, and the E. William Davis Jr., MD, Professor of Medical Ethics. The fellowship will begin July 1.

New Robotic Cardiac Surgery Director

T. Sloane Guy, MD, has joined WCM and NYP/Weill Cornell as head of the new robotic cardiac surgery program. He comes from Temple University, where he was chief of the Division of Cardiothoracic Surgery. In his new role, Guy leads a clinical team that performs innovative, minimally invasive procedures using small, dexterous robotic instruments. Says Leonard Girardi, MD '89, chair of cardiothoracic surgery and cardiothoracic surgeon-in-chief at NYP/Weill Cornell: "Very few institutions offer this kind of robotic surgery, and I'm confident that his long-standing proficiency and talent will keep us at the forefront."

Physician Organization Names COO

Edward Grab, a national leader in managing healthcare delivery systems at academic medical centers, has been named chief operating officer of WCM's Physician Organization. He comes to WCM from Boston, where he was executive vice president and COO of the Harvard Medical Faculty Physicians at Beth Israel Deaconess Medical Center. Grab's recruitment is among several leadership changes in the Physician Organization. Daniel Knowles, MD, was promoted from chief medical officer to president and CEO; Michael Stewart, MD, was named CMO.

TIP OF THE CAP...

Susan Bostwick, MD, professor of clinical pediatrics, elected president of the Academic Pediatric Association's board of directors for 2017; she'll serve as president-elect during 2016.

David Hajjar, PhD, professor of pathology and laboratory medicine and of biochemistry, named a nonresident senior fellow at the Brookings Institution's Center for Middle East Policy.

Catherine Hartley, MD, assistant professor of psychology in psychiatry, winner of a \$650,000, five-year NSF Faculty Early Career Development Award to support her work on adolescent decision-making.

Makoto Ishii, MD '08, an assistant professor of neurology and neuroscience in the Feil Family Brain and Mind Research Institute, given the Paul B. Beeson Career Development Award in Aging Research.

James Killinger, MD, assistant professor of pediatrics, awarded the Presidential Citation from the Society of Critical Care Medicine.

Ning Lin, MD, assistant professor of neurological surgery, elected to the Chinese American Medical Society's board of directors for 2016.

Andrew Schafer, MD, professor of medicine, named president-elect of the American Clinical

and Climatological Association for 2016–17. He was also appointed to the scientific advisory council of the Doris Duke Charitable Foundation.

Marco Seandel, MD, PhD, assistant professor of cell and developmental biology in surgery, of cell and developmental biology, and of medicine, winner of the Irma T. Hirschl/Monique Weill–Caulier Trust Award to study the mechanism by which the risk of congenital heart disease in children is influenced by genetic mutations in the sperm of older fathers.

Philip Stieg, MD, PhD, professor and chairman of neurological surgery, named president of the Brain Tumor Foundation.

WCM Boasts 'Hot' Researchers

Four WCM faculty have been named to a list of the most influential scientific minds of 2015. The roster-based on statistics maintained by Thomson Reuters-comprises investigators whom the media firm's editors consider "a special subset of 'hot' researchers whose very recent work has won distinction in the form of citations." They are: Lewis Cantley, PhD '75; David Calfee, MD, associate professor of medicine and of healthcare policy and research; BJ Casey, PhD, the Sackler Professor of Developmental Psychobiology; and Mark Rubin, MD, director of the Englander Institute for Precision Medicine and the Homer T. Hirst III Professor of Oncology in Pathology. Additionally, Thomson Reuters assessed which institutions had produced the most "hot papers" in HIV/AIDS in the previous two years-and announced that the two most prolific were WCM and Scripps Research Institute. It also revealed that four WCM researchers in microbiology and immunology had made the list of top-ten authors of hot papers in HIV/ AIDS. They are professors John Moore, PhD, and Per Johan Klasse, PhD; Rogier Sanders, PhD, an adjunct associate professor; and research associate Albert Cupo.

Drukier Prize Goes to Pediatrician

Sing Sing Way, MD, PhD, chair of infectious disease at Cincinnati Children's Hospital, has been awarded the inaugural Drukier Prize in Children's Health Research. The \$10,000 prize was established as part of a \$25 million gift, made to WCM in 2014, that also created the Gale and Ira Drukier Institute for Children's Health. Way was recognized for his research on how a woman's immune system tolerates the fetus and placenta during pregnancy, preventing rejection.



Cutting the ribbon: A ceremony in March officially opened the permanent laboratories of the Jill Roberts Institute for Research in Inflammatory Bowel Disease. From left: Ellen Scherl, MD, Jill Roberts, Augustine Choi, MD, Jessica Bibliowicz, and David Artis, PhD.



Rahul Sharma, MD

Sharma Tapped as ED Chief

Rahul Sharma, MD, has assumed the post of chief of the Division of Emergency Medicine at WCM and emergency physician-inchief at NYP/Weill Cornell. Sharma—whom Augustine Choi, MD, chairman of the Weill Department of Medicine, calls "an outstanding physician who has contributed to numerous advances in emergency care"—succeeds Neal Flomenbaum, MD, now the hospital's chief of emergency medical services. Previously WCM's executive vice chief of emergency medicine, Sharma holds a combined MD-MBA from Tufts.

Roberts Institute Celebrates New IBD Lab

The Jill Roberts Institute for Research in Inflammatory Bowel Disease hosted a ribbon-cutting ceremony in March to celebrate the opening of its permanent laboratory space on the seventh floor of the Belfer Research Building. Speakers included Jessica Bibliowicz, chairman of the Board of Overseers: Augustine Choi, MD, the Weill Chairman of the Weill Department of Medicine; Institute director David Artis, PhD, the Michael Kors Professor in Immunology; and Ellen Scherl, MD, the Jill Roberts Professor of Inflammatory Bowel Disease and director of the Jill Roberts Center for Inflammatory Bowel Disease, the Institute's close clinical collaborator. Established two years ago, the Institute and its five primary investigators have already made numerous advances in such areas as describing the molecular underpinnings of IBD and exploring how the immune system influences the disease's development and progression. "We're in a very powerful position to accelerate basic discoveries and to translate them to benefit patients," Artis says. "That's really what all of this work revolves around."

FROM THE BENCH



Experience Informs Physicians' Own End-of-Life Choices

In an special issue of JAMA on death and dying, WCM researchers report that physicians are less likely than the public to die in the hospital, or to have surgery or be admitted to the ICU in the last six months of their lives. The investigators say their findings indicate that doctors' understanding of the realities of intensive, inhospital care at the end of life affects their own treatment choices. Says co-senior author Holly

Prigerson, PhD, co-director of the Center for Research on End-of-Life Care and the Irving Sherwood Wright Professor of Geriatrics: "The findings provide a form of doctor testimonial recommending less aggressive end-of-life care and highlight the need for economic and human resources to support home deaths." The researchers reviewed data for some 666,600 people including about 2,400 physicians—in the Northeast.

Tackling Resistant Prostate Cancer

Neuroendocrine prostate cancer, a subtype that is resistant to treatment, pathologically resembles small cell lung cancer—a finding that could lead to better ways to combat the disease. With colleagues in Italy, WCM investigators used next-generation sequencing technologies and discovered the genetic, epigenetic, and molecular features that underlie neuroendocrine prostate cancer, which evolves from the typical form of the disease, adenocarcinoma. "While the two resistant tumor types adenocarcinoma and neuroendocrine prostate cancer—were genomically similar, they had distinct epigenomic profiles," says co-senior author Mark Rubin, MD, director of the Englander Institute for Precision Medicine, the Homer T. Hirst III Professor of Oncology in Pathology, and a member of the Meyer Cancer Center. "These changes could potentially explain why the altered cells no longer respond to anti-hormonal therapies." The work appeared in *Nature Medicine*.



Genomics Reveals Arabian Roots

Research on the New York and Doha campuses finds that indigenous Arabs are descendants of humans who migrated out of Africa before others continued on to colonize Europe and Asia. The investigators—including lead author Jason Mezey, PhD, associate professor of genetic medicine, and senior author Ronald Crystal, MD, chairman of the Department of Genetic Medicine and the Bruce Webster Professor of Internal Medicine—sequenced

JASON MEZEY, PHD

the genomes of 104 Arabian Peninsula natives and compared them with 1,092 genomes from worldwide populations. Their findings, published in *Genomic Research*, run contrary to the previous hypothesis that when humans migrated out of Africa they passed through the peninsula, colonized Europe and Asia, and later returned. Says Mezey: "The indigenous Arab population was relatively isolated and yet they flourished and developed, as did Europeans, as did Asians."

Breast-Conserving Surgery Poses Risks

Nearly a quarter of early-stage breast cancer patients who undergo partial mastectomy risk another operation within ninety days, researchers report in *JAMA*. The breast-conserving surgery involves removing the cancerous tumor plus a margin of healthy tissue, providing an alternative to full mastectomy. "Our study shows that re-operation can be considered an epidemic in the United States," notes Art Sedrakyan, MD, PhD, professor of healthcare policy and research. "Surgeons try to conserve the breast, but it is both stressful and potentially risky if women have to come back for a second surgery. That is why it's so important to develop stronger guidelines that recommend exactly how much tissue to remove, rather than leaving it up to individual surgical judgments."

Flavors Key to Vaping's Youthful Appeal

Since the flavor variety of e-cigarettes is such an attraction for youthful smokers, eliminating those options could discourage teens and young adults from "vaping," says Michael Pesko, PhD, assistant professor of healthcare policy and research. Pesko, who has done extensive research on smoking and e-cigarettes, notes that restricting flavors is a preferable strategy to increased taxation, because it would limit vaping's appeal to youth while keeping the devices affordable for older smokers who use them as an aid to quitting. "Governments are worried about young people using e-cigarettes," says Pesko who reported his investigations in *Addiction*, "but regulating them too harshly could send older smokers back to regular cigarettes."



Haitian AIDS Patients See Good Outcomes

In a research letter in the *New England Journal* of *Medicine*, WCM investigators report that one of the first groups of AIDS patients to receive free HIV drugs in a public health setting in the developing world is living as long as those in the U.S. Of the 910 patients who began antiretroviral treatment in the WCM-affiliated GHESKIO clinic in Haiti in 2004, 70 percent are still alive. The results are all the more remark-

MARGARET MCNAIRY, MD

able because the majority of those patients had advanced AIDS when they started treatment; many had associated conditions including tuberculosis; and most were severely underweight and lived on less than \$1 per day. All patients were asked to return to GHESKIO once a month for follow-up, but were responsible for taking their daily medications unsupervised. "These patients were literally on their deathbeds and living in very difficult conditions," says senior author Margaret McNairy, MD, assistant professor of medicine and the Bonnie Johnson Sacerdote Clinical Scholar in Women's Health. "This proves the long-term sustainability of efforts to provide AIDS treatment in developing nations."



JASON SPECTOR, MD

New Sterilizer Doesn't Hurt Electronic Devices

A new sterilization device can kill germs without harming electronics, says an article in *Plasma Medicine*. WCM investigators report that the Sterifre Countertop Sterilizer can rid cell phones of germs in ten minutes—offering a quicker, easier, cheaper, and more thorough way to clean common electronic devices, as well as a potential strategy for disinfecting biomedical equipment and other items used in healthcare. "I can

imagine these things populating hospitals, clinics, schools. You could even have one at home if you wanted to disinfect your baby's bottle," says Jason Spector, MD, professor of surgery, whose team tested the sterilizer on fiftyone cell phones as well as on less delicate items. Medical equipment is typically sterilized by using either toxic gas or high-pressured steam; because both methods harm electronic devices typically used in hospitals, there was no quick and thorough way to rid them of bacteria. The new sterilizer only requires air, industrial-grade hydrogen peroxide, and a power source. It's already commercially available on a limited basis, and FDA approval efforts are under way.

Lightbox

Inflammatory Topics

This microscopic image of a mouse intestine highlights experiments conducted in the lab of Gregory Sonnenberg, PhD, assistant professor of microbiology and immunology in medicine—to study potential approaches for treating inflammatory bowel disease in humans. Chronic inflammation was triggered in the mouse intestine to study the immune cells (depicted in yellow) that infiltrate the tissue (seen in green).



REGORY SONNENBERG, PHD



Talk of the Gown

Young Minds

all's

11

By studying the adolescent brain, Weill Cornell Medicine neuroscientists aim to change how the justice system treats juveniles n June 2015, twenty-two-year-old Kalief Browder hanged himself from a bedroom window in his childhood home in the Bronx. His suicide was a tragic end to a heartbreaking story: In 2010, when he was just sixteen, Browder was sent to Rikers Island Correctional Facility in New York City after being accused of stealing a backpack. He spent the next three years awaiting trial in one of the country's toughest jails, never having been convicted of any crime. And for nearly two years of that time, Browder was held in solitary confinement—during a period of teenage brain development when interacting with others is vital. He seemed to rally after his eventual release, earning a high school equivalency diploma and enrolling in community college. But he struggled with depression, and those close to Browder said he never really recovered from his prison trauma, particularly from long stretches of being locked alone in a cell for twenty-three hours a day.



"There's just this visceral reaction when I think of all that young

man endured," says BJ Casey, PhD, a neuroscientist and director of the Sackler Institute for Developmental Psychobiology at Weill Cornell Medicine, who followed news accounts of Browder's death. "And of course, I immediately thought of his mother. What is the worst thing that could happen to any parent? The loss of a child—and especially the loss of a child because of a system that is broken. You have to wonder: What can we do to make sure this doesn't happen again?"

For Casey, part of the answer lies in informing clinicians, courts, and elected officials about research that provides crucial insight into the maturing brain—and why adolescent behavior can differ so dramatically from that of children and adults. Studies show that adolescents undergo neurobiological changes that make them more prone to anxiety and depression and, under certain conditions, can impair their judgment and decision-making. Casey believes this information is key to helping treat youngsters with mental health problems, which peak during this period; one in five adolescents have a mental illness that will continue into adulthood. She also argues that new findings about the still-developing brain—including those published in a recent study led by Alexandra Cohen, a PhD candidate in neuroscience at the Sackler Institute—that reinforce the notion that full brain maturation can occur as late as one's twenties should play a significant role in how young people are treated by the justice system.

Such evidence has already influenced legal and social policies; Browder's death, for example, prompted New York City to abolish solitary confinement for sixteen- and seventeen-year-old detainees, and Mayor Bill de Blasio stressed the specific damage that isolation can have on a young person's mental stability. (Solitary confinement was later eliminated for those twenty-one and under.) President Obama followed suit earlier this year, recounting Browder's story when announcing a ban on solitary for juveniles in federal prisons, a move that he hoped would push more states to re-examine their rules. Casey says data on developing brains should be considered when it comes to other policies as well, including fair sentencing and at what age offenders should be regarded as adults. "We should all be held accountable for our actions and behavior, but it's about culpability," she says. "We need to think about that when looking at whether the punishment fits the crime under the circumstances."

Impulse Control

Teenagers stereotypically do impetuous, dangerous things—drive too fast, experiment with alcohol and drugs, play with guns—resulting in a 200 percent rise in deaths, most of them preventable, during this phase of life. For years, Casey says, many doctors attributed this solely to the lack of a mature prefrontal cortex, the part of the brain associated with reasoning. Yet, as Casey points out, younger children have immature brains but don't act the same way. So for more than a decade, she has used neuroimaging and behavioral experiments to show that additional changes are happening: around puberty, neurochemicals cause strong activations in the growing limbic system, the brain's emotional center. Connections between that system and the prefrontal cortex aren't completely >

'We should all be held accountable for our actions and behavior, but it's about culpability,' Casey says. 'We need to think about that when looking at whether the punishment fits the crime under the circumstances.' 'The work we've done shows that adolescence is a unique period that's very different from childhood and adulthood in terms of emotional processing,' says Francis Lee, MD, PhD. established, though, making it difficult for adolescents to shut down those feelings.

Casey explains that it's almost as if these emotional regions "hijack" the prefrontal cortex of the adolescent brain, which can make young people more susceptible to bad choices. "There's a real sensitivity to cues in the environment, both positive and negative," she says. There's other evidence that this is hard-wired. Francis Lee, MD, PhD, the Mortimer D. Sackler, MD, Professor of Molecular Biology in Psychiatry, has done experiments in mice that demonstrate similar developmental patterns in brain circuitry. One joint study with Lee and Casey, published in 2012 in *Proceedings of the National Academy of Sciences*, showed sharp differences in how adolescents handle fear compared to their older or younger counterparts; adolescent mice and humans both have a harder time learning that something that once frightened them is no longer a danger. "The work we've done shows that adolescence is a unique period that's very different from childhood and adulthood in terms of emotional processing," Lee says.

Casey has also conducted various experiments focused on impulsivity, a trait that often lands teens in trouble. For a 2013 Developmental Neuroscience study, she and MD-PhD candidate Michael Dreyfus asked eighty participants between ages six and twenty-seven to view a series of faces with calm or fearful expressions. With their brain activity being monitored by MRI, the subjects were asked to press a button each time they saw a neutral face, but to hold back from pressing it when they saw a rare fearful face (which implied that the person in the image was under threat). Casey's team was surprised to discover that adolescents, especially boys, were more likely than the other age groups to press the button at the threatened expression. "We were blown away by that," she says. "Usually if you see a potential threat, you avoid it." That reaction corresponded to enhanced activity in parts of the brain linked to emotion, suggesting that this age group might be biologically drawn to risk-taking. Casey says these findings add to a growing body of literature explaining why teenagers are sometimes unable to control themselves in the heat of the moment or stressful circumstances, which can be exacerbated when they're around their peers. "There's less capacity for them to regulate themselves in those situations," she says. "If that's the case, then that suggests diminished responsibility."

To spread that message, Casey has presented her work to legislators, state supreme courts, and judges across the country. In late January, she spent a morning at the U.S. District Court in lower Manhattan, where she asked more than two dozen federal judges to complete an impulsivity task similar to one she's given adolescents. In a game like whack-a-mole, the judges were told to say "whack" every time a certain picture popped up on a video screen, but to stay quiet if they saw a different image. "About half of them said 'whack,' even though they weren't supposed to," says Casey. The point? To encourage the judges to think from a young person's perspective. "I was trying to show them where their performance was relative to teenagers, because teenagers actually do pretty well on that task," she says. "Where teenagers break down is when they're under threat, and that's usually when criminal behavior occurs."

Legal Remedies

The idea that there are fundamental distinctions between juvenile and adult offenders has already gained traction. The U.S. Supreme Court decided in January that those sentenced as teenagers to mandatory life in prison should be allowed to petition for parole. As Justice Anthony Kennedy wrote: "Allowing those offenders to be considered for parole ensures that juveniles whose crimes reflected only transient immaturity—and who have since matured—will not be forced to serve a disproportionate sentence in violation of the Eighth Amendment." This was the latest in a string of cases that suggest young people should be treated differently; in the last decade, the court has referred to scientific research when banning capital punishment for juveniles and ruling that they can't be locked away for life for crimes other than murder.

But Casey and others at Sackler wonder about an even bigger question tied to the law: When exactly does an adolescent become an adult? Right now, it's a hazy legal area. Minors are typically prohibited from voting, buying cigarettes and alcohol, and serving on juries, yet twenty-three states currently have no minimum age for trying a child as an adult. In New York and North Carolina, youngsters are prosecuted as adults when they turn sixteen. Overall, more than 200,000 people under eighteen face prosecution as adults in U.S. criminal courts every year. "The age limits we've set in the past have not been based on anything guided by developmental science or behavioral science. Historically it's been arbitrary, and each state has a different law," Casey says. "That's concerning."

To that end, Cohen is lead author of a new study that concentrates on eighteen- to twenty-one-year-olds, who are legally considered adults but fall into a gray zone of neurological development. For a study published in February in *Psychological Science*, Cohen, Casey, and colleagues evaluated cognitive control for 110 thirteen- to twenty-five-year-olds. Once again under MRI imaging, subjects were asked to respond to different stimuli, but during



BJ Casey, PhD

periods when they were anticipating either hearing a loud, annoying noise or possibly winning up to \$100. They found that when people between eighteen and twenty-one performed tasks under negative conditions, their brains looked more like teenagers than older adults. "We're not really trying to conclude a firm numerical cutoff. In reality, there are so many factors that go into determining when an adolescent becomes an adult," Cohen says. "But we wanted the takeaway to be that it's important to consider contextual information when you're making a judgment of criminal responsibility or culpability, because that can drastically alter a situation."

Cohen repeats Casey's belief that adolescents should be punished for misconduct, particularly when it comes to more heinous crimes, but she notes that exposing still-developing teens like Browder to harmful conditions in adult facilities or imposing overly harsh sentences for misdemeanors or nonviolent felonies likely won't alter behavior or properly prepare youngsters for life after jail. "What the juvenile justice movement is trying to promote is rehabilitation versus locking someone up and throwing away the key," Cohen says. "The more we can rehabilitate these individuals and have them be contributing members of society, the more it will benefit all of us."

A Proactive Approach

The ideal solution, however, is to use this knowledge to aid troubled youngsters before they break the law. After all, the researchers note, as many as 70 percent of people who wind up in the juvenile justice system have a mental disorder. Clinicians like Dylan Gee, PhD—an assistant professor of psychology in psychiatry at Sackler who has treated young patients at Weill Cornell's Payne Whitney Clinic in Westchester County, as well as through the Child and Adolescent Outpatient Department at NewYork-Presbyterian hope that these data can help doctors more precisely treat distressed teens, who may then be less likely to act out. "There's so much that is in flux during this stage that often the clinical presentation is very complicated," Gee says. Most current treatments for young people with anxiety are largely based on those used for adults, such as cognitive behavioral therapy, which relies on exposing patients to a feared situation and gradually desensitizing them. Gee says that kind of therapy could be adjusted according to a patient's age; for instance, research indicates that actively engaging in a variety of reallife activities, rather than imagining scenarios in a therapist's office, may be particularly effective for teenagers.

Casey emphasizes that there's no need to think all teenagers are at risk. Much of their behavior is simply part of growing up—just as a baby learns to walk and talk—and the majority get through adolescence just fine. To worried parents, she says that finding safe outlets for young people to explore and experiment is essential; for example, rock climbing in a controlled environment could satisfy a bit of that impulse to take risks. "Why can't we use this time of passion and heightened sensitivity and channel that in positive ways?" Casey asks. "How can we put that toward something like community service? How can we encourage them to use those changes for something good?"

— Heather Salerno

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Wisdom of Crowds

At major events like Burning Man and Coachella, Eric Salk, MD '92, practices 'mass gathering medicine'

ate last summer, some 70,000 people flocked to a barren tract in Nevada's Black Rock Desert for the massive, weeklong Burning Man festival. On a dry lake bed hundreds of miles from civilization, they established what organizers of the annual event describe as "a temporary metropolis dedicated to community, art, self-expression, and self-reliance."

But what happens if, in the midst of this geographically isolated "crucible of creativity," someone gets sick or injured?

Coping with such calamities is the job of Eric Salk, MD '92. A veteran emergency physician, Salk works with CrowdRX, a company that provides healthcare services to a wide variety of



Eric Salk, MD '92

a consultant. "It depends on the environment-whether it's a festival spread out across twenty acres or if you're in a fixed stadium. Are you in a city with three hospitals a few blocks away, or all the way out at Burning Man, where you've got 70,000 people in the middle of the desert, 200 miles from the nearest hospital?"

unique; it's hard to come up with a for-

Treating patients under such circumstances is part of a growing subspecialty known as "mass gathering medicine." The field, Salk says, is getting more sophisticated and organized than in the past, when medical care at large events was often provided by local ambulance services, and doctors were hired on an ad hoc basis. In preparing CrowdRX's presence at a venue, he and his

colleagues consider not only location but existing resources, including transport times to local hospitals and factors such as the proximity of a trauma center. The nature of the event also dictates the likely complaints: at electronic dance music (EDM) shows, drug and alcohol abuse can be serious issues, while at triathlons, clinical staff may see sports injuries, heat exhaustion, and heart attack. "You see the

'We basically had to create an on-site hospital including X-ray, ultrasound, laboratory services, and the ability to fly the most critically ill patients out for evacuation.'



full spectrum," he says, "from the most minor scrapes and bruises to people who are critically ill to occasional fatalities."

Last year's Burning Man was Salk's first trip to the festival, and the first time CrowdRX serviced it. "We basically had to create an on-site hospital including X-ray, ultrasound, laboratory services, and the ability to fly the most critically ill patients out for evacuation," he says. "Burning Man gets every age, so we had to be prepared for kids coming in with fevers and sore throats, as well as

> people well into their eighties with cardiac complaints." Common conditions include "playa foot"-skin burns from going shoeless on the fine, alkaline soil—as well as eve abrasions and other effects of the event's notorious dust storms, which are so bad that visibility is counted in feet. "Burning Man was really impressive," says Salk, who got licensed to practice in Nevada so that he could provide hands-on care. "I'd seen



videos and read about it for years, but it's really hard to explain the extent of it. The level of creativity that people bring to it, the commitment, the spirit in this huge city that just pops up overnight in the desert—it's just unbelievable."

In addition to treating emergencies, Salk and his colleagues aim to prevent them from happening in the first place. They work with event organizers and community partners to mount harm-reduction campaigns—promoting, for example, adequate hydration or responsible substance use. At some EDM shows, they deploy peer ambassadors—often medical or nursing students—who mingle with the crowd to identify revelers who need help. Salk himself has worked numerous EDM events—and yes, he wears earplugs. "It's not my favorite type of music—I'm more of a Led Zeppelin and classic rock kind of guy," he says with a laugh. "But I must say that for all the bad press these festivals sometimes get, when I walk through the crowd, I'm always impressed with the positive energy and the supportive, loving feeling among the kids."

Salk hails from a prominent medical family: his uncle was polio vaccine pioneer Jonas Salk, MD, and his father, the late Lee Salk, PhD, was a renowned child psychologist who taught at WCM in the Seventies and Eighties. For Salk, who holds a master's in public health from UCLA, mass gathering medicine is a sideline; his full-time career is as an emergency physician in northwestern Connecticut, where he has also held medical leadership roles at hospitals and in his local community. He notes that, since the care at such gatherings is paid for by the event itself, the field offers a welcome respite from the less enjoyable parts of conventional practice, such as documenting charts or navigating insurance coverage. "I love emergency medicine, but practicing within our healthcare system can be stressful," he says. "At these festivals, we're able to practice medicine person to person, without a lot of paperwork; we're reimbursed, more often than not, with hugs and smiles. It reminds you of the fun, human side of practicing—why I went into medicine in the first place." — Beth Saulnier



Staying healthy: Bob Bancroft administers medication to his son Alex.

Tall Order

An ambitious study aims to understand how Crohn's disease stunts kids' growth hen Alex Bancroft was five, it was clear that something was awry with his digestive system. During kindergarten, his mom says, he was spending a lot of time in the bathroom. Doctors first thought he had a virus, but the symptoms persisted. Then a pediatric gastroenterologist diagnosed Alex with irritable bowel syndrome and put him on medication for it. But he didn't get any better—and on top of enduring diarrhea and fatigue, he wasn't growing. "He wouldn't eat, because he was afraid that he wouldn't make it to the bathroom in school," says his mother, Caroline Bancroft. "At age seven, he dropped down to about forty pounds."

Eventually, Alex's parents brought him to NYP/Weill Cornell, where he saw Thomas Ciecierega, MD, assistant professor of pediatrics. Ciecierega made the correct diagnosis—Crohn's disease, a type of inflammatory bowel disease (IBD) that is characterized by intestinal inflammation—and put the boy on the proper course of medication. "He started gaining weight and was more active," Caroline says. "You could see the life coming back."

Today, Alex is still a little short for his age, but the Long Islander is an active nine-yearold and avid lacrosse player. He'll have to stay on medication indefinitely, and the disease has other potential complications, like eye problems and arthritis. But for now, he's doing well. Says his mom: "This is the healthiest I've ever seen him in his life."

Someday, kids like Alex could benefit from research now under way at WCM. Neera Gupta, MD, director of research and a specialist at the WCM Pediatric Inflammatory Bowel Disease Center and an associate professor of pediatrics, recently launched a study to uncover why kids with Crohn's—especially boys—are often shorter than their peers. Growth is a dynamic marker of a child's health status, she notes, and it's an issue of central importance to patients, families, and providers.

Gupta, who is also a physician-scientist at the Jill Roberts Institute for Research in Inflammatory Bowel Disease at Weill Cornell Medicine, notes that roughly 25 percent of patients with IBD are diagnosed during childhood and adolescence. In the United States, there are about 5,000 new pediatric IBD cases each year—and they present unique challenges. Not only is growth impairment a major complication of pediatric-onset Crohn's disease that distinguishes it from the adult-onset version, she explains, but diffuse disease is more common in children at the time of diagnosis, and progression occurs more frequently in kids than in adults.

There are also sex differences in the presentation and course of Crohn's disease. In Gupta's previous studies, she found that girls tend to have a more severe course of disease and are more likely to need surgery, but boys are more likely to have growth problems. Her current work, funded by an NIH award of more than \$3 million, aims to figure out why.

The study will follow children and adolescent boys and girls for two years. After an initial screening to make sure they qualify, participants will come in every six months for a total of five visits, either at Weill Cornell or one of the other collaborating



Neera Gupta, MD

institutions. Procedures will include height and weight measurements, assessment of pubertal status, medical history, blood draw, hand x-rays (for bone age), and nutrient intake assessments.

Gupta's team will utilize the data to develop predictive models to identify which children are most likely to have persistent growth problems caused by Crohn's disease, ultimately helping clinicians to better determine a course of treatment. "One of the debates in our field is when to introduce the most aggressive therapies for Crohn's disease," Gupta says. "Some believe we should do it at the time of diagnosis, and some believe we should start with other therapies first. Most agree there are high-risk children who would benefit from early intervention with aggressive therapy—but we need to figure out who these high-risk children are. Because there is a very narrow therapeutic window in which we can intervene to improve growth, children who are at highest risk for persistent growth impairment may be candidates for early intervention with aggressive therapy."

After data collection is completed, doctors will be able to look at a combination of variables—including sex, race/ethnicity, disease location, bone age, inflammatory markers, hormone levels, and genetic markers—to determine whether a child is at high risk for growth impairment. The next step will be an interventional clinical trial assessing aggressive therapies in children who are at highest risk for remaining growth-impaired. Importantly, Gupta says, the study will improve understanding of the underlying mechanisms of growth impairment in Crohn's disease. It's known that impairment may result from inflammation, malnutrition, or the side effects of medications; despite this knowledge, it continues to occur frequently in children and adolescents. "We need to advance our understanding of the underlying mechanisms of growth impairment in Crohn's disease," Gupta says. "We hope that findings from our research will lead to improved treatments not only for the children identified as high-risk for persistent growth impairment, but for all children with IBD."

'Most [clinicians] agree there are high-risk children who would benefit from early intervention with aggressive therapy,' Gupta says, 'but we need to figure out who these high-risk children are.'

> Office visit: Pediatrician Thomas Ciecierega, MD, with Alex and his family

Gupta aims to complete data collection by 2019, but for now her team is still in the process of recruiting participants. The goal is 125—but that's challenging, in part because not every Crohn's patient in the specified age range will qualify for the study. Alex, for example, hasn't qualified so far, because his bone age hasn't

met the eligibility criteria. But his parents hope that work like Gupta's will someday ensure that other kids don't have to go through the ordeal that he has. "Ultimately," says his dad, Bob Bancroft, "what we're hoping for is a cure."

- Keri Blakinger



TALK OF THE GOWN



Jonathan Victor, MD '80, PhD

How the Nose Knows

Neuroscientist Jonathan Victor, MD '80, PhD, joins an NSF-funded effort on the fundamentals of smell hen we need to rescue people from collapsed buildings or to search for bombs, land mines, missing persons, or contraband—we typically employ dogs, with their finely tuned sense of smell, to locate them for us. But exactly how animals use that sense, known as olfaction, largely remains a mystery.

Among those aiming to solve it is Jonathan Victor, MD '80, PhD, the Fred Plum Professor of Neurology in WCM's Feil Family Brain and Mind Research Institute. Victor is part of a team of researchers that last fall received a \$6.4 million grant from the National Science Foundation aimed at uncovering the universal algorithms at work in the nervous system when animals use olfaction to navigate. An understanding of this neural circuitry could shed light on the human brain-and spur the development of technology to replicate the services that animals provide, thus keeping highly trained and often valuable animals out of dangerous situations. Other potential applications could lie in medicine or agriculture; for example, Victor says, "if we understand how insects use smell to navigate, we have the potential to alter their navigational strategy-for example, by selectively altering the neurons that carry out crucial computations-so that they could no longer search for us effectively."

The question at the heart of the project is how circuits and networks of neurons execute complex calculations related to smell. Is an animal using temporal cues, spatial cues, or a combination? Is it using its own life experience, or an innate understanding of the physics of odor and wind? As Victor puts it: "Do circuits carry out a function because of specialization at the synaptic level, the cellular level, the circuit level—or a combination of the above?"

The seven investigators, from institutions across the U.S., comprise experts in such fields as psychology, engineering, applied mathematics, and computational neuroscience. They

will quantify "odor plumes"—the way odors move in space—and measure how animals behave in response to them. The team includes researchers who study this response in humans, dogs, cockroaches, terrestrial mollusks, and hermit crabs; neuroscientists who work on mouse and

fly models; and a physicist who specializes in the dynamics of plumes. Victor brings to the collaboration a combination of mathematical and experimental approaches he has developed in work on taste and vision. "Olfaction is not only a matter of distinguishing one chemical from another," he explains. "The nervous system has to figure out how to move through space, sample this complex spatial pattern, and make decisions based on it. It was a total eye-opener to realize how interesting and challenging a problem this is."

The investigators came together under unusual circumstances. In a new funding method, the NSF invited thirty researchers from branches of biology, physics, and math to participate last summer in a five-day "Cracking the Olfactory Code" Ideas Lab workshop—an event that Victor describes as an odd combination of "what you might consider a high school mixer, 'American Idol,' and 'Survivor.' " The first couple of days included social exercises for scientists to meet and greet, as well as a form of "speed dating" in which participants would chat with someone for two minutes and then move on around a circle. Potential

'It was a total eye-opener to realize how interesting and challenging a problem this is.' collaborators were encouraged to think about big-picture questions they'd like to answer, and by the end of the week half a dozen groups had emerged to draft project proposals.

Soon after, the NSF selected three of the groups to share \$15 million it had

received through the federal government's BRAIN (Brain Research through Advancing Innovative Neurotechnologies) initiative, which President Obama announced in 2013. By studying different organisms, Victor's team expects to find a general strategy that transcends individual systems. "The brain of a fly, for example, has a profoundly different structure than the brain of a mouse, not just in size but in layout; the parts of one do not correspond to the parts of the other," Victor says. "Nevertheless, they both manage to implement the computations that allow them to navigate by smell."

- Andrea Crawford



TALK OF THE GOWN

Quality Control

Paul Casale, MD '82, is the new head of WCM's accountable care organization



Paul Casale, MD '82

'ACOs benefit patients by enhancing the coordination of care, improving quality of care, and reducing costs.' or the new executive director of the accountable care organization (ACO) of Weill Cornell Medicine, NewYork-Presbyterian, and Columbia University Medical Center, assuming the leadership of NewYork Quality Care is a homecoming of sorts. Interventional cardiologist Paul Casale, MD '82, not only earned his medical degree at WCM, but he completed his internal medicine residency at NewYork-Presbyterian/Weill Cornell before going on to a fellowship in cardiology at Mass General. Casale, who also holds a master's in public health from Harvard, comes to the post from Lancaster General Health/Penn Medicine, where he served as chief of the Division of Cardiology and medical director of quality. A national leader in the development of high-quality population health programs, Casale has more than three decades of experience in the field at the local, state, and national levels. Founded in January 2015, NewYork Quality Care comprises 4,000 physicians and serves some 30,000 Medicare beneficiaries.

Could you explain in a nutshell what an accountable care organization is?

An ACO is a group of physicians, often coordinating with a health system, who take responsibility for providing high-quality care for a population of patients. Implementation of ACOs has been a major initiative of the Centers for Medicare & Medicaid Services as it moves away from fee-for-service to a value-based payment system.

Why are ACOs important?

The rise in the cost of healthcare in the U.S., and the Medicare program in particular, continues to be a significant contributor to the national deficit. There is agreement that these rising costs are unsustainable, and the ACO is one of the building blocks in the movement toward a value-based payment system. In that arrangement, physicians are aligned with the health system in looking for ways to improve quality, enhance the coordination of care, and eliminate duplication of services.

Why do you think it's vital for WCM to participate in an ACO?

ACOs have been established across the U.S. in community-based health systems as well as large academic health organizations. Our ACO, NewYork Quality Care, is a combination of three entities—Weill Cornell, Columbia, and NewYork-Presbyterian. These three institutions are world leaders in providing healthcare, and to be successful in a value-based payment system, we need to work together to achieve the "triple aim" as described by the Institute of Healthcare Improvement: improving the patient experience, improving the health of populations, and reducing per-capita cost of care.

In general, how do ACOs benefit patients?

ACOs benefit patients by enhancing the coordination of care, improving quality of care, and reducing costs. For physicians to understand how well they are caring for a group of patients, it requires access to accurate and timely data on the quality and cost of care. Improving the ability of electronic health records to track performance measures and enhancing the information exchange among physicians and health systems will benefit patients.

Could you give an example of an outcome that illustrates how an ACO can help a patient?

When a patient suffers a heart attack, he or she enters the hospital and receives the needed care. A stent is placed in the blocked artery and the patient is discharged within a few days with new medications. Addressing behaviors that might contribute to him or her coming back with further heart problems is an important aspect of the follow-up care. For example, many patients with heart disease have diabetes or smoke. In our current system, patients receive counseling about diabetes management or smoking cessation during an office visit, but in an ACO a patient may receive additional care through an enhanced care management system, which often includes social workers, pharmacists, and community health workers. Pharmacists are an important member of the care team, because patients are often on a long list of new medications after a heart attack and are confused about why or how they should take them. In addition to the traditional home health nursing visits, in an ACO, a pharmacist or a community health worker could conduct a home visit to be sure the patient understands the correct medication dosing and the importance of the dosing schedule. It's extending the care a patient had in the hospital at the time of the acute event in order to manage the illness and enhance health.

How do you think WCM will benefit as an institution from participating in an ACO?

Putting patients first is always the priority in healthcare, and an ACO emphasizes a patient-centric approach. WCM's participation in an ACO will lead to better care coordination for our patients. WCM has a world-renowned Department of Healthcare Policy and Research, which has already written many important papers on the transition to a value-based payment system in the U.S. As we develop the ACO, there will be more opportunities for research using our own data to understand the impact of these payment models on patient care. In addition, WCM is educating the physicians of the future. This change in payment will be part of that future—not only in practice, but also as our alumni become leaders in their field.

How is NewYork Quality Care distinct from other ACOs?

Among the unique features of our ACO is the involvement of two world-class medical schools and one of the top ten hospitals in the country. There are challenges inherent in an ACO in an academic health system. One is that there are many medical students, residents, and fellows who help provide care—so there are more people who need to be educated and involved in the process of implementing new initiatives for the ACO. On the other hand, there are exceptionally bright physicians, nurses, and others who can be creative and innovative in helping advance ideas for care transformation in the ACO, as theory often doesn't translate into practice.

Are there ways in which having been a medical student and a resident at this institution will inform your approach to the job?

Interestingly, there are still quite a few people who were here when I was a student and a resident, and having those personal relationships is always helpful when leading change. My dedication to the success of the ACO is enhanced by the fondness and appreciation I have for the medical school and the hospital.

What do you find especially gratifying about practicing medicine in the context of an ACO?

As an interventional cardiologist, by the time my patients come to the cardiac catheterization laboratory, they may not have been managing their health very well—their diabetes, high blood pressure, cholesterol, smoking, and other life-style choices. After decades of practice, I see many patients come back to the cath lab for additional procedures. Although we can provide exceptional care with the advances in medical technology, there is much more to do in preventive care. For me, that's a growing passion—to develop tools to enhance prevention and health promotion. As we keep people healthy, we dramatically improve their quality of life.

— Beth Saulnier

'Among the unique features of our ACO is the involvement of two world-class medical schools and one of the top ten hospitals in the country.'

Medical History

A new book charts WCM's progress, from its nineteenth-century founding to the modern day



Building block: A ceremony marks the laying of the cornerstone at NYP/Weill Cornell on June 12, 1930.

he history of Cornell University Medical Collegenow Weill Cornell Medicine-is essentially the history of modern medicine," Dean Laurie Glimcher, MD, observes in her foreword to a new book that follows the college from its 1898 founding in rented rooms to its present status as one of the country's leading academic medical centers. As Glimcher observes, Weill Cornell Medicine: A History of Cornell's Medical School (Cornell University Press) begins in an era when general anesthesia was still not universal and heroin was considered a nonaddictive painkiller. But even as the book, written by Dean Emeritus Antonio Gotto Jr., MD, and his longtime editorial administrator Jennifer Moon, PhD, traces the growth of the college and the evolution of medical education through an era of rapid scientific advances, it also tackles more than a century of urban crises, international controversies, and public events from two world wars through the attacks of 9/11."There has always been an interweaving of the college's history and the history of New York and the United States," Gotto says. "Whether our faculty and students were fighting a cholera epidemic in the city or protesting the Vietnam War, the medical college has both shaped and been shaped by what was happening in society. We wanted this book to reflect that."

Gotto, the medical school's dean from 1996 through 2011, began work on the book soon after he stepped down from that post. He had become interested in the college's history through one of its most important early figures: Canby Robinson, who served as dean of Gotto's alma mater, Vanderbilt University Medical School, before coming to Cornell for a brief and controversial tenure from 1927 to 1934. Robinson oversaw the construction of what's now NYP/Weill Cornell, but conflicts with faculty members and the financial pressures of the Great Depression led to his departure—and he remains one of the only deans without a portrait hanging in the college. Says Gotto: "Learning about Canby Robinson made me wonder how other deans throughout our history had dealt with all our recurring challenges, and I wanted to piece together their experiences."

For help, Gotto turned to Moon, who holds a doctorate in American culture and has worked in administrative and editorial roles at the college since 2002. While brief overviews of WCM's past had been written over the years for anniversary events, there was no comprehensive history to draw upon, so Moon delved into the Medical College's archives and its wealth of records, as well as coverage from the *New York Times*, personal interviews, and other external sources. "We found that some of the same issues come up over and over in Weill Cornell's history—our relationships with other institutions, the difficulty of finding space for a growing medical center in New York City, the need for philanthropy," Moon says.

At the same time that the book follows these through-lines, it also highlights the defining moments of each era in the college's history, for good and ill. Weill Cornell was coeducational from its founding, and its early graduates included public health pioneer Connie Guion, MD 1917. During World War II, it served the nation by joining with New York Hospital to form the first hospital unit to be stationed in the South Pacific combat zone; in the Fifties, faculty participated in a mind-control research program run by the CIA. Gotto and Moon don't shy away from recounting the protests surrounding the Shah of Iran's treatment at NYP/Weill Cornell in 1979 or the death of Libby Zion in 1984, which led to a grand jury investigation, a civil trial, and a reevaluation of the conditions in which residents and interns worked. "We couldn't

'There has always been an interweaving of the college's history and the history of New York and the United States.'

present only the positive in our history," Gotto says. "To tell the story from the perspective of the college's leaders, we had to be accurate about what they were dealing with."

Those leaders are presented in short, self-contained biographies that appear throughout the book, and some extraordinary characters emerge. The college's first dean, charismatic Southerner and demanding micromanager William Polk, MD, was described as ruling the medical school "with gentle fury" by Cornell University historian Morris Bishop '14, PhD '26. Joseph Hinsey, MD, was dean during World War II, when Cornell ran an accelerated program to produce new battlefield physicians and medical students marched in formation along York Avenue. J. Robert Buchanan, MD '54, who served from 1969 to 1977, was instrumental in obtaining the air rights over FDR Drive that allowed for the expansion of NYP/Weill Cornell. The book also offers cameos of figures such as George Papanicolaou, MD, famous for the Pap smear but also the coauthor of a study infamous among Prohibitionists for its investigation of drunken guinea pigs. (The research showed no long-term ill effects of alcohol use.)

Weill Cornell Medicine: A History of Cornell's Medical School is punctuated with this kind of detail, as well as archival images, such as a dissecting classroom in the 1930s (complete with skeletons). As the book progresses to more recent years—including Gotto's own tenure—readers can learn the stories behind the renaming of the medical college for Sandy and Joan Weill, the founding of the Qatar campus, and the establishment of an affiliation with Houston's Methodist Hospital. "Alumni may turn to the book to learn more about the period when they were students here, but I think that they'll find surprises, too," Gotto says. "For me, it's been a very satisfying process, to see how Weill Cornell Medicine has been at the center of so much that's happened not just in medicine, but in the world." **Patients First**

The new history of WCM chronicles a then-revolutionary approach to clinical care

The establishment of the Cornell Pay Clinic, an innovative experiment designed to address the healthcare needs of the emerging middle class, helped extend the medical school's reach clinically. Created by Lewis Conner, MD,



one of the medical school's original instructors and a cardiologist who later cofounded the American Heart Association, it charged moderate fees and offered comprehensive clinical services to middle-income patients who could not afford private physicians but were not entitled to free care. A *New York Times* article announced its opening on November 1, 1921, and noted that it was "the first of its kind to offer general medical service in this city."

The decision to open the clinic was motivated by the results of a survey conducted by the Public Health Committee of the New York Academy of Medicine on the dispensary situation in New York City. The survey recommended the establishment of a clinic targeted at middle-class patients, which would be governed by a medical college or a hospital and involved in the teaching of students. Walter Niles, the medical school's second dean, described the needs of this segment of the population in the New York Times: "For some years there has been a growing recognition on the part of physicians, social workers, and others interested in public health that there is great need of some agency through which diagnosis and treatment by specialists can be brought within the economic means of persons of ordinary income. The great proportion of the city's wage earners are self-supporting, but they do not have sufficient margin of income to pay the office fees of specialists. It is estimated that more than two million persons in Greater New York are faced with the alternative of accepting charity or going without the skilled medical attention which their condition may demand."

The new clinic received a flood of media attention when it opened and was soon overwhelmed by visits. On its first day of operations, the clinic's seventy-six physicians treated more than 250 patients and scheduled appointments for 750 more the following week. In order to maintain the quality of service, the clinic had to turn away a large number of patients. Still, 18,803 people were seen during the clinic's first five months, and many returned for repeat visits, mostly for the treatment of chronic diseases.

Other facilities, including the Neurological Institute of New York, the Brooklyn Hospital Dispensary, a diagnostic clinic at Massachusetts General Hospital, and dispensaries in Chicago and Cleveland, were similarly geared toward middle-class patients, although they were not called pay clinics. What was unique about the Cornell model was that it offered both diagnosis and treatment, provided by a wide variety of specialists in a private office environment. This allowed for a personal relationship between doctor and patient—an amenity typically available only to the wealthy at that time.

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There's an App for That

Medical research expands to Android devices



Deborah Estrin, PhD

ast year, Apple unveiled a new platform that offers a streamlined way to create mobile applications linked to medical research. The technology, called ResearchKit, lets investigators more easily connect with the people whose diseases they're studying, allowing them to gather feedback on symptoms, as well as data on everything from a patient's weight to the air quality where they live. "When you can collect real-time information, you don't have issues with recall or bias," says Deborah Estrin, PhD, a professor of healthcare policy and research at WCM. "If you ask somebody how much pain they had over the last two weeks—as is typical in a doctor's appointment—they will answer the question differently than if you ask them how much pain they had today."

Five apps—focused on tracking such diseases as asthma, type 2 diabetes, and breast cancer—launched soon after ResearchKit was released; today there are more than a dozen, each free for study participants to download and set up to securely transfer the collected data back to the medical institution running the study they're in. But as Estrin points out, ResearchKit has a major draw-

back: less than 50 percent of smartphone users in the U.S own an iPhone and could therefore participate in the studies. Plus, iPhone users aren't a representative sample of the population, tending to be wealthier, more educated, and less racially diverse.

Wanting to address that disparity, Estrin developed a complementary version for Android, dubbed ResearchStack. Like ResearchKit, it will let programmers create apps connected

to medical research, but specifically for Android devices, whose owners tend to come from a wider spectrum of socioeconomic and ethnic groups. "The idea is to take advantage of the great data-collection instruments many of us hold in our purses or pockets," says Estrin, also a professor of computer science at Cornell Tech, "and to promote and enable these large-scale research studies across a larger segment of the population." After a beta test that began in February, ResearchStack 1.0 is set to be released this spring. The first app to be developed with it is Mole Mapper, which allows users to photograph their skin moles and track how they change and grow over time. It was created by a researcher now working at the National Cancer Institute in collaboration with Sage Bionetworks, a nonprofit that facilitates open science. The app—which already has an iPhone version—collects real-time data and sends it to melanoma researchers at the Oregon Health and Science University. The idea is to help users figure out when a mole has changed enough to require a medical evaluation, to foster early detection of malignancy, and to help researchers create better algorithms for melanoma diagnosis. Additional Android-compatible versions of all the ResearchKit projects are sure to come, Estrin says.

Estrin notes that the advent of ResearchStack is likely to make these study-facilitating apps more appealing to investigators studying all types of health conditions. Now that researchers are able to conceive apps that can be customized

> to work with both Apple and Android devices—thus allowing them to tap into much larger pools of participants—they will have stronger justification for seeking funds to develop them, which can be significant. "Increasingly, this will be the way that we conduct research," Estrin says. "With these apps, you're able to see how disease symptoms play out in the wild, and look at responsiveness to treat-

ments outside of the clinical setting. You can ask patients to check in much more frequently than you'd ever be able to through in-person appointments—and during those checkins, to not only share how they're feeling, but also provide useful information about their condition. That's the power of the smartphone."

'The idea is to take advantage of the great data-collection instruments many of us hold in our purses or pockets.'

Sterile Field

A physician-entrepreneur aims to make surgery safer in the developing world

ames Bernstein, MD '64, still has a note that Jonas Salk, MD, gave him when he was managing his lab at the legendary researcher's institute in La Jolla, California. "It needs help to happen," the message says, "and you are one who has been 'called.'" Salk, of course, is the physician-scientist who developed the first safe and effective polio vaccine, sparing untold millions from the crippling disease. That handwritten missive, Bernstein says, was a directive "to do something really big that would have an impact on lots and lots of people."

Now Bernstein—a surgeon, internist, and medical entrepreneur based in Washington, D.C.—is poised to follow his late mentor's advice. This spring, his company, dubbed Eniware, is launching a portable sterilizer that could save thousands of lives in developing nations where electricity is unreliable or non-existent and there is no practical way to sterilize surgical tools.

To understand the need for Eniware's device, Bernstein says, it's important to note that disinfection and sterilization are not the same: even when instruments are boiled or soaked in bleach for long periods, spores can survive. In refugee camps and field clinics—even in hospitals in impoverished nations—thousands die from post-operative infections, making relatively routine procedures like appendectomies and C-sections potentially life-threatening.

Louis Pasteur figured this difference out in the

late nineteenth century, when he invented the autoclave. But autoclaves, which destroy microbes using technology similar to that of a pressure cooker, require large amounts of electricity and distilled water. What makes Eniware's sterilizer different, and potentially impactful, is its use of nitrogen dioxide (NO2) gas, which sterilizes at room temperature. The results of a feasibility study, which Eniware funded, were published in *PLoS One* in June. It found that the technology "is well suited for low-resource environments and can sterilize challenging medical devices."

The Eniware device, called the Portable Sterilizer-25 Liter (PS-25), looks like a big black suitcase with a knob on the top. The interior contains a rack that holds surgical instruments inside pouches, which have indicators confirming exposure to the sterilizer. A chamber for a NO2-generating cartridge releases the gas, which is removed at the end of each cycle by an internal scrubber before the unit can be opened. The rugged kit requires no other supplies, and no electricity, heat, or water. The unit—which will be priced under \$2,000—can sterilize as many as a dozen instrument sets at once for less than \$20. Bernstein says the device would typically be used 300 to 500 times, at an annual cost of under \$5,000. "That is offset by the cost savings in avoiding the dire outcomes of sur-

gery with unsterile instruments; the PS-25 compares favorably to disposable surgery kits, which can cost as much as \$100 per set to use and dispose," he says. "We're using new technology that is portable and inexpensive to address a global problem." — *Franklin Crawford*



Open and shut case: James Bernstein, MD '64.

with the Eniware portable sterilizer. Below right: Jonas Salk's note to Bernstein.

TRANSFORMING CANCER CARE

Weill Cornell Medicine scientists are coaxing the immune system to fight back against tumors

BY ANNE MACHALINSKI

PORTRAITS BY TIFFANY WALLING / GETTY IMAGES FOR WCM

hen Ty Williams was diagnosed with stage IV prostate cancer in June 2011, he responded well enough to treatment that he could continue managing a corporate banking group without having to slow down or tell many of his colleagues that he was sick. But about two years later, that changed, as his once-stable disease started progressing rapidly. "When we looked at my scans, my wife and I were shocked," says Williams, now sixty. "It was obvious that the cancer had gotten much worse, and that we needed to do something really aggressive if I wanted to live."

Williams's oncologist, Scott Tagawa, MD, MS '10, the Richard A. Stratton Associate Professor in Hematology and Oncology at Weill Cornell Medicine, enrolled him in a clinical trial, which involved combining chemotherapy with an experimental method of delivering a toxic payload "directly into the tumor cells, regardless of where they are," says Tagawa, a member of the Sandra and Edward Meyer Cancer Center at Weill Cornell Medicine. For this to be possible, scientists had to harness a mechanism used by the immune system to find and suppress pathogens. They reprogrammed a protein that typically locates and neutralizes viruses or bacteria to instead seek out prostate cancer cells. They then attached a radioactive agent to it, which would be delivered directly into the cancer cells after the protein attached to its target, says Tagawa, an oncologist at NYP/Weill Cornell. For Williams, this cancer-seeking poison arrow, called a radiolabeled monoclonal antibody, "completely turned things around." Today, while he continues to see Tagawa once a month and regularly undergo treatment, his disease is more controlled—and chronic—than terminal, he says. "When I tell people I have cancer, it's the last thing they would ever believe," Williams says. "Even my family forgets I'm sick sometimes."

Based on success stories like his, immunotherapy is now considered the "fifth pillar" of cancer therapeutics, joining surgery, radiation, chemotherapy, and precision-targeted therapeutics. While the latter four attempt to remove or attack cancer cells directly, treatments under the immunotherapy umbrella harness >





Monica Guzman, PhD

Cancer immunotherapy traces its roots to the early 1890s, when a surgeon infected patients with strep bacteria in the hope that they'd have a strong response that might eradicate their tumors. a patient's own immune system to attack their disease from within. Today, scientists are making significant advances, offering patients with many types and stages of disease the chance of a lasting and dramatic remission.

But while there's a lot of excitement about immunotherapy's potential, these developments in no way mean that cancer will be rendered obsolete anytime soon. This is because, at least right now, only 10 to 30 percent of patients respond to these treatments, and in many cases, scientists don't understand why. With more research and clinical advancements, experts think that instead of finding a cure for cancer, we'll see more patients living with a controlled disease in the coming years, thanks in large part to immunotherapy. "Now that we have better surgery, less severe and more targeted radiation and chemotherapy, plus immune therapies, we are beginning to attack cancer in a scientific way rather than an empirical way," says Lewis Cantley, PhD '75, the Meyer Director of the Meyer Cancer Center and a professor of cancer biology in medicine. "Our goal is to figure out how to combine these therapies for each and every patient so that we can control their disease and help them live a healthy, normal life. Immune therapy is not going to be a cure-all for all cancer, but it's certainly going to be a remarkably good tool to use."

ancer immunotherapy traces its roots to the early 1890s, when New York-based surgeon William B. Coley, MD, infected patients with strep bacteria in the hope that they'd have a strong response that might eradicate their tumors. He had some success with this treatment, called "Coley's toxins," but never fully understood why it sometimes worked and often did not. Over the years, other scientists pursued aspects of his approach, with little success. It wasn't until scientists better understood how the immune system functions that they could research and develop smarter ways to use it to fight malignancies.

A major breakthrough in the field came from James Allison, PhD, now at MD Anderson Cancer Center in Houston. In the late 1980s, he discovered a protein called CTLA-4, which he found could inhibit the immune system's ability to alert fighter T cells —known for their ability to track down and kill pathogens—of tumor cells in their midst. Rendered invisible to the body's natural defenses, these tumor cells could multiply and thrive. Additional findings Allison made in the late 1990s led to the clinical development of the first-ever drug that blocks CTLA-4, thereby releasing the T cells' brakes, so that these immune cells are unleashed on the disease. His work to develop this type of drug, known as an immune checkpoint blocker, won Allison the Lasker Award— America's version of the Nobel—in 2015.

Immune checkpoint blockers are to date considered the most promising type of immune-based therapy. But scientists are studying other approaches as well. These include additional monoclonal antibodies, like the one used on Williams, which are programmed to find specific types of cancer cells and deliver medication directly to them; supercharged T cells, which are genetically altered in a lab to find tumor cells and tumor stem cells, and then multiplied into the billions before being infused back into the patient so that they can stage a massive attack; therapies to alter and engage the immune cell-rich area around tumors, called the microenvironment; and cancer vaccines, which would prevent the disease from developing in the first place.

Additionally, investigators are testing ways to combine immunotherapy with chemotherapy or radiation, and also studying how checkpoint blockers and other FDA-approved immunotherapy drugs might be used in earlier stages of the disease to produce the best outcome.

With new immune-based therapies and improved surgeries, radiation, and chemotherapy, death rates from cancer have dropped significantly in recent years. But doctors will still diagnose more than 1.6 million new cancers in the United States this year, and close to 600,000 people will die of the disease. Because only 5 percent of cancer patients will ever make it into a clinical trial, moving discoveries in labs into doctors' offices is critical.

Hope for Leukemia Patients

A promising form of immunotherapy involves the use of chimeric antigen receptor (CAR) T cells, which are genetically engineered to recognize a surface protein expressed on tumor cells. Currently, the T cells used in this type of treatment are taken from the patients themselves, a process that requires weeks of preparation before the cells are ready for infusion. Thus far, CAR T therapy has primarily been used in patients with acute lymphocytic leukemia (ALL); WCM has partnered with the drug company Cellectis to develop a form of the therapy for patients with acute myeloid leukemia (AML), the most common form of leukemia in adults. "Treatment with CAR T cells has shown impressive results in patients with acute lymphocytic leukemia, but the process of harvesting T-cells from sick leukemia patients can be logistically and clinically challenging," says Gail Roboz, MD, a professor of medicine. "We hope to be able to use T cells from healthy donors and engineer them to selectively attack CD123, an antigen present on AML stem cells."

Roboz, a member of the Meyer Cancer Center and an oncologist at NYP/Weill Cornell, is collaborating with scientists at Cellectis and with Monica Guzman, PhD, assistant professor of pharmacology in medicine, a leukemia stem cell expert. "Targeting stem cells in AML is important," says Guzman, "because most patients who go into remission relapse when the root of the disease-which can't be killed by standard chemotherapy-allows it to rise again and again." Guzman, who developed the first antileukemia stem cell therapies twenty years ago during her doctoral work at the University of Kentucky, says that a particularly exciting part of the Cellectis project is the possibility of faster access to engineered T cells by using healthy donors to generate an "off the shelf" product. Says Guzman: "For AML, which is incredibly fast moving, speed is important." She and Roboz hope the T-cells will grow and proliferate when their target is present, but slow down and eventually "commit suicide" when their target is eliminated. "The project is using breakthrough technology," says Roboz, "and the results have been exciting."

'Bridging the Gap'

Nasser Altorki, MD, head of the clinical lung cancer program and the Gerald J. Ford–Wayne Isom Research Professor in Cardiothoracic Surgery, is considering two clinical trials that would test various immune-based approaches to treating lung and esophageal cancers. One of those would use immune» With new immune-based therapies and improved surgeries, radiation, and chemotherapy, death rates from cancer have dropped significantly in recent years.



Nasser Altorki, MD

checkpoint inhibitors on pre-surgical patients with early-instead of advanced-disease. Some would get these inhibitors alone, while others would get them with "a very tiny dose" of radiation therapy, says Altorki, a member of the Meyer Cancer Center. After the cancer is removed, investigators would be able to compare the changes that occur before and after treatment, in the hope of better understanding why only a small percentage of patients currently respond to these therapies and whether addition of a tiny dose of radiation improves the results. A similar investigation would look at patients with esophageal cancer, and compare those given immune checkpoint blockers and chemotherapy before surgery to others who get those treatments plus radiation. Again, the goal would be to find out why some patients respond when others do not. "Asking these questions is very important, because it allows us to bridge the gap between laboratory research and patient care," says Altorki, a cardiothoracic surgeon at NYP/Weill Cornell. "We hope to ask very specific questions that we believe would lead to an improvement of the treatment paradigm."

Tumors into Vaccines

A final—and next-generation—area of immunotherapy research at WCM is focused on seeing how immune-based approaches might be able to enhance other types of therapy. Silvia Formenti, MD, chairman of radiation oncology and the Sandra and Edward Meyer Professor of Cancer Research, focuses on immunotherapy paired with radiotherapy, and how the latter might help the former transform patients' tumors into personalized vaccines directly at the site of their disease. Formenti says that a decade ago-before she arrived at WCM in April 2015-she started noticing that many of the effects of radiotherapy on tumors were in fact mediated by the immune system. "At that time, there were occasional reports in the literature that when a spot on the lung was treated with radiotherapy, the doctor would also see an effect far away-like in the liver," says Formenti, associate director of radiation oncology at the Meyer Cancer Center and radiation oncologist-in-chief at NYP/Weill Cornell. She thought this extremely rare occurrence might be caused by the immune system, which was somehow > continued on page 35

Targeting Pancreatic Cancer

Can immune suppression be reversed?

Douglas Fearon, MD, the Walter B. Wriston Professor of Pancreatic Cancer Research, is considering a new clinical trial to test whether a drug called AMD3100 can reverse the immune suppression process at work in the pancreatic cancer microenvironment. Unlike many other cancer types, pancreatic cancer has shown no response to immune checkpoint blockers. This is because the immune suppression mechanism at play affects fibroblastic stromal cells in the tumor's microenvironment, which then block T cells' entry to the tumor region, rather than affecting the T cells themselves. In recent animal models, administering AMD3100 to overcome the block to T cell accumulation in pancreatic cancer has meant that the T cells can do their work and destroy the tumor. Based on this finding, gastrointestinal oncologist Tong Dai, MD, PhD, an assistant professor of medicine, and Manish Shah, MD, the Bartlett Family Associate Professor in Gastrointestinal Oncology-both members of the Meyer Cancer Center-are hoping to direct the U.S. component of a phase 1 clinical trial that has been initiated in Cambridge, England, to test the drug's safety. This trial will determine whether the drug improves the tumor's immune response by comparing a pre-treatment biopsy to one collected post-treatment. "If it works out and if we uncover this fundamental reason why tumors suppress an immune attack, I think we'd find some of the same characteristics in lung cancer, colorectal cancer, prostate cancer, and others," Fearon says.

<image>

Manish Shah, MD

Modulating the Microenvironment Researchers attack a tumor's habitat

CAR T cells are currently demonstrating impressive activity against liquid malignancies, but these engineered T cells have shown minimal effects in solid tumors due to the immunosuppressive strategies at play within the mass itself. "When you surgically remove an ovarian tumor from a patient, more than half the mass is made up of non-cancerous cells," says Juan Cubillos-Ruiz, PhD, an assistant professor of microbiology and immunology in obstetrics and gynecology. Known as the tumor microenvironment, this noncancerous material contains endothelial cells that provide blood to the tumor, stromal cells that secrete growth factors, and also immune cells-which, in ovarian cancer, can comprise up to 40 percent of the whole. So what are those immune cells doing there, and why aren't they successfully attacking the cancer? "Because of several cancer-derived factors, these immune cells, which were the first responders and originally protective,



are made dysfunctional and instead help the tumor grow," says Cubillos-Ruiz, a member of the Meyer Cancer Center. In recent years, it's become clear that this process of turning immune cells pro-tumoral isn't unique to ovarian cancer, but is also found in breast cancer, lung cancer, and other solid tumor types as well. That's why Cubillos-Ruiz's team is investigating new strategies to modulate the tumor microenvironment and harness the protective function of immune cells within it, which he calls a "Trojan horse" approach.

In ovarian cancer, a tumor's toxic microenvironment modifies proteins located in the endoplasmic reticulum—the network of membranes that controls folding and secretion of proteins—which in turn triggers a transcription factor known as XBP1. Once it's activated, dendritic immune cells, which would typically alert T cells to fight an intruder, are turned off, and the tumor can thrive without anything to slow its growth. This process, known as the ER stress response, might be controlled if nanoparticles containing a XBP1-silencing molecule are injected at the tumor site, Cubillos-Ruiz explained in a groundbreaking paper published in *Cell* last summer, with Dean Laurie **>**

Juan Cubillos-Ruiz, PhD

Cubillos-Ruiz's team is investigating new strategies to modulate the tumor microenvironment and harness the protective function of immune cells within it, which he calls a 'Trojan horse' approach. Glimcher, MD, as senior author. Now, they're trying to find out if the same process occurs in other types of cancer, while working to develop a potent inhibitor that could one day be used in patients to shut down that pathway. Says Cubillos-Ruiz: "A drug like that would be a double-whammy strategy against cancer."

ivek Mittal, PhD, an associate professor of cardiothoracic surgery and of cell and developmental biology, is another scientist studying the role of the tumor microenvironment in mediating immune suppression in lung cancer. Mittal is identifying various modes that lung tumors use to elicit immune-suppressive pathways, and harness this information to tailor specific therapies to shut them down-which has led to combination immune therapies to hit the two or three most dominant pathways at the same time. Immunotherapies are also being combined with standard-of-care

chemotherapy, radiation therapy, and targeted therapies. Because all of this knowledge is coming from the tumor's microenvironment-not the cancerous cells themselves-it's like looking at the entire galaxy in relation to how it impacts one planet, Mittal says. His studies rely in part on active collaborations with surgeons, who often remove a full lobe of the cancerous lung that includes not only the tumor nodule, but also adjacent normal tissue. "From the same patient, we can compare a normal immune cell to its counterpart inside the tumor, and can identify what is being activated and what is being suppressed," says Mittal, a member of the Meyer Cancer Center. "By finding out more about how specific immune cells under the influence of the tumors might be contributing to the cancer's progression, we're uncovering new potential targets for therapies."



Vivek Mittal, PhD

'From the same patient, we can compare a normal immune cell to its counterpart inside the tumor,' Mittal says, 'and can identify what is being activated and what is being suppressed.' called to attention by the radiotherapy. From there she had an idea. "Maybe in some patients, when you irradiate one of the lesions, it will not only help the tumor respond and convene and kill some cells, but also acquire a memory that can be applied to regions away from the field," Formenti explains. "Somehow radiation will turn the tumor into a vaccine."

hile this approach will only work in a minority of patients, the effect can be prolonged and dramatic, Formenti says. One patient, whom she calls "Mr. P," had metastatic lung cancer, which had spread to his liver and bones; he came to her in 2012 for palliative radiotherapy in his hip. Before his appointment, he'd stumbled upon a story about her research using radiotherapy with immune checkpoint blockers in mice and, ready to enter hospice care, he begged her to try it on him. After treating one small lesion that was nowhere near his lung, "literally everything he had-everything-went away," Formenti says. Today, he is still healthy and disease free, and has never had another treatment. Since then, she has run a study with patients like him, and found that one out of three patients respond to this treatment, which shrinks their tumors or stops them from progressing when they weren't responding to chemotherapy. Now, she's working with a \$1.6 million grant from Bristol Mevers Squibb to combine two immune checkpoint blockers with radiotherapy in a trial to treat patients with metastatic disease and multiple tumors. She's leading three additional clinical trials at WCM, each combining immunotherapy with radiotherapy, and is both the principal investigator on an NIH-funded project and the leader of a Department of Defense breast cancer research program focused on combining radiation and immunity. And she is also part of a new strategic, preclinical research alliance with one of the Janssen Pharmaceutical Companies of Johnson & Johnson to develop new treatment approaches for various types of cancer.

While Formenti pioneered this field, she is no longer alone: there are now eighty-one clinical studies in the country combining immune-based therapy with radiotherapy. "We're in a huge immune-oncology revolution right now," she says, "and pharma is taking this on with the speed of light." But while there's a lot to be excited about, Formenti says, there's still a lot of work to be done. "We're looking at more and more targets for immune checkpoints, and for each of them, we'll have to figure out the best way to incorporate radiation," says Formenti, who is collaborating with cancer immunologist Sandra Demaria, MD, interim assistant professor of radiation oncology. "We'll need to design trial after trial until we find the correct way to do it."

Indeed, researchers have much yet to accomplish, including establishing the correct doses and protocols. At the same time, the healthcare system must address the often-astronomical price tag of immune-based drugs, which can cost into the hundreds of thousands of dollars per year. Despite these challenges, physicians and scientists have high hopes for future breakthroughs. "Immunotherapy is something that has captured the imagination of doctors and patients for decades, and for the very first time, we now have immune-based treatments that are working," Altorki says. "Hopefully this new phase of immunotherapy is the first leg of a sustained ascent."

'His Scans Look Great' For one patient, a terrific response

Seventy-eight-year-old Stanislaw Sniarowski of Bay Ridge likely wouldn't be alive today if not for an immune-based drug. A year ago, he was prescribed Opdivo to treat his stage IV lung cancer. Known as a checkpoint inhibitor, Opdivo works by reactivating T cells to detect and attack tumor cells, a response that his cancer had stunted. Opdivo received FDA approval in March 2015 for use in patients with advanced stage squamous non-small cell lung cancer after chemotherapy, and additional FDA approvals for similar immune-based drugs targeting lung cancer have followed. In the short time that these drugs have been commercially available, Sniarowski's oncologist, Ronald Scheff, MD, says they've already made a big impact among the fifty or so patients he's used them on. "Like a lot of treatments for lung cancer, only a certain number of patients are going to respond," says Scheff, an

More than two years after diagnosis, Sniarowski is 'back to doing normal activities,' his oncologist says.

assistant professor of clinical medicine and a paid consultant to Bristol Meyers Squibb, which makes Opdivo. "But for those who do, they can respond for a very long time."

Sniarowski, who Scheff calls "one of our superstars," had multiple recurrences of his lung cancer, which had initially been removed surgically, and was too sick to do much on his third type of chemotherapy; then Opdivo hit the market. Now, more than two years after diagnosis, "his scans look great, he's gained weight, and he's back to doing normal activities," says Scheff, a member of the Meyer Cancer Center and an oncologist at NYP/ Weill Cornell. Among those is dog-sitting his son's German shepherd and taking regular weekend trips to the Poconos. "He's not nauseated, there are no headaches—the treatment is like taking a vitamin shot," says his son, Mariusz Sniarowski. "Considering his condition and his age, he's doing great."

Resistance Novement

Carl Nathan, MD, is a leading voice in the campaign to develop new antibiotics—and conserve the ones we have

BY BETH SAULNIER PORTRAIT BY JOHN ABBOTT



ast fall, New York Giants tight end Daniel Fells suffered an ankle injury during practice. He later spiked a temperature of 104 and was rushed to the hospital, where doctors found that the wound was infected with methicillin-resistant *Staphylococcus aureus* (MRSA). As worried fans followed Fells's struggles in the media, he underwent multiple surgeries to excise the potentially deadly strain of bacteria, which doesn't respond to most antibiotics. While doctors were able to save his foot—and his life—his future in football remains uncertain.

For Carl Nathan, MD, stories like Fells's underscore a threat that he has devoted a great deal of energy to publicizing and combatting. For more than a decade, he has been advocating the development of new antibiotics and measures to curb the over-use that drives the evolution of drug-resistant strains.

The R.A. Rees Pritchett Professor of Microbiology and one of the world's leading authorities on tuberculosis, Nathan has written numerous academic articles on antimicrobial resistance—including pieces in *Nature, Nature Medicine, Science Translational Medicine,* and the *New England Journal of Medicine*—and been a global thought leader on the subject in the research community and beyond. But he notes that cases like Fells's are far more effective at making both average Americans and government officials understand the issue's urgency. "It makes no impact to talk about the threat numerically and statistically, with epidemiologic arguments," says Nathan, who marks his thirtieth anniversary at Weill Cornell Medicine this spring. "What gets people is the individuals: the face, the name, the personal story."

Why are you particularly interested in drug-resistant microbes?

I don't think it's hard to be interested; I think it's hard to justify ignoring it. We're not making new antibiotics, and each one that we have is becoming progressively less useful as resistance rises. People with bacterial infections are moving around more without adequate public health control measures. It's hard not to be alarmed.

What will become of modern medicine without antibiotics? Just think about it: Not only will people get pneumonia and die often rather than rarely, but consider elective surgery. Are you going to want to have your hip replaced if you can't protect against operative-associated infections? What's going to happen to trauma surgery? Or soldiers who live close together in barracks, and meningococcal disease spreads and you can't treat it? What about premature babies? What about cancer chemotherapy? It goes on and on.

How big a problem is this in the U.S.?

In this country, an estimated 23,000 people a year die from bacterial infections that used to be treatable and now are not. Gonorrhea, for example, was originally the easiest bacterial infectious disease to treat; it took a single injection of penicillin to cure it. There are now cases of gonorrhea in this country—somewhere between 1 and 5 percent—that you can't treat with anything, leading to pain, infertility, arthritis, and even death. Globally the

problem is much bigger. There are about a dozen species of bacterial pathogens where you now have some clinical isolates that are resistant to every antibiotic available.

Would you give an example of a global threat?

Probably the dominant form of antimicrobial resistance is expressed by *Mycobacterium tuberculosis*. This is the single leading cause of death from a bacterial infection in the world, even though it is curable—and to put those two things in the same sentence constitutes a societal indictment. In this country, we have very few cases of multi-drug-resistant tuberculosis [MDR-TB], but I just came back from Haiti—four hours away by plane—where they diagnosed about 16,000 new TB cases in 2014 alone, and hundreds of them are multi-drug-resistant. The fatality rate of MDR-TB in many places is about 70 percent. Treatment takes about two years and the drugs are toxic. The average patient is taking twelve to seventeen pills a day, plus a painful injection.

Is it hard to rally activism around this issue?

It is. This isn't a disease like HIV/AIDS, where there was a community of people who were afflicted and formed lobbying groups, protested, and demanded more funding. Here you have isolated people with no particular demographic to tie them together. They're not hemophiliacs, they don't have cystic fibrosis; they could be anybody or everybody. These are scattered, tragic events. And when they involve celebrities, are particularly gruesome, or the person who's affected is particularly photogenic or heartrending, they come into the news. If I were allowing myself to be cynical, I would say that when members of Congress or their loved ones are affected, this will move very quickly.

So what are you calling for?

Two things. One is an oversight structure, and another is cooperative research between the private, academic, and government sectors to overcome some of the obstacles for developing new antibacterials.

How would such an oversight agency be structured?

It isn't entirely clear, but the first issue is that these problems are global. Resistance moves in waves from one place to another, and it's futile to try to control it by only looking within a given nation. So there needs to be a global surveillance network where data are collected in a scientifically meaningful way and shared. Drug companies are almost exclusively multinational, so there needs >



A scanning electron micrograph shows the interaction of MRSA bacteria (in red) with a human white blood cell.

to be a coordinated effort on how to solve the economic problem that's facing antibiotic development. It basically means making a reward structure that is not dependent on the traditional one, because the opportunities for return on investment are so much smaller than for other classes of drugs that there are almost no companies left that have chosen to continue antibiotic discovery.

Why is it so hard for a company to make a profit on an antibiotic?

There are several reasons. There's a high rate of failure during the drug discovery process—and once the drugs are released, they're lost to resistance relatively quickly. Also, they're often curative in a relatively short time. A typical antibiotic course can be one to ten days, as opposed to lifelong for many other kinds of drugs, so the opportunity for making money is very limited.

With overprescription of antibiotics helping to drive resistance, could you describe the most common ways in which the drugs are misused?

In this country well over half the antibiotics produced are used in the food industry; they're administered to healthy animals, fish, and plants to increase production. Another problem in this and many other countries is overprescription of antibiotics to humans without diagnosis; most prescriptions are dispensed for viral infections where they have no benefit. A terrible problem overseas, especially in China and India, is profitmaking by doctors for writing prescriptions. Here at home, the doctor is paid for providing care, and the pharmacist and drug company make money from the prescription. In those countries, the doctor is selling the antibiotic and has an incentive to prescribe frequently and abundantly, and that's exactly what's happening.

If you're advocating for major cuts in antibiotic use in livestock, might that not face serious opposition from agriculture?

The argument is that it will raise costs and lower production but in parts of Europe that have banned using antibiotics relevant to human medicine in healthy animals for food production, those fears were not realized. Congress and the FDA have moved toward regulation, but for political reasons they've been unable to go the distance.

What words of wisdom do you have for the American pediatrician on the front lines, facing parents who demand she prescribe antibiotics for their sick child, even though she's quite sure it won't help?

I have great sympathy for her, and I'm not trying to tell her what to do, because her responsibility is to the patient and to weigh all the factors involved. Such as, if she offends the parents, they may not come back when it's really necessary, and there could be adverse effects on the child's health or even their life. I don't think the onus is on her.

Then what's the solution?

Quick, accurate diagnostics that can be used at the point of care. Then, that pediatrician can say to the parents, "Your child has reovirus, and unfortunately we don't have anything for it. An antibiotic is most likely to disrupt the healthy bacteria that help your child's immune system develop, so actually that might be harmful." I think that conversation would go very differently than, "I don't know what your child has, but I'm not willing to guess that it might be a bacterial infection, so I won't give you an antibiotic." If you have a diagnostic test that informs you about your patient's sample, that changes the equation.

Besides diagnostic testing and reducing antibiotics in food production, what can be done in the U.S.?

We can make efforts at conservation, which includes correct prescription. We can reduce the need for antibiotics by following appropriate procedures of hygiene and sanitation; for example, handwashing by medical personnel. We can encourage research and promote alternative methods—like vaccination, use of antibodies against bacteria, or novel strategies to block their resistance mechanisms. There are a lot of moving parts, and it requires oversight by an agency that can identify the points of control and undertake the appropriate combination of education, exhortation, regulation, surveillance, and funding.

Isn't this kind of thing the job of the World Health Organization?

The WHO should be doing everything I describe. But many people now consider it to be so hampered by political infighting that it's ineffective, and this was revealed by its sluggish response to the Ebola outbreak. So it's not clear that that's the locus where this could be best carried out. Perhaps it could be strengthened and reformed, and that would be a perfect setting in terms of the treaties that established it and the concept behind it. On the other hand, you might need a freestanding, treaty-based organization specifically for this problem, just to bypass that bureaucracy and start afresh.

Are global leaders starting to get it?

They are. For several years now, the World Economic Forum has prioritized antimicrobial resistance as a major threat to global security and economic advancement. The WHO has listed it as a top concern. The government of the United Kingdom has prioritized it as a chief concern in the sphere of medicine. President Obama has called for and received a national action plan for combatting antimicrobial resistance.

How optimistic are you that such an action plan can realistically be carried out?

It's really tough. The kind of discussion we're having is decades old, and nothing happened for a long time. There have been many panels, reports, and manifestos saying all of this. But some progress has been made. In 2004, I wrote an article in *Nature* calling for "open labs" to work on antibiotic development, meaning cooperative arrangements between drug companies, academics, and government researchers. Those labs have come into existence and they're incredibly effective; two examples are the TB Drug Accelerator of the Gates Foundation and the Tres Cantos Open Labs Foundation, located on the GlaxoSmithKline campus outside Madrid. There has also been a progressive seepage of understanding and appreciation of this problem from the medical and scientific sphere into the business community, and from there into government.



A 3-D illustration of drug-resistant Mycobacterium tuberculosis

So would you say you're optimistic that despite all the challenges, a solution can be found?

There is every reason to remain pessimistic, but I don't think it helps. It's like any big change in how society's structured. You hammer away, and nothing changes—then suddenly it starts to change, and it changes very quickly. There have been lots of things—women's right to vote; abolition; apartheid—where change seemed impossible and lots of people put their shoulder to the wheel and no one could tell if their effort was going to be wasted, but eventually these intractable problems gave way. So I'm hoping we're reaching the point in terms of the level of urgency, the growing knowledge in the business and government sectors, and the fact that this has reached collective attention at the level of the WHO. I think it's different now. We can't go back. We can only go forward.

Notebook

NEWS OF MEDICAL COLLEGE AND GRADUATE SCHOOL ALUMNI



Dear Alumni,

Spring is always an exciting season for Weill Cornell Medicine. Match Day was held on March 18 and we were delighted by the accomplishments of all our fourth-year students who matched at the absolute best residency programs across the country. I know that we all feel a sense of great pride as these students go on to represent our alma mater in the next phase of their medical journeys.

For more than 118 years, WCM graduates have made their mark on the medical community and the world at large. Our alumni include outstanding clinical leaders, pioneers in science and medicine, Nobel laureates, CEOs, U.S. Surgeon Generals, entrepreneurs, and prominent leaders across major government agencies and health systems.

As our world becomes increasingly interconnected, our dedication to solving health problems that transcend national boundaries continues to drive scientific innovations and discoveries. Many WCM students take advantage of global health service, training, and research opportunities during medical school, and the current issue highlights some interesting examples.

An alumnus and neuroscience professor at WCM, Jonathan Victor, MD '80, is developing algorithms to study how animals recognize and navigate toward odors. James Bernstein, MD '64, has founded a company that is launching the first portable sterilizer that does not require electricity, heat, or water. These are just two examples of the unique and globally impactful ways that alumni are applying their WCM education.

These distinguished alumni are an inspiration to the WCM community. As one of the top-ranked clinical and medical research centers in the country, we have built our reputation on a tradition of excellence inspired by our exemplary leaders, esteemed faculty, and outstanding students who go on to make medical discoveries and improve the health of patients both nationally and internationally. As the members of this year's graduating class prepare for their next chapter, please join me in congratulating them on their accomplishments and help me welcome them into our great association.

And please make plans to attend Reunion 2016 on Sept. 23–24! Stu Mushlin, MD '73, chair of the reunion committee, is planning a spectacular event—a great way to reconnect with old friends and reflect on all that you experienced at Weill Cornell Medicine.

Warm regards,

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

1920s

Spencer Kubo, MD '80, received the following letter from Rev. Ruben L. Dela Cruz, chief executive officer of Brokenshire Memorial Hospital in Davao City, Philippines. "While preparing a talk on the history of the hospital, I read that Herbert C. Brokenshire, MD '24, in whose memory and honor the hospital is named, is an alumnus of your medical college. In 1926, he came to Davao and served as hospital director of the Davao Mission Hospital until 1941 when he was called to active service by the US Navy during World War II. His life and work had a great impact in the Davao region and the island of Mindanao. Many people consider him an icon in medical service to people of all creeds and walks of life. Weill Cornell Medicine is mentioned often as we celebrate the life and ministry of Dr. Brokenshire. Our sincere thanks for molding such a dedicated physician."

1930s

Arthur D. Hengerer, MD '39, is 102 years old and recently made a donation to the General Scholarship Fund of WCM. He graduated 76 years ago and is still supporting his alma mater.

1940s

David S. Brown, MD '45, and Charlotte Rush Brown, MD '45: "We D & C Browns have enjoyed seventy-one years / Since CUMC launched our rewarding careers / And while not total fools / Being 95 brings rules / That frustrate contact with our few living peers."

Richardson K. Noback, MD '47: "My wife, Nan, BS Nurs '47, and I moved back to Kansas City, MO, in 2012 after living in the Southwest for nineteen years. We are enjoying living a few miles from our former home in a continuing care retirement community with a surprising number of former friends and colleagues. We are fortunate to be able to carry on our usual activities although with a reduced cruising range, so our previously frequent foreign travel has become rich memory. Our grandchildren are major interests as they show their parents' talents for medicine, the sciences, advanced degrees, and sports. One grandson—with a black belt—is in the pharmacology doctoral program at Johns Hopkins; another is in the MD-PhD program at the University of Berlin; another just completed his legal studies in Munich; and another is on his college hockey team. One granddaughter just completed her master's in English, and another is a fine tennis player and student council president."

1950s

Sarah Burton Nelson, MD '50, a retired psychiatrist, is enjoying life in Scottsdale, AZ, with her husband, Bernie Makowsky. At 91, Sarah still enjoys swimming, reading novels, staying in touch with her three children and six grandchildren, and socializing with longtime friends and the members of her assisted living community. She has many fond memories of her time at Weill Cornell Medicine.

Roy W. Menninger, MD '51: "After some 60 years of psychiatric practice, I closed my office last year. A few years after I returned to Topeka in 1961 to

join the Menninger Foundation, I was elected president and served in that role for a quarter of a century. Since so much of my time had to be spent on such nonclinical matters as management and fundraising, I took the opportunity to open a private office when Menninger left Topeka to become part of Baylor Medical College in Houston. It did provide for the long-delayed satisfaction of clinical practice, though I missed the collegiality and intellectual stimulation that made the Menninger Foundation in Topeka a truly unique institution. As I approached the tender age of 90, I recognized that retirement could perhaps be something more than nominal, and so it has been. My dreams of further travel have been sidelined by the slow development of an untreatable (and for some years, undiagnosed) myopathy, but my wife, Bev, and I are content to accept the limitations that living longer inevitably brings. The close proximity of and frequent visits with the families of our



Vintage view: An issue of *Weill Cornell Medicine*'s predecessor publication from 1972.

seven children is indeed a great satisfaction. It is a blessing that retirement and relative immobility make possible, and for that we are grateful."

David Wilcox, MD '55: "Jane and I have moved to a retirement home, North Hill, in Needham, MA. We're enjoying it."

Beverly Billinger Shaver '54, MD '58: "Jim and I moved four years ago from Phoenix to Evanston, IL, better to be near our four children and seven grandchildren. We still winter in Scottsdale, AZ, but are enjoying the cultural scene in Chicagoland. Would love to see any classmates who are in the area."

John Baldwin, MD '59: "I live in Twain Harte, CA, on the edge of Yosemite National Park at 4,000 feet, which means four great seasons. Jeannie and I kept our Carmel house and spend time there as well. Most of June I guide groups to Sitka, AK, for ocean halibut and salmon, which has been incredibly rewarding since the drought has all but eliminated my once-great California lakes and rivers. All best to the great friends of our wonderful class." ' Robin and I are blessed to experience our "Green Acres" life, alternating between a small farm in Amsterdam, NY, and our condominium at 65th and 2nd in the City.'

-GUS KAPPLER '61, MD '65 **R. Gordon Douglas, MD '59**: "My wife, Sheila, and I have become interested in food production and consumption, and their effects on health, CO2 emissions, water use and pollution, and animal ethics. How do we nourish ourselves and the global population while protecting our earth and its finite resources? We have started a program at Princeton that brings together faculty, post-docs, and graduate and undergraduate students to create a vibrant research and educational program. Among other activities, we held an enormously successful conference in February on how entrepreneurship can tackle our global food challenges, which excited students and faculty alike."

James E. Shepard, MD '59: "The years of fabulous dry weather here in Northern California have resulted in a water shortage. Accordingly, I use 1/10 cup of water to shave, and we catch shower water in buckets to water the lawn. This year there has been lots of rain. However, that has been minor compared to the blizzard in NYC. I can imagine just walking through the tunnel from Olin Hall to class while the faculty tries to make it through the snowdrifts."

1960s

Gideon G. Panter '56, MD '60: "I'm still in the private practice of gynecology, doing my surgeries at WCM. The problem with old geezer surgeons like myself is that the surgery gets less and less as the referring doctors either retire or die. I've been filling in the empty slots in my time by working with a company that developed a robotic control for the laparoscope camera. This eliminates an extra human from the operating field, and gives the surgeon detailed control of the camera. Imagine all the uses to which the relieved assistant could be assigned. By the way, I still have dinner most nights with the youngest of my seven children. She is a high school junior and I suspect that she might become a physician."

Clay Alexander, MD '61: "Medicine was a profession, back in the day, and it's become a business. There are numerous justifications for that, but I think older patients feel something is missing. After many decades of practicing both science and art during my general surgical years, the right brain has taken over. My fourth novel was recently published on Amazon. It's both challenging and fun to live multiple lives in those pages."

Conner Moore, MD '63: "I truly intended to be at the reunion, but the date coincided exactly with my 50th wedding anniversary and my sons had plans. I had dinner with Deb and **Marty Weiss, MD '63** in November in Los Angeles and he had high praise for the event. He had a long conversation with **Kirk Peterson, MD '63**—my roommate—who has practiced cardiology in San Diego. Marty was recently awarded a Dartmouth (Geisel) Medical School Alumni Award for Lifetime Achievement honoring his 20-plus years as chief of neurosurgery at USC. Marty was active in numerous specialty organizations, including as president of the American Board of Neurosurgery and was the editor of at least three specialty journals as well as being involved in countless research projects. Well done, Marty! I retired from practice in 2008 and authored *Black Bag to Blackberry: A Maine Pediatrician's 40-Year Journey.* WCM prepared me well for a challenging adventure. My eldest son, Christopher, is a pediatrician in Greeley, CO."

James E. Bernstein, MD '64: "Eniware, which I co-founded, is launching its PS-25 portable sterilizer this spring. This disruptive technology provides surgical instrument sterilization without heat, electricity, or water. (For more, see page 27.) My family is well and thriving."

James Baden '61, MD '65, is a retired surgeon living in Hilton Head Island, SC. He plays bridge, watches movies, and catches up on the hundred books he always wanted to read. Dr. Baden volunteers at the local clinic and sings with a barbershop harmony chorus. Travels to China, Australia, New Zealand, Russia, and Europe are on his wish list. He remembers anatomy class and Eliot Hockstein in Physical Diagnosis. **Spike Kunz, MD** '65, and **Gus Kappler '61**, MD '65, are two classmates he would like to hear from. He looks forward to the reunion.

Gus Kappler '61, MD '65: "Robin and I are blessed to experience our 'Green Acres' life, alternating between a small farm in Amsterdam, NY, and our condominium at 65th and 2nd in the City. We are looking forward to reuniting with medical school classmates at the 50th Reunion in September. I recently published Welcome Home From Vietnam, Finally, a truthful accounting of war's devastating effects on body, mind, and soul. I stress a preventive approach to PTSD in contrast to the DoD's current 'sink or swim' practice; one must consider how adolescent is the warrior's brain development. In mid-March I will present the 85th Evacuation Hospital's '70-71 Vietnam battlefield approach to general, vascular, and thoracic surgery at the Medical History of the Vietnam War Symposium in San Antonio, TX. Also in September, Robin and I will attend in La Jolla, CA, the biannual reunion of all those we have found from the 85th Evacuation Hospital, Phi Bai, Vietnam, '70-71. It is a time for renewing our brotherhood and healing."

Deborah Pavan Langston, MD '65: "On June 30, 2015, I officially retired as professor and surgeon in ophthalmology at Harvard Medical School/Mass Eye & Ear/Mass General Hospital. On July 1, I learned that I had been appointed to the board of trustees of those distinguished medical centers and my retirement became theoretical. I

am also still working with my fellows publishing a number of multi-year studies, but the greatest joys in my life are my two truly beautiful grandchildren (ages 4 and 6) and my daughter and son-in-law living just 20 minutes away. My son is a Wall Street success and my health is good."

Judith Axelrod, MD '67: "I am semiretired from my medical practice of infectious diseases, but still attend and teach one day a week in the ID Clinic at Mount Sinai St. Luke's Roosevelt, where I've been on the attending staff for 42 years. Otherwise, I travel, play tennis, and enjoy all the good things that NYC has to offer."

Charles H. Hennekens, MD '67, received the Alton Ochsner Award on Smoking and Health at the annual convocation of the American College of Chest Physicians. His seminal work on smoking includes being among the first to discover that for heart disease it is never too late to quit, but for cancer it is never too early. He was also among the first to demonstrate that in women of childbearing age, oral contraceptives pose a relatively small absolute risk of heart attack, but that cigarettes increase that risk about 13-fold. For those who use oral contraceptives and smoke, risk increases 40-fold. Dr. Hennekens has had a commitment to reducing premature deaths from smoking because he has lived eight years longer than any man in his immediate family, and all smoked cigarettes and died prematurely from their habit. He is the first Sir Richard Doll Professor and senior academic advisor to the dean of Charles E. Schmidt College of Medicine at Florida Atlantic University.

Richard Lumiere '63, MD '67: "I was saddened to hear of the death of Richard Muchnick, MD '67. He was one of our finest physicians and a testament to the education we received at Weill Cornell. Many in our class depended on his class notes, which always included a line next to the most salient points. I entrusted him with the care of many friends and family over the years. I must also note that I traveled with him on my first European trip during medical school. The impressions of that trip led me and my family to spend annual summers in the South of France and Tuscany over the past 40 years. In fact, one of the last places I visited in Tuscany was on a recommendation from Richard. He was a steady and stalwart physician and friend."

George Popel, MD '69: "I retired from the practice of ophthalmology in Wilmington, DE. I have three daughters and so far only two grandchildren."

1970s

Bill Goodhue, MD '70, received the Order of Military Medical Merit, Hawaii Chapter, Lifetime Achievement Award at the Honolulu Country Club December 8, 2015 annual holiday dinner, for service to the Army Medical Department and to the community. He retired in 2001 as a colonel from a 26-year Army pathologist career, then as Honolulu acting chief medical examiner in 2011. He is currently contract forensic pathologist for the City of Honolulu and clinical assistant professor of pathology at the John A. Burns School of Medicine at the University of Hawaii, and divides his time between his Honolulu home and his beach house on the north shore of Kauai.

Eric Thomas, MD '70: "Still working quite happily in private practice and now seeing some of the real advantages of private practice, namely the ability to define the medical and surgical dermatology procedures that are most satisfying. Also, I'm still bicycling. I just came back last fall from Corsica and am going to Provence this fall. My three kids are all gainfully employed: one in analytics in the Hillary campaign, one in commercial real estate in Manhattan, and one locally in public relations for a private school in Connecticut. Hope all of my classmates are doing well and are healthy and happy."

Gregory M. LaGana, MD '71: "I retired from active practice, but still do some pro bono consulting and volunteer teaching. Noelle and I have three grandchildren: Thomas, age 7, and identical twins Molly and Lucy, age 4. Classmate and dear friend Barry Levy, MD '71, and I continue to perform *Damaged Care: The Musical Comedy about Health Care in America* (see damaged care.com)."

Henry A. Pitt '67, MD '71: "For the past three years I've been the chief quality officer for the Temple University Health System. In 2015, Temple University Hospital received the Rising Star Award from the University Health System Consortium for improvements in patient quality and safety."

Robert G. Robinson, MD '71, received two national awards for his research on the neuropsychiatry of stroke during the past year. He received the highest award given by the American Neuropsychiatric Association, the Gary Tucker Award for Lifetime Achievement in Neuropsychiatry, presented at the national meeting in March in Orlando. He also received the yearly award by the American Psychiatric Association for



Build up: An Alumni Quarterly from 1973

research in geriatric psychiatry, the Jack Weinberg Award in Geriatric Psychiatry, at the annual meeting last May in Montreal. After 15 years as professor of psychiatry and neuroscience at Johns Hopkins and 21 years as the Paul W. Penningroth Professor and head of the Department of Psychiatry at the University of Iowa, Bob will retire this coming July.

James W. Husted, MD '72: "I have just retired from active practice of interventional radiology. After Weill Cornell, my internship at Bellevue, and a radiology residency at the University of Pennsylvania, I was fortunate to obtain a fellowship at H.U.P. in this exciting new field. I practiced at a large Philadelphia suburban hospital, where I was able to develop this sub-specialty as part of a group of twenty-five radiologists. Over 37 years, I participated in many national I.R. committees, coauthored 20 papers, and was elected to fellowship in both the American College of Radiology and the Interventional Radiology Society. Joan and I plan to relax, enjoy our four grandchildren, travel, spend more time in Ocean City, NJ, and indulge my passion for ocean sailing."

Allan Gibofsky, MD '73, was recently named a consultant to the Arthritis Advisory Committee of the Food and Drug Administration. He is currently co-director of the Inflammatory Arthritis Clinic at Hospital for Special Surgery and is a master of the American College of Rheumatology.

George Goldmark, MD '73: "My twin brother, **Harry, MD '73**, and I retired from the practice of orthopaedic surgery at the end of December. Following BS and MS degrees from MIT in electrical engineering, we attended WCM. We trained together at Hospital for Special Surgery, after which Harry moved to Massachusetts and I to New City, NY. He returned to New York in 1986, where we worked together in private practice for 29 years. Harry has retired to Aiken, SC, with his wife, Nancy, BS Nurs '73, and I will be spending my winters in Boca Raton, FL, with my wife, Loretta."

Benjamin A. Lipsky, MD '73, and his wife, Donna, just returned from a two-week visit to Seattle to see family (especially their two young granddaughters) and friends. They are in the fourth year of their European adventure, living and working in Oxford, UK. Ben has continued to conduct research (mostly on diabetic foot infections), sit on various international academic committees, teach at the University of Oxford, and lecture worldwide. This year he was elected to Fellowship in the Royal College of Physicians and Surgeons (Glasgow), where he will deliver the keynote address at their annual meeting.

William M. Scheld, MD '73: "Last October I received the David A. Harrison Distinguished Educator Award. This is a lifetime achievement award and the most prestigious teaching award

at the University of Virginia School of Medicine."

Marc E. Kaminsky, MD '74: "At the end of 2015, I retired from the practice of diagnostic radiology in Fort Wayne, IN. My wife and I plan to move to Hilton Head, SC, within the next six months. We have one son who is an attorney serving as a federal defender in Manhattan and lives with his wife and 18-month-old child in Brooklyn."

Joshua G. F. Nagin '71, MD '75, MBA '88: "I am happily retired after more than 30 years in the ER and I now try to make a few more bucks than I lose by playing golf. Ronna and I live in Bonita Springs, FL, and enjoy our five grandchildren, traveling, and the active retired life of Florida."

Lynda Rosenfeld, MD '76: "I remain at Yale where I am the director of the Clinical Cardiac Electrophysiology Fellowship Program and chief for the Inpatient Cardiology Teaching Service. I was recently promoted to professor of medicine and pediatrics."

Barry Weintraub, MD '77, opened Fifth Avenue Cosmetic Plastic Surgery in Manhattan in August 2015. Recently, he trademarked the Bedroom Eye Lift and the Bedroom Brow Lift, procedures that he says create a youthful, natural looking eye, and launched a state-of-the art surgical facility. Dr. Weintraub specializes in primary and revisionary rhinoplasty, as well as addressing the normal gravitational problems of aging.

Robert A. Schultz, MD '78: "Getting healthcare policy right is crucial for us all. My latest book, *From Both Ends of the Scalpel*, opens up the real world of medical care delivery to those thus far blessed with good health, and reminds those suffering from illness that their story is being told. Join me by getting the word out."

1980s

Jim Blankenship '76, MD '80: "After years of talking to WCM students who follow their rotation through WCM's affiliated medical facility in Tanzania with a climb up Mt. Kilimanjaro, last year my three kids and I gave it a shot. It was fun."

Sam Spigelman, MD '81: "Happy to say that my wife and I are happily back in the Big Apple for the past two years and loving every minute of it. I now work in pharma, a welcome change from clinical medicine. Expecting our first grandchild (can you believe it?), the first boy in our family for many years. Looking forward to seeing everyone at our 35th Reunion."

Stuart Knechtle, MD '82, has moved to Duke University Medical Center as executive director of the Duke Transplant Center. He and his wife, Mary Banks, live in Hillsborough, NC."

Steven Wexner, MD '82, is director of the Digestive Disease Center, chair of the Department of Colorectal Surgery at the Cleveland Clinic

' My twin brother, Harry, MD '73, and I retired from the practice of orthopaedic surgery at the end of December.' – GEORGE GOLDMARK, MD '73 Florida, affiliate professor at Florida Atlantic University College of Medicine, and a clinical professor at Florida International University College of Medicine. He is president of the American Society of Colon and Rectal Surgeons Research Foundation. Recently he was elected an honorary fellow by the European Surgical Association and the European Society of Coloproctology.

James Auran, MD '83: "The greatest moment in my medical career was when my daughter Emily told me she wanted to follow in my footsteps. The second greatest was when she walked into my office and announced that she had gotten into Columbia P&S, where she is now a first-year medical student. In January 2016, I became chief of the Department of Ophthalmology at Harlem Hospital Center, where I will supervise Columbia University ophthalmology residents while running a busy eve department in a city hospital. Just as I stepped up, my classmate (and personal physician) Gerald Hoke, MD '83, stepped down after 20 years as the chief of the Department of Urology at Harlem Hospital Center. The Class of 1983 has certainly had an impact in Central Harlem. How many other WCM classes can claim to have produced two department chairs in the same hospital?"

Susan Hirsch, MD '84: "We are celebrating our 34th anniversary this year. Our three sons are thriving: the eldest is getting his PhD in anthropology at the University of Chicago; our middle son is a reporter at North Country Public Radio, an NPRaffiliate in Plattsburgh, NY, where he was the 'man on the ground' during the Dannemora prison escape; and our youngest is a sophomore at Columbia University. It was awesome to see everyone at last year's reunion."

Roger Blumenthal, MD '85: "I am cochair of the American College of Cardiology/ American Heart Association subcommittee that is updating the blood pressure, cholesterol, risk assessment, and lifestyle guidelines. Over the past year, I greatly enjoyed spending time with WCM classmates **Steve Berger, MD '85**, **Dave Blaustein, MD '85**, and **Troy Elander, MD '85**. I look forward to seeing many classmates at our next reunion in September."

Paul E. Lynch, MD '85, co-edited *Sexualities: Contemporary Psychoanalytic Perspectives*, with Alessandra Lemma, published by Routledge in 2015.

Lisa Lavine Nagy, MD '86, has presented to closed Congressional hearings on veterans' health and was asked to write a protocol for treatment using environmental

medicine. She has lectured to the EPA and National Institute of Environmental Health Sciences and taught researchers in Nancy Klimas's Chronic Fatigue/Gulf War Research group how to apply these principles to the clinical management of those who have been exposed to mold, chemicals, and electricity and are now intolerant. She communicates for the American Academy of Environmental Medicine in many settings, such as on "The Doctors This Month" and soon on MSNBC about lead in the water of Flint, MI. She writes: "AMA policy is archaic and must move with the times. See www.lisanagy.com for my Penn Med intro lecture, which might help you or your patients one day. This is the future of medicine-getting to the cause of illness."

Bob Narayan, MD '86: "I am planning to go to my first reunion (30th) this year and have started contacting old buddies from med school to drum up some interest, as I would love to catch up. Also, I'm thinking of starting an alumni group in Northern California, where I practice. So if any WCM graduates are in Northern California, please contact me at bobnarayan @ yahoo.com. Hope to hear from you."

Stephen Rosenfeld, MD '86: "I'm currently the full-time Executive Review Board chair for Quorum Review, an independent IRB in Seattle. I'm also a member of the Secretary's Advisory Committee for Human Subject Protections for HHS. I live in Maine and telecommute to Seattle."

Theresa Rohr-Kirchgraber, MD '88, was recently chosen to receive the American College of Physicians Indiana Chapter 2016 Laureate Award, which honors Fellows and Masters of the College who have demonstrated by their example and conduct an abiding commitment to excellence in medical care, education, or research and in service to their community, their chapter, and the American College of Physicians. The award will be presented at the Annual Scientific Meeting in December 2016.

Scott Rodeo, MD '89, and Christine Frissora Rodeo '86, MD '90: "Our son is a Classics major in Arts & Sciences at Cornell and joined the Cayuga's Waiters *a cappella* group."

Howard L. Weiner, MD '89: "I've accepted the position of chief of neurosurgery at Texas Children's Hospital in Houston, TX, and professor of neurosurgery and vice chairman in the Department of Neurosurgery at Baylor College of Medicine. I'm sad to leave NYU Langone Medical Center after nearly 27 years."

1990s

Jeff Kauffman, MD '93: "My wife, Uschi, daughter Heidi, and I have moved from Sacramento, CA, to Franconia, NH, where I joined the Alpine Clinic. My office is at the base of Cannon Mountain. I continue to specialize in sports medicine and couldn't be happier with my new position."

Maria C. Shiau, MD '93: "I am currently working at the NYU Langone Medical Center Radiology Department, for the past ten years as a thoracic radiologist. For the past five years I have been the director of medical student education in radiology, overseeing the integration of radiology throughout the curriculum as well as running our dedicated four-week radiology course. In 2014, I was named Alpha Omega Alpha Teacher of the Year. In 2015, I was inducted into the National Hispanic Scholarship Fund Alumni Hall of Fame and YWCA Academy of Women Leaders."

Jose Ramirez, MD '94: "I am currently in Orlando, FL, going on 14 years. My wife, Pearl, and I have four wonderful kids. I am the program director for Pediatric Emergency Medicine Fellowship at Orlando Health and entering my seventh year in that role. Every so often Henry Park '90, MD '94, who is out in Tampa, and his family will get together with mine, and we have a great time. Over the years, Frank Lombardo '90, MD '94, Frank Wong, MD '94, and Tony Yen, MD '94, have come down."

We want to hear from you!

Keep in touch with your classmates.

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

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MD 12

Li-Ming Su'89, MD'94: "Just wanted to provide a brief update on my new position at the University of Florida College of Medicine. After joining the urology department of the UF College of Medicine in 2008 as the David A. Cofrin Professor of Urology, associate chairman of clinical affairs, and chief of the Division of Robotics and Minimally Invasive Urologic Surgery, I was recently named the chairman of the department. I will lead a department of 11 faculty members specializing in all areas of urology including urologic oncology, stone disease, general urology, trauma/reconstruction, female urology, pediatric urology, and andrology."

Seth M. Manoach '88, MD '95: "I am assistant professor of medicine in the Division of Pulmonary and Critical Care at WCM. I'm an intensivist at NYP/Lower Manhattan. I write and research with my colleagues at NYP. My wife, Bette Kim, is a cardiologist. We have two great kids, Max and Eli. That said, life has its ups and downs. My wife and I both lost our fathers and other family members this year. You live, you grow, you mourn, you celebrate. Time ticks on."

Mark Wurfel, MD '97: "I am now a full professor at the University of Washington in Seattle and hold the David J. Pierson, MD, Endowed Chair in Pulmonary and Critical Care Medicine. I've had the pleasure of working with an increasing number of WCM grads who have come to Seattle for internal medicine residency and even pulmonary fellowship. Looking forward to working with more of them."

2000s

Joshua Dines, MD '01: "I was promoted to associate professor of orthopaedic surgery at WCM. I'm the assistant team physician for World Series runners up, the New York Mets. On CBS News I talked about a new technique to treat irreparable rotator cuff tears. I'm editing my sixth textbook, this one on reverse total shoulder replacement, to be released at the end of this year."

Henry Wei, MD '02: "I'm Google's corporate medical director now."

2010s

Kira Segal, MD '12, and Matthew McCarthy, MD '11, were married on August 1, 2015. Their wedding was attended by fellow alumni Ali May, MD '10, Michael Day, MD '11, Rachel Day, MD '13, John Pena, MD '11, Sarah Van Tassel, MD '12, Dorothy Chyung, MD '12, Carlo Canepa, MD '12, David Phillips, MD '12, Elizabeth Gausden, MD '12, Gregory Bonci, MD '12, Kristin Gilbert, MD '12, Jared Gilbert, MBA '12, Steve Park, MD '12, Ethan Brown, MD '12, Joseph Pale, MD '12, Daniel Sonshine, MD '13, and Kaitlin Greene, MD '13.

ALUMNI

'51 MD—Patrick J. Mulrow of Jupiter Island, FL, formerly of Perrysburg, OH, December 3, 2015; professor emeritus, chairman of medicine, and leading researcher in hypertension, University of Toledo College of Medicine; also taught at Yale University; expert on the role of renin in the regulation of aldosterone production; former chairman, Council for High Blood Pressure Research; secretary-general, World Hypertension League; recipient of the Senior US Scientist Award from the Alexander Von Humboldt Foundation; author; singer of Irish songs; active in professional affairs.

'53 MD—John P. McCreary of Watertown, NY, November 11, 2015; retired radiologist; former president of Northern Radiology; provided radiological services at Samaritan Medical Center, Mercy Hospital, Carthage Area Hospital, Lewis County General Hospital, and River Hospital; veteran; Rotarian; woodworker; craftsman; active in civic, community, professional, and religious affairs.

'55 MD—Thane Asch of Tappan, NY, January 18, 2016; pioneer in modern mammography; retired professor, radiologist, and director of mammography at Columbia Presbyterian Medical Center; also taught at New York Hospital and Weill Cornell Medicine; veteran; traveler.

'56 MD—Richard K. Mead of Barrington, RI, January 11, 2016; primary care physician and cardiologist; associate professor emeritus, Brown Medical School; recipient of the Teaching Award from the Rhode Island Hospital House Staff, the Laureate Award from the American College of Physicians, and the Distinguished Teachers Award from Brown Medical School; veteran; assistant Scoutmaster; pianist; singer; book collector; active in community, professional, and religious affairs.

'61 MD—Richard J. Hastings of Woodstock, VT, December 31, 2015; chief of surgery, orthopaedist, and trustee at Central Suffolk Hospital; chairman of the Orthopedic Society of Suffolk County; veteran; volunteered at Bugbee Senior Center and Meals on Wheels; Civil War buff; tennis player; gardener; poet; quizmaster; active in community and professional affairs.

'62 MD—John K. Charlton of Scottsdale, AZ, February 23, 2015; chairman of the Dept. of Pediatrics and director of the Division of Nephrology, Maricopa Integrated Health System; pediatric clerk-ship director, assistant dean for student affairs, director of student counseling, and director of career counseling at the University of Arizona College of Medicine's Phoenix campus; clinical associate professor of pediatrics at University of Arizona College of Medicine in Tucson; also served on the staff of Phoenix Children's Hospital and St. Vincent de Paul; leading advocate for child abuse prevention; helped found the Crisis Nursery and served as its medical director; pianist; pilot; sailor; traveler; patron of theatre, opera, and the symphony; active in community and professional affairs.

'62 MD—Ronald A. Stroth of Scottsdale, AZ, February 9, 2016; anesthesiologist; veteran; world traveler.

'62 MD—F. Darwin Zahn of Scottsdale, AZ, December 25, 2015; general surgeon; pioneer in laparoscopic cholecystectomies; veteran; woodworker; fisherman; sportsman; musician; active in community and professional affairs.

'62 BA, MD '66—Richard H. Fine of San Francisco, CA, November 10, 2015; chief of the adult health center, San Francisco General Hospital and Trauma Center; cared for the poor, the homeless, AIDS patients in the early days of the AIDS epidemic, and prisoners; created one of the first outpatient clinics at a public hospital in the US; founded the first medical and psychiatric clinic to treat jail inmates; official physician for the Black Panthers; set up the Black Man's Free Clinic in Oakland, CA; ran a clinic for the American Indian occupiers of Alcatraz; active in civic, community, and professional affairs. Zeta Beta Tau.

'72 MD—Thomas L. Kennedy III of Fairfield, CT, October 31, 2015; pediatric nephrologist; chair of pediatrics, Bridgeport Hospital; clinical professor of pediatrics and acting chief of pediatric nephrology, Yale School of Medicine; also taught at the University of Connecticut Health Center; veteran; chairman, Fairfield Board of Health; marathon runner; avid reader; music enthusiast; active in community, professional, and religious affairs.

FACULTY

E. Darracott Vaughan Jr., MD, of Sheridan, Wyoming, April 22, 2016; the James J. Colt Professor of Urology; founding chairman, Department of Urology, 1978–2001; president, American Urological Association, American Foundation for Urologic Diseases, and American Board of Urology; winner of numerous awards including the Gold Cystoscope Award from the AUA, the St. Paul's Medal from the British Association of Urological Surgeons, and the Maurice R. Greenberg Distinguished Service Award from NYP/Weill Cornell; active in professional, community, and religious affairs.

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Post Doc

The Envelope, Please...

The Class of '16 marks a record Match Day

ourth-year students at Weill Cornell Medicine recently participated in the largest-ever Match Day on record. In mid-March, WCM faculty were on hand in Griffis Faculty Lounge to celebrate—and share a traditional champagne toast—with the members of the Class of '16 as they opened the fateful envelopes revealing where they'd spend the next three to seven years of internship and residency.

The students were among the more than 33,000 future physicians and osteopaths in the U.S. and abroad vying for some 30,000 residency positions. Of the WCM students who matched, 51 percent will pursue primary care residencies in internal medicine, pediatrics, family medicine, and ob/gyn. Some 39 percent of the matching students will stay in metro New York, with twenty matched to NewYork-Presbyterian—seventeen of them at NYP/Weill Cornell. "It's nice to have a face on the future," said Courtney Haviland '16. "It's starting to feel real." But, she added, "it's going to be hard to leave here."

Haviland landed a residency in pediatrics at Massachusetts General Hospital; happily, her fiancé, William Shrauner '16, will train in internal medicine at nearby Brigham and Women's Hospital. Among the many other elated future physicians was Evan Bander '16, who matched to his first choice: neurosurgery at NYP/Weill Cornell. "I came here knowing what I wanted to do," Bander said. "Every advantage was given to me: I got to work with great faculty and classmates, had the support of my family—and it got me here."





Game, set, Match!: Members of the Class of '16 who celebrated residency placements included (clockwise from top left) Milna Rufin, Kartik Viswanathan, engaged couple Monica Jeong and Will Cope, and Nick Maston (hugging a friend).



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