

weillcornellmedicine

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

SUMMER 2013

The Cancer Revolution

Lewis Cantley, PhD,
heralds a new era
in research



Students Salute Scholarship Donors

Student scholarships are essential for bringing the best and brightest to Weill Cornell, and they enable those students to continue their studies without the burden of debt. This year's Salute to Scholarship was an opportunity to honor both the generous scholarship donors and the hardworking scholarship recipients.

Held at Olin Hall on May 22, the event filled the room to capacity with guests eager to hear more from the Weill Cornell scholarship recipients and the donors who support them. In a highlight of the evening, students throughout the room stood and toasted their respective donors, sharing with the audience the powerful impact of this support and the many opportunities it provides.



Herbert Siegel (top row, far right) with his wife, Jeanne, Siegel Family Faculty Award recipient Dr. Domenick J. Falcone, Dean Glimcher, and the recipients of the Siegel Family Student Prizes.



"This support will allow me to pursue my field of interest in an academic environment, rather than in private practice, so that I can focus not only on my commitment to lifelong learning, but also to educating others."

Diana Mosquera, Class of 2014 and a student speaker at the event.



"We recognize that students are the key to building the future of our healthcare system. They are a driving force at this institution, and they are the reason we are here tonight."

Overseer Sandy Ehrenkranz, Chair of the Student Affairs and Education Committee on the Board of Overseers, Co-Chair of the Dean's Council, and a longtime volunteer and donor. The Ehrenkranz family has endowed the Ehrenkranz Family Scholarship.



"I have a long relationship with Weill Cornell, and I want to pass on that same experience to the students who will be my colleagues someday. It's the best gift that I can give."

Hazel Szeto, MD, PhD '77, who has contributed generous gifts to the Advancing the Clinical Mission scholarship and to the Class of 1977 Loan Fund, both of which provide necessary financial aid support for students beginning their medical careers.



Weill Cornell Medical College

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DISCOVERIES THAT MAKE A DIFFERENCE
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FEATURES

22 OPEN MIND BETH SAULNIER

Lewis Cantley, PhD '75, has been fascinated with understanding how things work ever since he was a boy in West Virginia, where his father taught him to make his own toys and design his own rockets. Today Cantley is one of the world's leading cancer researchers: the discoverer of a key pathway in cancer biology; leader of a \$15 million Stand Up To Cancer "dream team"; winner of the most lucrative prize in biology and medicine. His recruitment from Harvard last fall was both a coup for Weill Cornell and a vital step in the buildup of its bench-to-bedside research enterprise.

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28 THE BODY POLITIC BETH SAULNIER

In June, the Supreme Court ruled in a case that had been closely watched by the scientific community: *Association for Molecular Pathology v. Myriad Genetics*. To the joy of many researchers, the court ruled—in a rare unanimous decision—that human genes can't be patented in their natural state. Among those popping champagne corks was Christopher Mason, PhD. An assistant professor of computational genomics, Mason was among the experts who provided testimony for the plaintiffs—even giving genetics primers to their attorneys. Says Mason: "This will open the floodgates of new ideas, research, and techniques."

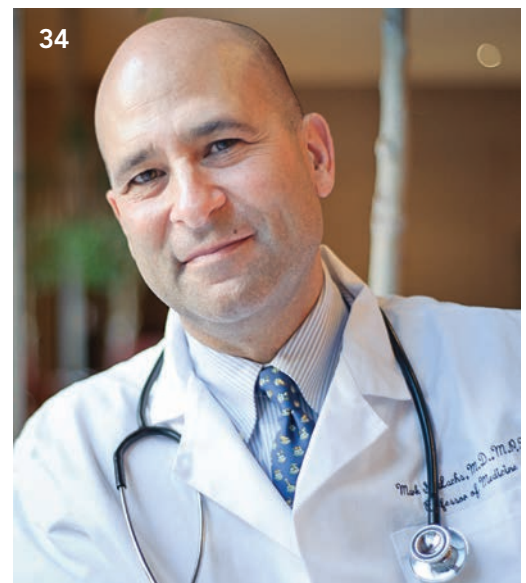
34 PROTECTIVE MEASURES BETH SAULNIER

Geriatrician Mark Lachs, MD, calls elder abuse "the most extreme form of age discrimination"—and he has devoted a career to studying it. Over the past quarter-century, Lachs and his Ithaca-based collaborator, gerontologist Karl Pillemer, PhD, have conducted some of the most comprehensive and frequently cited studies in the field. It's an all-too-common phenomenon, causing untold physical, psychological, and financial harm; in one recent study, Lachs and Pillemer found that roughly one in thirteen older New Yorkers had been abused in the past year.



MICHAEL AUSTIN / THEIS.POT.COM

Cover photograph by John Abbott



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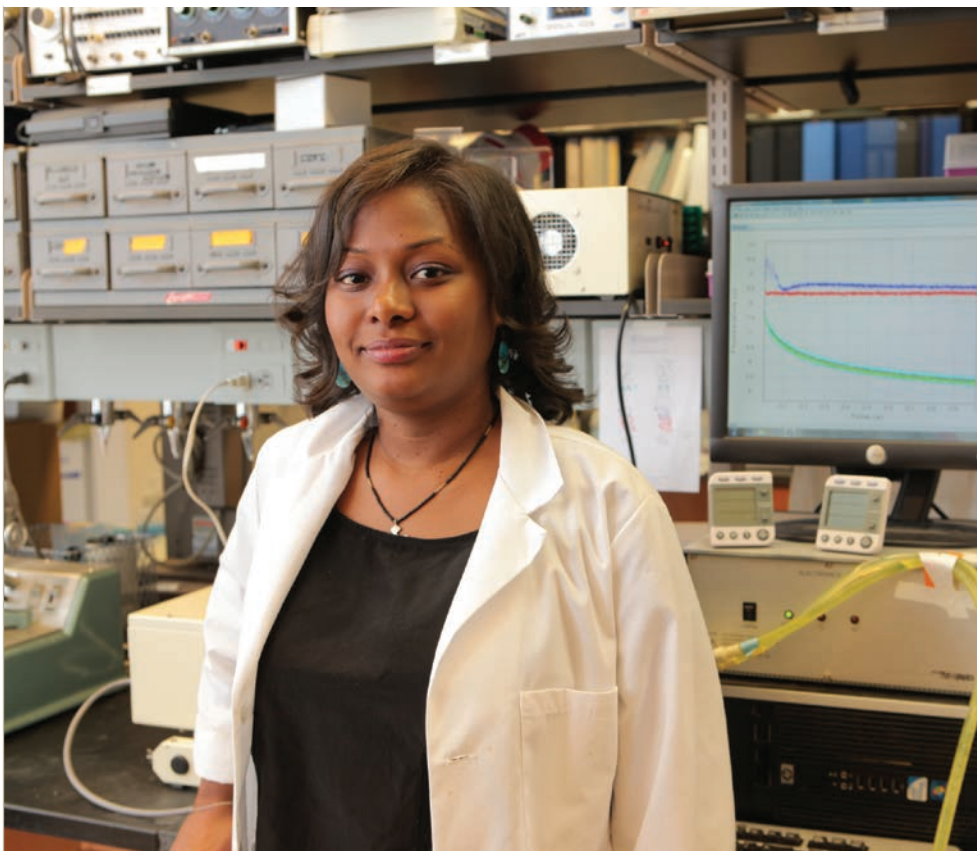
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The Innovation Issue

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



Medicine is entering an era of disruptive innovation. That term, coined by Harvard business professor Clayton Christensen, explains the way a niche idea or product—something that at first may appear insignificant or inconsequential—comes to redefine an industry. An example would be the way computers suddenly jumped from \$200,000 main-frame machines to affordable and ubiquitous personal devices.

Disruptive innovations are not iterative improvements to the status quo but profound transformations; they are new entrants to a field that shift the paradigm. That is why I often use the term to describe what's happening at Weill Cornell with our game-changing approach to biomedical research, particularly in the field of precision medicine.

In this edition of the magazine—our research issue—we highlight many examples of potentially disruptive innovations. We feature pioneering cancer researcher Lewis Cantley, PhD '75, who discovered an enzyme critical for cell survival that has therapeutic potential in treating cancer, diabetes, and more. Cantley joined the faculty last fall to direct our new Cancer Center, which promises to move treatment from one-size-fits-all approaches to individualized therapies.

We also highlight the work of Steven Lipkin, MD, PhD, and colleagues in uncovering a genetic technique that activates the molecular switch that launches metastasis in colorectal cancer. We cover the bench-to-bedside collaborations of Linda Vahdat, MD, and Vivek Mittal, PhD, who are working to develop therapies for types of metastatic breast cancer that currently have no hope for treatment. We announce our progress in bringing clinical trials at Weill Cornell and NewYork-Presbyterian under one umbrella, with

the establishment of a new joint office intended to spur discovery by streamlining logistics. In a conversation with Christopher Mason, PhD, of the HRH Prince Alwaleed Bin Talal Bin Abdulaziz Al-Saud Institute for Computational Biomedicine, we ask "Who owns your genes?" and discuss the vast research expansion that is expected to follow the recent Supreme Court decision limiting patents on the human genome. In addition, we take a close look at the work of pioneering geriatrician Mark Lachs, MD, and his collaboration with social scientist Karl Pillemer, PhD, from the Ithaca campus to address the serious problem of elder abuse in this country. As Lachs points out in the article, elder abuse has not received the kind of attention that has been devoted to child abuse or spousal abuse, yet it is a large and growing problem that is too often overlooked in medical settings.

These are just a few of the researchers you'll meet in this issue, which showcases the depth and breadth of investigations at Weill Cornell. And, of course, any one issue of *Weill Cornell Medicine* can only scratch the surface of the immense talent in basic science and translational medicine at our institution. You will continue to read much more about our research in upcoming issues.

We live and work in an exciting moment in medicine—an era of innovation, in which technological tools are illuminating biological processes to create enormous opportunities for improving human health. At the same time, the need for new therapies is great, as we confront alarming increases in obesity, Alzheimer's, and other debilitating diseases and as we reach the limits of existing approaches to many intractable conditions such as cancer and pain. Medicine is poised and ready for disruptive innovation. And at Weill Cornell, our clinicians, translational researchers, and bench scientists are working toward profound transformations and promising new avenues in patient care.

LISA BERG

The Belfer Research Building – **New Discoveries on the Horizon**



The Belfer Research Building, where breakthrough discoveries will lead to innovative treatments and cures, stands 18 stories high and has already made its mark on the Weill Cornell skyline. The state-of-the-art building, slated to open in January 2014, will be home to research efforts in key areas including cancer, cardiology, children's health, drug discovery, and neuroscience. Scientists will work, collaboratively, on some of the greatest health-care challenges that we face and will catapult Weill Cornell into a new era of personalized medicine. Recruitment is already well under way to bring more of the world's finest scientific minds to join the research powerhouse at Weill Cornell.

With only a few more months before it opens, building construction is full-speed ahead: the double-fritted glass curtain wall, designed to maximize energy efficiency, is now complete; the framing on each floor is in place; the open-design labs and offices are taking shape; the roof of the skylight terrace in the Starr-Greenberg Conference Center is installed; the conference rooms are nearly wired for high-end technology needs; and visitors on hard-hat tours can now catch glimpses of the many spaces where interdisciplinary collaboration will take place in this historic building.

"It is here where our physicians and scientists will
**be working to find the answers to the health
challenges of our time**, and bring hope and health
to people in New York and around the globe."

Sanford I. Weill
Chairman of the Board of Overseers



Weill Cornell Medical College

A construction worker installs the wiring in one of the almost completed open-design lab spaces in the building.





The double-fritted glass curtain wall on the façade of the Belfer Research Building is designed to maximize energy efficiency.



The stairwell in the double-height lounge on the fifth floor allows an abundance of natural light from the windows. The lounge will be a pleasant space for researchers to collaborate with colleagues.

"The Belfer Research Building will double our research space and greatly enhance our capacity to deliver cutting-edge, translational medicine to our patients. **Now is the time to seize the moment by bringing more leading lights to our campus,** and to this building, to keep us in the vanguard of exceptional scientific discovery and patient care."

Laurie H. Glimcher, MD
Stephen and Suzanne Weiss Dean
Provost for Medical Affairs

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BRYAN DERBALLA

Autism Center Opens on Westchester Campus

This summer, the Westchester psychiatric campus celebrated the completion of its new Center for Autism and the Developing Brain. Unveiled at a dedication ceremony in June, the 11,000-square-foot NewYork-Presbyterian/Weill Cornell Medical Center facility is housed in a former recreational center that was renovated specifically to treat people with autism. It will offer integrated treatment and comprehensive services for patients and their families, from diagnostics for small children to vocational training for adults. It will be led by Catherine Lord, PhD, professor of psychology in psychiatry and in pediatrics, an internationally known autism expert. “Our focus on the lifespan and on interdisciplinary, evidence-based assessment and treatment is an innovative approach not commonly found at even the most highly respected programs in the country,” Lord notes.

The Center has numerous design elements intended to be soothing and appealing to people with autism, including natural light, color-coded rooms, soundproofed floors and walls, a circular floor plan, benches to allow for respite stops while navigating the

halls, and more. The facility also features a gymnasium filled with carefully chosen play equipment, observation rooms allowing monitoring and recording of treatment sessions, and cozy waiting areas designed to welcome families. “Diagnosis is just a start,” Lord says. “By evaluating the strengths and weaknesses of each patient, and by monitoring and measuring that individual’s response to a variety of approaches, we will fine-tune our ability to deliver the best possible short-term treatments. We also see our core identity as a hub from which we can connect patients and families to the wealth of programs and services in their own community.”

According to a 2012 report from the CDC, one in every eighty-eight American children has been diagnosed with an autism spectrum disorder—a 23 percent rise over 2009.

Play room: Architect Jaques Black (left) and director Catherine Lord, PhD, in the gym of the new Center for Autism and the Developing Brain

Graduates Are 'The Future, Period,' Dean Glimcher Says at Commencement

The traditional commencement ceremony in Carnegie Hall celebrated the conferral of degrees on 259 students in the Class of 2013. The graduates included 71 PhDs, 39 physician assistants, 20 masters of science, and 129 MDs, 35 of them from the Qatar campus. "As medicine changes, you are the next generation of discoverers," Dean Laurie Glimcher, MD, told the graduates. "It is your role—indeed your obligation—to seek new ways of doing things, to innovate and to discover."

In addition to Glimcher and Cornell President David Skorton, MD, the speakers included newly minted physician Bem Atim, MD '13, who was chosen to give commencement remarks on behalf of his class. "My classmates have done asylum work for torture survivors, staffed clinics for the uninsured, and cared for pediatric burn victims," noted Atim, who is bound for a psychiatry residency at NYU. "These men and women—these great and good men and women—remind me that, no matter how dark and sinister the world may seem, there is much more good in it than bad."

In her speech, Glimcher said that the graduates are the future of global medicine. "But I think you're even more than that," she added. "I think you might just be the future, period. If change is coming as fast as they say it is, we need leaders in all fields of endeavor who have qualities beyond the ordinary."



AMELIA PANICO

Cum laude: Cornell President David Skorton, MD, applauds the graduates from the Carnegie Hall stage.

TIP OF THE CAP TO...

Medical students **Daniel Cook '14** and **Andrew Gregg '15**, selected as Howard Hughes Medical Institute Research Fellows.

Genetic medicine chairman **Ronald Crystal, MD**, the Bruce Webster Professor of Internal Medicine, winner of the Sten Eriksson Distinguished Scientific Achievement Award from UMass Medical School and the Alpha-1 Foundation.

R. Gordon Douglas Jr., MD '59, former president of Merck Vaccines, winner of the Award of Distinction from the WCMC Alumni Association.

Orli Etingin, MD, the Lisa and Sanford B. Ehrenkranz Professor in Women's Health, winner of Weill Cornell's Maurice R. Greenberg Distinguished Service Award.

Domenick Falcone, PhD '81, associate professor of pathology and laboratory medicine and of cell and developmental biology, winner of the Siegel Family Faculty Award.

Oliver Fein, MD, professor of clinical medicine and of clinical public health, recipient of the David R. Calkins Award in Health Policy Advocacy from the Society of General Internal Medicine.

Neurology chairman **Matthew Fink, MD**, the Louis and Gertrude Feil Professor in Clinical Neurology, and Joseph Safdieh, MD, vice chairman of neurology for education, elected fellows of the American Neurological Association.

Neurology professor **Kathleen Foley, MD '69**, former chief of the Pain and Palliative Care Service at Sloan-Kettering, awarded the Medal of Honor from the American Cancer Society.

Dean **Laurie Glimcher, MD**, winner of the Advancing Women in Science and Medicine Award for Excellence from the Feinstein Institute for Medical Research. She was also elected to the board of trustees of the New York Blood Center.

Pharmacology chair **Lorraine Gudas, PhD**, the Revlon Pharmaceutical Professor of Pharmacology and Toxicology, recipient of the Future of Health Technology Award.

Roy Gulick, MD, chief of the Division of Infectious Disease, elected to the Association of American Physicians.

Medicine professor **Jeffrey Laurence, MD**, winner of the Visionary Award from the Red Ribbon Foundation for pioneering AIDS research.

Associate dean for clinical research **John Leonard, MD**, the Richard T. Silver Distinguished Professor of Hematology and Oncology, named chair of the Lymphoma Committee of the Alliance for Clinical Trials in Oncology.

Madhu Mazumdar, PhD, chief of the Division of Biostatistics and Epidemiology, named a fellow of the American Statistical Association.

Stefano Rivella, PhD, associate professor of genetic medicine in pediatrics, elected director of the International Biolron Society.

William Schaffner, MD '62, winner of the Health Achievement Award from the National Meningitis Foundation.

Research professor of neuroscience in pediatrics **Susan Vannucci, PhD**, honored by the National Organization of Italian American Women's Greater New York Region.

Chelsea Clinton Gives Grand Rounds Lecture

Board of Overseers member Chelsea Clinton gave a Global Health Grand Rounds talk in May, describing the work of the Clinton Health Access Initiative (CHAI) to a standing-room-only crowd in Uris Auditorium. The nonprofit, on whose board Clinton sits, works to improve health outcomes in the developing world by negotiating the prices of medicines and diagnostics, expanding access to new technologies, establishing locally sustainable health-care models, and more. “The only way any of this will be systemic,” Clinton said, “is if those of us who think we are pretty good at disrupting the status quo can actually have that work disseminated and sustained by those who are really good at implementing and really good at procuring.”

CHAI was established in 2002 as the Clinton HIV/AIDS Initiative; it later expanded its focus and changed its name. In addition to HIV/AIDS, it works to combat malaria, expand vaccination, and lower infant mortality in some thirty countries worldwide. After the lecture, MD-PhD student and global health activist Sandip Kishore, PhD '11, said that Clinton's comments “help provide a roadmap on where great universities and motivated student-faculty collectives can strike.”

Second Brain Tumor Biotech Summit Held

The Weill Cornell Brain and Spine Center hosted its second annual Brain Tumor Biotech Summit in June, bringing together 175 leaders in medicine, research, and industry to accelerate new treatments and promote funding for emerging therapies. Held in conjunction with Voices Against Brain Cancer, the event featured some thirty lectures and panel discussions showcasing advances in vaccines, nanotechnology, stem cell biology, gene therapy, and more. It drew a variety of participants, from neuroscientists and oncologists to hedge fund managers, investment bankers, and representatives of the biotech industry, nonprofits, and pharmaceutical companies. “The Summit is an amalgamation of thought leaders in the areas of science, industry, and venture capital who collectively have already expanded the boundaries in brain tumor research, leading to novel ideas and new clinical trials,” says Philip Stieg, MD, PhD, chairman of the Department of Neurological Surgery. “This year's Summit forged new, game-changing relationships, and I'm excited to see the advancements in brain tumor treatments that will be catalyzed as a result.” According to the American Cancer Society, more than 23,000 people in the U.S. are diagnosed with brain or spinal tumors each year. More than 14,000 of them will die of their disease.

Downtown Hospital Merges with NYP

Weill Cornell physicians are now practicing in Lower Manhattan, thanks to a merger between NewYork-Presbyterian and New York Downtown Hospital. Now known as NewYork-Presbyterian/Lower Manhattan Hospital, the 180-bed facility is the sixth NYP campus and the borough's only remaining hospital south of 14th Street. Its 140 physicians are now members of the Weill Cornell faculty and of the Weill Cornell Physician Organization. In tandem with the merger, the Physician Organization opened a multispecialty practice on William Street, half a block from the hospital. Michael Stewart, MD, senior dean for clinical affairs, says that in addition to offering high-quality care, NYP/Lower Manhattan will “enable easier referrals and transfers, if needed, to our center on the Upper East Side for more advanced health-care services.”



CHLOE APPLE SELDMAN / IRA FOX

Global thinker: Chelsea Clinton gave a Global Health Grand Rounds talk entitled “Changing the Model.”

NewYork-Presbyterian Tops U.S. News List

Once again, *U.S. News & World Report* has named NewYork-Presbyterian the top hospital in the New York metro area. Of the more than 4,800 facilities the magazine evaluated nationwide, only 3 percent are ranked in even one adult specialty; NYP was ranked in fifteen, as well as in ten pediatric specialties. Among its highest ratings were third place in three areas: cardiology and heart surgery; neurology and neurosurgery; and nephrology. NYP also landed a coveted spot on the magazine's eighteen-hospital “honor roll” marking overall excellence, tying with UCSF Medical Center for number seven.

Davisson Leads Team on Hypertension Grant

Researchers at Weill Cornell and the University of Iowa have been awarded a five-year, \$10.6 million federal grant to study the role of the brain in links between obesity and high blood pressure. The award, from the NIH's National Heart, Lung, and Blood Institute, funds three separate but linked studies focusing on neural pathways and mechanisms that lead to obesity and hypertension; they will also explore the role of the hormones angiotensin and leptin in regulating weight and blood pressure.

The Weill Cornell-led study will be headed by cell and developmental biology professor Robin Davisson, PhD. “Both obesity and hypertension, and the combination of the two, are serious health problems worldwide,” says Davisson, who also holds an appointment in biomedical sciences in the Veterinary college on the Ithaca campus. “Our studies are going to lend insight into some of the very basic mechanisms that cause those diseases to occur. Ultimately, what we learn could lead to therapeutic interventions that are different from what we do today.”

JASON KOSKI / UP



Robin Davisson,
PhD

FROM THE BENCH

Scientists Explore Biology of Blood Disorders

Two recent studies shed light on the molecular biology of three blood disorders: beta-thalassemia, HFE-related hemochromatosis, and polycythemia vera. The work involved researchers at six American and European institutions who explored the intricacies of how the body regulates iron and produces red blood cells. Published in *Nature Medicine* and the *Journal of Clinical Investigation*, the findings offer novel targets in treating the diseases. "When you tease apart the mechanisms leading to these serious disorders, you find elegant ways to manipulate the system," says Stefano Rivella, PhD, associate professor of genetic medicine in pediatrics.

Hypertension Soars in Sub-Saharan Africa

Diseases driven by high blood pressure are on the rise in sub-Saharan Africa, says a Weill Cornell professor of medicine and pediatrics working at the affiliated Weill Bugando Medical Centre in Tanzania. In the *Journal of Hypertension*, Robert Peck, MD, reports that nearly half of the deaths and admissions at Bugando in a three-year period were due to hypertension-driven illnesses such as stroke and other cardiovascular diseases. "This is a striking finding," he says, "because most people assume that stroke is a disease of the developed world." The study found that hypertension was the leading cause of death, after HIV. One reason for the increasing prevalence of high blood pressure—afflicting nearly 20 percent of adults in the region—is a move toward more sedentary lifestyles and Western diets. Tanzania has the world's lowest ratio of physicians to population, at one per 50,000 patients.

A Proposed Pathway for Surgical Innovation

In an article published in the *British Medical Journal*, Art Sedrakyan, MD, PhD, associate professor of public health and cardiothoracic surgery, and colleagues outlined a vision for evidence-based surgery and device research. "Currently, there is no dynamic research framework to systematically detect devices and surgeries that don't offer any benefits to patients or may even be harmful," says Sedrakyan, who heads the FDA medical device epidemiology net-

work (MDEpiNet) science and infrastructure center. The authors suggest ways in which clinical trials, observational databases, and registries can be used to assess the quality of devices and surgical techniques.

Epigenetics Key to Common Childhood Leukemia

Epigenetic changes—the turning on and off of genes—may be as important as genetic alterations themselves in causing pediatric acute lymphoblastic leukemia (ALL), the most common childhood cancer. Ari Melnick, MD, the Gebroe Professor of Hematology/Oncology, and a pathologist at St. Jude Children's Research Hospital published their findings in the *Journal of Clinical Investigation*. They report that a mechanism called cytosine methylation plays a previously underappreciated role in the development of leukemia. Their study involved tissue samples from 137 St. Jude patients with B-cell leukemia and thirty with the T-cell version, representing all major subgroups of ALL. "The data show that aberrant epigenetic gene programming can now be considered a hallmark of acute lymphoblastic leukemia, occurring in all patients regardless of the presence of genetic mutations," Melnick says, adding that the finding offers the opportunity for development of epigenetic targeted therapies.

Circuit Development Shows Origins of Brain Disorders

Recent work by Weill Cornell researchers could shed light on a variety of brain disorders. In *Cell*, pharmacology professor Samie Jaffrey, MD, PhD, and colleagues describe a mechanism that guides the wiring of neural circuits in the developing brain. Faulty wiring, they report, occurs when RNA molecules embedded in a growing axon are not degraded after they give instructions that help steer the nerve cell.

"The brain is quite 'plastic' and changeable in the very young," Jaffrey notes, "and if we know why circuits are miswired, it may be possible to correct those pathways, allowing the brain to build new, functional wiring." The work could have implications for such disorders as epilepsy, autism, schizophrenia, and mental retardation.



Samie Jaffrey, MD, PhD

Exploring the Source of Childhood Asthma

Common childhood asthma may not be caused by allergens or inflammation after all; researchers have linked it to an overactive gene that interrupts the synthesis of lipid molecules. "This is a completely new pathway for asthma pathogenesis," says Stefan Worgall, MD, PhD, chief of the Division of Pediatric Pulmonology, Allergy, and Immunology. The discovery, published in *Science Translational Medicine*, could represent a boon to patients. "Our findings are not only valuable in understanding the pathogenesis of this complex disease, but provide a basis to develop novel therapies, especially asthma agents based on a patient's genotype," Worgall says. Nearly 10 percent of Americans aged seventeen and under have asthma, making it the most common serious respiratory illness of childhood. It affects some 7 million children, leading to 640,000 emergency room visits, 157,000 hospitalizations, and 10.5 million missed school days annually, according to figures from 2009.



Stefan Worgall, MD, PhD

Anti-Cocaine Vaccine Nears Human Trials

A novel anti-cocaine vaccine has cleared a key testing hurdle in primates, with human trials expected within a year. According to lead investigator Ronald Crystal, MD, the vaccine "eats up the cocaine in the blood like a little Pac-Man before it can reach the brain." Says Crystal, chair of the Department of Genetic Medicine: "We believe this strategy is a win-win for those individuals, among the estimated 1.4 million cocaine users in the United States, who are committed to breaking their addiction to the drug. Even if a person who receives the anti-cocaine vaccine falls off the wagon, cocaine will have no effect." The vaccine combines bits of the common cold virus with a particle that mimics cocaine's structure, prompting an immune response. "The immune system learns to see cocaine as an intruder," says Crystal, the Bruce Webster Professor of Internal Medicine. "Once immune cells are educated to regard cocaine as the enemy, they produce antibodies against cocaine the moment the drug enters the body."

Talk of the Gown

Insights & Viewpoints



JOHN ABBOTT

Linda Vahdat, MD

Heavy Metal

Is copper the key to treating triple-negative breast cancer?

Oncologist Linda Vahdat, MD, has helped bring to market the last four major breast cancer drugs, playing a leading role in developing two of them. Director of the Breast Cancer Research Program and professor of medicine at Weill Cornell, she has devoted her career to treating patients with advanced stages of disease, earning a stellar reputation for translational research. But when Vahdat started sharing an idea for a new therapy—one that involves depleting patients' copper levels—she was met

with deep skepticism.

"I'm an established investigator, and then all of a sudden, I'm talking about copper depletion," recalls Vahdat, a native New Yorker who first investigated cancer at high school science fairs. "People thought it was a little bit of a crazy notion, but many were willing to quietly follow along to see how it developed. I'm sure more than one colleague thought I had shifted my focus to a more alternative and complementary medicine approach compared to my hardcore approach—which I have not!"

Undaunted by obstacles inherent to approaching a disease a new way—which, she says, made her feel as if she had “a full-time job pushing a boulder uphill”—Vahdat enrolled her first patients in a clinical trial for a copper depletion drug called tetra-thiomolybdate (TM) in 2007. Originally slated to run for two years, the clinical trial continues today; earlier this year she published the first Phase II results in the *Annals of Oncology*. “The bottom line is, we are very encouraged by our trial results. We have many people in our clinical trial who, statistically speaking, shouldn’t even be alive,” Vahdat says. “We have kept extending the duration that patients are kept on the trial because we have scientific evidence that we are interfering with processes that we believe are critical to tumor progression, and the net result is that we may be preventing tumors from recurring. If this is so, we feel we have a moral obligation to keep providing them with TM and continuing to study its effect.”

Copper depletion has shown particular efficacy in patients with triple-negative cancer, so-called because the tumors test negative for estrogen, progesterone, and HER2 receptors and therefore do not respond to hormonal therapies or to Herceptin. Between 15 and 25 percent of breast cancer diagnoses fit this profile and as a result have a poor prognosis; once such a tumor metastasizes, patients have a median survival rate of just nine months. The second woman Vahdat enrolled in the study had triple-negative breast cancer that had spread to her liver. Luckily, she was able to undergo therapy to remove all traces of it prior to starting on the TM trial. Surprisingly, at the end of two years in the trial, she was well and disease free—an observation that was not what one would expect. This inspired Vahdat to look closely at how copper depletion affects that population. “You have to be open-minded,” she says. “This is part of being a scientist. You have to be able to process observations and try to make sense of them.”

After seeing positive results, Vahdat was eager to understand the mechanism by which copper depletion might work, above and beyond what could be learned from the clinical trial. She proposed a study with longtime collaborator Vivek Mittal, PhD, associate professor of cell and developmental biology in cardiothoracic surgery. They had begun working together several years earlier, when Mittal’s lab was looking for microRNA—the noncoding



ABBOTT

Seeking a cure: Vahdat with members of her lab

RNA molecules that regulate gene expression—involved in breast cancer metastasis. Earlier this year, Vahdat and Mittal co-authored a paper in which they identified a microRNA that is highly suppressed in metastatic triple-negative breast cancer. When its function is restored in mouse models, tumors do not spread. Vahdat and Mittal are now in talks with pharmaceutical companies to further pursue that angle of research.

They have also done extensive work investigating how new sites are prepared for metastasis, a process in which primary tumors recruit bone-marrow derived progenitor cells to establish niches where new tumors can grow. “What we thought could be happening is that depletion of copper might be destroying this pre-metastatic niche,” Mittal explains. “If you destroy those niches, the primary tumor will not be able to metastasize.” As a first step, Mittal’s lab depleted copper in mice whose breast cancer had spread to the lungs, reaching levels as low as Vahdat had in human patients. They observed that depletion did not stop the primary tumor from growing—but did affect its ability to metastasize. The lab is now conducting experiments on a copper-dependent enzyme essential to the establishment of pre-metastatic niches, and Mittal is confident they will soon detail the full mechanism by which copper depletion prevents metastasis.

Mittal admits he wouldn’t normally

have been interested in testing such a strategy in the lab. But when Vahdat showed him her early clinical data, he got excited. “She is treating triple-negative breast cancer patients. There is no therapy for these people—yet this copper depletion is clearly benefiting them,” he says. “You can discover a lot of interesting things in humans, then study the nuts and bolts in mouse models and figure out better ways of treatment to go back to the patient.”

Vahdat and Mittal agree that the need to develop therapies to fight metastasis is dire, since all currently available drugs target only primary tumors. “The focus has to move to metastasis, because the primary tumor is not what kills people,” Mittal says. And time, Vahdat says, is of the essence. “These patients are desperate for something,” she says. “The longer we take, the more people will die. And I really feel like we could be on to something important.” While cautioning that they are still gathering data, Vahdat notes that copper depletion has the potential to become standard therapy for triple-negative breast cancer in the way that Tamoxifen is for hormone-receptor positive disease. The foundation for the next set of clinical trials is being laid to assess, once and for all, if this is an effective strategy. Still, Vahdat admits, “Every time I say ‘copper,’ I think it’s a little bit crazy. But it is what it is, and there’s the science to back it up.”

— Andrea Crawford

Lab Partners

Weill Cornell and
NewYork-Presbyterian
join forces on clinical trials

When pediatric hematologist-oncologist James Bussel, MD, initiated his first clinical trial at Weill Cornell back in 1981—on the use of intravenous gamma globulin in the treatment of the blood disease ITP—it got rolling under what was basically a gentlemen's agreement. "I talked to the pharmaceutical company, and they said they'd give me some money," says Bussel, professor of pediatrics at Weill Cornell and an attending pediatrician at NewYork-Presbyterian Hospital. "We got Institutional Review Board approval and went ahead with no contract and no real budget."

In the thirty-plus years since, such informality has gone the way of the slide rule. Physicians who want to initiate trials now face a maze of logistical and administrative barriers including intensified regulatory burdens, increased institutional review, spiraling research and development costs, and dwindling federal dollars. "They've generally gotten much harder," says John Leonard, MD, the Richard T. Silver Distinguished Professor of Hematology and Medical Oncology and associate dean for clinical research. "The regulatory burdens are heavier. More steps are required. And the costs are higher because the steps are greater."

Among the biggest hurdles: negotiating a contract between the institution and its funding partner, and developing a budget that meets institutional standards. Contracts can get hung up on issues of indemnification and intellectual property rights, while detailed budgets must integrate with billing so that services for trials are separated from patients' clinical bills. "Let's say you order a blood count, liver test, and iron levels on a patient in a trial," Bussel offers as an example. "Your budget has to be developed such that the system will know that the blood count and liver test are part of the study, and should be paid for by it, whereas the iron levels are just clinically indicated testing that have nothing to do with it. That level of detail is present in almost every aspect of a trial."

Until recently, most of these functions have been left to the departments and individual investigators to navigate. (Bussel, for his part, hired a full-time nurse to handle his trials' administrative aspects to make sure to maintain compliance.) But in January, in an effort to streamline the process, Weill Cornell launched a Joint Clinical Trials Office with NewYork-Presbyterian Hospital. "Our big-picture goal is to increase high-impact clinical research that synergizes with our other missions," says Leonard, who is directing the initiative. "We want to grow the clinical research activities here in a way that fosters and benefits other aspects of the institution, whether it be patient care, laboratory research, or education."

An active clinician-scientist, Leonard has played a pivotal role in



BANANA STOCK

developing novel treatment strategies for lymphoma, establishing Weill Cornell as one of the world's leading centers for monoclonal antibody-based therapies. His current research focuses on targeted treatments—understanding why people with the same disease can have vastly different responses to the same drugs. In addition to participating in investigator-initiated trials at Weill Cornell, Leonard chairs one of the National Cancer Institute's lymphoma clinical research groups and oversees NCI-funded trials across the country. He notes that while other institutions offer trial support in various ways, the joint collaboration is unusual. He's in the process of setting up a leadership team for the office, which will have oversight of some 2,000 clinical trials occurring at NYP and Weill Cornell at any given time. Says Leonard: "We are working to provide investigator support, scientific and feasibility review, financial management, and regulatory compliance under one umbrella."

One way the new office will expedite processes is through the establishment of master agreements—documents that establish the terms and conditions of the relationship between the institution and the pharmaceutical company or other funding sponsor, so individual trials don't have to re-invent the wheel. "Improving the efficiency and speed with which clinical studies are implemented at the Medical Center will benefit investigators, sponsors, and patients," says Gene Resnick '70, MD '74, chief medical officer of Aptiv Solutions, which designs and implements clinical trials for pharmaceutical and medical device companies, including some at Weill Cornell. "The Joint Clinical Trials Office is a terrific initiative that will only make Weill Cornell more attractive to biopharma and medical device companies as a trial partner."

The office was the brainchild of Dean Laurie Glimcher, MD, and NYP President Steven Corwin, MD, who have prioritized collaboration between the hospital and Weill Cornell. Although most trials originate at the Medical College, Leonard says there is significant overlap of services including information technology, pharmacy, labs, and radiology. "It became clear that it was best to work together," he says. "Trials attract patients, who attract physicians. They greatly benefit both institutions."

— Renée Gearhart Levy

Power of Prediction

Computer model forecasts the spread of Alzheimer's

According to a RAND Corporation study published in the *New England Journal of Medicine* last spring, the costs of treating dementia could soar as high as \$511 billion a year by 2040—when the condition is expected to afflict some 9.1 million Americans. Facing those dire numbers, researchers and clinicians welcome any advantage that might help to stave off an epidemic of suffering for patients, their families, and society at large.

At Weill Cornell, Ashish Raj, PhD '05, and colleagues are creating a novel weapon in that battle. But the members of his lab aren't neuroscientists; their graduate degrees are in such fields as engineering, physics, applied math, and even astronomy. Raj, an assistant professor of computer science in radiology, is spearheading an effort to design computer models that can predict the course of neurodegenerative conditions—not just Alzheimer's and frontal temporal dementia but also Parkinson's, multiple sclerosis, stroke, and more. "Our theoretical model can have an impact on real-world health care," says Amy Kuceyeski, PhD, an instructor in mathematics in radiology who joined the project as a postdoc. "That's the most exciting part."

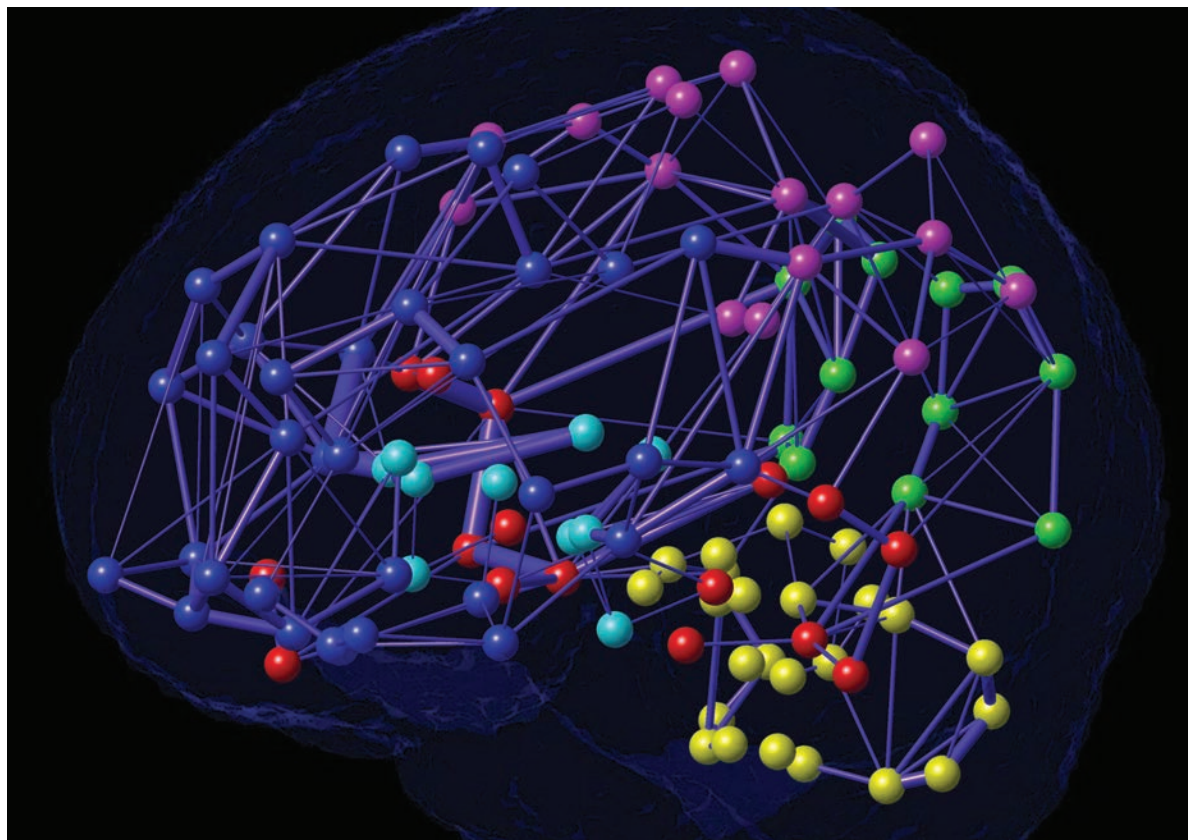
Their work, first published in *Neuron* in 2012, used hundreds of brain scans from the Alzheimer's Disease Neuroimaging Initiative to create an algorithm that can anticipate the progress of neuronal damage over time. Eventually, it could serve as a predictive tool for physicians, patients, and their families. "Suppose you're suffering memory problems and suspect you have Alzheimer's," says Raj, who earned his doctorate on the Ithaca campus. "We can put your MRI into the model, and it will tell you how the disease will develop over time—five, ten, fifteen, twenty years down the line. Basically, you get a weather map of how it's going to evolve—how much of it you'll get and where. Because each part of the brain has a specific functional role, we can predict what kind of deficit you're likely to

encounter and whether you're going to have memory, attention, or motor problems."

The central thesis of Raj's work rests on the fact that the brain is an interconnected network of neurons—and like any network, its structure influences its behavior. Alzheimer's, he notes, takes a reliable path: the damage starts in the temporal lobe, moving to the parietal lobe and then to the frontal. "It happens to every single patient, and you have to wonder what is going on—it's not random," he says. "We're confident that this

Brain waves: An illustration of neural connections demonstrating the path of Alzheimer's disease

EVE M. LOCASTRO



model is capturing the dynamics of the disease." While he stresses that the work is in its early stages, he can envision its clinical benefits. By knowing what part of the brain the disease will strike next, physicians could focus on strengthening those areas through such treatments as transcranial magnetic stimulation, deep brain stimulation, or stem cell therapy. If Alzheimer's path can be predicted, in other words, its damage may not be inevitable.

— Beth Saulnier



Art Sedrakyan, MD, PhD

ABBOTT

The Next Step

Registry consortium aims to aid development and use of evidence-based orthopaedic implants—and avoid costly failures

In 2005, a new implant/prosthesis promised to revolutionize hip replacement. Rather than the industry standard metal-on-polyethylene, which could be expected to last fifteen years, the device boasted a metal-on-metal joint, which industry researchers claimed would last a lifetime. Around the world, orthopaedic surgeons began to implant this new device into patients. But major problems soon became apparent.

“The wear rate turned out to be very high, which led to much earlier failure in hundreds of thousands of patients,” says Art Sedrakyan, MD, PhD, associate professor of public health and director of a patient-centered comparative research program in the Department of Public Health that houses the FDA medical device epidemiology network (MDEpiNet) science and infrastructure center. “In addition, patients were experiencing substantial metallosis—elevated levels of metal ions in the blood.” In other words, the alloy employed—a blend of chromium and

cobalt—was covertly poisoning patients. And at the joint ends, friction flaked off bits of metal, which lodged in muscle tissue and caused chronic pain.

To aid in catching defective devices before they become medical disasters—Sedrakyan estimates that half a million recipients of this device could need follow-up surgery—the Device Center of the Food and Drug Administration has established the International Consortium of Orthopaedic Registries (ICOR). It is led by an international steering committee, and Sedrakyan serves as principal investigator of the grant to support its development. While in the past a loose global network of orthopaedic device registries struggled to catalog and assess patient and doctor feedback on joint replacement outcomes, ICOR hopes to streamline communication, enhancing and coordinating data. “Critically evaluating current technologies is ICOR’s goal,” says Sedrakyan. “We need to be able to spot poorly performing products quickly, so they won’t be used in hundreds of thousands of patients before

we’re able to see their shortcomings.” Though issues with this implant began appearing just two years after its 2005 release, he notes, an official recall was not issued until 2010.

ICOR’s inaugural meeting, held in May 2011, brought together seventy-three stakeholders from twenty-nine registries representing fourteen countries—offering diverse perspectives on the flaws in orthotic device testing and research. Public health department chair Alvin Mushlin, MD, sees enormous promise in ICOR, including the potential to serve as a blueprint for other international consortia. “This is really a model,” says Mushlin. “It started with orthopaedic devices, but there are other areas in medicine and surgery in which we could come together and collaborate to provide better information about the safety and effectiveness of medical devices.” In fact, in April 2013, following on the success of ICOR, an international cardiovascular device initiative was started by Sedrakyan in conjunction with the FDA and in partnership with leading cardiovas-

cular experts around the world.

Beyond working with extant data and research, ICOR hopes to raise the bar for device development and testing. For a drug to be approved by the FDA, it must undergo an exhaustive series of trials to demonstrate safety and efficacy—but that's not the case in the device world. "Historically, devices have not been used as commonly as drugs," says Sedrakyan, "so the fiscal sense of doing big expensive trials for a small market product just didn't add up." But with the number of hip and knee replacements expected to balloon to three million annually by 2035, orthopaedic devices are no longer a special-case, small-market industry. "These insufficient studies on device safety have real potential to harm people," says Sedrakyan, "and everyone who's a part of ICOR understands that."

Along with the ground to be gained in testing and research, the information collected by ICOR will help guide device development. In the past, the orthopaedic device industry has effectively been working in the dark—trying out various innovations without the benefit of feedback from patients or surgeons. This sort of disconnect was particularly apparent in the case of another recalled implant that was approved in 2008. It featured a variety of interchangeable stem and neck options, known as a "modular neck," which broke the implant into a series of components that could be customized to a patient's particular anatomy. "This was promised to be a big advancement, but it turned out not to be," says Sedrakyan. "There is emerging evidence that all those extra parts led to earlier than expected failing."

However, other companies jumped on the bandwagon, developing their own products that capitalized on the new technology. A 2006 article in *Orthopedics* even hailed the modular-neck hip as the "keystone to functional restoration" in hip replacement. Sedrakyan argues that this kind of well-meaning but ultimately misguided innovation could be recognized early and prevented by a stronger interface among patients, industry, and the medical community through the development and analysis of information about devices in the registry system. "If doctors can learn immediately that a certain modification doesn't lead to improved outcomes, then the industry won't pursue further developments in that same track," says Sedrakyan. "More feedback, more progress."

— Kristina Strain

Genetic Diversity

WCMC-Q Genomics Core facilitates a variety of research, on the Doha campus and beyond

GOOGLE IMAGES



Key crop: The Genomics Core's achievements include sequencing the genome of the date palm, a staple of the Middle Eastern diet.

Once upon a time, in the ancient past of genetic analysis—say, a decade ago—sequencing a genome was an expensive, lengthy proposition. Happily, times have changed. Now, the WCMC-Q Genomics Core can sequence the equivalent of eight human genomes in ten days—at a dramatically lower cost. "The price drop over the past ten years is shocking," says the Core's director, Joel Malek, PhD, assistant professor of genetic medicine. "It has fallen at least 1,000 fold per DNA sequence—if not 10,000 fold." Then there are the technological advances that have driven costs down in the first place. For example, Malek says, whereas researchers studying a genetically inherited disease might previously have been limited to sequencing just part of a subject's genome, now faster techniques

make it practical to sequence all of it—allowing them to shine their investigative flashlights over a much wider area. "The technology is moving so fast," he says. "Every day you could walk in and say, 'This really wasn't feasible a few weeks ago, but with the technology improvement we can consider it as a viable option.'"

And, as Malek notes, these days such analysis isn't just for genomes anymore. Having realized it's a "very robust, consistent technology," he says, researchers are applying it to an ever-widening variety of topics. "Now it's used for detecting infections, predicting cancer outcomes, looking at what genes are turned on and off, trying to figure out what proteins are regulated," he says. "With one core, you can support many different kinds of research."

Located on the Doha campus, Malek's facility boasts state-of-the-art equipment—

he estimates it's worth between \$5 million and \$6 million—and a staff of eight. In addition to supporting other researchers, not only at the Qatar branch but in New York and Ithaca as well, they conduct their own investigations. Many of those projects have close relevance to the emirate, such as exploring common genetic disorders—a pressing issue in Qatar, where about a third of marriages are between first cousins. The Genomics Core has also sequenced the genome of the oryx, a variety of antelope that is Qatar's national symbol; the species is classified as “vulnerable,” and the findings are hoped to strengthen genetic diversity in the emirate's captive breeding program. It has also done extensive work on the date palm, a crop essential to the Middle East. That research—whose funding has been renewed for another five years, with a \$4.5 million grant from the Qatar Foundation—is currently focused on establishing the genetic basis for such traits as drought hardness and salt resistance. “The Core is absolutely, critically important,” says M. Elizabeth Ross, MD '79, PhD '82, the Nathan Cummings Professor of Neurogenetics and Development. “It has been a focal point for building research programs, because one of the unique aspects of the region is the population and its character.”

Based in New York, Ross has traveled to Doha every six to eight weeks for the past couple of years, spearheading a neurogenetics program on the Qatar campus. She has high praise for the strides Malek and his staff have made in developing the Core, which she calls “a pioneer in the region.” Says Ross: “Just about anyone can purchase the equipment—it's how you use it that makes all the difference. Joel has been incredibly successful in building a highly capable team. The group has been wonderful to work with; they've been receptive to collaborating with investigators, and they take a real interest in the projects that come their way. It's more than just a service core.”

Arash Rafii, MD, PhD, an associate professor of genetic medicine in obstetrics and gynecology on the Doha campus, has been working with the Genomics Core on studies of how ovarian cancer metastasizes from the primary tumor to the peritoneal cavity. He notes that while the Core's equipment isn't particularly rare—if need be, he could send his samples to any number of facilities in the Middle East and

beyond—the close interaction with its staff enriches the enterprise immeasurably, on both sides. “By doing it here, we raise the level of everyone who is involved in this project,” he says. “It's creating know-how instead of just outsourcing a technology.” Rather than simply receiving shipped samples and doing the required analysis, the Core's staff can visit Rafii's lab and observe him in the OR—not only getting them more invested in the project, but broadening their knowledge base and making them more sophisticated researchers in their own right. “They feel that each sample is special,” Rafii says. “They see that there are patients behind what we're

doing, and it inspires them.”

Ross notes that the Doha core has another practical advantage: it gives all Cornell-affiliated researchers another analytical option, in addition to the genomics facilities in New York and Ithaca. “One thing that's cool about this is that we have three campuses we can rely on,” she says. “Each has a slightly different focus—so with the three of them, we cover a lot of territory in terms of expertise. Throughput capacity can be an issue when you've got a lot of projects cooking. It's great to know that when one particular core has more work than it can handle, there's another we can turn to.”

— Beth Saulnier

Sound Minds

A surgeon and a bioengineer design lifelike ears for kids born without them

Microtia is a congenital birth defect in which one or both outer ears is missing or deformed. Occurring in from one to four out of every 10,000 births, it's relatively common—but it remains a surgical challenge. “There's a lot of it out there,” says Jason Spector, MD, associate professor of surgery, “and it's very difficult to reconstruct.” For such children and their parents, the options are far from ideal: either an artificial implant, which runs a high risk of infection, or one crafted from the patient's own rib cartilage, which entails a painful recovery.

In both cases, the results tend to be mediocre. The outer ear, after all, is a marvel of construction. Made of an especially elastic type of cartilage, it's firm but pliable, yielding to the touch but readily regaining its form. It serves an important function in directing sound to the inner ear—and, obviously, it's an essential aesthetic feature of the human head. Children with microtia generally undergo reconstructive surgery around the time they start school—not only for physiological reasons, but to spare them the inevitable teasing on the playground.

Within the next few years, though, kids and parents may have a much better option. Spector and Ithaca-based biomedical engineer Larry Bonassar, PhD, have had highly encouraging results in a project to bioengineer ears. Their ultimate aim: to craft anatomically exact ears from a patient's own cells—natural implants that would not only be functional and attractive, but sidestep issues of tissue rejection. “The quality of the results is very high,” Bonassar says of the work, reported in *PLOS One* in February. “It's the most robust cartilage that I've ever seen anybody grow. It has all the molecular characteristics that we look for.” Adds Spector: “When you slice it up under a microscope, the histology looks exactly like native auricular cartilage.”

The team's initial work employed tissue taken from cow ears and used to form a gelatin-like solution, which was then either shaped in an injection mold or extruded with a 3-D printer. The implants, made in Bonassar's lab, were shipped to Spector via the campus-to-campus bus and inserted under the dorsal skin of rats—where the new ears have thrived. Now, Bonassar is working with human tissue Spector obtains in the OR, with the long-range goal of



Hear, hear: In the Ithaca lab of Larry Bonassar, PhD (right), a 3-D printer forms an artificial ear (above).

growing enough ear cartilage for each patient—one ear requires some 250 million cells—through samples taken from their own bodies, possibly nurtured with their bone marrow and stem cells and, potentially, growth factors. Thanks to advances in computer imaging, bioengineers can scan a patient's normal ear—most cases of microtia are unilateral—and create a perfect mate, a quick and painless process that wouldn't require kids to be sedated.

Since their work was reported in the media, both Spector and Bonassar have received dozens of queries from parents around the world, clamoring to know when the technology will be available. Another growing constituency, Bonassar notes, is war veterans; thanks to advances in body armor, soldiers are surviving previously fatal injuries but are left with disfiguring wounds. With a significant amount of preclinical work still to be done, the researchers estimate it will be another

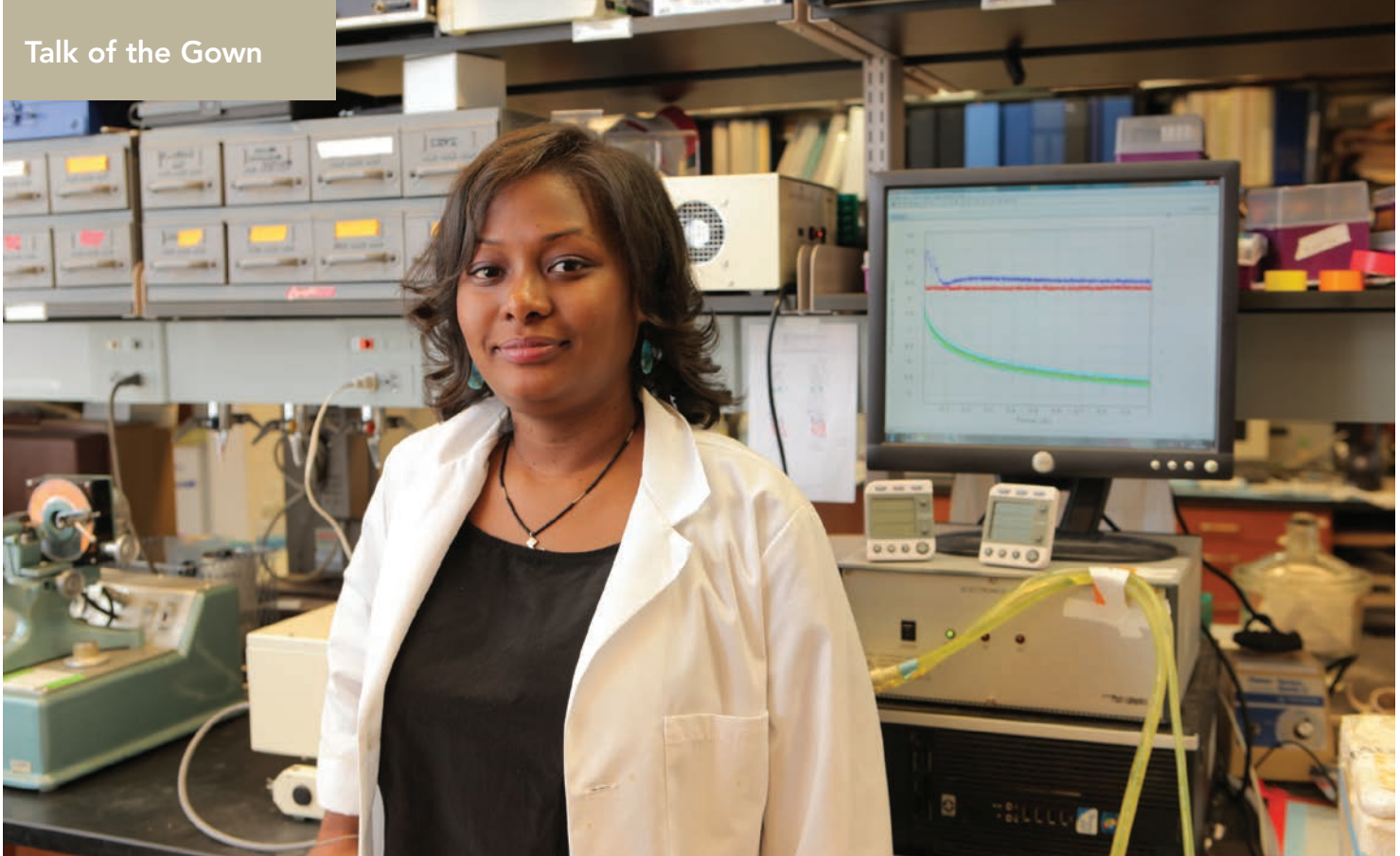


LINDSAY FRANCE / CORNELL UNIVERSITY PHOTOGRAPHY

three to five years until the ears are implanted in humans. "The idea that you can literally print up a perfect replica of a normal ear is something that people are hopeful and excited about," Spector says.

"I don't want to disappoint them. I want to make this technology a reality, because it would make such a huge difference in the lives of these children."

— Beth Saulnier



ABBOTT

Nicole Ramsey

Bitten by the Science Bug

Already a veteran researcher, MD-PhD student Nicole Ramsey is preparing to battle malaria from bench to bedside

The package arrived just in time for Nicole Ramsey to do the research that would become the final chapter of her doctoral thesis. Known as the Malaria Box, the small rectangle represents some big ambitions: it's a stack of plastic trays containing dozens of drugs with the potential to fight a disease that, according to the WHO, kills one African child every minute of every day.

Compiled by the nonprofit Medicines for Malaria Venture, the box is much in demand among researchers worldwide. They can get it free of charge—but first, they must prove that their project merits it. Ramsey, an MD-PhD student studying the effects of promising antimalarials on the cellular membranes known as lipid bilayers, passed muster. She's currently wrapping up her thesis, which explores how a drug's effect on lipid bilayers may

predict toxicity—steering researchers away from compounds likely to prove undesirable. “It’s a validation that the people who give out the samples believe this approach will be helpful in making decisions about what drugs to develop further,” says Olaf Andersen, MD, director of the Tri-Institutional MD-PhD Program and Ramsey’s thesis adviser. “One of the problems with the treatment of malaria, and many other diseases of the developing world, is that there’s not a lot of money available for drug development. So the more hints you can get to reduce the risk of failure later on, the better off you are.”

This fall, it’s back to medical school for the future physician-scientist, who’s planning a career in academic medicine. After completing her MD she’ll specialize in pediatrics, with a likely concentration in infectious disease; even as a busy graduate

student, Ramsey took time each week to shadow that subspecialty service at Weill Cornell. “As much as I love research, I also love interacting with patients and taking care of them,” says Ramsey, whose favorite leisure activity is finding online discounts for the city’s cultural and culinary delights. “Someday I’d like to see my research helping people—to be part of the whole process.”

Ramsey grew up in Canarsie, Brooklyn, in a medical household: her mother is a visiting nurse, her father a respiratory therapist. (Her younger sister is following in her MD-PhD footsteps, matriculating at Albert Einstein this summer.) Ramsey attended high school at Bronx Science—commuting two hours each way—and earned an undergrad degree in biology at Howard University. She first came to Weill Cornell the summer after her freshman

year through the Gateways to the Laboratory Program, which encourages underrepresented minorities to pursue an MD-PhD through a ten-week immersion in medicine, surgery, and bench science.

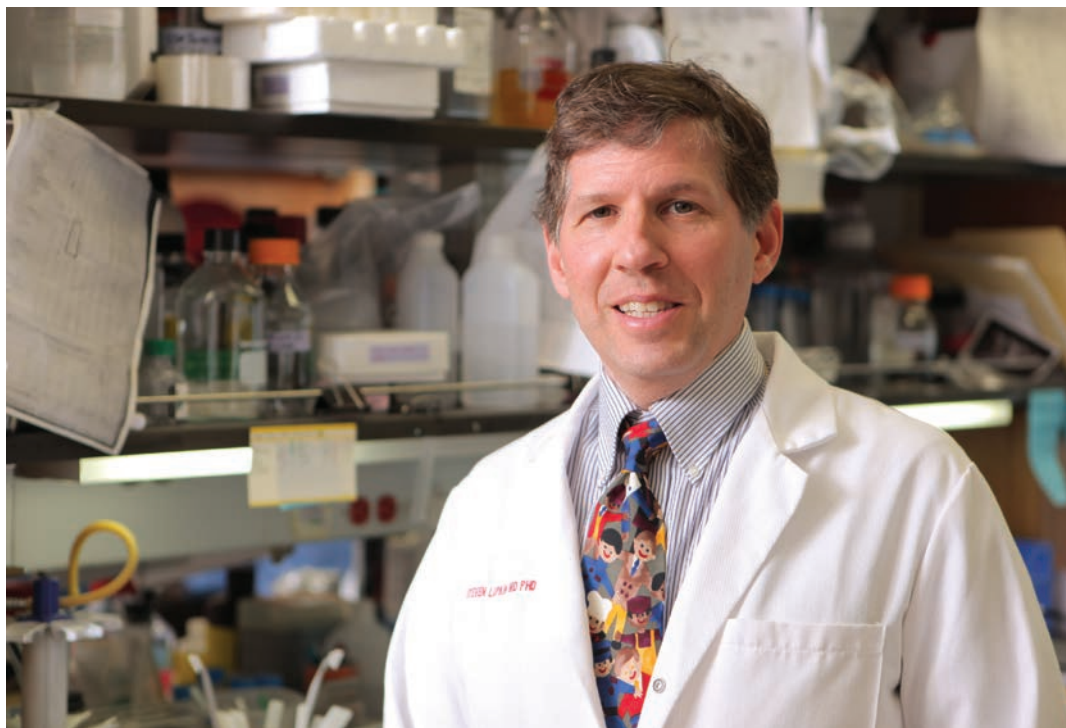
Ramsey already had some research experience; as a high school student she'd interned in the nutrition department at Columbia, doing obesity-related work on yeast that, a decade later, would garner an author credit in the *Journal of Biological Chemistry*. She continued to pursue research throughout college, including a summer in the West African nation of Mali, where she was inspired to focus on malaria. In 2011 she won a United Negro College Fund/Merck Institute for Science Education Fellowship, a highly competitive award that carries a grant of more than \$50,000. "She will achieve great things," says Carla Boutin-Foster, MD, MS '99, the Nanette Laitman Clinical Scholar in Public Health/Community Health and assistant dean for faculty diversity, who was Ramsey's first-year medical school mentor. "She's an excellent student and role model. As a young African American woman, an MD-PhD, she is a wonderful example of scholarship, intelligence, and patient advocacy."

On top of her thesis work and medical studies, Ramsey has been active in Weill Cornell student outreach groups. She's the head of Motivating Action through Community Health Outreach (MACHO), which combats the childhood obesity epidemic by encouraging exercise and healthy eating among kids in minority neighborhoods. Inspired by another initiative, known as Achieving Successful and Productive Academic Research Careers (SPARC), that Boutin-Foster established to offer career development for women and underrepresented minorities on the junior faculty, Ramsey pitched a version for high school and college students. The result, an annual conference at Weill Cornell, draws busloads of participants from as far away as Rochester and Philadelphia. "We often think of research as being siloed, not connecting to the population," Boutin-Foster observes. "But Nicole is creating a paradigm where we're able to translate skills and understanding of basic science, like teaching kids about nutrition in a way that resonates with them. That's what we're advocating for—more students like Nicole, who believe their science degree can change the world."

— Beth Saulnier

Message Received

Working with an Ithaca-based engineer, Steven Lipkin, MD, PhD, has revealed 'GPS genes' that can drive colon cancer metastasis



ABBOTT

Steven Lipkin, MD, PhD

According to the American Cancer Society, this year more than 140,000 Americans will learn they have colorectal cancer. Early detection and treatment can provide a five-year survival rate of nearly 100 percent, but more than four in ten Americans skip the colonoscopies that can catch the disease before it metastasizes. As a result, many tumors are detected only after they have spread—making it imperative for researchers and physicians to understand why cells metastasize and how to stop the process. "All too often, if there are multiple metastases we have little hope of curing the patient and can only try to slow down the whole process," says Steven Lipkin, MD, PhD. "There's a critical need to study the biology of metastasis, so we can develop new drugs that could save patients whose tumors have advanced."

Lipkin, an associate professor of medicine and of genetic medicine, has devoted his career to studying a range of gastrointestinal maladies. He became interested in colon cancer because of its ubiquity—it's the second most common cancer in the U.S.—and because many aspects of the disease remain a mystery. "We still don't understand colon cancer very well and have only scratched the surface, unfortunately," says Lipkin. "It's a complex problem. All kinds of receptors and cell messaging systems are involved."

Throughout the body, chemical messengers called chemokines shepherd cells to different locations in the body through a complex series of signaling pathways, guiding the immune response. For example, immune cells migrate to the skin when you nick your fin-

ger with a knife or to the lungs when you get pneumonia. As a colon tumor grows it's able to co-opt this system, breaking off pieces of itself and sending them into circulation. Meanwhile, the chemokines act as oblivious escorts, taking these cells to new tissues and establishing new cancers. Up until now, the exact chemokines involved have been unknown to researchers. "The problem we want to address is that there aren't good models showing how colon cancer metastasizes," says Lipkin. "If we're able to develop a better model, we're better able to understand the whole process, and we can create a better system to screen potentially lifesaving drugs."

Recently, a cross-disciplinary collaboration has helped shed light on the specific factors at work in colon cancer metastasis. With Xiling Shen, PhD, an assistant professor of electrical and computer engineering at Cornell's Ithaca campus, and Shen's graduate student Huanhuan Joyce Chen, Lipkin has made a breakthrough: the discovery that a chemokine called CCR9 and its ligand receptor CCL25 regulate the movement of colon cancer cells. "The presence of CCR9 keeps them essentially stuck in the colon," says Lipkin. But, he explains, as the cancer grows, its cells become less like the normal colon cells they evolved from and lose their ability to produce the "stay put" signal. The factor keeping colon cancer contained disappears. "It's like when you turn off an electromagnet and all the little iron filings go away," says Lipkin. "That's when metastasis happens."

This elaborate cell messaging system, which makes colon cancer metastasis so fascinating, is precisely what makes it difficult to study: replicating the CCR9/CCL25 pathway outside the human body has been impossible. Mice, the usual lab animal of choice, share none of the biochemical nuances found in human chemokine pathways. "Mice are pretty good models if you're doing infectious disease studies and testing antibiotics; there, the correlation to humans is very strong," says Lipkin. "But in oncology, 80 percent of the drugs that are put into clinical trials with mice end up failing somewhere along the way." Dogged by the unpredictability of this imperfect system, colon cancer researchers like Lipkin have logged many hours laboring over promising treatments that turned out to be unsuccessful.

Now, thanks to the expertise that Chen and Shen have brought to the project, the CCR9/CCL25 pathway has been engi-

neered into mice. That has been the key to creating a reliable lab model. Colon cancer cells inside an engineered mouse behave the way they would in a human—staying local when the pathway is activated and migrating when it is turned off. "Now we can imitate the human gut microenvironment," says Shen. "By engineering the chemokine 'switch' into mice, we are able to recapitulate the natural route of metastasis and the natural environment for colon cancer." Chen shuttles back and forth between Shen's lab in Ithaca and Lipkin's in Manhattan, engineering the chemokine mechanism into different colon cancer cell lines and culturing them. "Now we can study metastasis in a petri dish," says Chen. "We can use this discovery to engineer a new mouse model."

Shen and Lipkin's collaboration arose serendipitously when Shen traveled to Weill Cornell to give a lecture and Lipkin invited him to contribute to his research. Now, the two scientists are forging a non-traditional partnership that is as much about educating each other as it is about sharing research. With their first round of research published in the *Journal of Clinical Investigation*, the three collaborators are at work on a paper describing the engineering principles that make the chemokine switch possible. "Problems like these require people to go outside their comfort zones," says Shen. "I had to understand medicine; Steve had to understand engineering. It's about more than just bringing your own expertise to the table."

— Kristina Strain

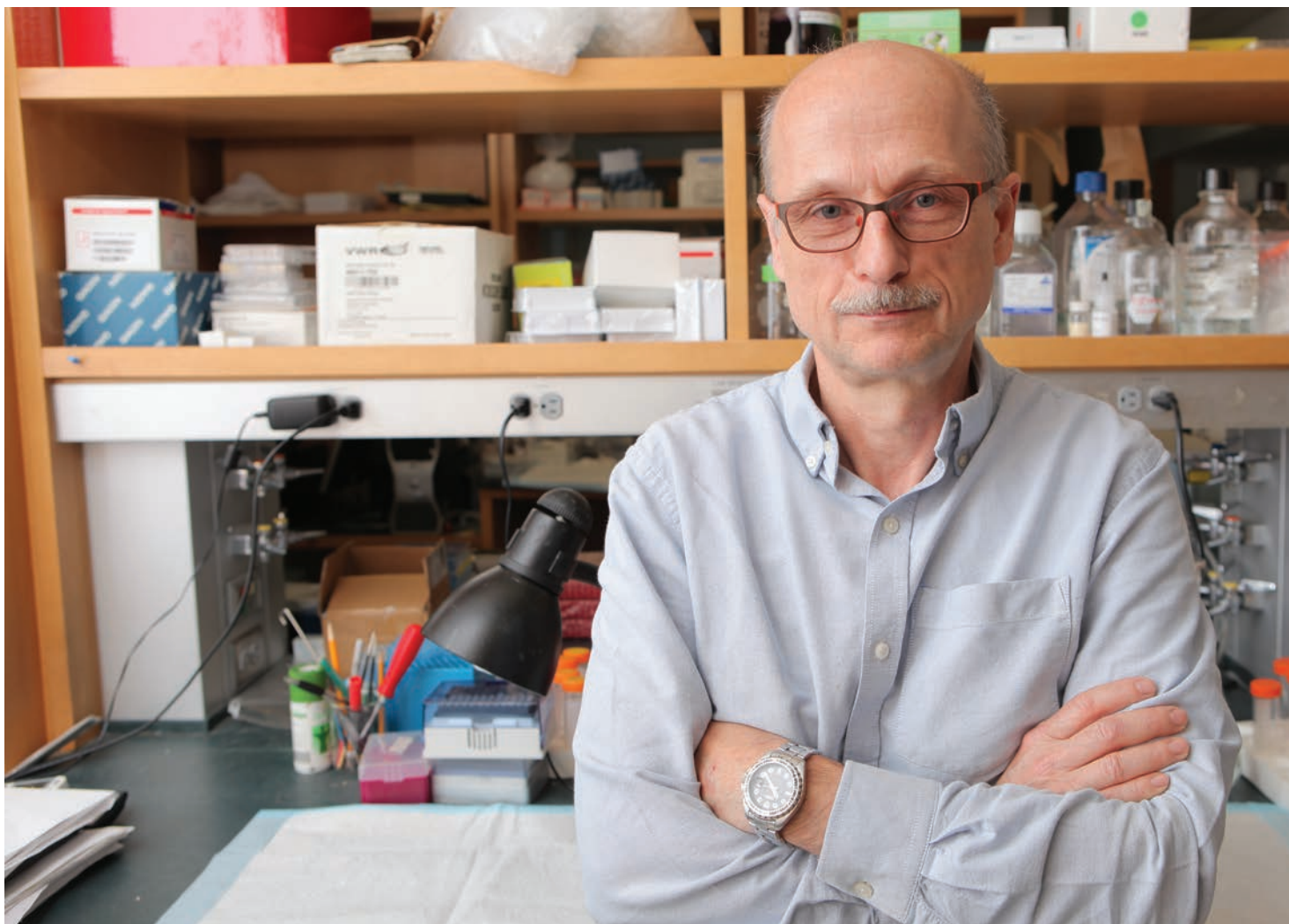
The Gestation Equation

How does the maternal environment affect the developing brain?

Expectant mothers know the dangers of exposing their babies to substances that can harm them, such as alcohol, tobacco, raw fish, and too much caffeine. But now pregnant women may have something else to worry about: stress. According to researchers led by Miklos Toth, MD, PhD, professor of pharmacology, children born to mothers who suffer from high levels of stress during pregnancy have an increased risk of psychiatric conditions such as anxiety and depression throughout their lifetimes. While predisposition to disease has typically been thought to be transmitted across generations by genetic mutation, Toth and his colleagues have found that the gestational environment also plays an important role.

They call it "maternal programming"—a term that describes the influence of the mother's body during sensitive periods of development that produces persistent effects in offspring. The research, which was funded by the NIH and the Brain and Behavior Research Foundation (formerly NARSAD), shows that gestational factors are essential for both the proper development of the fetal and neonatal brain and the establishment of normal adult emotional and cognitive behavior. Conducting experiments on mice, Toth and his lab members have shown that environmental perturbations can lead to developmental abnormalities in offspring that manifest in adolescence and adulthood as mental and cognitive disorders. "This is a major finding and quite surprising," says Francis Lee, MD, PhD, professor of psychiatry and pharmacology. "The assumption has always been that these conditions would have to be transmitted genetically. Translating this to humans, it means that it should be important to minimize stress and anxiety during pregnancy, particularly during the third trimester."

In Toth's experiments, normal mice placed in stressful living environments while pregnant not only displayed signs of anxiety themselves, but produced offspring that displayed symptoms of anxiety—and sometimes a symptomatic second generation as well. Similar models testing for depression showed the same findings. "It was puzzling," says Toth, who also holds an appointment in neuroscience. "How can you have a dis-



ABBOTT

Miklos Toth, MD, PhD

ease that looks like it is genetically transmitted yet is totally not genetic? At a fundamental level, this is unusual compared with what we are used to in Mendelian genetics."

Although fetal brain development occurs throughout pregnancy, it is during the third trimester that circuitry relating to emotions and psychiatric disorders is particularly vulnerable. How and why remain unclear; Toth is currently working to determine the mediator of this mother-to-offspring effect. "We are trying to outline certain pathways," he says, "from the very beginning of the insult, step-by-step, through the placenta to the fetus and the fetus's brain, to see what kind of cell is targeted." Toth says there is some evidence that factors in the altered gestational environment reach the developing brain across the placenta, and also through lactation postnatally, through cytokines and chemo-

kines—proteins produced by immune cells. "Somehow the molecules, if produced in excess, may no longer serve an immunological role and can adversely affect the offspring," he says.

A second question is what happens in the developing fetus to cause lifelong deficits in function—and in some cases, in a second generation as well. Toth and his team are looking for epigenetic marks, changes in gene expression or cellular phenotype, caused by mechanisms other than changes in the underlying DNA sequence. "We do know that if the maternal environment is adverse, certain genes are very sensitive and they make a permanent change," he explains. "Through this whole complicated pathway, the mother alters how synapses function in the offspring brain. And all the depression and anxiety behaviors that we talk about are based on how the synapse works."

Answering these questions could have important clinical relevance. If researchers can identify the signaling pathways between mother and offspring, Toth says, they could potentially be neutralized during pregnancy; likewise, finding the epigenetic biomarker could lead to pharmacologic methods to revert those areas of the brain to normal architecture and function. Beyond the sphere of psychological disorders, the research could help to explain how myriad diseases and disorders are passed down. "The federal government invests enormous amounts of money to find genes, with the sole purpose of finding the modifications of such genes in individuals with a disease," he says. "But as our research demonstrates, focusing on the genes alone may not be sufficient to answer why some people get diseases such as depression and others do not."

— Renée Gearhart Levy

Open Mind

Lewis Cantley, PhD '75, is poised
to lead a bench-to-bedside revolution
in cancer research

By Beth Saulnier

Photographs by John Abbott

When Lewis Cantley was a boy growing up in West Virginia, he once asked his father if they could buy some fireworks for the Fourth of July. “Why do you want to *buy* firecrackers?” his father responded. “Go make your own.” The senior Cantley gave his son the recipe for gunpowder, and young Lew went to work; before long, he’d graduated to building rockets. Similarly, Cantley’s go-kart was a custom design, powered by a souped-up lawnmower engine—which the boy optimized after studying the vagaries of internal combustion. “From my earliest memories,” says Cantley, PhD '75, “I was always extremely curious about how everything worked.”

Cantley’s father was largely self-educated. He didn’t go to college, but he soaked up knowledge on a wide variety of topics, even reading the encyclopedia from A to Z. “He was in the Coast Guard during World War II, so he learned Morse code, which he taught me when I was quite young,” recalls Cantley, now the Margaret and Herman Sokol Professor in Oncology Research in the Division of Hematology and Medical Oncology, the Professor of Cancer Biology in Medicine, and director of the Cancer Center at Weill Cornell and NewYork-Presbyterian Hospital. “He also learned a lot about navigation, the tides, what controlled the weather. So when I would ask a question like ‘Why does it rain?’ instead of saying, ‘Because God makes it rain,’ he would say, ‘Well, the moisture collects, it rises, gets to a high temperature, cools in the high atmosphere, causes drops of a certain size, and at some point the drops become so large that they begin to fall.’”



The family never bought toys. If Cantley admired a plaything that a kid down the street had, his father would show him how to build it—and the boy would pass the knowledge on to his friends. “By the time I was sixteen I could take a car engine completely apart and put it back together, and it would run,” he says. “So that curiosity, and the confidence that I could figure out how anything worked, was what drove me. It also made me totally unafraid to ask questions about anything, because I figured I could understand it at some level.”

That mindset has served Cantley well over the past four decades. He’s now one of the world’s leading cancer researchers: the discoverer of a key pathway in cancer biology; leader of a \$15 million Stand Up To Cancer “dream team”; winner of the most lucrative prize in biology and medicine. His recruitment from Harvard last fall was both a coup for Weill Cornell and a vital step in the buildup of its bench-to-bedside research enterprise. “It was a huge splash around the country,” Dean Laurie Glimcher, MD, says of Cantley’s hiring. “I knew it was a great recruit, but I did not anticipate what a buzz would be created. It immediately raised the image of both Weill Cornell and NewYork-Presbyterian Hospital. A number of colleagues e-mailed me to say, ‘Thank you for recruiting Lew Cantley—you really put us on the map.’”

Prostate cancer expert Mark Rubin, MD, calls Cantley’s hiring a turning point for the Medical College, noting that his arrival has

‘I knew it was a great recruit,’ says Dean Glimcher, ‘but I did not anticipate what a buzz would be created. It immediately raised the image of both Weill Cornell and NewYork-Presbyterian Hospital.’

sparked excitement among the many faculty members eager to collaborate with him. “Lew Cantley brings a lot to the Weill Cornell community,” says Rubin, the Homer T. Hirst Professor of Oncology in Pathology and director of the Institute for Precision Medicine at Weill Cornell and NewYork-Presbyterian. “His lab is established and strong, and it will continue to do excellent science. As an internationally recognized researcher, Lew will help recruit some of the world’s top scientists, because they’ll want to work with him and the teams he’s building, to ask fundamental questions related to how metabolism affects cancer.”

John Leonard, MD, associate dean for clinical research, lauds Cantley as not only a world-class scientist, but one who is intensely committed to bringing discoveries to the bedside. “It’s remarkable how patient-focused he is,” says Leonard, the Richard T. Silver Distinguished Professor of Hematology and Medical Oncology. “Many people would be content to continue to write papers, win grants, and get acclaim, but he is focused on taking it to the next level—and always with an eye toward, ‘How are we ultimately going to use this to help patients?’”

For Cantley, the move offered not only the chance to get in on the ground floor of Weill Cornell’s institutional revolution—a shift

symbolized by the construction of the \$650 million Belfer Research Building—but the opportunity to work in an intensely collaborative environment at a propitious moment: the dawn of truly personalized medicine. “Over the years, there has been a very fragmented approach to cancer,” Cantley observes. “You have the basic scientists who know the pathways and understand the biology, the clinicians who treat the patients, and the pharma companies who make the drugs—and they’re three completely isolated groups of people. We have to bring them all together as a team. So when you design a clinical trial, you have the basic scientists suggesting the biomarkers; you have a mechanism teasing out the mutations in each individual patient; and then, based on that, you put the patient on the right trial. This needs to be done in a seamless manner. And it’s not done in a seamless manner anywhere—but the opportunity to do that here is better than at any other institution I know of.”

Cantley’s arrival roughly coincided with the founding of the Institute for Precision Medicine, a translational research hub launched in January to offer targeted treatments based on a patient’s genetic profile—including genomic analyses aimed at helping patients with advanced disease and those who have become drug resistant. In addition to developing personalized therapies, the Institute will build a comprehensive biobank to further research and clinical care, and will inform preventive medicine by identifying patients at risk for cancer, heart disease, neurological disorders,

and more. “This Institute will revolutionize the way we treat disease, linking cutting-edge research and next-generation sequencing in the laboratory to the patient’s bedside,” says Rubin. “We will use advanced technology and the collective wealth of knowledge from our clinicians, basic scientists, pathologists, molecular biologists, and computational biologists to pinpoint the molecular underpinnings of disease—information that will spur the discovery of novel treatments and therapies.”

Among the key targets in personalized cancer medicine is an enzyme whose discovery established Cantley’s scientific reputation two decades ago. Known as phosphoinositide 3-kinase (shortened as PI3-kinase or PI3K), it’s a signaling pathway that plays an essential role in as many as 80 percent of cancers, including those of the breast, ovaries, and endometrium. “In addition to discovering the enzyme and its function, Dr. Cantley has been involved in figuring out which types of tumors commonly contain mutations of the gene that encodes PI3-kinase, and he is now developing clinical trials whereby individuals that have this type of mutation can be treated with PI3-kinase inhibitors,” notes Andrew Dannenberg, the Henry R. Erle, MD–Roberts Family Professor of Medicine, who has done extensive research on the connection between cancer and inflammation. “That’s a remarkable odyssey and body of work—from discovering the gene to understanding its function to figuring out how it’s regulated and what it controls downstream, all the way to determining its role in cancer and how often it’s mutated, and providing the basis for personalized cancer investigation.”

The PI3K pathway has been the focus of the Stand Up To Cancer team that Cantley is leading, a sixty-researcher effort that wraps up in October after four years. The work was also cited in the awarding of the first Breakthrough Prize in Life Sciences last February. Cantley was one of eleven recipients of the prize, whose sponsors include founders of Google and Facebook—and which carries a \$3 million cash award for each winner. “Once I heard there was a prize like that, I wasn’t surprised that he was one of the winners,” says Rubin.

"It's the inaugural event, and they wanted to send an important signal of how important this award is—and Lew clearly is a well deserving recipient." (The prize's large cash award—more than double that of the Nobel—initially prompted Cantley's wife to ask, "Are you sure this isn't a joke?" But no: the \$3 million was indeed received—on his sixty-fourth birthday, no less.)

Cantley's wife—Vicki Sato, PhD, a former immunologist and pharmaceutical executive who now teaches at Harvard Business School—will divide her time between Boston and New York for the foreseeable future. The couple has two daughters, one a PhD student in chemical biology at Harvard, the other a professional ballroom dancer who fell in love with the art as a Harvard undergrad. Once an avid basketball player, Cantley had to give up the sport due to chronic injuries; these days, his favorite leisure activity—other than reading mysteries or histories—is snorkeling. "It's one thing I can do without my knees and back bothering me, just following fish around in the Caribbean," he says. "The beauty of it is just overwhelming. You find things that you've never seen before."



SABCS/TODD BUCHANAN

Key player: Cantley describes the role of PI3K during a breast cancer symposium in San Antonio in 2012.

Cantley was the second in a family of four children—Linda, Lew, Larry, and Lloyd—and the eldest boy. Their father worked for Union Carbide; their mother started college when Cantley was eleven and his youngest brother just three. The kids, who would all become straight-A students, helped her study. Surprisingly, the future cancer researcher never took a biology course after high school. "I was really interested in chemistry, physics, and math," he says with a laugh, "probably from working with gunpowder and trying to figure out how to make my rocket get off the ground."

He majored in chemistry at West Virginia Wesleyan College, graduating *summa cum laude*. On Cornell's Ithaca campus, he earned a PhD in physical biochemistry with a minor in theoretical physics. "Again, I took no biology courses and not even any biochemistry," he says. "It wasn't until I started doing research where I was interested in the question of how you couple an electrical gradient into manufacturing a high-energy chemical that I got interested in metabolism and cell regulation. I was interested in photosynthesis, how to capture light and convert that into fixing carbon or making ATP [the cellular fuel supplier adenosine triphosphate], generating energy. Asking those simple questions—which turned out not to be that simple—got me deeper and deeper into biology. And as I got interested in how cells regulate metabolism, that got me interested in cancer, because cancer cells are professionals at doing this. In fact it's the ability to do this that makes them cancer cells."

When Cantley first identified PI3K in 1984, he didn't realize he had discovered something revolutionary—that it was a key player in transforming normal cells into cancerous ones. He knew it was a lipid kinase that co-purified with a variety of oncoproteins, but

believed it was involved in a well-known reaction that had been discovered in 1949. "That was exciting, but it didn't make a whole lot of sense because we couldn't tie why making that lipid would cause the cell to be transformed," he says. "We had a variety of ideas for why it might be doing it. But people had worked on that lipid for forty years, and there still wasn't a clear tie to why that would be relevant to cancer."

His "eureka" moment didn't come until 1988, while comparing PI3K—then dubbed type 1 PI kinase—with a related enzyme associated with normal cells. "I thought they were making the same product, because by chemical analysis they had exactly the same mass, and they partitioned by various assays in the same place," he says. "But one day, we were looking at the data and found there was a one millimeter difference in the rate at which they migrated in the solvent. So that meant they were chemically different. For four years we had assumed they were chemically identical, and that had locked us into assuming it was this well-established molecule. On that day, I knew we'd made a major discovery—that we'd opened up a whole new field—because people had looked for forty years to see if there were any isoforms of this lipid, and nobody had seen any. I went home that night and said, 'This is going to completely revolutionize cancer.' To physicists, this would be like finding a quark no one had ever seen before."

But at the time, Cantley was something of a voice in the wilderness. Other researchers didn't find his results credible, and he couldn't get funding to pursue the findings. His reaction to the naysayers—including one luminary who pledged to eat his hat if it were true? "I ignored them," he says. "I knew it was right. In some ways it doesn't matter what other people believe, as long as you know it's right. And I had other sources of money; it was only one



Next generation: Cantley with members of his lab, which researches signaling and metabolic pathways related to cell growth and oncogenesis.

of ten things I was doing in the lab. But I could not get a grant to fund this. So I siphoned off money from other things, because I knew this was far more important, and that people would eventually understand it."

The story exemplifies one of Cantley's firmly held beliefs: don't assume that the received wisdom is complete, or even necessarily correct. "What we know about biology is about 5 percent of what actually goes on in biology," he observes. "People read huge volumes of medical textbooks and so forth and say, 'Everything is already understood; my job is just to memorize it, to dot the I's and cross the T's on what other people have done.' That's not at all the case. We're at this time in biology where, in five or ten years, we're going to be shocked at the complexity of things we never appreciated."

A prime example: Once upon a time, physicians and scientists assumed that all cancers were more or less the same. These days, they know that nothing could be further from the truth; breast cancer alone has multiple subtypes, each requiring a different therapy. "We'll be breaking cancers into smaller and smaller subgroups," Cantley says. "Maybe only 5 percent of breast cancer patients will have a particular type—but if we have a drug that works for those 5 percent, and the next year we get another 5 percent, and the next year another 5 percent, in twenty years that adds up to a lot of people. That's how we're going to make progress. The problem we had

in the past was that pharmaceutical companies weren't interested in making a drug that didn't work for everybody; at least, it had to work for all breast cancer patients, all lung cancer patients, or all colorectal cancer patients. With that attitude, they failed over and over and over."

For the most part, Cantley doesn't talk about *curing* cancer—he talks about treating it, shrinking tumors, extending longevity, improving quality of life. He describes today's efforts to understand the disease as "almost an engineering problem." By way of analogy, he cites the space race of the mid-twentieth century. "If the U.S. government had said in 1920, 'Let's go to the moon,' nobody would have been convinced it was possible. How could you build a rocket with sufficient thrust? Was it possible to escape the atmosphere? There was no pure, clear, scientific understanding of what would be required to do it. We didn't have computers. So you could spend \$1 trillion toward going to the moon in 1920, but it would have been a waste. But in 1960, when we decided to go to the moon, any theoretical physicist would have said, 'Yes, of course we can. We need rockets that have this thrust, and we know how to make them. We need to calculate the trajectory, and we know how to do that.' Computers were getting started. So it wasn't a matter of, 'Is it possible to get to the moon?' It was, 'Let's fine-tune the engineering.'"

When President Richard Nixon declared war on cancer in 1971,

'Diseases are complicated. And the technologies you have to use to solve important questions are complicated.'

Cantley says, it was akin to attempting a flapper-era moon shot. "It was thought that one silver bullet would cure everybody," he says. "And so they were looking for a magic potion, without any knowledge of what was going on." But Cantley is confident that today we're closer to the Sixties-era pledge that led to man walking on the lunar surface. If one of his loved ones had cancer, he says, he'd be "extremely hopeful" that the current bench-to-bedside work will lead to effective therapies. "We're talking about having a foot in the door—and we're also talking about a scientific approach to get to the end," he says. "In the past, even with chemotherapy and radiation, we didn't know why some people responded and some didn't; now, with these targeted therapies, we do know. It's not, 'Let's randomly try another set of poisons and see what happens.' Because that's what we've been doing for thirty years."

It's increasingly accepted that close collaboration across disciplines—breaking down the traditional silo approach to research—is essential to tackling any complex scientific problem in today's hyper-specialized, tech-driven world. And indeed, when Cantley is asked what kind of atmosphere he aims to foster in his lab, a spirit of collaboration is at the top of the list. "Biology is complicated," he says. "Diseases are complicated. And the technologies you have to use to solve important questions are complicated." For example, a single journal article could entail expertise from a variety of fields—describing the crystalline structure of a molecule, offering proof that a gene that encodes it is implicated in a particular disease, chronicling the effects of a mutation, and more. "No one person can do all that," he says. "In fact, it's hard for any one lab to do all that. It's typically three, four, five, even ten collaborators from multiple labs, all getting together to solve a problem. And if you want to take it all the way to a clinical trial, you've got to get surgeons, oncologists, and anesthesiologists involved and develop the biomarkers for it. So all of this requires teams. In the past, everybody just did it on their own, completely isolated, and that made things incredibly slow."

Although Cantley is best known as a cancer researcher, he's done well-respected work in other fields. (Perhaps the most exotic: analysis of tissue from a 68-million-year-old *Tyrannosaurus rex*, which confirmed that birds are the dinosaur's closest living relatives.) A particular area of interest is the link between the PI3K pathway and insulin resistance, which can lead to type 2 diabetes. "One of the many normal functions of PI3-kinase is to mediate insulin responses," he explains. "Almost everything insulin does to control glucose homeostasis in the body, it does through PI3-kinase."


And these days, he notes, Americans are getting a whole lot of glucose—in the form of sugary sodas, desserts, even seemingly savory foods like bread and crackers. Cantley says that when he was growing up, none of his classmates were overweight—but when he went home to West Virginia during graduate school, he found that obesity had hit epidemic levels. "What changed so fast?" Cantley muses.

"Two or three things happened in the mid- to late Sixties. Everybody says that people quit exercising, but that's bull; in the Seventies, running was the most popular thing to do. My relatives never changed their exercise. So what did they change? Well, Coca-Cola." Cantley recalls that as kids, he and his siblings relished the small glass bottles of Coke that their mother would allow them on their weekly outings to the grocery store—a treat that came in six-ounce servings. "That was our allotment of Coca-Cola for the week," he notes. "In the Sixties it went up to twelve ounces, then to sixteen—and it was now cheap, sweetened with corn syrup instead of sucrose."

Today, sodas commonly come in liter bottles or giant fast-food cups. And while some have decried New York Mayor Michael Bloomberg's effort to ban large portions of sweetened drinks as overly paternalistic, Cantley supported it, considering it a public health issue. As he once told the *New York Times*: "Sugar scares me." He never eats dessert; in his office, where boxes of Chinese green tea are stacked up on a shelf, the sugar packets are there only as a courtesy for guests. And as Cantley noted in a 2012 episode of "60 Minutes," in addition to its obvious role in obesity and diabetes, sugar is increasingly implicated in certain types of cancer. "What we're finding now is that a lot of cancer cells have insulin receptors," he says. "Imagine that you drink a Coca-Cola, and you're insulin resistant—which means that your insulin levels have to go up really high to get your liver, muscle, and fat to respond. The cancer cell is sitting there on the side, insulin's going up; it hits the cancer cell and tells it to take up the glucose. While the other tissues are at a disadvantage, the cancer cell wins. So this is setting yourself up for insulin to drive the growth of cancers—and we find that there's a subset of cancers that often have insulin receptors highly expressed. They include endometrial cancers, breast cancer, prostate cancer, and colorectal cancers—and those are the cancers that often correlate with diabetes and obesity. So that cannot be coincidental."

The link between obesity and cancer is an area of interest to Dannenberg, and one where he and Cantley plan to collaborate in the future. Dannenberg calls Cantley's body of work "truly transformative," noting that his interdisciplinary investigations of PI3K for the past three decades have given him a unique perspective and skill set that will be invaluable to Weill Cornell's research enterprise. "His decision to come here also illustrates his belief in the goals of the institution," Dannenberg notes. "As a remarkable basic scientist—but also one who takes pride in translating basic findings to the clinic—it should be an enormous opportunity both for him and for our institution to grow in new directions."

Dannenberg says that Cantley has "many virtues that one wishes to see in a leader": he's approachable, humorous, focused, passionate, experienced, committed, and helpful. Glimcher describes her former Harvard colleague as "absolutely charming, low key, friendly, modest, intensely collegial, and collaborative." She adds that for Cantley, it's all about the science—and never about garnering accolades. "He's a good example of Harry Truman's comment that it's amazing how much you can get done if you don't care who gets the credit," Glimcher says. "That's Lew." ●

A portrait of Christopher Mason, PhD, a man with short brown hair and a slight smile. He is wearing a white lab coat over a light blue dress shirt and a blue and white striped tie. He is standing in a laboratory setting with shelves of equipment and a large circular device visible in the background.

Christopher
Mason, PhD



The Body Politic

Geneticist Christopher Mason, PhD, celebrates the Supreme Court decision in favor of 'genetic liberty'

By Beth Saulnier

Few Supreme Court decisions have bench scientists popping champagne corks—but this one did. In mid-June, the high court unanimously ruled that human genes can't be patented. Among those closely watching the case, *Association for Molecular Pathology v. Myriad Genetics*, was Christopher Mason, PhD. An assistant professor of computational genomics in the Department of Physiology and Biophysics and the HRH Prince Alwaleed Bin Talal Bin Abdulaziz Al-Saud Institute for Computational Biomedicine, Mason was among the experts who provided testimony for the plaintiffs—even offering genetics primers to their attorneys. In March, *Genome Medicine* published the results of a study in which Mason and colleagues found that, due to the broad scope of many gene patents, as much as 100 percent of human DNA could be deemed off-limits to researchers.

The high court's decision was a powerful moment for Mason, who started mapping his career path as a geneticist while in the eighth

grade. “I was fascinated by how you start life as a single cell, and that in that one cell there is a complete genetic, dynamic recipe to create an entire human being that eventually is composed of trillions of cells,” he says. “But we barely understand the grammar of life’s molecular code, even if we can clearly see the letters in the book.”

Mason holds a dual bachelor’s degree in biochemistry and genetics from the University of Wisconsin, Madison, and a PhD in genetics from Yale. His lab uses functional genomics and high-throughput methods in three main areas: neurogenetics, tumor evolution, and synthetic biology. As he puts it on the lab’s website: “We leverage clinical cases which can reveal the most about the human genome: the most peculiar cases in human genetics, the most aggressive cancers, and the most striking brain malformations.”

Mason spoke to *Weill Cornell Medicine* shortly after the court rendered its decision—amid such heady headlines as (in *Forbes*) “Supreme Court Breaks Myriad Monopoly.”

Weill Cornell Medicine: How does it feel to have contributed to an outcome that has such broad implications for research?

Christopher Mason: It’s gratifying and humbling—one of the proudest moments of my career. In 2006, I saw what I believed was an injustice, and I was able to fight for seven years, all the way to the Supreme Court. You don’t just want to be a geneticist or a researcher, you also want to be a good citizen. I feel like I’ve not only

contributed to science, but to society at the same time, which is relatively rare.

WCM: Could you describe the moment when you got the news?

CM: My inbox exploded with a barrage of e-mails, tweets, and text messages. I was extremely excited—I felt liberated. Before, there were certain pages of the book of life that we weren’t allowed to look at; we can now examine

GOOGLE IMAGES



Decision of the Court

How the justices ruled, in their own words

Section 101 of the Patent Act provides: “Whoever invents or discovers any new and useful...composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.” We have long held that this provision contains an important implicit exception: Laws of nature, natural phenomena, and abstract ideas are not patentable. Rather, they are the basic tools of scientific and technological work that lie beyond the domain of patent protection.

As the Court has explained, without this exception there would be considerable danger that the grant of patents would “tie up” the use of such tools and thereby inhibit future innovation premised upon them. This would be at odds with the very point of patents, which exist to promote creation. The rule against patents on naturally occurring things is not without limits, however, for all inventions at some level embody, use, reflect, rest upon, or apply laws of nature, natural phenomena, or abstract ideas, and too broad an interpretation of this exclusionary principle could eviscerate patent law. As we have recognized before, patent protection strikes a delicate balance between creating incentives that lead to creation, invention, and discovery and impeding the flow of information that might permit, indeed spur, invention. We must apply this well-established standard to determine whether Myriad’s patents claim any new and useful composition of matter, or instead claim naturally occurring phenomena.

It is undisputed that Myriad did not create or alter any of the genetic information encoded in the BRCA1 and BRCA2 genes. The location and order of the nucleotides existed in nature before Myriad found them. Nor did Myriad create or alter the genetic structure of DNA. Instead, Myriad’s principal contribution was uncovering the precise location and genetic sequence of the BRCA1 and BRCA2 genes within chromosomes 17 and 13. The question is whether this renders the genes patentable.

* * *

Myriad found the location of the BRCA1 and BRCA2 genes, but that discovery, by itself, does not render the BRCA genes new compositions of matter that are patent eligible. Indeed, Myriad’s patent descriptions highlight the problem with its claims. For example, a section of the patent’s detailed description of the invention indicates that Myriad found the location of a gene associated with increased risk of breast cancer and identified mutations of that gene that increase the risk. In subsequent language Myriad explains that the location of the gene was unknown until Myriad found it among the approximately eight million nucleotide pairs contained in a subpart of chromosome 17.

Many of Myriad’s patent descriptions simply detail the iterative process of discovery by which Myriad narrowed the possible locations for the gene sequences that it sought. Myriad seeks to import these extensive research efforts into the patent eligibility inquiry. But extensive effort alone is insufficient.

Nor are Myriad’s claims saved by the fact that isolating DNA

from the human genome severs chemical bonds and thereby creates a non-naturally occurring molecule. Myriad’s claims are simply not expressed in terms of chemical composition, nor do they rely in any way on the chemical changes that result from the isolation of a particular section of DNA. Instead, the claims understandably focus on the genetic information encoded in the BRCA1 and BRCA2 genes. If the patents depended upon the creation of a unique molecule, then a would-be infringer could arguably avoid at least Myriad’s patent claims on entire genes by isolating a DNA sequence that included both the BRCA1 or BRCA2 gene and one additional nucleotide pair. Such a molecule would not be chemically identical to the molecule “invented” by Myriad. But Myriad obviously would resist that outcome because its claim is concerned primarily with the information contained in the genetic sequence, not with the specific chemical composition of a particular molecule.

* * *

It is important to note what is not implicated by this decision. First, there are no method claims before this Court. Had Myriad created an innovative method of manipulating genes while searching for the BRCA1 and BRCA2 genes, it could possibly have sought a method patent. But the processes used by Myriad to isolate DNA at the time of Myriad’s patents were well understood, widely used, and fairly uniform, insofar as any scientist engaged in the search for a gene would likely have utilized a similar approach, and are not at issue in this case.

Similarly, this case does not involve patents on new applications of knowledge about the BRCA1 and BRCA2 genes. Nor do we consider the patentability of DNA in which the order of the naturally occurring nucleotides has been altered. Scientific alteration of the genetic code presents a different inquiry, and we express no opinion about the application of [Section 101] to such endeavors. We merely hold that genes and the information they encode are not patent eligible simply because they have been isolated from the surrounding genetic material.

Edited and condensed from the unanimous decision of the Supreme Court in Molecular Pathology v. Myriad Genetics, written by Justice Clarence Thomas. Legal citations have been removed for clarity.

‘Myriad found the location of the BRCA1 and BRCA2 genes, but that discovery, by itself does not render the BRCA genes new compositions of matter that are patent eligible.’

'The 9-0 decision was an unequivocal liberation of the genome. Clearly, both the conservative justices and the liberal justices believed that people should own their own genes, both inside your body and when purified from your body.'

them freely in both research and clinical settings. The mood is nothing short of euphoria, a wondrous sense that a long-standing dark cloud hanging over us is now gone.

WCM: Do you consider this an unambiguous victory?

CM: I would call it a near-complete win. What was rejected were patents on DNA—that it is not the property of a company or institution; that your genes are yours, even if they're isolated from your body; and that it's a natural product. What was upheld is what's called "complementary" DNA, or cDNA. Because you have to synthesize it—extract it from cells and perform some biochemistry—the Supreme Court says that cDNA is new. Myriad has claimed that because they have cDNA patents they still have ownership over the genes, but that is a wild overstatement. More than 99 percent of all genetic testing is done on DNA; cDNA is harder to work with and less accurate.

WCM: How quickly do you think this change will be felt?

CM: It's already happening. Literally within hours of the decision, I had phone calls and e-mails from multiple people saying, "Let's start a genetics company, let's start sequencing patients, let's invent new methods." This will open the floodgates of new ideas, research, and techniques. It will increase competition and drive down costs.

WCM: What about the argument that the loss of patents will stifle biotech investment?

CM: I think this will spur innovation in the right places, like new diagnostic and analytical methods—more on processes and on truly modified DNA, where you actually have created new molecules. We have already seen multiple companies announce research and testing plans and reduced costs. This is a win for researchers and patients.

WCM: How did you get involved in this cause?

CM: I've been interested in the subject since I was a postdoctoral researcher in 2006, looking for specific genes that were associated with brain malformations. It became clear that you often don't know the cause of the disease, so you'll look at five or twenty genes at a time; sometimes you'll have a list of 100. And I came across a study indicating that as many as 18 percent of human genes were patented. That was surprising—first, I didn't realize you could patent

genes; and second, it meant that just by doing my normal research in the lab I would have a one in five chance of infringing on a patent. It was essentially unavoidable.

WCM: Can you give a sense of how broad the patents were?

CM: Take the BRCA1 gene as an example: Myriad's patent claimed any molecule that has a fifteen-nucleotide stretch that matches something from BRCA1. That would be the equivalent of opening up a book and having someone tell you, "I own the copyright on the word 'the.' " My point in the *Genome Medicine* paper was that the risk was unclear. There were some genes that were without question patented, like BRCA1, and the BRCA1 patent unquestionably also matched 700 other genes. But for the vast majority of genes that partially overlap a patent, it created a large legal uncertainty.

WCM: How did the patents and threat of litigation affect the scientific community?

CM: At the dawn of personalized medicine, we were ironically at our most restricted as to what genes you could and could not target. No one knew how bad the risk was; should you take it? The American Association for the Advancement of Science reported that 50 to 58 percent of researchers had their work delayed or changed due to patents. Some breast cancer experts and others simply stopped their research. They've essentially lost fifteen years waiting for these patents to be struck down.

WCM: What was it like to be at the Supreme Court for oral arguments?

CM: It was humbling and exciting. You imagine the justices as these grandiose, all-knowing figures—but they clearly struggled with how to interpret the science. Another striking thing was that I've been working on the case for seven years, and it all boiled down to a thirty-minute argument on each side.

WCM: Were you surprised that the decision was unanimous?

CM: I was pretty sure we'd win on DNA, but I thought we'd have 6-3 decision, maybe 5-4. The 9-0 decision was an unequivocal liberation of the genome. Clearly, both the conservative justices and the liberal justices believed that people should own their own genes, both inside your body and when purified from your body.

WCM: Does this case indicate that the patent

system—which dates back to the eighteenth century—isn't equipped to handle some modern technology?

CM: That is a complicated question. There have been proposals put forth for a two-tiered system; since some sectors are more dynamic than others, like software and biotechnology, maybe the patents there could be shorter. It's true that twenty years is an extraordinarily long time in genetics. Every experiment we're doing in my lab today either couldn't be done, or couldn't even have been imagined, five or ten years ago.

WCM: While the case was being considered, actress Angelina Jolie announced she'd had a prophylactic double mastectomy after learning she carries the BRCA1 mutation and was at high risk for breast and ovarian cancer. How has her story shaped public dialogue?

CM: It highlighted the struggle of making that decision—the real-world consequences of these mutations. In her *New York Times* op-ed, she pointed out that the cost of the BRCA1 test is extremely high, because it could be done by only one lab, which could charge a monopolist's price—in this case, \$3,000. Now, without the patents, other firms can offer the same test, which has already lowered the cost to \$500 and offered better versions. Another issue is that there was no way for people like her to get a second opinion. If you want to decide whether to get a root canal, you can get opinions from ten different dentists—but there was no such opportunity available for the genetic-based decision to remove your breasts and ovaries.

WCM: Have you had your own genome sequenced?

CM: I did, last year. According to one of Myriad's patents, you weren't supposed to sequence your BRCA1 gene or do comparisons on it. So I actually made a haiku with the letters that were in my BRCA1 gene and presented it at a talk as an example of further infringement.

WCM: Wait—you made a haiku out of your DNA?

CM: It's hard, actually. You have only four letters—A, C, G, and T. But when DNA becomes RNA, your A's turn into U's, and you sometimes have N in a place where you don't get a good base call, so I allowed six letters.

WCM: So how did it turn out?

CM: *A gaunt gnat gang can't
cut a taut act; an ant can't
taunt a taut, tan tau. ●*



MICHAEL AUSTIN / THEISPOT.COM



Protective Measures

For a quarter-century, geriatrician Mark Lachs, MD, and social scientist Karl Pillemer, PhD, have collaborated to study elder abuse

By Beth Saulnier

Let me tell you something," Mark Lachs, MD, says with a laugh. "You never want to follow Mickey Rooney."

In March 2011, Lachs offered expert testimony on elder abuse before a U.S. Senate committee. The previous witness was Rooney—the ever-popular performer of stage and screen who made his debut as a toddler, grew up before America's eyes, and continued acting well into old age. Then ninety, Rooney had recently made headlines for revealing a personal tragedy: he'd been financially and emotionally victimized by a relative. "What other people see as generosity may in reality be the exploitation, manipulation, and, sadly, emotional blackmail of elders and people who are vulnerable," Rooney told the Special Committee on Aging. "My money was taken, was used. When I asked for information . . . I was told it was none of my business." He went on to describe being "completely stripped of the ability to make even the most basic decisions," such as where to go and what to do. "Over the course of time," he said, "my daily life became unbearable."

With tears welling in his eyes, Rooney concluded with a message to fellow elders who had suffered abuse. "You're not alone, and you have nothing—*nothing*, ladies and gentlemen—to be ashamed of," he said. "You deserve—yes, you *deserve*—better. You all have the right to control your own life. Everyone does. You have the right to control your life and be happy. Please, for yourself, end the cycle of abuse and do not allow yourself to be silenced anymore."

As Lachs recalls it, Rooney's words brought the house down. "Here was this beloved man who was unbelievably articulate about the way he was exploited," says Lachs, the Irene F. and Roy I. Psaty Professor of Clinical Medicine and co-chief of the Division of Geriatrics and Palliative Medicine. "Those of us who have worked in this area for decades had been trying to bring public awareness to this—and here there were paparazzi."

Rooney's story—as well as another high-profile case in the news at the time, in which the son of centenarian socialite Brooke Astor was convicted of misappropriating millions from her estate—brought much-needed attention to an issue that has long been a focus of Lachs's



PETE MAROVICH / CORBIS

Cautionary tale: In 2011, actor Mickey Rooney testified on Capitol Hill about his experiences as a victim of elder abuse.

research. Over the past quarter-century, Lachs and his Ithaca-based collaborator, gerontologist Karl Pillemer, PhD, have conducted some of the most comprehensive and frequently cited studies in the field of elder abuse. “It’s really the most extreme form of age discrimination,” says Lachs, who spoke at the White House’s 2012 symposium marking World Elder Abuse Awareness Day. “We think about job discrimination against older people, or lack of courtesy, or the ways in which older people are undertreated in health-care or social-service environments. But this is the most heinous and egregious form of mistreatment.”

Lachs and Pillemer have helped shape discussion of an issue that is becoming increasingly serious. While overall rates of elder abuse aren’t necessarily going up—and, in fact, may be dropping somewhat due to improved awareness—the aging population means that raw numbers of abuse cases will inevitably rise. U.S. Census data indicates that by 2030 a fifth of the nation will be over sixty-five. “Elder abuse is a huge phenomenon,” says Ronald Adelman, MD, the Emilie Roy Corey Professor of Geriatrics and Gerontology and Lachs’s co-chief, “and it will only increase as our demographics change, now that we have 10,000 Americans turning sixty-five every day.”

The day that Lachs testified before the Senate committee, the Government Accountability Office (GAO) released a report on elder abuse, noting that the most recent national study—published in 2009 by researchers at the Medical University of South Carolina—found that 14.1 percent of non-institutionalized older adults had experienced abuse (physical, psychological, or sexual), neglect, or financial exploitation in the previous year. “This study and three other key studies GAO identified likely underestimate the full extent of elder abuse, however,” the report stated. “Most did not ask about all types of abuse or include all types of older adults living in the community, such as those with cognitive impairments.”

That tip-of-the-iceberg phenomenon was the subject of a major



A. KINLOCH

Mark Lachs, MD

study Lachs and Pillemer presented at the second New York State Summit on Elder Abuse, held in November 2010. It was based on telephone interviews of more than 4,100 New Yorkers aged sixty-plus and extensive queries of nearly 300 agencies, both governmental and otherwise, that respond to abuse cases. Their report, “Under the Radar,” concluded that for every case that’s reported, nearly

twenty-four are not. Overall, it found that 7.6 percent of respondents—about one in thirteen—had experienced some type of mistreatment in the past year. The most common form was financial exploitation, at 4.2 percent, followed by 2.2 percent reporting physical abuse. “The numbers are just stunning,” says Lachs, who has consulted with the World Health Organization on the issue. “If you heard about a disease affecting 5 to 10 percent of the population, the CDC would be out in force tomorrow. It would be considered a major public health crisis. It affects not only the person being victimized; it affects our public welfare systems, which will be bankrupted by this. Everyone is talking about Medicare and Medicaid. Our data suggest that elder abuse is a factor for nursing home placement, for mortality, and probably for health-care utilization.”

Elder abuse comes in a variety of forms: it can be physical, emotional, financial, and—in cases so rare they’re difficult to study—sexual. It can also take the form of neglect, in which needed care is withheld. “I would suggest that physicians need to have their antennae up high, particularly if a patient is not doing well despite resources—losing weight, missing visits,” Lachs says. “Frequently, if my suspicion is significant, I’ll start with asking about general safety. ‘Tell me about your neighborhood. Have you ever been robbed? Do you feel safe going out?’ And then I will slowly move to questions of, ‘Is your son or daughter ever rough with you? Have you been made to wait for food, medicines, or care? Have you ever been hit, slapped, or punched?’ Quite often the answer is no. But if you see fifteen or twenty patients over the age of sixty, you will have encountered an elder abuse victim—and most internists and family doctors see that number or more in a day. It’s out there, and so the opportunities to detect and meaningfully intervene are there.”

According to Lachs, the single most common subtype of abuse is financial exploitation, as Rooney so poignantly described. In an economic downturn, Lachs notes, Social Security checks and carefully tended nest eggs can be especially tempting. In 2011, Met Life and Virginia Tech released the results of a study of elder financial abuse, estimating annual losses at more than \$2.9 billion, a 12 percent increase from three years earlier. “Older adults often have significant financial resources that are the target of misuse, if not by family members then by unscrupulous people trying to sell financial services or rip them off with home improvements or investment scams,” Lachs says. “The government has become very interested in this, because older adults who are essentially impoverished by this become wards of the state in some form. When you lose your nest egg as a seventy-year-old, it’s different from when you’re forty or fifty, because there’s no way to replenish it if you’re not working.”

And while someone like Brooke Astor may have ample resources to live on despite heavy losses, Lachs points out that such crimes still have a societal cost. “The resources that are absconded with are often earmarked for community philanthropy,” he says. “In the case of Brooke Astor, that money would have gone to art and culture. I’ve been called to look at elder abuse cases in which an estate that was to be directed to a church, synagogue, youth organization, or park was rifled by an unscrupulous eleventh-hour confidante. Even if you don’t have an older person in your life right now, if you use those community resources you should be aware that it’s another way in which society suffers.”

Lachs traces his passion for geriatrics to being raised by grand-



UNIVERSITY PHOTOGRAPHY

Karl Pillemer, PhD

parents who were “strong, cognitively and physically.” His interest in studying elder abuse began while doing a Robert Wood Johnson clinical fellowship at Yale in the late Eighties, when he witnessed abuse cases while working in the emergency department of a New Haven hospital. “There were almost no physicians involved—which was in stark comparison to child abuse, where there were fellowships even then,” recalls Lachs, who earned an MPH from Yale. “For my mentor I had to select a person who was a child abuse expert, because there were very few clinicians in aging who wanted to study domestic violence.”

Another early mentor was Pillemer, who had conducted seminal studies of elder abuse in the Boston area—work that remains among the most cited in the field. His PhD dissertation in sociology, earned at Brandeis in 1985, was the first that did comprehensive case comparisons on the issue. His findings were nothing short of revelatory. “There was a dominant worldview, based on very small case studies, that elder abuse was a problem of family caregiving,” says Pillemer, now the Hazel E. Reed Professor in Cornell’s Department of Human Development. “The idea was that old people get sick, frail, and disabled, hard to care for, and cantankerous. Their nice and otherwise well-meaning caregivers can’t handle it anymore and get mad and hit them or withdraw and neglect them. They basically blamed the victim. That seemed suspicious, because the fields of child abuse and spousal abuse started out the same way.”

Pillemer’s work revealed that, in fact, the opposite was true. It wasn’t that the elder abuse victims were dependent on their abusers; their abusers were dependent on *them*. “The older adults may have had some impairments—they weren’t completely healthy—but most often they were supporting a deviant and dependent adult child, or a spouse who was a substance abuser or had Alzheimer’s. The person abusing them was highly dependent, such as a mentally ill or drug-addicted kid who couldn’t hold down a job and was living with the older person.” Pillemer explored the issue in a much-cited article in *Social Problems* entitled “The Dangers of Dependency,” noting that such cases are exquisitely complex. In the case of a dysfunctional adult child abusing a widowed mother, for example, the abuser might be providing enough help—say,

'Older people who are victims may be isolated in such a way that they see nobody in the course of a calendar year other than their primary care physician and the abuser.'

doing the grocery shopping or picking up prescriptions—to make them seem essential. Says Pillemer: “Since old people don’t want to go into nursing homes, for some of them being occasionally pushed around by your adult son is worth it, if the son is doing enough to prevent institutional placement.”

In recent years—particularly since David Skorton, MD, became president of Cornell—the University has encouraged and fostered research collaborations between the Medical College and the Ithaca campus. The past decade has also seen an explosion of interest in bench-to-bedside investigations. Lachs and Pillemer’s long-standing relationship is, as the latter puts it, “a poster child for translational research”—the embodiment of inter-campus collaboration long before it became an institutional priority. “It’s a continual feedback loop,” Pillemer says. “Physicians see issues in the clinical world that lead to research questions, which then prompt studies, which then lead to interventions.”

For example, Lachs’s observations as a nursing-home physician inspired a study of resident-to-resident abuse, published in 2008, that found that 2.4 percent of residents had been the victims of physical violence and 7.3 percent had experienced verbal aggression—just in the previous two weeks. “That emerged from Mark seeing this problem over and over, and how difficult it was for staff to intervene. We wouldn’t have gotten the idea for the project if it hadn’t been for Mark’s clinical experience,” Pillemer says. “And if it weren’t for Mark I wouldn’t be attuned to, for example, delirium and its role in a person’s ability to give meaningful information about an elder abuse incident, the role of cognitive impairment in somebody’s reliability as a witness, or the role of agitation in resident-to-resident abuse. Similarly, without me, Mark might not be as attentive to the role of the family system, race, or socioeconomic status. Our publications reflect this more holistic view.”

Lachs and Pillemer’s collaboration began as the field of elder abuse research was starting to come into its own. Pillemer notes that just as the Sixties saw shifts in understanding about child abuse, and the Seventies about spousal violence, the Eighties saw the beginnings of widespread awareness about abuse of the elderly. (Pillemer says: “We used to joke that we were like the Flat Earth Society—this small group of people trying to call attention to an issue that seemed if not exotic, then rare, and people didn’t quite know what to do about it.”) And while there are commonalities with other forms of domestic violence, elder abuse can be especially thorny to

uncover. “If a child comes to school with a black eye or doesn’t come at all, there’s some modern-day equivalent of a truant officer who looks into that,” Lachs says. “Older people who are victims may be isolated in such a way that they see nobody in the course of a calendar year other than their primary care physician and the abuser. So I teach residents and medical students that the once-a-year blood pressure visit and physical exam may be the only opportunity to detect mistreatment.”

Then, as Lachs notes: “You have the additional complexity that the caregiver is often the abuser”—the very person accompanying the victim to the doctor’s office. Adelman recalls a long-ago case that taught him the importance of giving elderly patients the chance to speak candidly. “Every time I would see the woman as an outpatient, her daughter was present,” he says. “She’d been admitted to the hospital and as I was making rounds she said, ‘Doctor, I must speak to you alone. Every time you saw me, my daughter was in the room and I couldn’t tell you what was going on. My adolescent grandchildren are stealing my money, and I couldn’t buy my medicines. That’s why I ended up in the hospital.’ I learned that every time you see a patient, you need to see them alone. It may be just during the physical exam. If a family member doesn’t want to leave, why is that? Are they trying to hide something? Or if you want to send help into the home, like a visiting nurse, and they won’t accept it, what’s going on there? You always must have time for privacy.”

Adelman also describes a pair of hospitalized patients whose contrasting situations underscore the nuance and complexity of parsing abuse cases. Both involved overdoses of the heart drug Digoxin—but for completely different reasons. One man got too much Digoxin and not enough of his diuretic because, as it turned out, his daughter was illiterate and unable to read the labels. The other was far more unsettling. “It was a second marriage, and the wife, who had congestive heart failure, wanted to go to her son’s wedding,” Adelman recalls. “The husband didn’t want her to go, and he was in charge of the medicine, so he gave her too much Digoxin and she ended up in the hospital.” The former was a mistake that could be prevented by color-coding the bottles; Adelman did just that, and the patient’s medications were properly dosed from then on. The latter was intentional abuse requiring a much more challenging kind of intervention. “You have to think about elder abuse—but it’s not always elder abuse,” he says. “People can fall and have a hip fracture, and they can also be pushed and have a hip fracture.”

Pillemer notes that as researchers, he and Lachs take a “very restrictive” view of elder abuse. Neglect, for example, must involve a perpetrator who is in a recognized position of trust and responsibility. “One of the ways that the field has been criticized is that, as someone once put it, some definitions of elder abuse hold people to a standard of behavior exceeded only by the Sermon on the Mount,” Pillemer says. “‘Emotional neglect’ could include not calling your mother often enough. People lumped every bad thing that could happen to an older person, from being touched by a grifter to receiving solicitations in the mail for bogus charities. We feel that elder abuse needs to be seen as analogous to child abuse and spousal abuse to make any conceptual sense.”

In 2009, the Medical College teamed up with more than twenty-five government, academic, and nonprofit organizations to launch the New York City Elder Abuse Center, which is dedicated to treating and preventing elder abuse in the city and beyond, with Weill Cornell faculty in key roles. They include Lachs, the Center’s med-

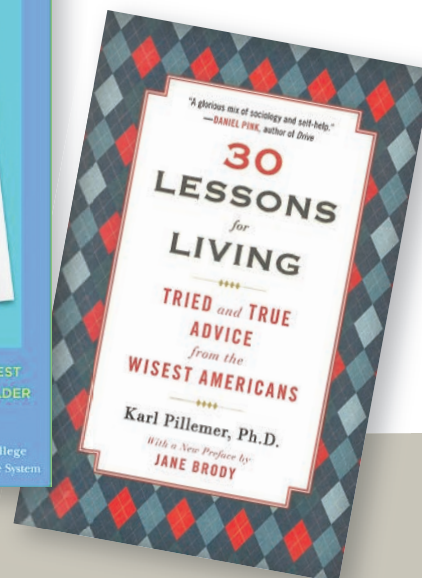
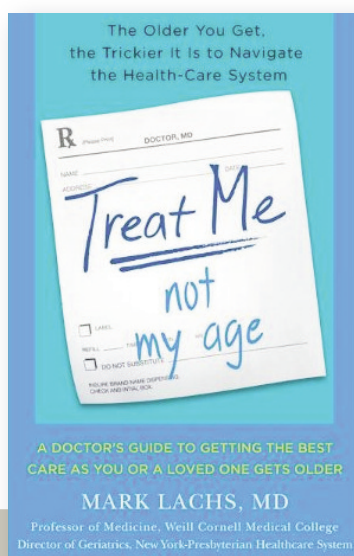
ical director, as well as Risa Breckman, LCSW, assistant professor of gerontological social work in medicine, its executive director, and Veronica LoFaso, MD, associate professor of clinical medicine, its geriatrician. “There has been very little public awareness of elder abuse and neglect,” observes Breckman, who has worked in the field for more than thirty years and co-authored a seminal book on the subject with Adelman in the Eighties. “The newspapers might report it, but the storyline is not clear for people. You hear about individual cases, but the public is not understanding this as a human rights issue, a public health issue, a criminal justice issue. There hasn’t been an effective, government-led public awareness campaign. We’re still in the beginning of doing that kind of primary prevention.”

Breckman stresses the need for additional research on all aspects of elder abuse, from its effect on victims to intervention strategies to the psychopathology of abusers themselves. “You name it,” she says, “our field needs it.” There’s also a growing demand for practitioners with expertise in elder abuse. With the aim of fostering the next generation of advocates, the Center offers a summer internship for undergraduates—aimed not only at educating them about abuse, but exposing them to the varied lives of elders. “A lot of the time, unless younger people have positive relationships with their grandparents, they may not understand the value of older adults,” Breckman says, “so to introduce them to elder abuse and neglect is like asking them to dive into the deep end of the pool. All of a sudden we’re going to tell you the scariest stuff about aging—that’s not the best way to start.”

The New York City Elder Abuse Center has used the “Under the Radar” data to estimate that each year some 120,000 older adults are abused in their own homes in New York City alone—and that 96 percent of cases go unreported. The reasons why so few come to light range from victim isolation to cognitive impairment to the fear that any intervention will lead to placement in a nursing home. Another all-too-common reason: shame. “It’s hard to think of a

greater parenting failure,” Pillemer observes, “than your son or daughter beating you up.”

In their report, the researchers chronicled patterns of abuse—noting that overall, spouses or partners and adult children were responsible for 40 percent of the mistreatment reported in the survey. Spouses or partners were most often cited as the perpetrators of physical and emotional abuse; financial exploitation was most often attributed to adult children, grandchildren, other relatives, friends, or home health aides. Of those who were abused, just over a quarter cited more than one perpetrator. “Abuse occurs concurrently,” Lachs says. “It’s uncommon to see someone who was physically abused who’s not also verbally abused, neglected, and financially exploited. There’s a great deal of overlap.” The findings underscore the complex, multifactorial nature of elder abuse—and the magnitude of the problem that Lachs and Pillemer have spent a combined half-century trying to understand. “Theirs has been an incredibly complementary, deep, and abiding collaboration,” Adelman says. “Their work has brought a lot of clarity to a field that desperately needed it.” ●



Further Reading

Popular books by Lachs and Pillemer

Mark Lachs’s most recent general-audience book begins with an anecdote from a medical colleague. A geriatric patient named Morris comes in and complains that his right knee hurts. The doctor asks his age, and the man says he’s 101.

“Well, what do you expect at your age?” the physician asks.

The patient gets up angrily. “The problem with that, Doc,” he says, “is that my left knee is also 101, and it doesn’t hurt at all!”

The 2010 book is entitled *Treat Me, Not My Age: A Doctor’s Guide to Getting the Best Care as You or a Loved One Gets Older*. In it, Lachs offers advice on navigating the geriatric health-care system—from a discussion of “medical ageism” to tips on everything from choosing a doctor to dealing with the stresses of retirement to crafting an advance directive. It includes such practical matters as advising families to carry their own copies of medical records and to visit a hospitalized relative at mealtimes to make sure the older person is eating. As the “New Old Age”

columnist in the *New York Times* put it in a review of the book: “We need a guy like this.”

Pillemer’s latest, published last fall, is *30 Lessons for Living: Tried and True Advice from the Wisest Americans*. In it, he gathers wisdom from more than 1,000 people over sixty-five from many walks of life, whom he asked to share the most important lessons they’d pass on to today’s young people. The participants have, among them, some 30,000 combined years of married life and 3,000 children. The topics on which they offer wisdom range from relationships and childrearing to career, health, spirituality, and more. (Marital bliss tip number one: wed someone like yourself.)

As Pillemer writes: “There are things about life—secrets if you will—that are probably impossible for younger people to know firsthand. We need to consult those who have already traveled the roads, byways, dead ends, and unexpected detours to understand which directions our lives should take.”

Notebook

News of Medical
College and Graduate
School Alumni



R. Ernest Sosa, MD '78

Dear fellow alumni:

As always, it was a busy but exciting spring at Weill Cornell.

We held our final "Alumni-to-Student Knowledge" (ASK) session of the academic year on May 8. At the request of the students, this session featured alumni who are pursuing innovative careers outside of traditional medicine.

Sponsored by the WCMC Alumni Association, the ASK program addresses students' desire for increased interaction with alumni and provides a unique forum where they can discuss educational, career, and lifestyle decisions in a relaxed and friendly environment. Over the past couple of months we've hosted sessions featuring alumni who practice in general surgery, transplant surgery, and cardiothoracic surgery as well as in rheumatology and orthopaedic surgery. We look forward to hosting more ASK sessions in the 2013–14 academic year. If you're interested in participating, please contact the Office of Alumni Relations.

I had the pleasure of traveling to Doha to attend the commencement celebration of our Qatar campus in May. I was so impressed by the students' enthusiasm. Most have matched into great residency programs here in the United States and eagerly look forward to this new challenge. Back in the States, I was thrilled to learn that more than seventy-five members of the graduating class made symbolic gifts of \$20.13 to establish the Class of 2013 Scholarship Fund. The Alumni Association matched their efforts dollar for dollar, and we presented Dean Glimcher with a check for nearly \$3,000 at Convocation.

On May 30, I proudly sat onstage at Carnegie Hall as the Class of 2013 received Doctor of Medicine degrees and became the newest members of the Alumni Association. Overall, 98 percent of the Class of 2013 matched to top fifty hospitals around the country. We're so proud of our graduates! This fall, we look forward to welcoming the Class of 2017 and seeing the cycle begin anew.

Also at commencement, we honored R.

Gordon Douglas Jr., MD '59, with the WCMC Alumni Association Award of Distinction. Established in 1949, it recognizes an alumnus or alumna who has demonstrated exceptional achievement in academic medicine in the areas of education, research, and patient care, and who has brought honor and acclaim to the Medical College. Dr. Douglas's illustrious career includes stints at the National Institute of Allergy and Infectious Diseases, the University of Rochester, and Weill Cornell, where he served as chairman of the Department of Medicine and Physician-in-Chief of NewYork-Presbyterian Hospital until 1990. He went on to become president of Merck Vaccines and was instrumental in the development and distribution of an extraordinary number of new and innovative vaccines. Dr. Douglas is founding chairman of Aeras, a nonprofit biotech company whose mission is to develop new vaccines for tuberculosis.

In early June, the Office of Alumni Relations hosted dinners in the Los Angeles area. These intimate gatherings were great opportunities for alumni to learn more about what's going on at the Medical College and to connect with fellow graduates. The office will be planning more of these events in 2013–14, so be on the lookout for events in your region.

On June 21, we hosted the annual Dean's Circle Dinner with Dean Glimcher. This special event honors the generosity of the Medical College's most prestigious giving society. We were pleased to recognize more than fifteen alumni who have made significant contributions to their alma mater this year. It is never too late to join the Dean's Circle and help our students in need. Please contact the Office of Alumni Relations at (646) 317-7419 for details.

As always, thank you for your continued support of the Alumni Association, the Medical College, and our students. Weill Cornell would not be the special place it is without you.

Best and warmest wishes,

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



IRA FOX

Construction sight: A view of the Belfer Research Building, which is nearing completion on East 69th Street

1940s

Gil Smith '44, MD '47: "I will turn 90 this September. I seem to be doing pretty well. Maybe that is partly due to my wonderful wife, Linda. In terms of activities, I go to the gym three times a week and am in an ongoing Spanish class. The latter is fun, but I doubt that I will become a professor."

1950s

Charles A. deProsse '46, MD '50: "I am living and thriving in retirement in Iowa City. I was recently honored by the Emma Goldman Clinic, a feminist health clinic, for many years of service to, and support of, women's reproductive rights. For the past 17 years, fundraising activities by the Clinic have provided money for the deProsse Access Fund, used to defray some of the cost of an abortion for women unable to raise enough to pay for their procedures."

Russel H. Patterson, MD '52: "Julie and I are in good shape, not counting mild

dementia and stiff joints. We live in NYC, but go to Vermont most weekends. We go to several neurosurgical meetings each year, where we see old friends and keep up with what's new in the specialty. The children are all well, and so are the five granddaughters."

Calvin Kunin, MD '53: "I was saddened to learn of the death of our dear classmate **Betty Coryllos** on March 6, 2013, at the age of 83. Betty was the most self-directed person I have ever known. Her goal as a young woman was to become a pediatric surgeon—and she made it! We are all better off because of people like Betty. My wife, Ilene, and I reside in Columbus, OH, during the warm weather and in Tucson, AZ, during the winter. My current hobby is bird photography. Several of my photographs have been published in the *New England Journal of Medicine* as 'photofillers.' We joined a birding group led by an expert guide for a trip to San Blas, Mexico, in

January 2013. This place has an extraordinary abundance of birds not seen in the U.S. We look forward to more birding as the weather warms in southern Arizona. I just returned from my twentieth annual visit to Taiwan. Most of my time is devoted to working with young investigators to evaluate their research and provide advice on how to write manuscripts. I was the keynote speaker at a conference held in Taiwan to develop a nationwide 'Antibiotic Stewardship' program. I am a permanent consultant to the Taiwan National Health Research Institutes. This is hard work, but I am rewarded by fine meals and good fellowship. They gave me a few days off to photograph the native field, forest, and seashore birds. The secret to retirement, as all of you know, is to keep busy, read widely, maintain an exercise routine, enjoy friends and family, eat well, and vote your conscience. I am trying to do all of this, as did Betty. I can be reached at ckunin@columbus.rr.com."

'I was recently honored with a *Festschrift* by the Brigham and Women's Hospital and Children's Hospital for my 53 years of service.'

Donald P. Goldstein, MD '57

Richard T. Silver '50, MD '53, professor of medicine and director of the Leukemia and Myeloproliferative Center at NewYork-Presbyterian/Weill Cornell Medical Center, received the award for Lifetime of Achievement, Dedication, and Service to Weill Cornell Medical College in December 2011 and the Lifetime Achievement Award from the SASS Foundation for Medical Research at its annual dinner dance in November 2012.

Kenneth Hubel, MD '54, is retired and living in North Liberty, IA. His interests include family, photography, travel, big band jazz on the alto sax, the free clinic in Iowa City, trying to remain limber, and accepting change. He remembers most an elective at Fort Defiance on the Navajo Reservation.

Donald P. Goldstein, MD '57: "I'm still clinically active in gynecologic oncology although I stopped performing major surgery in 2006. I see patients at Dana Farber Cancer Institute and Brigham and Women's Hospital and manage all the chemotherapy for patients at the New England Trophoblastic Disease Center, which I started in 1965. I was recently honored with a *Festschrift* by the Brigham and Women's Hospital and Children's Hospital for my 53 years of service. Many of my former residents and fellows returned and presented papers about the work we have been doing in the field of trophoblastic disease and pediatric and adolescent gynecology. The sixth edition of our popular textbook, *Pediatric and Adolescent Gynecology*, was dedicated to me. All this is very satisfying after a busy and rewarding career, which is not over quite yet."

W. Walter Menninger, MD '57, the retired head of the Menninger Foundation, was consulted and credited on film director Baz Luhrmann's recent film of F. Scott Fitzgerald's *The Great Gatsby*. According to Luhrmann, Menninger helped provide a bookending device that allowed Nick Carraway, the narrator, to be more than a disembodied voiceover.

Bernie Siegel, MD '57: "This September I will have another book, *The Art of Healing*, coming out from New World Library. It will contain my experience as a surgeon and counselor of cancer patients as well as 70 drawings by patients, health-care practitioners, and others to reveal how to make the invisible visible related to diagnosis, treatment, and more. I hope this book creates an awakening in medicine and brings together the fields of mind, body, and spiritual medicine by sharing what is familiar and appropriate to some and unfamiliar and inappropriate to other practitioners and their journals."

Michael Stone '54, MD '58: "I am a professor of clinical psychiatry at Columbia. My wife and I recently returned from London and

Amsterdam, where we met with my colleagues in forensic psychiatry. I have been working with TV producers to launch a new series, 'The New Evil'—a sequel to my previous Discovery Channel series, 'Most Evil,' where I interviewed serial killers and other high-profile murderers, emphasizing the 'why?' factor: what led these men and women to do the things they did? I have also written several articles on the biological underpinnings of certain patients with 'borderline personality.' I am working on a new book that will address issues like problematical custody cases, the dangers of marijuana in adolescents, and violence and the mentally ill. Beth and I are patrons at the Metropolitan Opera and make Lincoln Center our second home."

John Baldwin, MD '59: "Greetings to classmates and old friends. We have continued to enjoy our High Sierra home in Twain Harte, CA, and the old "castle" in Carmel, which is a great place when the snow here is up to your waist. I serve as surgical chairman for Tri-County Tumor Board, which meets twice a month, and am close to UCSF Surgical. However, our interests now are guiding 'big fish' trips to Glacier Bay and Sitka, Alaska, and outdoor winter sports including skiing and snowboarding. Both Jeannie and I have been blessed with excellent health and mobility that have allowed us to do the things we have always loved, right up to the scary 80 number, which is coming up fast. Lots of hugs to all of you, and thanks for the memories that remain as vivid as if they were yesterday. 'Toward the end, they speed up the tape,' as my dad said."

Thomas C. Carrier, MD '59: "In May 2013, I returned to Weill Cornell to attend a dinner at which our classmate, **R. Gordon Douglas Jr., MD '59**, was honored with the Alumni Award of Distinction. This award 'recognizes an alumnus who has demonstrated exceptional achievement in academic medicine, in the areas of education, research, or patient care and who has brought honor and acclaim to the Medical College.' The following day, Gordon delivered an address to the Class of 2013 at Commencement. At Weill Cornell, he served as professor and chairman, Department of Medicine, and physician-in-chief of the New York Hospital. From there he went on to Merck as president of the vaccine division, overseeing the development of many vaccines in use today, including those for hepatitis, chicken pox, HPV, and herpes zoster, among others. Since leaving Merck, Gordon has focused on the development of a tuberculosis vaccine, with several currently in clinical trial. Fellow classmates **Tom Fahey, MD '59**, and **Henriette Abel Stackpole, MD '59**, were also in attendance at the awards dinner."

James E. Shepard, MD '59: "My wife and I

have just returned from an interesting trip to the Baltic states plus the Ukraine and St. Petersburg. Apparently, doctors educated in Estonia stay there if they are in general practice, but if they are specialists they move 45 miles across the Baltic Sea to Finland, where they make more money."

1960s

Elizabeth Barrett-Connor, MD '60: "I continue to teach epidemiology at UCSD, which is still fun. I have received several recent awards recognizing my teaching: American Heart Association Population Science Award 2012, Endocrine Society Mentoring Award 2012, University Professor Lectureship (UCSD) 2012, and the American Heart Association Council on Epidemiology and Prevention Mentoring Award.

"I also consult for Centers of Excellence here and abroad. The one in Northern Ireland is of particular interest to my husband, whose family sailed from Belfast to Charleston before the Civil War. We are both enjoying his retirement, where we share many books and Turner Classic Movies, and he regularly shops and prepares fantastic dinners. I tell all women doctors they should marry a pediatrician.

"Jim brought two children, 6 and 10, into my life and we had three together; their various waves of graduations kept us busy this summer. Lena graduated Phi Beta Kappa and *magna cum laude* from Pomona College. Rosie was salutatorian from a 500-student high school in the Orlando, FL, area; she heads to the University of Vermont this fall with a President's Scholarship. (These are my husband's grandchildren from his first marriage, so I can brag; this clan includes two young men in Atlanta, one finishing and one starting college.) Our combined effort: sons married fantastic women and they have four children now, ages 2 to 4. Daughter Caroline, our only clinician, has a wonderful boyfriend and works as a nurse practitioner in women's health at UCSD.

"I know we are fortunate to have reasonable health, with children and grandchildren nearby, and are still traveling—not too many countries left on our bucket list."

Anthony Saidy, MD '62, sent word of his new book, *1983, a Dialectical Novel* (Seagull Press). Dr. Saidy, a retired public health physician, is also the author of several chess books, including *The Battle of Chess Ideas* and *The World of Chess*. He was instrumental in getting Bobby Fischer to Iceland in

1972 for his match against Boris Spassky.

William Schaffner, MD '62, professor and chair of preventive medicine at Vanderbilt University School of Medicine, was awarded the Health Achievement Award by the National Meningitis Association. Dr. Schaffner is an expert on vaccine-preventable diseases and vaccine-related public policy. He also received the *Nashville Business Journal's* 2013 Health Care Hero Award for Lifetime Achievement.

Ralph A. O'Connell, MD '63, is stepping down as dean and provost of the School of Medicine at New York Medical College. He continues on the faculty as professor of psychiatry and behavioral sciences and vice chair for research.

Burt Dudding, MD '64: "I've recently moved from Middlebury, VT, to Mesa, AZ, where my wife, Pauline Mills (BEd, University of Edinburgh, 1991; MD, University of Nevada School of Medicine, 2004), has begun working for Banner Health in one of their new primary health-care clinics in 'the Valley.' Our almost-7-year-old twins, Connor and MacKenzie, are enjoying the backyard pool, and when we're not in the pool we're inside in the cool. I retired

from medicine in 2004 and in the past nine years have actively pursued my lifelong passion for music and become a church musician, most recently having served for three years as organist and choir director for a Congregational church in Cornwall, VT. I do have a more important and full-time job as the stay-at-home parent for the twins, a kind of 'Dr. Mom' with aspirations to become a 'homeroom father' at their new school in Mesa. I can't think of a better job for a retired pediatrician. I would welcome news from any classmate. And while I'm still trying to figure out Facebook, it's probably safer to reach me by e-mail at badud ding@aol.com."

Larry Raymond, MD '64, director of occupational and environmental medicine at Carolinas HealthCare System and professor of family medicine at UNC Chapel Hill, writes: "Yes, we do have air quality issues in the Old North State, as we Carolinians call our home (and my adopted one). So I'm happy to serve as the lead physician (AKA, head cheerleader) for this advocacy group of over 300 health professionals across North Carolina. I think the late, great Prof. Walsh McDermott would approve, as he was a most articulate voice for all matters affecting the health of the commons, and a role

WCMC-Q



Oath of office: Graduates of WCMC-Q mark a rite of passage at Commencement in Doha.



AMELIA PANICO

Getting to Carnegie Hall: The Class of '13 was all smiles at Commencement.

model for many of my classmates of 1964.”

Peter Tsairis, MD '65: “My life’s work now, in conjunction with my wife of nearly 50 years, is fostering and administering the work and mission of the Alexia Foundation for World Peace, founded initially as a tribute to our daughter, Alexia, a photojournalist student at the Newhouse School at Syracuse University. On December 21, 1988, she was taken from us by a terrorist’s bomb aboard Pan American flight 103 over Lockerbie, Scotland. The Foundation aspires to give voice to social injustice and to cultural differences so as to promote global understanding through photojournalism. If you are interested in more details and the work we fund, visit our website, thealexiafoundation.org.”

Robert E. Curran, MD '66: “I received the Dean’s Excellence in Teaching Award from Brown University Alpert Medical School in June (along with many others). I’m not sure if the award is deserved, but at least it suggests that I am still in the game. The teaching is fun. The practice is fast dwindling by design.”

Paul Schellhammer, MD '66: “My wife, Ann (Cornell School of Nursing '65), and I relocated to a retirement community earlier this year in view of my prostate cancer and

eight-stent cardiac profile. Soon thereafter, Ann was diagnosed with an aggressive duodenal cancer that was not controlled by surgery or chemotherapy. She was an example of courage and calm and is my hero. In recalling the fond memories of the mid-Sixties on 69th and York, I consider my ‘real stroke of good fortune’ to be a freshman year Olin Hall mixer where we met.”

Richard Lumiere '63, MD '67: “I’m working 19 hours a week in gynecology at offices on Central Park South, NYC. I’ve been in contact with **Dean Edell '63, MD '67**, reminiscing about medical school and Dr. Lampe’s course in anatomy. I’m currently taking a one-month break in the South of France with my wife, Bianca, who was a dietetic intern at NYH. We were introduced by Diane Sachs, a nurse at the hospital and fellow Cornellian from Ithaca. She visited us two years ago, and we thanked her again for the introduction. We are very good friends of **Ed Ambinder, MD '68**. We also saw **Richard Muchnick '63, MD '67**, for a second opinion regarding an eye problem of Bianca’s. It seems like all the doctors trained at Cornell turned out to be the best. What a great education. I

remember Dean Hanlon telling us that half of what they taught us was right and half was wrong. Our task was to figure out which was right.”

Jeffrey S. Borer, MD '69: “On September 28, I will be honored at the annual awards and fundraising dinner of the Association of Black Cardiologists, in Washington, DC, with receipt of the Association of Black Cardiologists Diversity in Cardiology Award, which I will accept on behalf of my cardiology program at SUNY Downstate Medical Center. We were cited for the diversity of our faculty and trainees in a major academic medical center.”

Steven G. Gabbe, MD '69: “I am completing my fifth year as the senior vice president for health sciences at the Ohio State University and the chief executive officer of the Ohio State University Medical Center. Like all academic medical centers, ours is working through a significant transformation in health care, in part associated with the Patient Protection and Affordable Care Act. We are also 18 months away from the completion of a major expansion of the Wexner Medical Center, including the jewel of this project—a 420-bed James Cancer Hospital and Solove Research Institute and Critical Care Center. My wife, Dr. Pat Gabbe, and I have become avid tandem bicyclists. This interest grew out of our desire to ride in Pelotonia, an Ohio State fundraising event to support cancer research. Each year, we’ve ridden the 50-mile route.”

Nick Hardin, MD '69: “I have just retired from both the University of Vermont College of Medicine and active practice of pathology. Throwing away all the papers, photographs, and copies of reports and syllabi was a trip down memory lane. I was reminded of the patients from whom I learned so much, and the house staff and students I helped to train and educate. I still have a ways to go on clearing out the office, but am making progress. Looking forward to the time when ‘every day is a Saturday,’ and I can spend more time with my wife, Susan, and our children and grandchildren. However, I have already signed up to teach three labs on cardiovascular disease in the fall.”

1970s

Gerald F. Abbott, MD '71, was inducted as a fellow in the American College of Radiology during the ACR annual meeting in May. Dr. Abbott is an associate radiologist at Massachusetts General Hospital and an associate professor at Harvard Medical School.

Ken Kelleher, MD '72: "Currently I'm on an exciting ocean cruise of the Red Sea, all expenses paid. We were supposed to be looking for pirates, but they have all given up the job. So we just float around."

William Kleinman, MD '72: "I'm still working full-throttle. I'm president of the Indiana Hand to Shoulder Center and professor of orthopaedic surgery at Indiana University Medical Center. I've been married to Susie for 35 years. I've been in the same practice for 35 years (though it's a heck of a lot bigger than when I started). Two daughters' weddings are coming up in the next year. My son remains footloose and fancy-free. My best wishes to all my classmates, who I miss greatly."

Donald D. Wilson, MD '72, is pursuing a new career as an amateur paleontologist. He has recently published "Concretions as sources of exceptional preservation, and decay as a source of concretions: examples from the Middle Devonian of New York," *Palaios*, 2013, v. 28, p. 305-316. CT images were used to elucidate the origins of an enigmatic rock.

Benjamin Lipsky, MD '73: "I have transitioned from my positions at the University of Washington to living in Oxford, where I am affiliated with the medical school and Green Templeton College. I also work 25 percent time as a visiting professor of medicine (infectious diseases) at the University of Geneva. My wife is the bursar (CFO/COO) of one of the University of Oxford colleges (Kellogg), and we travel around the U.K. and Europe frequently. We also return to Seattle every few months, as our elder daughter and her husband have had our first grandchild."

Vincent "Vinny" de Luise, MD '77: "I enjoyed seeing many classmates at our 35th Reunion dinner at Petrossian Restaurant last fall. I continue to participate in the Humanities and Medicine Committee and Music and Medicine Initiative at WCMC. I have retired from clinical practice and continue to teach in ophthalmology. I am at Harvard this year in a postdoctoral fellowship program exploring new avenues in curriculum design for the medical humanities."

Steven Koenig, MD '77: "Last month, I joined **David Kanarek, MD '77,** and his family to celebrate the wedding of his daughter, Emily, at Ravinia in Highland Park, IL. David looks terrific and is enjoying his concierge practice in internal medicine. I continue to work full time at the Eye Institute of the Medical College of Wisconsin, practicing cornea and refractive surgery. I still love the work, but sailing, beekeeping, and managing a vineyard remain wonderful diversions this time of year."

Robert Schultz, MD '78, recently published *Autobiography of a Baby Boomer*, in which he tells the story of his travels on the hippie trail through Europe, North Africa, the Middle East,

and Asia and his discovery of the conventional joys and responsibilities of having a family. Dr. Schultz is retired from private practice of orthopaedic surgery, but teaches in the Department of Orthopaedics at Duke University.

1980s

Ethan Dmitrovsky, MD '80, former professor and chair of the Department of Pharmacology and Toxicology at the Geisel School of Medicine at Dartmouth, was appointed provost and executive vice president at the University of Texas MD Anderson Cancer Center. He will also be responsible for the Moon Shots Program, an effort to rapidly reduce mortality in several major cancers.

Carolyn H. Grosvenor, MD '80: "I am still working in primary care at the local VA and on faculty at SUNY Albany School of Public Health. I am also the assistant director of clinical preventive medicine for the New York State Preventive Medicine Residency Program. The highlight of the past two years is that I have become a medical missionary. In 2012 I went to Honduras, this year to Ecuador, and next year I plan to go to Haiti. This has been a life-changing experience for me. I am still married to Wayne (37 years), who took early retirement to pursue his musical interests."

Bob Friedlander, MD '81: "After 26 years I am leaving New Hampshire Oncology-Hematology to do a fellowship in palliative medicine at MSKCC. I plan to return home to New Hampshire after the fellowship to begin my second career!"

Philip M. Murphy, MD '81, was elected as a 2013 fellow by the American Academy of Microbiology. Dr. Murphy is chief of the Laboratory of Molecular Immunology and chief

'After 26 years I am leaving New Hampshire Oncology-Hematology to do a fellowship in palliative medicine at MSKCC.'

**Bob Friedlander,
MD '81**

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'I plan to work with the Alliance for Smiles in Harbin, China, this July. Life is good, and giving back makes everything more worthwhile.'

E. Anne Wuerslin, MD '81

of the Molecular Signaling Section, LMI, at NIH. His laboratory studies G protein-coupled chemottractant receptors, host defense and inflammation, and genetic risk factors in infectious and immune-mediated diseases.

E. Anne Wuerslin, MD '81: "I'm still working across the fine Rocky Mountain states of Colorado and Wyoming as a locums pediatrician for Colorado Children's Hospital of Aurora, CO. I'm busy with my volunteer jobs as a Copper Mountain Ambassador and ski guide for my eleventh season, and working as a master gardener for Larimer County in Fort Collins. I plan to work with Alliance for Smiles in Harbin, China, this July with volunteer medical work for children and adults with cleft lip and palate and other plastic surgery needs. Life is good, and giving back makes everything more worthwhile."

Michael M. Alexiades, MD '83: "I'm having my first book, a medical thriller called *Night Harvest*, published in October 2013. It's about a medical student who gets involved in a series of murders."

Louise Abel, MD '84: "Boudinot Atterbury, MD '84, and I have lived in Santa Fe, NM, for the past 18 years. It has been 25 years since we came out west to work with the Indian Health Service. I'm in the private practice of general internal medicine and love it. Keeping up with all the

changes in medicine has been hard, but we have traveled the world and have really rewarding work. I'm reaping the rewards of having been in practice now for more than 15 years here with the same patients. Boud has been a hospitalist these past five years. He is about to re-enter outpatient internal medicine, in a local clinic that started out as an AIDS clinic. He is looking forward to that. He is now on the clinical faculty at UNM Medical School. Our three daughters have graduated from college and now we are empty-nesters. We look forward to the next reunion to catch up with our colleagues and friends back east."

Christopher Plowe '82, MD '86, received the American College of Physicians Award for Outstanding Work in Science as Related to Medicine at the annual ACP meeting in San Francisco in April 2013. This award has been given to several Nobel laureates since 1958. Dr. Plowe is an investigator at the Howard Hughes Medical Institute and professor and leader of the Malaria Group, Center for Vaccine Development, at the University of Maryland School of Medicine.

Stuart Rubin, MD '87: "As the second half of 2013 gets under way, the Rubin family will be approaching three milestones. Lisa '85, PhD '93 in Pharmacology, and I will be celebrating our 25th wedding anniversary. Our younger son, Daniel, just graduated from Williamsville East High School and will be starting his undergraduate education at Vanderbilt University. Our older son, Matthew, will be graduating from the Georgia Institute of Technology in December."

Theresa Rohr-Kirchgraber, MD '88, and Paul Kirchgraber, MD '88, are living in Indiana and will see their youngest off to college this year. They hope to enjoy being empty-nesters. Theresa is running for president of the American Medical Women's Association (AMWA) and asks all of you who are members to keep a look-out for the ballots. She was recently an invited speaker at the American Medical Association annual meeting and gave talks on motivational interviewing and the 24-hour diet history. Paul has been flying all over the world in his position as global medical director for Covance Central Labs. He is enjoying his summer with the kids and trying to get in the daily exercise needed to keep him young.

1990s

Deborah M. Kado, MD '91: "In August 2012 we moved our family (two daughters: Anna, an incoming junior, and Sarah, an incoming sixth grader) from Los Angeles down the coast to La Jolla, CA. After about 20 years in LA, my husband, Paul Mischel, MD '91, relocated to the Ludwig Cancer Institute and the Dept. of Pathology at UCSD, and I moved from the UCLA Dept. of Orthopaedic Surgery to UCSD's Dept. of Family and Preventive Medicine/Epidemiology and Dept. of Internal Medicine/Endocrinology. In July 2013, everyone (including two rescue dogs) is thrilled with their new home, school, and work environment."

Tamara Rozental, MD '99: "I was recently promoted to associate professor in orthopaedic surgery at Harvard Medical School. I work at Beth Israel Deaconess Medical Center in the Department of Orthopaedic Surgery, specializing in hand and upper extremity surgery."

Jeffrey Yao, MD '99: "We welcomed our first child, Madeline Grace Yao, born on April 13, 2013."

2000s

Michael S. Irwig, MD '00, has been promoted to associate professor of medicine at George Washington University. He lives in Dupont Circle in Washington, DC, with two cats named Andro and Gen.

Erin Thelander Dalton, MD '02: "Holden

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Keep in touch with your classmates.

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Connor Dalton was born on July 7. His proud big sister, Callan (2 years old), is already showering him with kisses."

Diane E. McLean, MD '02: "I am currently an attending psychiatrist at Lincoln Medical and Mental Health Center in the Bronx, NY, and have a small private practice in child and adolescent/adult psychiatry. Life is busy at home with Rose, now 6-1/2, and James and Annabelle, both 3-1/2. Best wishes to everyone in the Class of '02."

Hina Talib, MD '06: "I completed a residency in pediatrics also at Weill Cornell. I just completed my fellowship in adolescent medicine and will be starting as an assistant professor of pediatrics at Children's Hospital at Montefiore/Albert Einstein College of Medicine this August. My clinical interests include pediatric and adolescent gynecology, contraception, adolescent health, and mental health. My research interests include HIV testing in Bronx adolescents. I am currently running a randomized control trial on the treatment of vitamin D deficiency in Bronx teens."

Kelly Vranas Ullery, MD '08: "My husband, **Brant Ullery, MD '08**, and I both completed our residencies at the University of Pennsylvania (I chose internal medicine and Brant chose general surgery), and we just started our fellowships at Stanford University Medical Center (I am doing pulmonary/critical care and Brant is doing vascular surgery). We also welcomed our first daughter, Emerson Grace, in August 2012."

2010s

Prabhjot Singh, MD '11: "I'm the chair of the One Million Community Health Worker Campaign (1millionhealthworker.org), which was launched at the World Economic Forum in January and endorsed by the African Union. As we work on global health issues, we are bringing the best lessons back to the U.S. in the form of City Health Works, a Harlem-based social enterprise that is supported by Robin Hood and the Robert Wood Johnson Foundation. Love to hear about other alumni experiences in primary care system design: psingh@ei.columbia.edu."

Faculty

Mark Rubinstein, a forensic psychiatrist and retired clinical assistant professor of psychiatry at Weill Cornell, recently published his second novel, *Love Gone Mad* (Thunder Lake Press).

In Memoriam

'42 MD—Robert M. Kiskaddon of Punta Gorda, FL, March 24, 2013; practiced internal medicine in Youngstown, OH; taught at Northeastern Ohio University; president, Mahoning County Medical Society; Rotarian; musician; sailor; active in community, professional, and religious affairs.

'45 MD—Hugh F. Lena of Niantic, CT, June 28, 2013; chief of general surgery and president of the medical staff, Lawrence Memorial Hospital; president, New London County Medical Association; veteran; received a special papal award from Pope Paul VI; active in community, professional, and religious affairs.

'45, '47 MD—Ernest Gosline of Clinton, NY, April 8, 2013; psychiatrist and psychoanalyst; director and commissioner of Community Mental Health, Oneida County; researched psychiatric treatments at Rockland State Hospital; veteran; commander, 331st General Hospital; author; musician; active in community, professional, religious, and alumni affairs.

'50 MD—James B. Given III of West Hartford, CT, and New Suffolk, NY, June 18, 2013; anesthesiologist, Hartford Hospital; veteran; golfer; sailor; hiker; active in professional and alumni affairs.

'51 MD—James H. Pert of Glenmont, NY, March 5, 2013; associate of Research University of Toronto, Canada; national research director, American National Red Cross; creator and director of New York State Blood Resources; organized the Vaccinia Immune Globulin national and international programs to fight complications of smallpox immunization; at the National Cancer Institute, developed a method of preparing platelet concentrates for use in cancer chemotherapy and organ transplants; associate professor of medicine at George Washington University School of Medicine and Albany Medical College; instructor of medicine at WCMC; veteran; author; active in community and professional affairs.

'52 MD—Richard Lennihan of Westminster, DE, June 12, 2013; vascular surgeon, Christiana Care Hospital; first physician in Delaware to perform vascular surgery; marathon runner; birdwatcher; veteran; supported Eritrean orphans; active in community and professional affairs.

'55, '58 MD—Gerald Glick of Chicago, IL, July 12, 2013; cardiologist; professor emeritus of medicine, Rush Medical College.

'62 MD—Nicholas L. Tilney of Boston, MA, March 13, 2013; Francis D. Moore Professor of Surgery and senior surgeon and director of the Center for Transplantation, Brigham & Women's Hospital; head of the renal transplant service at Brigham & Women's Hospital; director of the Surgical Research Laboratory, Harvard Medical School; author; active in professional affairs.

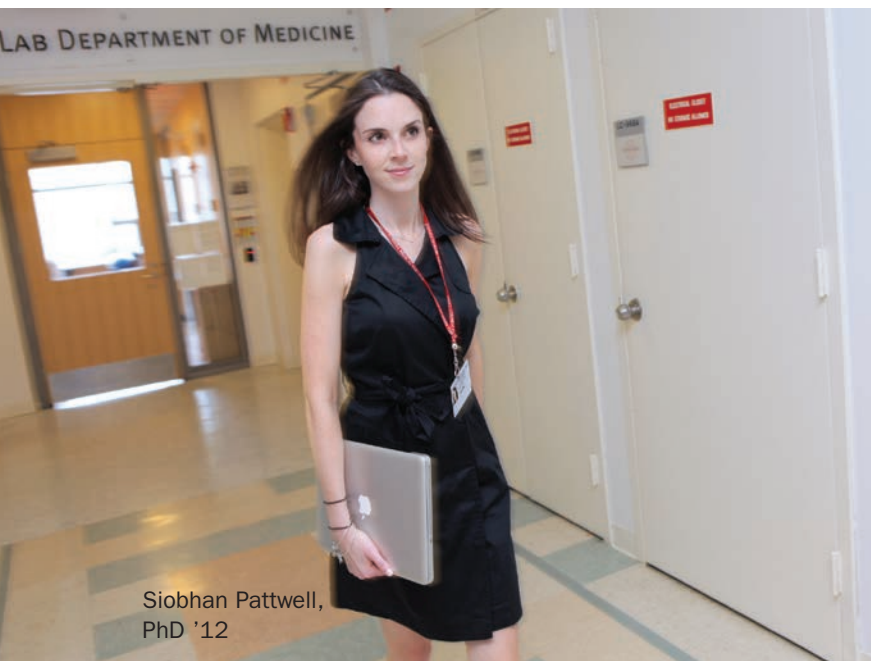
'59, '63 MD—Robert L. Wegryn of Westfield, NJ, May 5, 2013; medical director, Center for Hope Hospice; attending surgeon, Trinitas Regional Medical Center; chief and attending surgeon, Elizabeth General Medical Center; president, Union County Medical Society; recipient, Auxiliary Physician of the Year award, 1992; recipient, New Jersey Hospice Physician of the Year, 1997. Theta Delta Chi.

'66, '70 MD—George L. Wineburgh of Frankfort, IN, May 15, 2012; radiologist; discovered widespread tuberculosis in Tortola, BVI, and extensive asbestosis in northern New York State; gardener; active in civic affairs. Zeta Beta Tau.

'67, '73 MD—Richard M. Linchitz of Glen Cove, NY, May 22, 2013; medical director.

Scary Smart

Siobhan Pattwell, PhD '12, came to Weill Cornell to study brain tumors—but made a breakthrough in how adolescents process fear



Siobhan Pattwell,
PhD '12

JOHN ABBOTT

When Siobhan Pattwell was a Lafayette College undergrad, she did a pediatric oncology internship in London. It was often grim, challenging work. “The sickest kids with cancer in Europe would come to that hospital,” Pattwell recalls, “and one of them would pass away every few days.” Hour after hour, she’d sit in meetings where parents were told that nothing could be done—and at the end of the summer, she resolved to devote her talents to discovering new treatments. Says Pattwell: “I did a 180 from planning to attend medical school to wanting to pursue cancer-focused research.”

Long interested in neuroscience, the New Jersey native came to Weill Cornell to study brain cancer, ultimately joining the lab of psychiatry and pharmacology professor Francis Lee, MD, PhD. She went on to complete her PhD in 2012, stay for a postdoc, and earn kudos for her thesis research—which, as it turned out, had surprisingly lit-

tle to do with brain tumors. Last year, Pattwell was named to *Forbes* magazine’s “30 Under 30” list in science and medicine for her work on how adolescents process fear. “She’s fantastic,” Lee says. “She’s organized, disciplined, and very clear thinking—but most important, she can see something that doesn’t fit, switch gears, and figure out something that had never been understood before.”

Mentor BJ Casey, PhD, is similarly effusive. “She’s brilliant, with an uncanny sense for uncovering novel developmental discoveries and following through with the breadth of a senior scientist,” says Casey, the Sackler Professor of Developmental Psychobiology. “She is already a role model for junior scientists and peers, and one of the most grounded individuals I know.”

In experiments in humans and mice described in the *Proceedings of the National Academy of Sciences*, Pattwell made a major discovery: it’s much harder for adolescents to recover from frightening experiences than it is for children or adults. “Even though we still don’t understand the exact molecular mechanism, it suggests that we missed something,” Lee says. “And she found it.” For the rodent experiments, a tone was paired with a foot shock; in humans, a colored square preceded an aversive sound. Soon, the warning alone prompted fearful behavior—either freezing in mice or sweaty palms in humans. Pattwell then repeatedly exposed the subjects to the signal without the negative consequence, a common therapy called extinction learning. While children and adults responded well, adolescent fear was more intractable. “We found that an area in the prefrontal cortex is controlling the ability to reassess that a cue is safe,” Pattwell says, “and it’s not active in the same way in adolescence as during younger and older ages.” The discovery has implications for treating anxiety: without proper treatment, trauma suffered as a teen can persist throughout life. “All the therapies, whether pharmacological or behavioral, have been designed for a mature neural framework,” Pattwell observes, “because everyone studies the adult brain.”

Pattwell notes that the fear studies aren’t entirely unrelated to her initial passion; many of the pathways involved in learning, memory, and neuroplasticity are also involved in brain cancer. “Anytime anything is changing or growing,” she says, “certain signaling pathways are activated and molecular targets are involved.” This summer, Pattwell returned to oncology, moving a few blocks to Sloan-Kettering to work under cancer biologist Eric Holland, MD, PhD. This fall she’ll relocate with his lab to Seattle’s Fred Hutchinson Cancer Research Center. “As scientists, most of us can pride ourselves on being linear, logical thinkers,” Lee says. “But you also need to be open to new ideas, and Siobhan exemplifies that. Even as a graduate student, she was absolutely independent. Fear learning is not an area of focus in my lab. That she was able to work on her own and flesh out the story to this conclusion is quite remarkable.”

— Beth Saulnier

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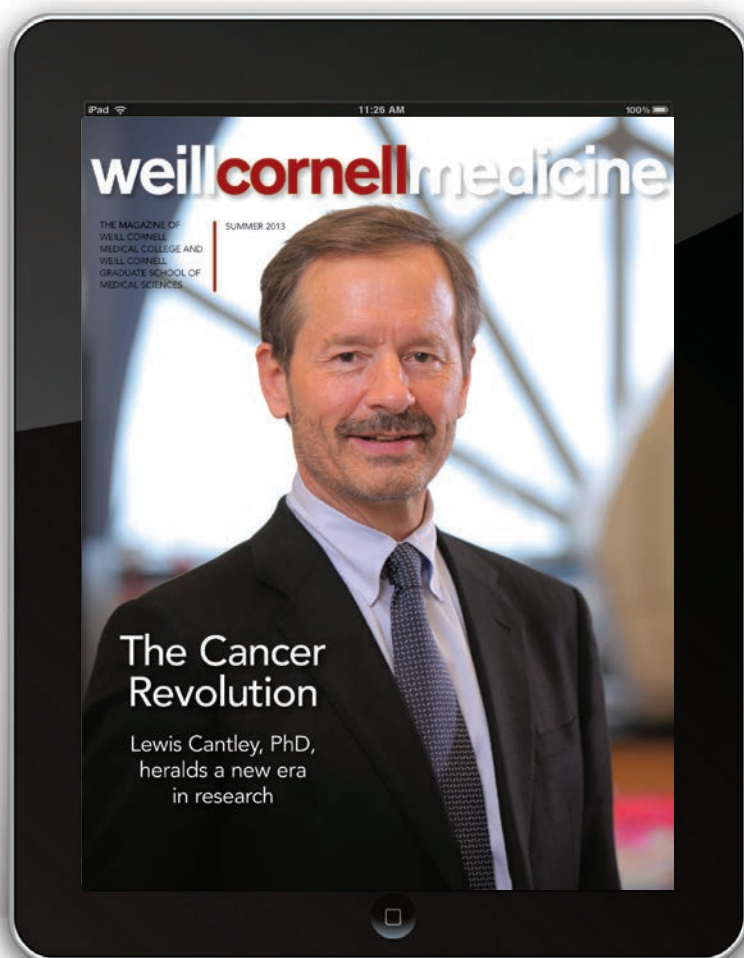
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