

Columbia Medicine

Columbia University Vagelos College of Physicians & Surgeons

2018 ANNUAL REPORT

Financially Speaking

A future without
medical school debt

Precision Medicine

Moving data to
patient care

MEDICINE PRESENT & FUTURE

TECHNOLOGY FROM ACADEMIC
MEDICINE IS DRIVING NEW TREATMENTS
TO PATIENTS NOW



Features:



4

Revving Up Medical Research as Innovation Engine

Researchers are using technology transfer, robotics, phone apps, and other technology to identify treatments for diabetes, Alzheimer's, cancer, and infectious diseases. What was once the domain of industry is now considered a routine part of academic medicine research, and Columbia offers tools to help faculty move their innovations to the marketplace.

10

Precision Medicine: Promise (Being) Fulfilled

Minimizing “variants of unknown significance” is one of the goals of precision medicine research, and mining data from a more diverse population—the goal of the federal All of Us Research Program—will speed that goal. Already, precision medicine shows promise in diagnosing some patients thought to have schizophrenia with a virus instead and offering new treatments for thyroid problems and sarcoma.

16

What Financial Freedom Means to Tomorrow's Doctors

Five VP&S alumni discuss how scholarships shaped their careers amid news that future generations of graduates will benefit from the generosity of Diana and Roy Vagelos'54 and others who have made it possible for students with financial need to get through medical school without borrowing money.

<http://ps.columbia.edu/>



20

Righting a Wrong: David McDonogh, Denied Degree in 1800s, Receives Posthumous MD

When we discovered that David McDonogh, a black medical student at VP&S in the 1840s, was not officially recognized as a student or graduate, we were determined to right a 171-year-old wrong. Dr. McDonogh, who completed his studies in 1847, received his posthumous MD diploma from Columbia at the 2018 graduation ceremony, and a scholarship in his name will help other students who have overcome adversity.

Departments:

2 Dean's Message

22 2018 Year in Highlights

30 Philanthropy News

34 VP&S News

39 About VP&S

- Trustees Committee on the Health Sciences
- CUIMC Board of Advisors
- Other CUIMC Advisory Groups
- CUIMC Administration
- Vagelos College of Physicians & Surgeons Administration
- Executive Committee of the Faculty Council
- Department Chairs
- University Centers and Institutes and Directors
- Affiliated Hospitals
- Facts and Statistics

On the Cover

New drugs and other innovations that can benefit patients are increasingly coming out of the work done in medical school labs. With the help of Columbia Technology Ventures and other systems, VP&S researchers can identify collaborators to move their ideas to commercial use, learn how to file for patents, get tips on how to launch their own companies, or find other support necessary to move their discoveries along the path of commercialization. Story, Page 4.

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2018 Annual Report

Editor: Bonita Eaton Enochs

Principal Writer: Sharon Tregaskis

Contributing Writers:

Avichai Assouline, Susan Conova,
Alla Katsnelson, Joseph Neighbor,
Odelia Ghodsizadeh

Art Director: Eson Chan

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Christopher DiFrancesco,
Chief Communications Officer

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Office of the Chief Executive and Dean of the Faculties of Health Sciences and Medicine

Columbia University Irving Medical Center
630 W. 168th St.
New York, NY 10032

Communications Office

Vagelos College of Physicians & Surgeons
701 W. 168th St., Box 153
New York, NY 10032
Phone: 212-305-3900
Fax: 212-305-4521

Office of Development

Columbia University Irving Medical Center
630 W. 168th St., P&S 2-421
New York, NY 10032
Phone: 212-342-0088



JORG MEYER

The Year That Rang Out the Old and Rang In the Next 250 Years

The year during which we celebrated our 250th anniversary celebration can be summed up in a remarkable comparison: We started the year as the College of Physicians and Surgeons at the Columbia University Medical Center, and we had two Nobel Prize winners on our active faculty. We finished the year as the *Vagelos* College of Physicians and Surgeons at Columbia University *Irving* Medical Center—and we had *three* Nobel Prize winners on our active faculty.

The 2017-18 year was not only a celebration of our legacy in medical education, research, and patient care but also a time for thoughtful planning that will ensure our continued leadership in academic medicine. By developing new programs, establishing new departments, recruiting renowned faculty, and growing our research portfolio, we are building the future of a medical school that has not just survived for 250 years but has thrived over 10 generations of organizational changes, shifts in societal norms, and technology that continues to shape how we learn, study disease, and advance patient care.

Three Nobelists:
Richard Axel, Joachim
Frank, and Eric Kandel



The stories in this report reflect the best of a year that has been punctuated by remarkable headlines. A gift from the estate of Herbert Irving, who died in 2016, and Florence Irving, who died earlier this year, enabled us to join with New York-Presbyterian Hospital to rename our shared campus the Columbia University Irving Medical Center. The naming is a fitting tribute to the Irvings, whose friendship and philanthropy have long supported our cancer programs and many other programs, including the work of junior and senior researchers. They also tirelessly championed the great care they received from Columbia physicians.

We also rededicated the medical school by changing our name to the Roy and Diana Vagelos College of Physicians and Surgeons—VP&S. This new name aligns the school with a name that has long symbolized ingenuity, leadership, vision, and generosity. For example, this year the Prix Galien USA Committee renamed its award for individual service to improve the state of human health as the “Roy Vagelos Pro Bono Humanum Award for Global Health Equity” in recognition of his historic act of moral leadership while CEO of Merck in donating ivermectin to treat and prevent river blindness in 34 countries.

Roy and Diana Vagelos not only lent us their name, they generously provided a scholarship endowment that was then supplemented by more than \$25 million in matching gifts from generous alumni, faculty, and friends who responded to the couple’s challenge to support this worthy effort. Starting this August, the endowment allowed us to eliminate loans and instead to provide scholarships for all of our medical students who have financial need. The scholarship program funded by these gifts will make VP&S affordable to all, and it will enable our graduates to pursue their professional dreams without being encumbered by repayment of medical school loans.

At graduation this year, we honored a man who completed his studies at VP&S 171 years earlier. David Kearney McDonogh was born an enslaved person in New Orleans and after he became a free man by attending college in Pennsylvania, he started medical studies with a mentor at Columbia. Because of his color, however, he was never formally recog-

nized as a student let alone allowed to graduate. We rectified that wrong by giving him a posthumous MD degree, which we presented to Patricia Worthy, Dr. McDonogh's great-great-granddaughter, at our graduation ceremony in May. You can read more about Dr. McDonogh's life and work inside this report.

In research, Joachim Frank, PhD, shared the 2017 Nobel Prize in Chemistry for his groundbreaking work creating and applying cryo-electron microscopy. He joins Eric Kandel, MD, and Richard Axel, MD, as our three Nobel Laureates on the active VP&S faculty.

We also can boast of our rapidly growing NIH funding. Columbia is the only leading medical school to exceed the change in the NIH budget for eight consecutive years. During that time, VP&S has had the second largest absolute increase in NIH funding of any medical school in the nation—a testament to the rigorous basic and clinical research done by our renowned faculty.

One large award from the NIH supports our part of the national precision medicine initiative, the All of Us Research Program, which has great potential to improve the health of many by gathering genetic information from individual volunteers across the full spectrum of American life. We are proud to lead the New York consortium and grateful for the many members of Upper Manhattan who have committed to participating in this important endeavor.

In education, we launched two new departments this year: the Department of Emergency Medicine, chaired by Angela Mills, MD, whom we recruited from the University of Pennsylvania, and the Department of Medical Humanities and Ethics, chaired by longtime faculty member Rita Charon, MD, PhD, founder of the field of narrative medicine. Another new recruit, Jordan Orange, MD, PhD, joined us from Baylor to chair the Department of Pediatrics.

Students have new degree options. The University approved a new joint degree, the MD/MS in biomedical engineering with Columbia's Fu Foundation School of Engineering and Applied Science. A new master's degree program in genetic counseling will begin enrolling students next year.

In patient care, we saw record numbers of visits to the Columbia faculty practice organization as we opened new locations throughout the New York area. Patient care will get a boost when a shared electronic health record, being developed in partnership with NewYork-Presbyterian and Weill Cornell, is imple-



mented. This large undertaking, years in the making, will greatly benefit patients and clinicians.

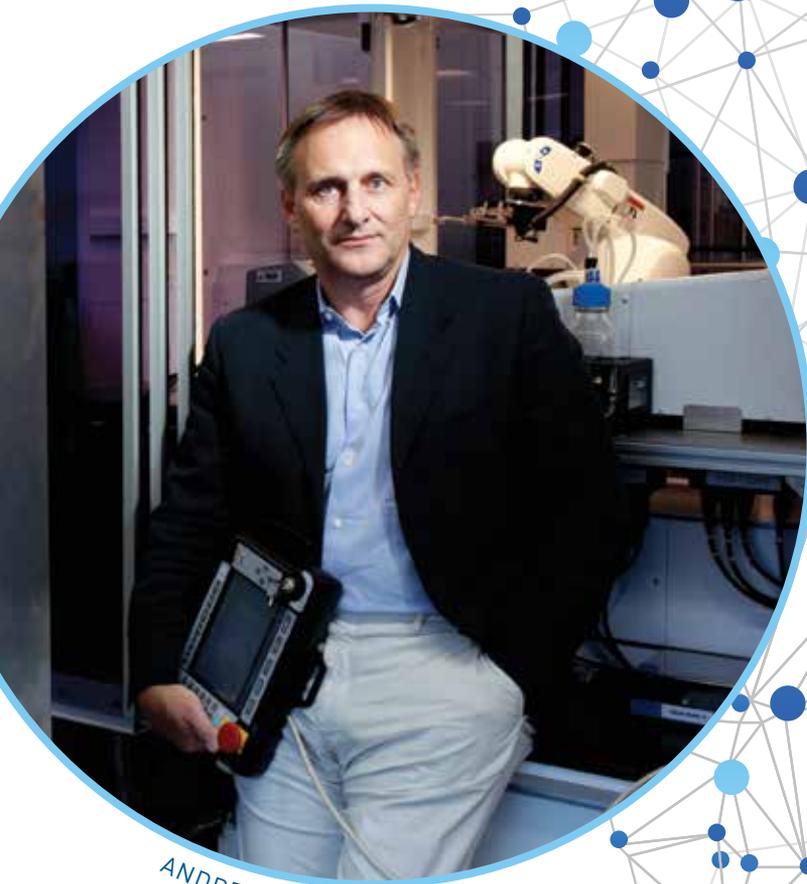
These technical and programmatic innovations will help us build on our future as educators, caregivers, and investigators, but we also know the importance of our physical infrastructure. A full year of enjoying our new Vagelos Education Center building, which still turns heads on Haven Avenue, was followed by renovation of our Alumni Auditorium, another facility that is enjoyed as a shared space by many in our neighborhood. By next summer, Haven Plaza, a pedestrian area created by closing the block of Haven Avenue, off Fort Washington Avenue, will offer a vibrant space for everyone in our community and the surrounding neighborhood to use—to relax, enjoy a meal or a conversation with a friend, participate in arts and cultural activities, or shop at the weekly greenmarket.

Our historic 250th year was one of great accomplishments, made possible by truly remarkable alumni, faculty, students, staff, and friends. It was a year of celebrating our past and planning our future, a future that promises to be as special as our past was remarkable. Thank you for the many ways you help us make VP&S such an extraordinary place.

With best wishes,

Lee Goldman, MD, Dean
lgoldman@columbia.edu

Columbia President
Lee Bollinger, left,
and VP&S Dean Lee
Goldman, right, with
Roy and Diana Vagelos



ANDREA CALIFANO



ORIN HERSKOWITZ



KAREN DUFF

INNOVATION ENGINE: MEDICAL RESEARCH

Researchers at VP&S are rewriting the course of scientific investigation, intent on speeding up the process of discovery that will help patients with cancer, Alzheimer's disease, diabetes, and other intractable diagnoses.

In cancer, Andrea Califano, PhD, the Clyde and Helen Wu Professor of Chemical Systems Biology and chair of the Department of Systems Biology, decided to turn cancer treatment theory on its head. The first wave of research in pursuit of personalized oncology focused on clues embedded within individual tumors. Decode the nucleic acids gone awry within the DNA of a particular patient's cancer, or so the thinking goes, to identify treatments tailored to target that specific mutation.

It's a fine theory, says Dr. Califano, but investigators still have a lot of work to do before the vast majority of cancers yield to that approach. "Only maybe 25 percent of patients have a mutation that could be defined as actionable," he says.

For more than a decade, Dr. Califano has championed what might be considered an end run around cancer mutations, focusing instead on identifying and blocking the networks of normal proteins—known as master regulators—hijacked by deranged DNA to spur tumor formation and sustain tumor growth. Prevent the signals those proteins send on behalf of a cancerous mutation, and the cancer itself screeches to a halt.

In February, the New York State Health Department approved for clinical use two tests based on Dr. Califano's work. Marketed under the names DarwinOncoTarget and DarwinOncoTreat—and developed by DarwinHealth, a Manhattan-based biotech firm co-founded by Dr. Califano in 2015—the tests are available to oncologists and researchers through the Laboratory of Personalized Genomic Medicine in the Department of Pathology & Cell Biology. DarwinOncoTarget identifies all proteins in an individual's tumor that are acting abnormally and for which an FDA-approved or investigational drug already exists. DarwinOncoTreat homes in on the entire complement of master regulator proteins responsible for launching and maintaining a specific tumor to predict the drugs that, by interfer-

PATIENTS WITH DIABETES, ALZHEIMER'S, CANCER STAND TO BENEFIT FROM TECH TRANSFER

ing with these proteins, will most likely benefit the patient.

"Our tests find between five and 20 pharmacologically actionable targets per sample," says Dr. Califano, noting that the tests include all FDA-approved compounds, not just those developed to treat cancer. "Oncologists can decide how to proceed based on toxicity, literature knowledge, and their experience using those drugs."

Startups like DarwinHealth have become an increasingly common vehicle for speeding innovative treatment approaches conceived within VP&S laboratories into clinical use, says Orin Herskowitz, Columbia University's senior vice president of intellectual property and tech transfer and executive director of Columbia Technology Ventures. This year, more than 400 inventions emerged from the University's research laboratories, generating more than 200 patent applications. Among the 100-plus licenses issued this year to commercial partners, more than two dozen were written to startups founded by Columbia faculty and students.

Among them, the contingent representing VP&S stands out. "Increasingly, the most transformative therapeutics, diagnostics, and devices with the highest potential to save and improve patients' lives are being launched via startups emerging from university research labs," says Mr. Herskowitz. "VP&S researchers are incredibly innovative and driven to see their inventions make an impact on the world, so not surprisingly many are turning to entrepreneurship and working with venture capital investors to make sure this happens as quickly and effectively as possible."

Consider, for example, the story of Ceracuity, co-founded in 2015 by Karen Duff, PhD, deputy director of the Taub Institute for Research on Alzheimer's Disease and the Aging Brain and a professor in the Department of Pathology & Cell Biology. Based in New York City, Ceracuity licensed a collection of small molecules developed by Dr. Duff and collaborator Wai Haung Yu, PhD, assistant



DONALD LANDRY

professor of pathology & cell biology, to spur autophagy—the process by which the healthy brain quickly and effectively clears abnormal, toxic proteins—as a treatment for Alzheimer’s, Parkinson’s, and frontal temporal lobe degeneration linked to tauopathy. “Think of it like a garbage truck,” says Dr. Duff, “taking out the recycling. We wanted to enhance the effectiveness of the garbage truck.”

President Jimmy Carter signed the Bayh-Dole Act in 1980, opening the door for investigators and their academic institutions to patent and license discoveries made in federally funded research enterprises. By the time Dr. Duff moved to the United States for her first academic post, in the early ’90s, universities were beginning to take a more proactive approach to educating faculty about intellectual property rights and facilitating patent applications, but academics were expected to stay in their lane. “When I first started working on neurodegenerative diseases,” says Dr. Duff, “there was a strict separation between people doing lab-based research and people doing therapeutic development.” Over the past decade, however, cultural shifts within academia and within industry have converged to spur increasingly dynamic crossover among academics, drug companies, and biotech startups. Even so, says Dr. Duff, getting to the point where an academic can form her own company and see her intellectual property all the way from laboratory to FDA approval is still relatively rare. “This is a huge landscape change.”

Dr. Duff, who was actively involved in commercialization of transgenic mouse models before joining Columbia, credits the Ceracuity launch to a serendipitous introduction facilitated by Jeffrey Lieberman, MD, the Lawrence C. Kolb Professor and Chair of the Department of Psychiatry. A group of investors had decided to apply their business experience to end Alzheimer’s and approached Dr. Lieberman, who also directs the New York State Psychiatric Institute, for access to faculty whose research might be relevant. “There’s a lot of frustration that pharma isn’t moving fast enough,” says Dr. Duff, who attended the roundtable discussion Dr. Lieberman organized and presented an overview of her lab’s work. “There’s an opening and the need for the right drug, the right business model to get medicine in people’s hands more quickly.”



GORDANA VUNJAK-NOVAKOVIC

After the event, Dr. Duff replied promptly to an email from the investors, asking about her vision for Alzheimer’s therapeutics. “I was just looking for a donor,” she says of the resulting correspondence. “It became clear they wanted a company format.” Together, Dr. Duff and Dr. Yu decided to explore the prospect, with Columbia Technology Ventures staff facilitating negotiations with the investors. “We patented the small molecules, Ceracuity licensed them, and the partnership has gone on from there,” says Dr. Duff, whose bona fides now include the titles co-founder, scientific advisory board chair, and member of the board of directors for Ceracuity, which completed its second round of seed funding in June.

Applied Therapeutics Inc., which initiated its first phase 1 clinical trial in February 2018, is slightly farther along the commercialization track for a diabetes treatment based on research by a group led by Donald Landry, MD, PhD, the Samuel Bard Professor and Chair of the Department of Medicine. Also a founder and board member of Tonix Pharmaceuticals, Dr. Landry holds more than 34 patents on an array of small compounds and has a long-standing relationship with the CTV team. When biotech consultant Shoshana Shendelman, a Columbia PhD graduate, approached Columbia looking for licensing opportunities for her clients, the CTV team included Dr. Landry’s patent for a compound to block the aldose reductase enzyme, which has been implicated in a laundry list of disease processes, including diabetic retinopathy and cardiomyopathy.

“I found the technology to be a really compelling opportunity for a biotech,” says Dr. Shendelman, who decided to license the technology herself and launched Applied Therapeutics Inc. to bring Dr. Landry’s work to the clinic.

Dr. Landry traces his induction into the world of commercialization to his work with catalytic antibodies when he developed the first artificial enzymes to degrade cocaine as a treatment for overdose and addiction. In his first 10 years at VP&S, Dr. Landry



hired chemists to produce small molecules necessary for the cocaine research and other projects and then had to retrain those individuals to handle more biological applications in order to keep them on his lab staff. To maintain chemists as chemists, Dr. Landry approached Merck, offering the company first option for licensing small molecules developed by his group in exchange for \$1 million, and with this deal the Organic Chemistry Collaborative Center (OCCC) was founded. The center spurred a substantial increase in small molecule development for investigators across the university, as CTV presented each new protein or pathway discovered by Columbia investigators to OCCC to assess its potential for drug development.

This innovative program led to the intellectual property at the heart of Applied Therapeutics, a triumph for the lead chemist on the project, Andrew Wasmuth, and Dr. Landry's other colleagues at the OCCC. "Currently there is no cure for diabetes, and patients suffering from the complications of diabetes normally have a much lower quality of life," says Dr. Landry. "Developing any treatment that can interrupt the pathophysiology of complications like diabetic cardiomyopathy and retinopathy would drastically change the natural history of the illness both in terms of survival and quality of life."

To make sure all Columbia faculty and students have the tools they need to transform their discoveries into real-world products, CTV runs or helps to run a network of five lab-to-market accelerators, each tailored to a particular industry. Three are dedicated to biomedical innovation, including the Translational Therapeutics Resource (TRx). A collaboration among the Irving Institute for Clinical and

“The environment at Columbia is special because the deep level of expertise and leadership in so many different areas enables the University to attract the best partners who work with investigators to transform ideas into treatments.”

Translational Research, Columbia Technology Ventures, the medical center's Clinical Trials Office, and, most recently, the Herbert Irving Comprehensive Cancer Center, TRx was established by the Irving Institute's director, Muredach Reilly, MBBCh, to leverage Columbia's proficiency in target discovery and advance novel therapeutics from the lab along the path of commercialization.

Dr. Reilly began envisioning TRx even before he was recruited to Columbia in 2016. "There's incredible basic science and clinical expertise and discovery at Columbia and many individual examples of faculty in basic and clinical research moving toward commercialization, licensing, and therapeutic programs," he says, "but there was no systematic program for bringing together all of the services and activities to guide investigators from discovery of a protein, gene, or target to commercialization."

Often referred to as the "valley of death," the period that stretches from discovery to commercialization can be especially daunting in the case of drug development, spanning several years and often at great cost. "We were really focused on putting together an integrated program that would help investigators move successfully through that

process," says Dr. Reilly. "We coalesced a set of core labs for screening, organic chemistry, small molecule development, experimental validation in animal laboratories—everything an investigator needs to go from the more scientific realm to the science of commercialization."

The VP&S commitment to supporting and facilitating commercialization was central to his own enthusiasm about joining the faculty in July 2017, says TRx co-director Akiva Mintz, MD, PhD, professor of radiology and radiology's vice chair for translational imaging, who came to Columbia with multiple patents and experience in early-stage drug development. "One of the challenges I faced at prior institutions and companies was between the exciting discovery and translation into clinic in the valley of death," he says. "You can have a very good idea and it goes nowhere, because people with expertise in discovery aren't necessarily the ones with knowledge in the procedural steps required by the FDA. The environment at Columbia is special because the deep level of expertise and leadership in so many different areas enables the University to attract the best partners who work with investigators to transform ideas into treatments."

Investigators typically get their feet wet with the TRx boot camp, an eight-week series offered every winter with guest lectures covering such topics as identifying target customers, working with the FDA, and pitching prospective investors. Boot camp alumni are eligible to apply for TRx pilot awards, which combine a grant of up to \$75,000 with a tailored mentorship team whose participants are chosen for their experience in business, venture investment, the FDA application process, or some other facet of commercialization. Winners in 2017 included teams developing compounds to suppress appetite, treat cancer, and halt the progression of a specific type of schizophrenia.

"It's not just, 'Here's a phone number,'" says Dr. Mintz, "but being with them on the journey, making sure things get done and they have the right partners."

Gordana Vunjak-Novakovic, PhD, University Professor, the Mikati Foundation Professor of Biomedical Engineering, and director of the Laboratory for Stem Cells and Tissue Engineering, has launched four companies in the past five years, all based on research discoveries in her lab, which is located on the CUIMC campus. "There's super-qualified help from CTV," she says. "They support the filing and protecting of intellectual property and they helped on multiple occasions to get free advice from people who are skilled at filing FDA applications." For scientific investigators, she says, the world of patent applications might as well be conducted in a foreign language, making the CTV legal team a particularly valuable resource. "You know what your innovation is, but what comes back from the lawyers is this completely incomprehensible document," says Dr. Vunjak-Novakovic. "I'm absolutely sure that working in isolation we would never have these successes."

To cultivate awareness of the commercialization process, Dr. Vunjak-Novakovic invites postdoctoral fellows, graduate students, and her research associates to participate in the TRx boot camps and the Columbia Biomedical Accelerator. In 2017, she and Lynne Johnson, MD, professor of medicine, received a TRx pilot award for an impregnated bandage to promote healing of bedsores and diabetic ulcers. "The TRx grant is funding critical experiments that prove the technology was viable," she says.



UNDER DEVELOPMENT:

Physicians, Scientists as Inventors

For professionals in academic medicine, the work all boils down to helping more people achieve greater well-being. This year, VP&S faculty and students pursued several tools in pursuit of that goal.

ROLLING WITH IT

For the 50,000 people in the United States who are diagnosed with Parkinson's disease each year, falls and fall-related injuries are a major issue. Sunil Agrawal, PhD, professor of mechanical engineering and of rehabilitation & regenerative medicine, and his research team designed a lightweight, wearable robotic device—the Active-Tethered Pelvic Assist Device (A-TPAD)—to investigate how Parkinson's affects a person's ability to recover their balance after a perturbation. The device can be programmed to push or pull the pelvis in a desired direction as a person walks on a treadmill. After just one training session with repeated waist pull perturbations, participants demonstrated improved unperturbed walking.

SWEET SUCCESS

Clinicians urge people with diabetes to make tactical meal choices to reduce blood sugar spikes, but results can vary. A team of Columbia data scientists has developed a personalized algorithm that predicts the effect of particular foods on an individual's blood sugar levels. Integrated into an app named Glucoracle, the algorithm uses personalized data collected during a “training” week to forecast a person's future glycemic responses. “While we know the general effect of different types of food on blood glucose, the detailed effects can vary widely from one person to another and for the same person over time,” says David Albers, PhD, assistant professor of biomedical informatics. “Even with expert guidance, it's difficult for people to understand the true impact of their dietary choices, particularly on a meal-to-meal basis. Our algorithm, integrated into an easy-to-use app, predicts the consequences of eating a specific meal before the food is eaten, allowing individuals to make better nutritional choices during mealtime.”

HEART HEALTHY

Although heart disease is the No. 1 killer of women in the United States, many women are underdiagnosed and unaware of their risk. Sonia Tolani, MD, and Natalie A. Bello, MD, assistant professors of medicine, developed the Love My Heart app to raise awareness among women. Using a series of 12 questions, the app determines a woman's personal risk of developing heart disease and offers a personalized heart plan with realistic goals to support healthy weight, healthy diet, exercise, and smoking cessation. Users select goals, such as skipping dessert or getting off the subway a few stops early, and receive prompts throughout the day to log their progress. “A large number of women—about 80 percent of us—have at least one risk factor for heart disease, but only 16 percent of us have had a discussion with our health care provider about those risks,” says Dr. Tolani. “We hope the app sparks new conversations among women and with their providers.”

CALIBRATING CHEMO

For many women with breast cancer, the first line of treatment is neoadjuvant therapy—several months of chemotherapy to kill active cancer cells, reduce tumor size, and possibly even eliminate the need for surgery. A new optical imaging system developed in the laboratory of Andreas Hielscher, PhD, a professor in the engineering school who has a joint appointment in radiology, uses near-infrared light to assess blood flow in the breasts so clinicians can see how a patient's vasculature changes and how the blood interacts with the tumor. “Patients who respond to neoadjuvant chemotherapy have better outcomes than those who do not, so determining early in treatment who is going to be more likely to have a complete response is important,” says Dawn Hershman, MD, professor of medicine and leader of the breast cancer program at the Herbert Irving Comprehensive Cancer Center. “If we know early that a patient is not going to respond to the treatment she is getting, it may be possible to change treatment and avoid side effects.”

LOOKING GOOD

Gabrielle Loeb, a 2018 graduate, and a medical student, Shirin Sadri, envision a role for augmented reality to boost the efficacy of surgeons performing minimally invasive endovascular procedures, including cerebral angiography. Working with a team under the mentorship of Steven K. Feiner, PhD, director of Columbia Engineering's Computer Graphics and User Interfaces Lab, Dr. Loeb and Ms. Sadri led the development of a hands-free interface to allow surgeons to view and interact with patient-specific anatomical models on a head-worn display, while making both hands available intraoperatively. The project was awarded first prize in the research category at this year's student research day, where Ms. Sadri invited judges to try out the wearable augmented reality device tested in the team's research. Dr. Loeb presented the work at the annual meeting of the Society of Interventional Radiology, and the work also was presented in Germany at the Institute of Electrical and Electronics Engineers conference on virtual reality.

MICRO RECORDER

Through a few clever molecular hacks, a team led by Harris Wang, PhD, assistant professor of pathology & cell biology and of systems biology, has converted a natural bacterial immune system into a microscopic data recorder, laying the groundwork for a new class of technologies that use bacterial cells for everything from disease diagnosis to environmental monitoring. Using the CRISPR-Cas system, the researchers modified an ordinary laboratory strain of the ubiquitous human gut microbe *Escherichia coli*, enabling the bacteria to not only record their interactions with the environment but also time-stamp the events. “Such bacteria, swallowed by a patient, might be able to record the changes they experience through the whole digestive tract, yielding an unprecedented view of previously inaccessible phenomena,” says Dr. Wang. Other applications could include environmental sensing and basic studies in ecology and microbiology, where bacteria could monitor otherwise invisible changes without disrupting their surroundings.



Dr. Vunjak-Novakovic sees her team's myriad patents and commercial ventures as an extension of a culture of innovation and problem solving within the VP&S community, as well as her own open-door policy welcoming clinicians on a quest for solutions. One of the largest projects underway in her lab aims to bioengineer functional lungs to make up for the shortage of organs available for transplant. "That started with a visit from a cardiothoracic surgeon who brought us a problem he was struggling with six years ago," she says, "and now we're en route to clinical trials." On other occasions, a collegial clinician has spared the team from wasting time on a misguided approach. "You need the end user of your prospective technology to prevent you from doing something that is irrelevant," says Dr. Vunjak-Novakovic. "They also help direct our research in a way that is most applicable, allowing a seamless application in the clinic."

Biophysicist David Brenner, PhD, director of Columbia's Center for Radiological Research, embarked on his research to find a better way to kill drug-resistant bacteria after a friend in his hometown of Liverpool, England, died from a surgical site infection after a routine hip replacement in 2012. Such deaths have been on the rise since the introduction of antibiotics in the 1940s, as the emergence of drug-resistant bacteria outpaces new antibiotic development. Deaths related to drug-resistant bacteria are even threatening to outpace deaths from cancer over the next few decades. Dr. Brenner said: "I got to thinking, 'The drugs-based strategy isn't working. My own expertise is in physics. So I wondered whether we could take a different approach, a physics-based approach.'"

Scientists have long known that ultraviolet (UV) light—which spans 200 to 400 nanometer wavelengths—efficiently kills all bacteria, drug-resistant and drug-sensitive. That's why hospitals use ultraviolet lamps to sterilize operating theaters. But because UV light also damages human cells—causing skin cancer and cataracts—these UV lights can only be used to sterilize inanimate objects when no people are present. "Even if you clean the room completely," says Dr. Brenner, "as soon as people come in they bring the bugs in with them, no matter how much they scrub."

Using basic physics ideas and generously supported by a startup gift from Lynn Shostack, a member of the CUIMC Board of Advisors, Dr. Brenner and his colleagues started testing whether a type of ultraviolet light known as far-UVC—with wavelengths in the 200-220 nanometer range—might safely kill bacteria and viruses. They picked these wavelengths because they are absorbed very quickly by any biological material, so they can't penetrate even the dead cell layer of the skin and can't reach or damage the key cells in the skin or the eye. But bacteria and viruses in the air are far smaller, so far-UVC light can penetrate and kill these microbes. "The two big advantages of far-UVC light are that it doesn't harm people and it doesn't care about drug resistance, because it kills bacteria and viruses in a different way from drugs," says Dr. Brenner.

Knowing that any resulting device would require FDA approval, Dr. Brenner checked in with the Columbia Technology Ventures team early on and received funding from a private foundation and through the Columbia-Coulter Translational Research Partnership, where would-be entrepreneurs pitch their ideas for development



capital. "In principle far-UVC light is both effective and safe," says Dr. Brenner, "but we needed to demonstrate this in as many ways as we could." In a series of papers in the journals PLOS One and Radiation Research, he and his colleagues detailed their findings suggesting that far-UVC light effectively kills drug-resistant bacteria during surgical procedures without harming the patient.

More recently, in a paper published in the journal Scientific Reports, the team expanded its vision, showing that far-UVC lamps efficiently kill airborne microbes, such as influenza. That may make it possible for public spaces—airports, airplanes, medical offices, schools, even food prep facilities—to be equipped with overhead far-UVC lamps. "We want to safely kill airborne microbes like influenza, TB, and measles, whilst of course not harming the good bacteria that make up the human microbiome," says Dr. Brenner.

While all faculty receive a percentage of licensing fees generated by their intellectual property and many serve on the scientific advisory boards of their respective startups, Columbia has strict policies in place to prevent conflicts of interest that might arise for faculty researchers, including a prohibition on executive posts in startups for faculty. Dr. Brenner focuses on the far-UVC science and technology development and is happy to put the entrepreneurial side of the story in the hands of the Columbia Technology Ventures team; through the team's efforts, Dr. Brenner and colleagues were awarded their first U.S. patent for the technology.

From her perspective, Dr. Vunjak-Novakovic says policies that preserve a chasm between scientific innovators and entrepreneurial development promote both job creation and the long-term success of the resulting companies. Her former postdoctoral fellows Nina Tandon, PhD, and Sarindr Bhumiritana, PhD, now serve as chief executive officer and chief scientific officer, respectively, of Brooklyn-based Epibone, which the trio co-founded with Sidney Eisig, DDS, the George Guttman Professor of Clinical Craniofacial Surgery and director of oral and maxillofacial surgery in the College of Dental Medicine. "The best way to ruin your company is to run it yourself," she says. "It's like not letting your child leave home. You have to find capable people to work there and let them do their jobs."

For scientists intent on making a difference in the lives of real people, says Dr. Vunjak-Novakovic, commercialization promises unparalleled opportunities. "The reason I went into biomedical engineering is to see what engineering can do for medicine," she says. "The end goal is to translate science from the laboratory into the clinic." ♦



Precision Medicine: Promise (Being) Fulfilled

Patients Benefit from Unique Diagnoses, New Treatments

Conner James Walker was 10 months old when he started having fevers. Over the next two months, the fevers were more frequent. When his mother, Denise, took him to the hospital for what she imagined must be dehydration due to the latest fever, doctors diagnosed the 1-year-old with cancer—acute myelogenous leukemia, or AML.

Conner went into remission after treatment for AML. But six months later, he was diagnosed with recurrent AML, which prompted a referral to Columbia for a bone marrow transplant. Conner underwent the standard tests that precede any transplant, but Denise and her husband, Chris, were invited to enroll Conner in Columbia's Precision in Pediatric Sequencing Initiative (PIPSeq), a program funded by the Sohn Foundation to offer genomic testing of all pediatric tumors within the tristate region.

PIPSeq was a game-changer for the Walker family. The sequencing of Conner's genome

revealed that—in addition to AML—he has a mutation in the RET gene, which predisposes carriers to medullary thyroid carcinoma, a stealthy malignancy that forms within the thyroid gland during middle age, remains asymptomatic until it has advanced, and is associated with a poorer prognosis than more common forms of thyroid cancer.

Because RET is a dominant mutation that can be genetically inherited from a single parent or spontaneously develop during development, Conner's pediatric oncologists at Columbia urged Mr. and Mrs. Walker to have the entire family tested. They learned that Conner's father and three of Conner's siblings have the RET mutation. Although none of the children had symptoms, Mr. Walker had a palpable nodule in his throat and underwent a biopsy, performed by Jennifer Kuo, MD, director of the thyroid biopsy program and the endocrine surgery research program.

By Sharon Tregaskis

When Conner Walker was referred to Columbia for a bone marrow transplant, his family was invited to enroll him in the Precision in Pediatric Sequencing Initiative, which combines insights from a panel of tests to sequence the DNA associated with a child's tumor and the rest of the patient's genome. The sequencing revealed a mutation that prompted testing of his entire family, ultimately providing family members with important information about their future health. Precision medicine has the potential to help many others by uncovering genomic and other biological insights to inform their health care decisions. Photo courtesy of the Walker Family.



Jennifer Kuo

to rich troves of data that reveal both genetic quirks we inherit from our parents and genetic mutations that emerge sporadically in response to environmental factors or a failure in the quality control process of DNA replication and translation. Any given mutation could mean nothing, something, or—as in the case of the Walker children—something in the future. “If you look for that many mutations, you’re going to find something,” says Dr. Kuo. “What that something means, we don’t necessarily know at this time.”

For clinicians, then, the trick is figuring out how to make the most of such data. “In the case of the Walker family, genetic testing revealed a mutation for which the clinical significance is known. It is tied to a specific disease and there is a treatment plan,” says Dr. Kuo. “But we could have easily found a mutation of which the clinical significance is not known.”

The list of such mutations is getting shorter all the time. “Major advances are being made in the development of tools that make it possible to connect differences in a single individual’s DNA sequence with the diagnosis and treatment of specific diseases,” says Dr. Maniatis, whose own research delves into the molecular mechanisms of amyotrophic lateral sclerosis (ALS, or Lou Gehrig’s disease). “Genetic studies are having an enormous impact on our understanding of neurodegenerative diseases such as ALS and Alzheimer’s disease by identifying disease mechanisms, cellular pathways, and possible drug targets.”

Consider how Dr. Kuo’s own clinical practices have shifted in the past five years, as investigators mine the data that have accumulated due to a basic fact of aging: The older you get, the higher your chances of developing a thyroid nodule. In the vast majority of these cases, the growth is benign, but the standard of care is to rule out malignancy by taking a needle biopsy. Historically, pathologists examined cells extracted from the nodule under a microscope, reporting their findings in accordance with the Bethesda classification system, a standardized system of six categories with associated risks of malignancy. In response to cytology findings in the murky middle of the scale—neither emphatically benign nor obviously malignant—patients and physicians alike have tended to opt for surgery. “Although thyroid surgery is a low-risk procedure,” says Dr. Kuo, “we were subjecting a lot of patients to unnecessary surgery for benign nodules.”

The silver lining of all those surgeries was a wealth of data—including the actual patient outcomes and complete pathological workups of the nodules. By analyzing DNA and RNA sequences from malignant nodules, as well as those that were benign, scientists developed molecular profiling tests to narrow the field of uncertainty and focus on the 5 percent of nodules that pose a danger. At Columbia, says Dr. Kuo, the new profiling tests have led to a dramatic reduction in the number of patients who choose surgery merely out of an abundance of caution, giving them greater confidence in the watchful waiting approach. “The ultimate goal of all of this is to gain a better understanding of the diseases that afflict our patients,” she says. “That allows us to offer patients more options in the care that they receive, which ultimately allows them to choose the path that is best suited for them.”

A week later, Dr. Kuo removed Mr. Walker’s thyroid gland and lymph nodes involved in the disease. “With our early intervention,” she says, “there is a very good chance that he has been completely cured and will remain cancer-free.” Using algorithms developed to predict the trajectory of the particular RET variant manifested by the Walker family, doctors will monitor Conner and his affected siblings, by monitoring their hormone blood levels over the coming decades for signs that a tumor is forming before it turns into cancer so that their thyroid glands can be removed prophylactically before the tumor poses a risk.

Such is the promise of precision medicine—plumb terabytes of data on hundreds of thousands of patients and their families to integrate insights from electronic health records with genomic and other biological data, plus behavioral and environmental parameters, to optimize the health and treatment protocols for individual patients. “Recent studies of large patient cohorts have revealed the incredible potential of combining genetic data and electronic clinical records,” says Tom Maniatis, PhD, director of Columbia’s Precision Medicine Initiative, a collaboration of all of Columbia University and New York-Presbyterian Hospital. “These data not only identify potential causes of disease, they reveal targets for drug development and treatment.”

Meanwhile, the cost of genomic sequencing has fallen dramatically, giving patients and their doctors increasingly affordable access

To hasten the kinds of insights that PIPSeq conferred on the Walker family—and that genetic profiling of biopsy materials offers—the National Institutes of Health has launched All of Us, a historic campaign to collect data from 1 million or more people living in the United States. Columbia heads the All of Us New York City consortium, one of several regional networks through which participants can enroll. “The billions of data points from All of Us will add up to one of the most powerful health research resources that we’ve ever had,” said NIH Director Francis Collins at the May 6 launch of the All of Us Research Program at Harlem’s Abyssinian Baptist Church.

The ambition of the effort vastly exceeds that of the ongoing Framingham Heart Study, named for the town in which 5,209 residents were recruited in 1948 and whose health and lifestyle—as well as those of their partners, children, and grandchildren—have yielded thousands of papers on an array of factors in human health and disease, including vital insights into cardiovascular disease. “From that study, [researchers] discovered that smoking, high cholesterol, and high blood pressure are major risk factors for heart attack and stroke,” says Dr. Collins. “Believe it or not, before this, we didn’t know those things, and many people thought that heart disease was just an inevitable part of aging.”

Perhaps even more important than the scope of All of Us is its emphasis on recruiting a nationally representative sample of par-

ticipants. “This program marks an amazing opportunity to bring together the communities we serve and our research community to advance health,” says David Goldstein, PhD, the John E. Borne Professor of Medical and Surgical Research in Genetics & Development, director of the Institute for Genomic Medicine at VP&S, and principal investigator of the NYC All of Us consortium. “This bold program will work with our communities to make sure not only that the promise of precision medicine is realized but that it is done so in partnership with the community.”

In the New York City area, more than 4,000 people have already enrolled; 81 percent are from communities typically underrepresented in medical research because of race, ethnicity, sex, or gender.

“Mining data from a more diverse population will provide vital insights. Doctors will have a better idea of what variations mean and how they may influence disease occurrence and response to therapy.”

“As recently as 2016, more than 80 percent of studies based on genomic profiling were on people of European descent,” says Kevin Gardner, MD, PhD, professor and senior vice chair of pathology & cell biology, who is helping to lead the Department of Pathology & Cell Biology’s precision medicine initiatives, particularly in underrepresented minority communities. “Getting sequences from European populations doesn’t account for the diversity we would see in African patients.”

Researchers do not want the genomic revolution to exacerbate disparities in access to evidence-based treatment, says Dr. Gardner, who spent nearly three decades at the NIH, most recently as acting scientific director for the National Institute on Minority Health and Health Disparities. With the right approach, he says, precision medicine has the potential to combat disparities in disease outcomes and treatments. “The goal of All of Us is to catch up, to increase diversity and participation in clinical trials.”

The effort promises profound gains for people who have historically been underserved, says Dr. Gardner, whose own research delves into disparities in breast cancer prognoses among ethnic groups. “In profiling genomics of patients, we see differences, variations,” he says. When such variations occur infrequently, or only in select subpopulations, scientists often lack the data and clinical information to understand their implications, dismissing them as “variants of unknown significance.”

“We want to minimize these variants of unknown significance. Mining data from a more diverse population will provide vital insights. Doctors will have a better idea of what these variations mean and how they may influence disease occurrence and response to therapy.”

For people coming to terms with a sarcoma diagnosis, such treatment insights are critical, says orthopedic oncologist Wakenda Tyler, MD, associate professor of orthopedic surgery at



VP&S and chief of musculoskeletal oncology at NYP. “Every patient who walks in with a sarcoma has a unique disease,” says Dr. Tyler. “Their sarcoma will not genetically be the same as any other sarcoma we see that year.”

Nationwide, sarcoma survival rates five years after diagnosis hover at just 50 percent. Through a project spearheaded by Gary Schwartz, MD, chief of hematology/oncology and associate director of the Herbert Irving Comprehensive Cancer Center, every sarcoma biopsy is genetically sequenced, a service not yet available in most hospitals. The results inform the personalized treatment protocol Dr. Tyler recommends. “A patient may still need surgery and radiation,” she says, “but we can also offer targeted therapies to home in on particular

genetic features of the tumor.” Already, she says, survival rates are inching upward. “Half of the patients who walk through the average oncologist’s office aren’t going to be alive in 10 years. The targeted therapies aim to increase that number to 60 or 70 percent.”

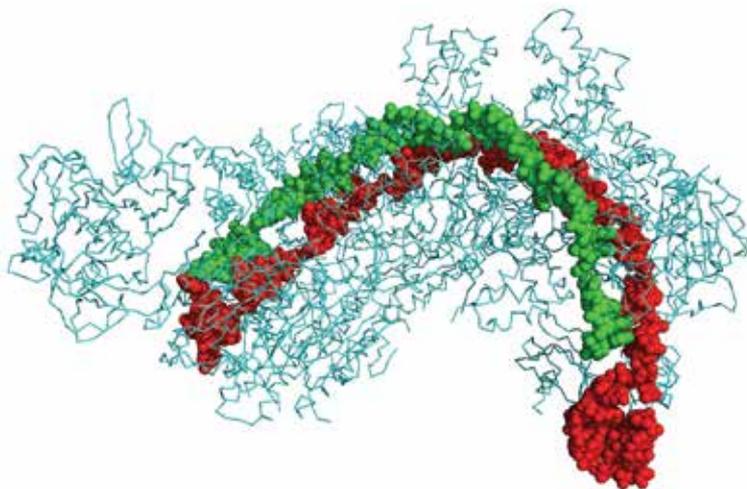
Meanwhile, because nearly every sarcoma patient undergoes surgery—which can radically alter mobility and function—Dr. Tyler has embarked on a project to connect high-risk patients with rehabilitation medicine even before their operations. For many people, the pain and impeded movement caused by a tumor forces them to compensate—favoring one leg over the other, for example. As a result, many have functional deficits or mobility impairments even before the tumor is removed, making physical and occupa-

CRISPR: Accelerating Development of Mouse Models of Human Genetic Diseases

Scientists have been tinkering in the mouse genome for more than a century, starting with conventional breeding to amplify and isolate naturally occurring variations within captive populations of house mice. As scientific understanding of DNA and its role in genetic inheritance accumulated, scientists began directly manipulating DNA itself, scrambling the order of nucleotides to discover how genotype informs phenotype.

Early methods were pure happenstance. Using X-rays or chemicals known to derange DNA replication, researchers were able to induce genetic mutations and study the resulting physiology. Technological innovations in recent decades have given scientists ever greater control of their tinkering, allowing them to turn on or off target genes to create “knockin” or “knockout” animals.

In June, the Columbia Precision Medicine Initiative announced the launch of five projects funded by a gift from Roy and Diana Vagelos to accelerate the development of mouse models of human genetic diseases. The new projects make use of CRISPR, a gene editing technique that allows scientists to precisely target snippets of DNA, swapping in and out nucleotides within a living cell to model the exact mutations found in patients.



Recipients of funding:

Lorraine N. Clark, PhD, associate professor and assistant medical director of pathology & cell biology, will use mouse models to determine the disease mechanism underlying the Gaucher disease gene, glucocerebrosidase (*GBA*) p.E326K variant. Among the *GBA* variants associated with Parkinson’s disease, p.E326K is one of the most prevalent and may represent a novel therapeutic target.

Simone Sanna-Cherchi, MD, the Florence Irving Assistant Professor of Medicine, will investigate the mechanisms by which mutations in *TRIM8* define a novel syndrome characterized by childhood epilepsy, focal segmental glomerulosclerosis (FSGS), and vesicoureteral reflux. The work may illuminate the pathogenesis of FSGS, one of the most common causes of kidney failure, in which progressive scarring of the glomeruli leads to permanent kidney damage.

Steven Siegelbaum, PhD, the Gerald D. Fischbach, MD, Professor and Chair of Neuroscience and a professor of pharmacology, will investigate the role of *HCN1* gene variants associated with human early infantile epileptic encephalopathy, a severe and often intractable seizure disorder that contributes to a progressive disruption of brain function, often accompanied by developmental delay and various neurological and non-neurological comorbidities.

Carol M. Troy, MD, PhD, professor of pathology & cell biology and of neurology, will investigate how *CRADD* mutations associated with developmental impairments among isolated Mennonite populations reveal new insights into the role of a metabolic pathway also implicated in Alzheimer’s pathology.

Ai Yamamoto, PhD, associate professor of neurology and of pathology & cell biology, will explore the role of *Wdfy3* in autophagy and the resulting processes of development and degeneration of the central nervous system.



Wakenda Tyler



Sander Markx

tional therapy vital contributions to ongoing quality of life. “We get so obsessed with shrinking the tumor, the radiation, the surgery, we forget about functionality,” she says. “This way, when patients are at their weakest point, postoperatively, they’ll already have a network of physicians and staff who are aware of the functional issues and ready to support them.”

In the world of psychiatry, where diagnoses typically result from a patient’s observable behaviors, precision medicine promises similarly profound shifts in clinical care. In an effort to more fully characterize

“In psychiatry you hope to control symptoms, but you don’t strive for a cure. It’s incredibly humbling to be providing precision medicine for the people who have the least resources.”

the forms of schizophrenia most resistant to treatment, Sander Markx, MD, director of the Department of Psychiatry’s Center for Precision Neuropsychiatry, and postdoc research fellow Anthony Zoghbi, MD, have embarked on a project to provide whole genome sequencing and assessment for neuronal autoimmunity for up to 3,000 patients in New York state’s psychiatric facilities. “Folks in inpatient facilities are the sickest of the sickest,” says Dr. Markx. “They’re so much sicker and so impaired cognitively that they usually can’t take care of themselves and they live their entire lives in state facilities.”

In addition to gaining clarity about the genomic corollaries to schizophrenia, Dr. Markx hopes to identify biomarkers that sug-

gest a diagnosis of neuronal autoimmunity, in which a tumor or virus triggers an immune reaction to proteins within the brain that are typically protected by the blood-brain barrier. “The literature is overflowing with people who have a virus, followed by schizophrenia-like presentation,” he says. “They’re very sick, with seizures and autonomic instability, blood pressure and heart rate fluctuation.” Due to the atypical and severe symptoms these patients exhibit, their doctors frequently conduct a comprehensive physiological assessment in addition to psychiatric screening. When cerebrospinal fluid analyses reveal the antibodies behind their symptoms—and sometimes even an undiagnosed cancer—treatment with immune-suppressants interrupts the autoimmune attack, reversing both the neurological and psychiatric symptoms.

Dr. Markx hypothesizes that the population of such patients may be far larger than previously recognized, because only a subset of people with neuronal autoimmunity exhibits severe autonomic and neurological instability at the onset of the condition, making their initial presentation difficult for clinicians to distinguish from schizophrenia. Already, the team has transferred one patient to Columbia for treatment; after 20 years of severe and refractory psychosis, she has begun showing early signs of recovery in response to intensive treatment with high-dose intravenous steroids. “If we can refine her treatment,” says Dr. Markx, “we might be able to get her back to a normal life.” Three other patients who have similar biomarkers also are scheduled for transfer and comprehensive treatment at Columbia. “Typically in psychiatry you hope to control symptoms, but you don’t strive for a cure,” says Dr. Markx. “It’s incredibly humbling to be providing precision medicine in this way, for the people who have the least resources.” ❖



Mary Killackey finished medical school at Columbia in 1998 with \$80,000 in student loan debt. That might sound like a lot, but she considered herself lucky to get out with a relatively small amount of debt.

Now chair of surgery at Tulane University in New Orleans, Dr. Killackey grew up in Philadelphia, the fifth in a tight-knit family of six children. She credits her parents for encouraging her and her siblings to pursue their dreams, no matter the upfront cost. Deciding between two strong choices for medical school—Columbia, where tuition ran about \$45,000 a year, and Temple University in Philadelphia, which was about one-third the cost because she was eligible for in-state tuition—Dr. Killackey didn't hesitate. "People say, 'Go to a state school; it's cheaper,'" she says. "But I cannot tell you how many doors have been opened for me because of the schools I went to, ultimately landing at Columbia for medical school. The truth is, schools like Columbia have funding to allow students with financial need to attend."

What Financial Freedom Means to Tomorrow's Doctors

By Alla Katsnelson

Illustrations by Daria Kirpach

Because of her family's modest income, about half of her medical school tuition was covered through grants. Even so, her debt weighed on her as she mapped out her career path. Although she was always drawn to the procedural nature of surgery, she also considered internal medicine. Transplant surgery, she says, turned out to be the ideal combination of both. "But at the time, I thought about it," she says. "I thought, 'If I go to primary care, if I go into family medicine, I'm going to be saddled with this debt forever.'"

Mary Fairbanks'87 graduated more than a decade before Dr. Killackey and did go into family medicine. "Honestly, in 1987, the kind of indebtedness we were getting into was nothing like what students take on today," she says. She received grants from several sources but still had to borrow about \$30,000 to finance her medical degree. With the help of a grant she received after graduation and the support of her family, she was able to pay off her loans within six years. That meant that when a friend suggested opening a

practice together, she could jump at the opportunity. "We had no money to start with," she says. "If I had been burdened by a big monthly loan payment, there's no way I could have done that."

"Debt makes an incredible difference," agrees Elvis Camacho'17. "It definitely influences you when you're applying for different specialties."

This is exactly the kind of burden that Roy Vagelos'54 and his wife, Diana, intend to vanquish with their historic \$250 million gift to the medical school, which was renamed in their honor in December 2017. Some \$150 million of the donation announced in December will fund an endowment that will replace loans with scholarship support for medical students who qualify for financial aid.

Starting with the 2018-19 academic year, VP&CS will eliminate need-based loans from the financial

Vagelos Gift
Takes Debt Off
the Table for
Most Students

aid packages that students receive. That means that all students eligible for financial aid, which includes more than half the student body, will receive some assistance, and about 20 percent of students—those with the most need—will receive scholarships covering their full tuition. And although the school cannot award scholarships retroactively to replace loans made in previous years, it did manage to help students who graduated in May 2018 by replacing a portion of their need-based loans with scholarships of \$5,000 each.

The Tradition of Debt

Hefty debt is perhaps as much a staple of medical school as is dissecting a cadaver. Indeed, almost 75 percent of all medical students in the United States graduate with debt; in 2016, the median amount of debt nationally was \$190,000, including undergraduate debt. VP&S has long tried to meet its students' needs by limiting loans for students with limited financial means to less than

“I had students call me after they received their financial package, just crying. It’s a dream come true. They’re going to be able to graduate from Columbia with no debt.”

\$30,000 each year and providing the rest as need-based scholarships. The school also has a strong commitment to educating students about managing the debt they take on. “The financial aid office was incredibly user friendly and really on the students’ side,” says Dr. Killackey. “They really took care of me.”

“For students who come from lower-income families, \$100,000 in debt may appear to be as much as a million,” says Hilda Hutcherson, MD, senior associate dean of the Office of Diversity and Multicultural Affairs. “The thought of taking on six-figure loans was always a shock. It used to cause a lot of angst and anxiety and worry about how they were ever going to be able to pay that amount of money back.”

For the Vagelos family, the generous gift is also a fitting one: When Dr. Vagelos was in medical school in the 1950s, he was a scholarship student, as was his wife in her time at Barnard College. Neither Roy nor Diana had accumulated any student debt by the time they graduated, allowing them to pursue their dreams. Dr. Vagelos has said that the aim is to give students the opportunity to follow their true calling in medicine and to provide the opportunity for more students to forge paths in fields such as family medicine, pediatrics, and geriatrics, specialties that often provide salaries far lower than those earned in most lucrative specialties. The scholarship program also will allow more medical students to enter careers in biomedical research that pay less but are vital to the future of medicine. The scholarship program is a first among mainstream U.S. medical schools.

After the Vagelos gift was announced, Dr. Hutcherson says, “I had students call me after they received their financial package,

just crying. It’s a dream come true. They’re going to be able to graduate from Columbia with no debt.”

Not only will the new funds help aspiring doctors focus on being successful medical students, she predicts it also will help change the demographics of incoming students. Just look at what happened when Ivy League colleges started replacing loans with scholarships in financial aid packages for prospective undergraduates from low-income families, she says. “Students who before would have found it difficult to attend an Ivy League school now saw it as a possibility.

“Columbia is a special place. The education that students have access to is unparalleled,” she says. “So it’s nice that we can now offer this education to more students from needy families.”

Dr. Camacho, who plans to go into academic medicine, wholeheartedly agrees. Even college was not on the radar when he was a child growing up in Miami, having moved there from Puerto Rico with his family. Medical school was even less a possibility. At age 17, he joined the Marines, where combat and time as a volunteer in hospitals made him realize that his passion lay in medicine. By the time he was in college and medical school, Dr. Camacho says, Columbia showed strong support for a diverse student body. “But to open up opportunities for people who come from very impoverished backgrounds, regardless of their color, will make an even richer environment for everybody.”

Despite the great need for doctors in the United States, the barriers to becoming one are growing. “The reality right now is we have an aging population, we have fewer doctors, and costs are very high for becoming a health care practitioner,” says Alex Porter’93. Dr. Porter is chief medical officer for Sui Generis Health, a medical products and policy company based in Atlanta. Because paying for



Rosa M. Mendoza de Perez’14, currently a postdoctoral clinical fellow in the Center for Family and Community Medicine and an assistant attending in clinical medicine, posed with her husband, Diego Perez Escobar, and with Dr. and Mrs. Vagelos at the 2017 Crown Awards. Dr. Mendoza has credited scholarships from Dr. and Mrs. Vagelos and others with supporting her through Princeton and VP&S.



health care is in flux, the financial costs of medical education add a level of uncertainty to pursuing a career in medicine. “The large cost of medical school is a deterrent, especially for people who want to go into general practice or work in underserved areas or conduct research. That’s not conducive toward us getting completely caring and motivated people who dream of caring for patients.”

Also, he adds, the steep increase in the cost of college over the past two decades means that most students are already carrying significant debt by the time they apply to medical school.

Cristina Carpio’09 notes that medical school debt is especially long-lasting. The daughter of Ecuadorian immigrants who came to the United States so she and her siblings could have more opportunities, Dr. Carpio is now a trauma surgeon and critical care doctor at South Shore Hospital, part of the Brigham and Women’s network in the Boston area. She feels fortunate to have received grants from Columbia to cover half of her tuition. Yet almost a decade after graduating she expects to be paying loans for another 10 years; many classmates are looking at 20 or 30 years, and she knows of two people from her medical school class who still owe more than \$250,000. “That debt is the longest-term relationship you’ll ever have. It could be longer than a marriage.”

Dr. Carpio, who grew up in Queens, knew she wanted to be a doctor at around age 10, when she began accompanying her diabetic grandmother to a Spanish-speaking doctor in Manhattan so her grandmother could communicate in her own language. After college, Dr. Carpio made a beeline for her goal, heading straight to medical school. At such a young age, though, it’s hard to appreciate how much long-term planning that medical school debt demands, she says, including the role it plays in planning milestones such as starting a family, buying a home, or saving for the future. Her relatively small debt has been helpful for her family, since she can see

a future without debt in a short time. “It will have a generational impact because I’m able to save to help my daughters go to college.”

For Dr. Killackey, a tremendous stroke of fortune a few years into her career showed her just how constraining medical school debt could be. After a general surgery residency at the University of Rochester, then a fellowship in transplant surgery at Mount Sinai, she was recruited to the transplant program at Tulane in the aftermath of Hurricane Katrina. She had a gut feeling, she recalls now, that she could really have an impact there.

She benefited from a federal program designed to retain doctors in New Orleans in the aftermath of the hurricane. The government program paid off her higher education debt. Overnight, her debt was gone. “The weight that lifts off of you—it’s indescribable,” Dr. Killackey says.

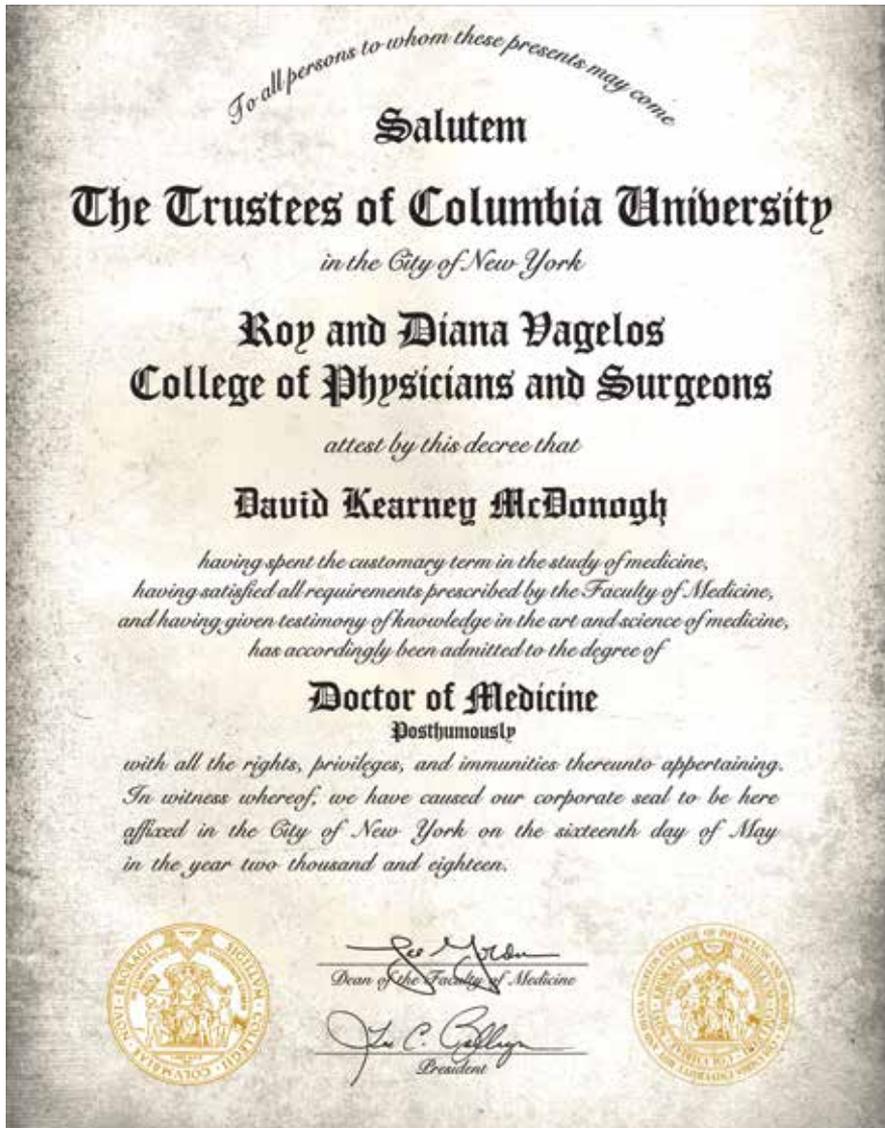
With that financial freedom, the prospect of staying in academic medicine—where salaries are significantly lower—became more viable. Perhaps more importantly, she experienced a dramatic shift in her outlook. “Once that debt was gone,” she says, “I felt I could really be true to the profession.”

She involved herself in teaching and in the quality and regulatory issues that affect transplant medicine. “That allowed me to progress, to get visibility, and to learn leadership.” Two years ago, she became the first woman appointed chair of the Department of Surgery at Tulane, although she was more than a decade younger than most people are when they become chairs.

“It’s just incredible,” says Dr. Killackey, musing on the fact that the careers of all qualifying graduates of VP&S—and, perhaps, all graduates someday—will benefit from those scholarships. “It makes me really proud to be a Columbia graduate, and it certainly makes me want to give back and support this effort, because it meant so much to me.” ❖

RIGHTING A WRONG:

David McDonogh, Denied Degree in 1800s, Receives Posthumous MD



American society was different in 1767 when Columbia opened a medical school, and the school’s changes during the past 251 years reflect the evolution of American culture in ways large and small. “Taking stock of history inevitably forces us to re-examine the past in the context of our present-day values as well as the values of that moment in history,” said Lee Goldman, MD, dean, at this year’s graduation ceremony.

Taking stock in the context of graduation resulted in granting an MD 171 years after it was earned by David Kearney McDonogh. “This award was considered unthinkable in the mid-19th century when McDonogh was training to become a physician, but it fully reflects our values of today,” said Dr. Goldman. “When our current VP&S leadership learned of this past wrong, we were determined to correct it.”

Dr. McDonogh’s life began in New Orleans, where he was born an enslaved person in August 1821 on the plantation of John McDonogh, who had amassed a fortune as a merchant and plantation owner. According to Russell Irvine, a Georgia State University faculty member who researched black students who studied at Vagelos College of Physicians and Surgeons in the 1800s but were not given diplomas because of the color of their skin, John McDonogh was ambivalent about the “peculiar institution” of slavery. He was a supporter of the American Colonization Society (ACS), a society that opposed slavery but also opposed the right of those freed from enslavement to live as free Americans. The ACS, founded in 1817, was dedicated to the education of freed African-Americans so they could be deported to Liberia to “civilize” that colony.

Dean Lee Goldman with Patricia Worthy, who accepted the posthumous MD degree on behalf of her great-great-grandfather



The ACS found sympathizers at VP&S, where other students of African descent studied—under restrictive conditions—starting in the early 1830s.

Before David McDonogh found his way to VP&S, he studied at Lafayette College in Easton, Pa., where John McDonogh sent two of his most talented “enslaved persons.” Lafayette’s president was an ardent colonizationist. David McDonogh was expected to study to be a minister, but he asked John McDonogh for permission to add medicine to his missionary training. John McDonogh gave him permission to study with a physician and pharmacist in Easton.

David McDonogh was frustrated by the time he graduated from Lafayette in 1844, intent on continuing his quest to become a doctor. By then he was emancipated after

living in a free state, but he was told that no New York medical schools would admit him. Instead Dr. John Kearney Rodgers, a VP&S professor, secured admission for him to Columbia medical lectures. The medical school did not formally register David McDonogh in its medical school while he attended lectures or formally identify him as a graduate once he completed studies in 1847, but history strongly suggests that he was fully qualified to receive a medical diploma from Columbia.

He began a career as a doctor when Dr. Rodgers appointed him to a staff position at the New York Eye and Ear Infirmary, and he identified himself as a Columbia medical graduate throughout his career. He is widely considered to be the nation’s first African-American ophthalmologist. (When John Kearney Rodgers died in 1850, according to an American Academy of Ophthalmology article, Dr. McDonogh took Kearney as his middle name to honor his mentor.)

Even by the time Dr. McDonogh died in 1893, VP&S was still not accepting African-American students. That changed in 1904, when Travis J.A. Johnson matriculated and became the first recognized African-American graduate of VP&S in 1908. Today, more than 20 percent of VP&S medical students are underrepresented minorities, making the school one of the most diverse among the nation’s top medical schools.

Five years after Dr. McDonogh’s death, McDonough Memorial Hospital opened

in his honor on West 41st Street. (His tombstone spells his name McDonogh but the hospital name and other documents, including his will, suggest he may have changed the spelling of his name at some point.)

Dr. McDonogh had two children, but only one—a daughter—survived to adulthood. The only known descendant of Dr. McDonogh, his great-great-granddaughter, Patricia Worthy, accepted his posthumous MD degree at this year’s graduation ceremony.

“Dr. McDonogh earned—but never received—his medical degree from our school in the 1840s. But today, we are posthumously awarding David Kearney McDonogh the degree Doctor of Medicine,” Dr. Goldman said at graduation. In addressing Ms. Worthy, he added, “It’s a great honor to have you here, and on behalf of Columbia University, it’s a privilege for me to present you with Dr. McDonogh’s diploma.”

Much of the 250-year anniversary of VP&S in 2017 was spent envisioning the future, Dr. Goldman said, by celebrating the school’s remarkable past. “Many of the achievements of our faculty and graduates helped shape the way that medicine is practiced throughout the world. By granting the MD degree posthumously to Dr. McDonogh, we add another name to the list of Columbians who have contributed to the VP&S legacy.” ❖

David McDonogh Memorial Scholarship

VP&S has established a \$1 million scholarship in Dr. McDonogh’s name, funded by Diana and Roy Vagelos’54, whose initial gift launched the 250th Anniversary Scholarship Challenge.

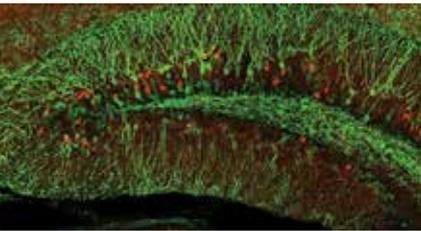
The McDonogh Scholarship will provide financial support to medical students who have overcome adversity or hardship in their pursuit of a medical education.

“We can think of no better way to honor Dr. McDonogh and his legacy,” said Lee Goldman, MD, in announcing the scholarship.

2018 Research Highlights

Memory Trace

It may be possible to access memories “lost” to Alzheimer’s disease—at least in a mouse model, reports a study in the journal *Hippocampus*. The researchers, led by Christine A.



Denny, PhD, assistant professor of clinical neurobiology (in psychiatry), taught healthy mice and those with Alzheimer’s to associate a lemon scent with a mild electric shock. A week later, the healthy mice remembered the scent and its consequences, but the Alzheimer’s mice did not. The researchers used laser light to stimulate the memory-storing neurons and access the “lost” memory. Says Dr. Denny: “This has exciting implications for those of us who research the brain.”

Drug Problem

A new model of Alzheimer’s disease may explain why clinical trials of potential Alzheimer’s drugs so often fail. Neurons are comprised of different compartments, and proteins continuously shuttle among them, says Scott Small, MD, the Boris and Rose Katz Professor of Neurology and director of the Alzheimer’s Disease Research Center in the Taub Institute at Columbia, in an article in *Trends in Neuroscience*. Traffic jams in and out of those neuronal compartments

lead to Alzheimer’s disease. Most drugs tested in clinical trials, however, are directed against amyloid that accumulates outside of neurons. Many such drugs will not relieve the traffic jams, Dr. Small says.

Sniff Test

An impaired sense of smell is an early sign of cognitive decline, preceding the clinical onset of Alzheimer’s disease. D.P. Devanand, MBBS, MD, professor of psychiatry, and colleagues have leveraged that effect to determine if patients with mild cognitive impairment (MCI) may respond to drugs called cholinesterase inhibitors, which are used to treat Alzheimer’s. In the study, published in the *Journal of Alzheimer’s Disease*, 37 participants with MCI underwent odor identification testing, then were treated with a cholinesterase inhibitor for 52 weeks. Those who had greater declines on the test saw greater cognitive improvement from the drug.

Dementia Drop

Dementia, including Alzheimer’s disease, is declining among northern Manhattan seniors, following national and global trends, according to a study in the *Journal of Alzheimer’s Disease*. The risk of dementia fell in all ethnic groups—by 48 percent in African-Americans, 40 percent in whites, and 36 percent in Hispanics. “Though we can’t know for certain, it’s possible that more timely diagnosis, the lifelong influence of better education, and aggressive treatment of vascular risk factors may be important reasons

for the decline in dementia rates,” says James Noble, MD, assistant professor of neurology, who co-led the work.

Aha!

A study led by Michael N. Shadlen, MD, PhD, professor of neuroscience, has identified the brain’s “aha!” moment—that flash in time when you suddenly become aware of information, such as knowing the answer to a difficult question. “Essentially, the act of becoming consciously aware of a decision conforms to the same process that the brain goes through to complete a decision, even a simple one—such as whether to turn left or right,” says Dr. Shadlen. While preliminary, the study, published in *Current Biology*, raises the possibility that the human brain’s most complex thought processes may soon be understood at a biological level.

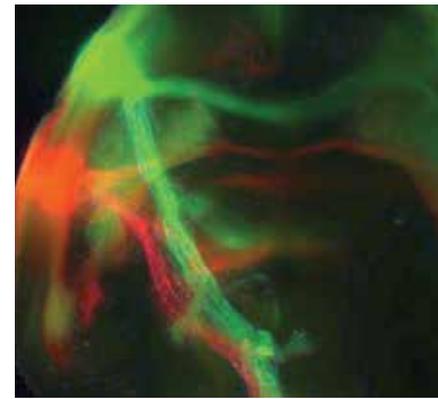
Bone Hormone

Age-related memory loss may be reversed by boosting blood levels of osteocalcin, a hormone produced by bone cells that also favors glucose homeostasis, male fertility, and adaptation to exercise, according to a study published in the *Journal of Experimental Medicine*. Gerard Karsenty, MD, PhD, the Paul A. Marks Professor and Chair of Genetics & Development, previously found that osteocalcin plays a role in memory and that its levels decline after early adulthood in humans. To determine whether memory loss could be reversed by restoring this hormone back to youthful levels,

he and his colleagues gave aged mice infusions of osteocalcin, which did improve their memory.

Taste Test

Molecules called semaphorins help connect taste receptor cells to the right neurons, according to a study led by Charles S. Zuker, PhD, professor of biochemistry & molecular biophysics and of neuroscience. The discovery, published in *Nature*,



provides new insights into how the tongue keeps its sense of taste organized despite the rapid turnover of the cells in its taste buds. In a second *Nature* paper, Dr. Zuker demonstrated that the brain’s underlying desire for sweet, and its distaste for bitter, can be erased by manipulating neurons in the amygdala.

GPS Scramble

Disruptions to the brain’s center for spatial navigation precipitate some of the severe memory deficits seen in schizophrenia, according to a study published in *Nature Neuroscience*. The researchers focused on a brain region called CA1, in the hippocampus, which plays a role in both naviga-

tion and in episodic memory, comparing CA1 activity in mice genetically modified to mimic schizophrenia to that in healthy mice. The schizophrenia-like mice had more trouble remembering familiar environments and adapting to changes in those environments, and their brain cells—tracked with two-photon microscopy—also lacked adaptability. Joseph A. Gogos, MD, PhD, professor of physiology & cellular biophysics and of neuroscience, co-lead the work with Attila Losonczy, MD, PhD, associate professor of neuroscience.

Mental Reversal

When observing a scene, the brain first processes details—spots, lines, and simple shapes—and uses them to build internal representations of more complex objects, such as cars and people. Researchers have long assumed that recalling a scene occurs in the same order as detecting it, but the brain actually reverses the order of processing—larger concepts first, then details, according to a study in the *Proceedings of the National Academy of Sciences*. “The work will help to explain the brain’s underlying cognitive processes,” says lead author Ning Qian, PhD, associate professor of neuroscience and of physiology & cellular biophysics.

Version Control

Researchers have identified a key process that fine-tunes how neurons transmit electrical signals, or action potentials, to communicate with other cells. Chaolin Zhang, PhD, assistant professor of systems biology and of biochemistry & molecular biophysics, and Hynek Wichterle,

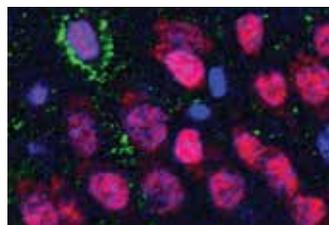
PhD, associate professor of pathology & cell biology, neuroscience, and neurology, zeroed in on the Rbfox family of proteins, which are enriched in neurons and previously were linked to neurodevelopmental disorders. Rbfox genes regulate a process called splicing, leading to production of modified versions of proteins critical for neuronal maturation, they reported in *Neuron*.

Kidney Failure

Each year, nearly 20 percent of deceased-donor kidneys recovered for transplantation are instead discarded. Reporting in the *Journal of the American Society of Nephrology*, Sumit Mohan, MD, associate professor of medicine, and colleagues raised concerns that biopsies underestimate organ quality. “It’s a complex issue,” says Dr. Mohan, whose team reviewed nearly 1,000 kidney biopsies that were processed by pathologists at Columbia and linked them to subsequent long-term function of the organ in recipients. “Our findings suggest that biopsy results should be used not to discard organs but instead used in limited circumstances to inform recipient selection.”

Brain Gain

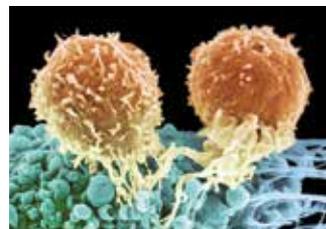
The human brain makes new neurons throughout life, according to the most definitive study on the question to date, published in *Cell Stem Cell*. Maura Boldrini, MD,



PhD, a research scientist in psychiatry and a member of the Columbia Stem Cell Initiative, and colleagues used molecular probes and mathematical modeling to track neurogenesis in brains from 28 healthy donors ages 14 to 79. Older brains retain the ability to make new neurons but may become less able to form new connections between them and keep them supplied with oxygen, they found.

Immune Booster

Cancer immunotherapy drugs work for only a minority of patients, but a report in *Cell* suggested that a generic drug now used to increase blood flow may be able to improve the effectiveness of the drugs. A team led by Sankar Ghosh, PhD, the Silverstein and Hutt Family Professor and Chair of Microbiology & Immunology, found that in mice with melanoma, the drug pentoxifylline boosts the effectiveness of

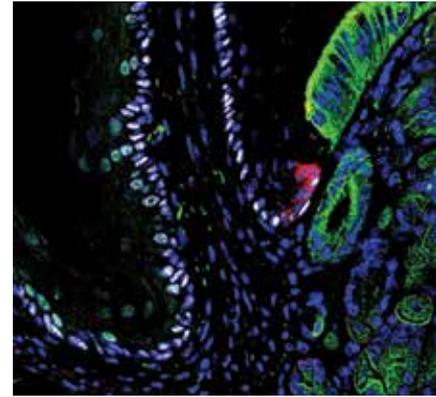


immune-checkpoint inhibitors, a type of immunotherapy now commonly used in the treatment of melanoma and other cancers. In a related study, published in *Immunity*, Dr. Ghosh and colleagues reported insights into the role of c-Rel protein in cancer immunity.

Big Reveal

Jianwen Que, MD, PhD, associate professor of medicine, and colleagues have identified cells

in the upper digestive tract that can give rise to Barrett’s esophagus, a precursor to esophageal cancer. The discovery of this “cell of origin,” reported in *Nature*, promises to acceler-



ate the development of more precise screening tools and therapies for Barrett’s esophagus and esophageal adenocarcinoma. Incidence of esophageal adenocarcinoma has risen by 800 percent over the past four decades, but little progress has been made in screening and treatment. If esophageal cancer is not detected early, patients typically survive less than a year after diagnosis.

Tumor Trigger

BRCA1 and BRCA2—so-called tumor-suppressor genes—help ensure that breast and ovarian cells grow and divide at a normal pace. If these genes become mutated, cells are likely to reproduce uncontrollably, a common prelude to cancer. In *Molecular Cell*, a team led by Alberto Ciccio, PhD, assistant professor of genetics & development, identified three genes in BRCA1/2-deficient cells that fuel genome instability during a critical DNA repair process, causing lesions that can lead to tumor formation. Says Dr. Ciccio: “Our studies raise the possibil-

ity that inhibition of these genes could reduce the occurrence of breast and ovarian cancer in BRCA1/2 mutation carriers.”

Broken Barrier

The blood-brain barrier keeps viruses and toxins from slipping into the central nervous system, but in multiple sclerosis, immune cells break through it to attack nerve cells. Using new microscopy techniques, Dritan Agalliu, PhD, assistant professor of pathology & cell biology (in neurology and pharmacology), and colleagues observed how these cells slip through the damaged barrier. According to their study published in *Cell Reports*, contacts between endothelial cells break down early in multiple sclerosis, before clinical manifestations of the disease emerge, allowing immune cells to enter the brain. Tightening junctions between the barrier’s endothelial cells could prevent immune cell leakage. Dr. Agalliu’s laboratory is currently working to develop methods to restore blood-brain barrier function in multiple sclerosis and other autoimmune diseases of the brain.

Diabolical Synergy

A study led by Antonio Iavarone, MD, professor of neurology and of pathology

& cell biology, and Anna Lasorella, MD, professor of pediatrics and of pathology & cell biology, has revealed that the fusion of two adjacent genes causes cancer by kicking mitochondria into overdrive and increasing the amount of fuel available for rampant cell growth. Drugs that target this pathway can prevent tumor growth, the team found. Published in *Nature*, the findings extend work by the same team published in 2012 in *Science*, identifying the fusion as a cause of some cases of a particularly aggressive form of brain cancer.

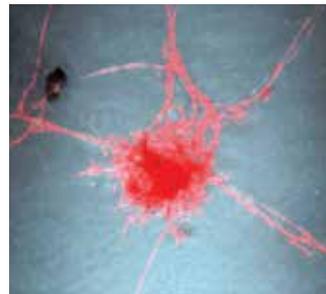
Double Whammy

Researchers led by Wendy Chung, MD, PhD, the Kennedy Family Professor of Pediatrics (in Medicine) and director of the hereditary cancer program, in work with GeneDx, a genetic testing company, have identified two new genes that increase the risk of breast cancer: MSH6 and PMS2. The study, published by *Genetics in Medicine*, suggested that each gene approximately doubles a woman’s risk of developing breast cancer by age 60. The two genes were previously known to cause Lynch syndrome, an inherited condition that also raises the risk of colorectal, ovarian, stomach, and endometrial cancer.

Stress Response

Stress spurs pancreatic cancer by triggering the release of “fight or flight” hormones, according to research published in *Cancer Cell* by Timothy C. Wang, MD, the Dorothy L. and Daniel H. Silberberg Professor of Medicine, and colleagues. Beta blockers, commonly used medications that inhibit these hormones,

were found to increase survival in a mouse model of the disease. An additional analysis of patients with advanced pancreatic cancer revealed that those



who were taking beta blockers for another condition lived approximately two-thirds longer than those who were not taking the medications.

Dynamic Disease

PNAS reported studies of a mouse model of amyotrophic lateral sclerosis (ALS) showing that one of the body’s natural defenses against the disease—a cellular “clean-up process” called autophagy—suppresses ALS disease progression early on but in later stages advances the disease’s deadly spread through the spinal cord. “One of the biggest challenges to treating ALS is that its disease progression is dynamic,” says Tom Maniatis, PhD, the Isidore S. Edelman Professor and Chair of Biochemistry & Molecular Biophysics. “In the *PNAS* paper we’ve identified a cellular process that likely plays a central role at the very beginnings of the disease, which could open the door to treatments that stop ALS before it has a chance to gain a foothold in the body.”

Eating Machines

Every second in the human body, 1 million cells die and are devoured by other cells

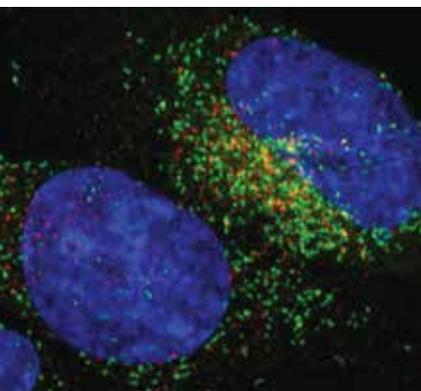
known as macrophages, which have extraordinary appetites. Researchers led by Ira Tabas, MD, PhD, the Richard J. Stock Professor of Medicine and professor of pathology & cell biology (in physiology & cellular biophysics), detailed in *Cell* the mitochondrial processes that are central to the outsized rate of digestion central to macrophage function. The new findings could help researchers improve the appetite of macrophages, which play a critical role in such chronic diseases as heart disease, lupus, and chronic lung disease.

Growth Factor

New findings about hematopoietic stem cells could enhance bone marrow transplantation, often used to treat blood cancer. *Science* reported on a key growth factor that, in mice, keeps blood-forming hematopoietic stem cells (HSCs) in a healthy state inside bone marrow. Without the growth factor, HSCs cannot maintain themselves or create new blood cells. The source of the growth factor—the liver—came as a surprise, says senior author Lei Ding, PhD, assistant professor of rehabilitation & regenerative medicine and of microbiology & immunology. All other known factors needed for HSC maintenance are supplied locally by the bone marrow.

Highways to DNA Repair

A cell’s DNA can be damaged 100,000 times a day, and the damage can lead to mutations that cause cancer. “But cells have ways to repair the damage, and as researchers learn more about these techniques, we may be able to exploit them to develop new anti-cancer thera-



pies,” says Jean Gautier, PhD, professor of genetics & development in the Institute for Cancer Genetics and associate director of research at Columbia’s Herbert Irving Comprehensive Cancer Center. Reporting in *Nature*, Dr. Gautier and colleagues revealed that DNA repair falters when cells cannot move damaged DNA to repair centers within the nucleus.

Brain Food

An inflammatory dietary pattern may increase inflammation in the brain and speed up brain aging, says a study published in *Current Alzheimer Research* and led by Yian Gu, PhD, assistant professor of neurological sciences. Researchers found that cognitively healthy elderly adults who consumed nutrients prevalent in such a diet—characterized by low intake of calcium, vitamins D, E, A, B1, B2, B3, B5, B6, folate, Ω -3, and unsaturated fatty acids and high intake of cholesterol—had higher levels of inflammatory markers, less gray matter, and worse visuospatial cognition than those who consumed fewer of these nutrients. The less well-preserved brain gray matter may explain the cognition impairment.

Blood Thinner

Aspirin does not increase heart failure events in heart failure patients who are taking one of the first-line therapies: angiotensin-converting enzyme—ACE—inhibitors or angiotensin receptor blockers—ARBs—according to research published in *JACC: Heart Failure*. “These findings allay concerns regarding the safety of aspirin for heart failure patients,” says

Shunichi Homma, MD, the Margaret Milliken Hatch Professor of Medicine and deputy chief of cardiology.

Triglyceride Triumph

Cells use triglycerides as fuel, but high triglyceride levels are associated with an increased risk of cardiovascular disease. Unlike cholesterol, which can be lowered with statins, triglyceride levels can only be modestly reduced with drugs, and results on heart disease outcomes are mixed. *Cell Metabolism* has published research from the lab of Utpal Pajvani, MD, PhD, a Herbert Irving Assistant Professor of Medicine, pointing to a possible strategy to lowering triglycerides: In mouse studies, researchers showed that inhibiting an enzyme in the liver significantly reduced triglyceride levels.

Mammalian Tether

Researchers have discovered an elusive protein that tethers two key organelles in mammalian cells, they reported in *Science*. The protein, called PDZD8, mediates communication between the mitochondria and the endoplasmic reticulum by using calcium ions as messenger molecules. “This research stands to advance our understanding of how cells and in particular neurons function and, as a result, the cellular basis of some of the most complex and persistent diseases we face, including neurodegenerative disorders such as Alzheimer’s where this organelle interface has long been suspected to be defective,” says Franck Polleux, PhD, professor of neuroscience, who led the work. Using powerful new imaging technol-

ogy, the team peered into a 30 nanometer-wide space between these organelles where PDZD8 resides and functions to tether these two organelles.

Freeze Frame

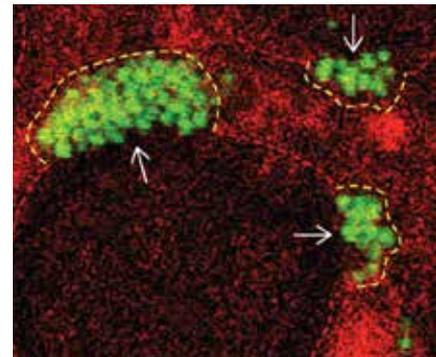
In two papers published in *Nature*, Alexander Sobolevsky, PhD, associate professor of biochemistry & molecular biophysics, and colleagues detailed insights into cellular processes derived from cryo-electron microscopy, a technique pioneered by 2017 Nobel Laureate Joachim Frank, PhD. One paper describes new insights into the function of the AMPA-subtype glutamate receptor, which is involved in memory and learning. The second paper focuses on TRPV6, which enables epithelial cells to absorb calcium. The team’s findings will help elucidate how abnormalities in calcium absorption contribute to cancer.

Inflammation Adjuster

Excessive abdominal fat raises the risk of insulin resistance and type 2 diabetes in part through inflammation, but researchers have had a hard time determining what causes such inflammation in fat cells. According to a study in *Nature* led by Ira Tabas, MD, PhD, the Richard J. Stock Professor of Medicine, a liver enzyme called DPP4 is at least partly to blame. Blocking its production in the liver soothed inflammation in abdominal fat cells and improved insulin resistance in obese mice. Says Dr. Tabas: “If we can develop ways to target liver DPP4 in people, this may be a powerful new way to treat obesity-induced type 2 diabetes.”

Infectious Agent

The bacterium *Staphylococcus aureus*, especially the epidemic USA300 strain, is a major cause of pneumonia among hospital patients. A team of researchers from the Department of Medicine and the Department of Pediatrics—Jaime Hook, MD, Naeem Islam, PhD, Dane Parker, PhD, Alice Prince, MD, Sunita Bhattacharya, MD, and Jahar Bhattacharya, MD, DPhil—used real-time imaging in a live mouse lung to investigate USA300 infection. The bacterium bunched up in nooks of the lung’s air sacs within 10 minutes of injection. The antibiotic vancomycin, which



can kill USA300 bacteria in vitro but is often ineffective in pneumonia patients, only worked when a gene that helps the bacteria form biofilms had been inactivated. The study, published in the *Journal of Clinical Investigation*, notes that targeting the gene or otherwise busting up biofilms could prevent lung damage.

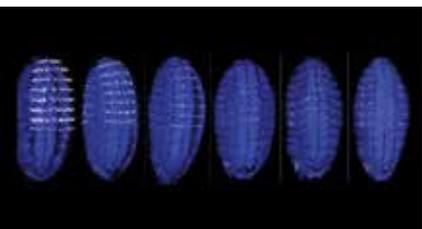
Fat Fix

For years, researchers have been searching for therapies that can transform an adult’s white fat into brown fat—a process called browning—as a treatment for obesity and

diabetes. Li Qiang, PhD, assistant professor of pathology & cell biology, and colleagues have created such a therapy in the form of a medicated skin patch that shrinks local fat and raises the body's overall metabolism. The new treatment, described in ACS Nano, is made by encasing a drug in nanoparticles that gradually collapse in the body, releasing the drug into nearby tissue. It was tested in obese mice but has not yet been tested in humans.

DNA Spotlight

Researchers led by Richard S. Mann, PhD, the Higgins Professor of Biochemistry & Molecular Biophysics (in Systems Biology), have developed a computational tool that shines



a light on the genome's most hard-to-translate segments. Dr. Mann studies Hox genes, which encode proteins called transcription factors that turn other genes on and off to coordinate development. He found that these factors guide different features of growth by binding to low-profile regions of the genome. In a study published in Proceedings of the National Academy of Sciences, Dr. Mann's team collaborated with the lab of Harmen Bussemaker, PhD, professor of biological sciences at Morningside and professor of systems biology, to use a sophisticated new computer algorithm to probe those so-called low-affinity DNA regions.

Reversing Relapse

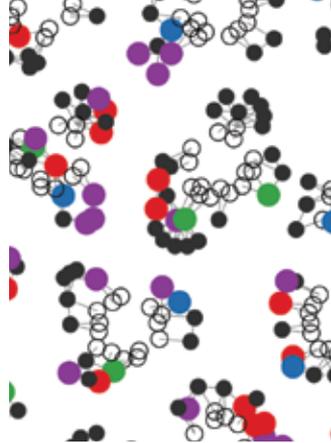
Most children with acute lymphoblastic leukemia can be cured, but the prognosis is dismal for about 20 percent of patients who relapse after treatment. A study published in Nature found that a mutation in a gene called NT5C2 leads to relapse in many ALL patients but also makes these cancer cells vulnerable to a class of drugs called IMPDH inhibitors. "By understanding the mechanisms of resistance, we are now positioned to design new strategies to curtail the occurrence of relapse," says Adolfo Ferrando, MD, PhD, professor of pediatrics, pathology & cell biology, and systems biology in the Institute for Cancer Genetics, who led the work.

Dampening Diabetes

Inhibiting a protein called FOXO1 is a promising strategy for treating type 2 diabetes, but drugs that inhibit FOXO1 stimulate fat production, causing side effects such as weight gain. A study led by Domenico Accili, MD, the Russell Berrie Foundation Professor of Diabetes and director of Columbia's Diabetes Research Center, found that in mice, FOXO1 works with a protein called SIN3A to limit lipid production. They screened 1 million small molecules, finding several that partially inhibit FOXO1, leaving SIN3A signaling intact. Such molecules, described in Cell, point to a new class of diabetes drugs.

Electronic Heritability

Researchers generally conduct genetic studies to determine the extent to which a disease runs in the family, but for



some diseases such analysis is impossible because no associated genes are known. A study led by Nicholas Tatonetti, PhD, the Herbert Irving Assistant Professor of Biomedical Informatics, and David K. Vawdrey, PhD, assistant professor of biomedical informatics, revealed that electronic health records can be used to estimate disease heritability. The results, published in Cell, matched those obtained through genetic data. Hospital records provided data from a very diverse group of patients in New York City, allowing the researchers to stratify disease risk for different ethnicities in ways that had not been done before.

Kidney Rx

Chronic kidney disease is usually diagnosed by lab tests and sometimes by kidney biopsy. "Because CKD is usually silent in the early stages, it may not be detected until an individual develops advanced kidney failure, at which time standard tests are unrevealing," says Ali G. Gharavi, MD, the Jay Meltzer, MD, Professor of Nephrology and Hypertension (in Medicine) and chief of nephrology. Dr. Gharavi led a study demonstrating that DNA sequencing can identify genetic forms of chronic kidney disease that are unrecognized by a standard workup, potentially allowing earlier and more precise diagnosis and treatment.

Talent Search

PTEN is best known as a tumor suppressor, a type of protein that protects cells from growing uncontrollably and becoming cancerous. But it turns out that PTEN has a second previously unknown talent: Working with another protein, CFTR, it helps to control inflammation and assists in the clearance of airway



infection, especially in patients with cystic fibrosis. The findings, published in Immunity by a team led by Alice Prince, MD, professor of pediatrics (in pharmacology), explain why people with cystic fibrosis are particularly prone to respiratory infections and suggest a new approach to treatment.

Suicide Uptick

Suicide attempts among American adults are on the rise, with a disproportional effect on younger, socioeconomically disadvantaged adults with a history of mental disorders, according to research led by Mark Olfson, MD, professor of psychiatry, and published in JAMA Psychiatry. "The patterns seen in this study suggest clinical and public health efforts to reduce suicide would be strengthened by focusing on younger patients who are socioeconomically disadvantaged

and psychiatrically distressed,” says Dr. Olfson. The risk of suicide for youth is especially high in the months after surviving a deliberate self-harm attempt, according to another study published in *Pediatrics* by Dr. Olfson and colleagues.

Violence Screen

It may be possible to predict violent behavior—as well as episodes of psychosis—in people at high risk of developing psychosis, according to a study led by Gary Brucato, PhD, a clinical psychologist and researcher at Columbia and the New York State Psychiatric Institute. The study, published in *Neuropsychopharmacology*, followed 200 individuals at high risk of psychosis over two years and showed that

both thoughts of violence and recent violent behavior were associated with future acts of violence, which occurred an average of seven days after the development of psychotic symptoms. These findings demonstrate how to more effectively screen for violent ideation, the researchers say.

Brain Chemistry

Ever more women are taking antidepressants—particularly selective serotonin reuptake inhibitors (SSRIs)—during pregnancy. Clinicians are divided on whether the drugs are safe and whether and how they affect the developing fetus. A study in *JAMA Pediatrics*, led by Jonathan Posner, MD, the Suzanne Crosby Murphy Associate Professor of Psychiatry, and Jay

Gingrich, MD, PhD, the Sackler Institute Professor of Developmental Psychobiology (in Psychiatry), detailed differences in the volume and wiring of certain brain regions among infants who had been exposed to SSRIs, especially during the third trimester. “Our new findings suggest that SSRIs may be having an effect on offspring,” says Dr. Posner, “but more research is needed to confirm that.”

Medication-Associated Depression

A third of American adults use medications that may raise the risk of depression, reported a study by Mark Olfson, MD, professor of psychiatry. More than 200 medications that have depression as a potential adverse effect were included in

Dr. Olfson’s study. The findings indicate that 38.4 percent of U.S. adults use one or more of these medications, putting them at greater risk of concurrent depression.

Tumor Avatars

Researchers led by Michael M. Shen, MD, professor of medicine, genetics & development, urology, and systems biology, have created patient-specific bladder cancer organoids that mimic many of the characteristics of actual tumors. Bladder cancer is the fifth most common cancer in the United States, yet it is one of the least understood. The use of organoids, tiny 3-D spheres derived from a patient’s own tumor, may one day help guide treatment of patients.

2018 Patient Care Highlights

Cardiomyopathy Excellence

Morgan Stanley Children’s Hospital at New York-Presbyterian has been designated an accredited center of care by the Children’s Cardiomyopathy Foundation. The hospital offers a wide range of services related to pediatric cardiomyopathy, including heart transplants, high-quality imaging, interventional cardiology, genetic testing, pediatric cardiac electrophysiology, and cardiac intensive care. The high volume of pediatric cardiomyopathy patients—over a 12-month period, the hospital cared for 238 patients with pediatric cardiomyopathy—factored into the hospital’s designation, as did its variety of clinical services, expertise,

academic affiliation, and status as a research hospital.

ED Expansion

New York-Presbyterian’s Morgan Stanley Adult Emergency Department has been renovated and expanded. The space doubled from 22,000 to 45,000



square feet during the four-year renovation funded by Morgan Stanley and other donors. The ED is now equipped with 88 expanded treatment bays. New features include acute care treatment units that offer patients state-of-the-art diagnostic and treatment tools for quick emergency intervention to mitigate long-term damage from stroke, cardiac arrest, and other acute conditions.

Early Psychosis Treatment Model

OnTrackNY, a program for individuals with early psychosis, decreased hospitalization rates from 70 percent to 10 percent and doubled rates of participation in education and employ-

ment. The program, directed by Lisa Dixon, MD, the Edna L. Edison Professor of Psychiatry, is based on a new treatment model called coordinated specialty care and provides a multidisciplinary team approach to treatment, including medication, psychotherapy, support with school and work, case management, and family support to help young people recover from psychosis.

In the Community

More than 60 medical center students led by the VP&S Class of 2018 volunteered for a health and wellness fair at the Fort Washington Men’s Shelter in the Amory. At the event, sponsored by the newly established Office of Service-Learning, students

staffed health and wellness stations within the shelter's corridors to offer information and basic medical exams to the shelter's residents.

Obesity Challenged

Two unique multidisciplinary programs help children and adults who suffer from obesity. COMMiT—the Comprehensive Obesity and Metabolism Management and Treatment—program brings surgeons, internists, endocrinologists, gastroenterologists, nurses, and dieticians together to provide a multifaceted approach to weight loss. FIT—Family Improving Health Together—provides comprehensive care for obese children ages 2 to 9 and tailors a personalized and holistic plan so the entire family can adopt dietary and exercise interventions.

Music at the Bedside

Students have found a way to mix their passion for music with patient care. The Music at Bedside Program's goal is to soothe and entertain patients enduring painful conditions while encouraging collaboration between students and palliative care professionals. Students play weekly in the cardiac medicine and neurosurgery units, where patients



are recovering from surgery or suffer from chronic illnesses that keep them hospitalized for long stretches.

Rh Disease Treatment Milestone

Fifty years after its development by Columbia physicians, RhoGAM is still in use today to prevent Rh disease, one of the most severe and devastating diseases affecting fetuses



and newborns. The drug was developed in the 1960s by Columbia researchers John Gorman, MD, and Vincent Freda, MD, together with a pharmaceutical company researcher, William Pollack, PhD. In February, Columbia researchers and physicians joined guests from around the world to celebrate RhoGAM's 50-year legacy.

Spine Hospital Naming

The spine hospital at New York-Presbyterian was renamed the Daniel and Jane Och Spine Hospital in recognition of a gift from its namesake longtime supporters. The hospital, collaborating with VP&S, opened the comprehensive spine hospital in 2015 with the recruitment of three of the world's leading orthopedic spinal surgeons, Lawrence Lenke, MD, surgeon-in-chief and director

of spinal deformity surgery; K. Daniel Riew, MD, director of cervical spine surgery; and Ronald Lehman Jr., MD, director of degenerative and minimally invasive spine surgery. All three surgeons are professors of orthopedic surgery at Columbia.

Mother-Centered

The Mothers Center at NYP and Columbia moved into a new, state-of-the-art space where services are centralized to provide comprehensive, multidisciplinary care before, during, and after a high-risk pregnancy due to maternal complications. The 5,300-square-foot outpatient center is the first in the nation to consolidate all relevant specialists that a pregnant woman may need to maintain and optimize her health and the health of her baby, says the center's visionary, Mary E. D'Alton, MD, chair of the Department of Obstetrics & Gynecology.

Joining Forces

Columbia doctors from three specialties—otolaryngology, dermatology, and ophthalmology—have opened the Center for Facial, Aesthetic, and Reconstructive Surgery to offer a variety of synergetic services at a single ColumbiaDoctors location. The new center provides patients with a unique interdisciplinary approach, Mohs surgery five days a week, and cosmetic and laser services.

N4C

Neurological dysfunction and psychiatric disorders are highly prevalent in patients who have experienced cardiac arrest. Neurology's new NeuroCardiac Comprehensive Care

Clinic (N4C), the first of its kind in the country, is a "one-stop shop" that offers multidisciplinary, coordinated care to help cardiac arrest survivors reach their full potential. The program was founded by Sachin Agarwal, MD, assistant professor of neurology. The neurocardiac team has specialists in neurocritical care, neuropsychiatry, neuropsychology, neurorehabilitation, and pastoral care to provide coping strategies to patients and their caregivers.

Mining for Rare Diseases

DISCOVER—Diagnosis Initiative: Seeking Care and Opportunities with Vision for Exploration and Research—is a unique center designed to



diagnose and develop novel treatments for rare and complex diseases. The program, directed by Wendy Chung, MD, PhD, the Kennedy Family Professor of Pediatrics (in Medicine), has discovered more than 40 rare diseases. The program's case management team works with about 50 specialists throughout the medical center and sees an average of three to four patients a week, most of them children.

Baby Hearts

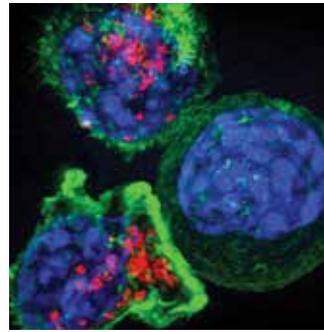
The Vivian and Seymour Milstein Family Infant Cardiac

Unit at NewYork-Presbyterian is a state-of-the-art, 17-bed unit solely dedicated to providing specialized neonatal cardiac intensive care to infants with complex heart disease. It became the first neonatal cardiac intensive care unit in the United States when it opened in September 2017. The new unit—with five single beds, five double-bed pods, and two isolation rooms—is staffed by physicians, nurses, and nurse practitioners who have special

expertise in cardiac physiology and intensive care.

Cell Therapy as Precision Treatment

The first T-cell therapy—CAR-T, in which a patient's own T cells are genetically enhanced to identify, attack, and kill cancer cells—was approved by the FDA in 2017 to treat some children with acute lymphoblastic leukemia and some adults with lymphoma. Prakash Satwani, MD, associate professor of pedi-



atrics, leads the CAR-T program at NYP's Children's Hospital. Ran Reshef, MD, associate professor of medicine and director

of translational research in the Blood and Marrow Transplantation and Cell Therapy Program, spearheaded the launch of CAR-T cell therapies for adult lymphoma and treated the first patients at Columbia. Pawel Muranski, MD, assistant professor of medicine and of pathology & cell biology, was recruited to Columbia in 2017 to establish a lab to manufacture CAR-T cells and other cell therapies for patients in clinical trials.

2018 Education Highlights

Interprofessional Day of Action

More than 1,800 students, faculty, and staff participated in the medical center's first Interprofessional Day of Action on April 5. All health professions schools canceled classes to enable full participation for the event, which will be held annually. Throughout the day, students attended seminars and interactive workshops that conveyed the necessity of teamwork among health care professionals and taught teamwork skills. The Interprofessional Day of Action was created by Columbia Commons IPE, a group formed by Rita Charon, MD, PhD, chair



of medical humanities and ethics at VP&S.

New Dual-Degree Program

VP&S students have a new dual-degree option. The MD/MS degree in biomedical engineering is an integrated program offered with the Fu Foundation School of Engineering and Applied Sciences to a select group of third-year medical students who will earn MD and MS degrees in five years to prepare them as innovative leaders in science, engineering, and medicine.

New Departments

VP&S has two new departments: the Department of Emergency Medicine and the Department of Medical Humanities and Ethics. Emergency medicine combines faculty from the Department of Medicine's division of adult emergency medicine and faculty from the division of pediatric emergency medicine within the Department of Pediatrics.

The department is chaired by Angela M. Mills, MD, a recruit from the University of Pennsylvania. Medical humanities and ethics combines faculty from multiple departments and will have divisions devoted to ethics, narrative medicine, and professionalism and health care justice. Longtime faculty member Rita Charon, MD, PhD, chairs the department.

Research Showcase

Students who conducted research during medical school shared their work with fellow students and faculty at the annual VP&S Student Research Day. The 73 students presented research on a range of topics, from testing the accuracy of machine learning classifiers to identify stroke patients, to development of an augmented reality system for cerebral angiography, to the effect of race and socioeconomic status on outcomes after pediatric allogeneic hematopoietic cell transplantation. Twelve projects were honored



in four research categories: research year, summer project, scholarly project, or MD/PhD.

Genetic Counseling Degree

A new two-year master's program in genetic counseling will be offered at VP&S beginning in Fall 2019. The program, directed by Amanda Bergner, MS, associate professor of genetic counseling (in genetics & development) at CUMC, will educate students in clinical genetics, counseling, communication, genomic medicine, and precision medicine. Students will be taught by genetic counselors, researchers, and physicians and will complete clinical internships at NewYork-Presbyterian Hospital.



HELP FROM OUR FRIENDS

THIS PAST YEAR HERALDED A NEW ERA for Columbia's medical school. As we marked our 250th anniversary, we saw the significant impact that philanthropy can have on our institution and on the medical landscape. We successfully launched and



Diana and Roy Vagelos

completed our 250th Anniversary Scholarship Challenge, which was spearheaded by Roy and Diana Vagelos to provide each of our medical students with a financial aid package that eliminates the need for loans, freeing our graduates from burdensome debt. Early in 2017, Dr. and Mrs. Vagelos announced this \$25 million challenge grant, which was then matched by faculty, alumni, and friends over the rest of the anniversary year. This effort was followed by the announcement of additional contributions totaling \$250 million for our scholarship programs, initiative in precision medicine, and a professorship, bringing the lifetime giving by Dr. and Mrs. Vagelos to more than \$310 million. In recognition, we fittingly renamed our school the Roy and Diana Vagelos College of Physicians and Surgeons (VP&S). This

closely followed the renaming of the larger campus as Columbia University Irving Medical Center, in recognition of Herbert and Florence Irving. The Irvings' generosity has helped make the Herbert Irving Comprehensive Cancer Center one of the world's elite cancer centers and continues to benefit our cancer programs. This report highlights other programs that have thrived from the support of our many friends during this historic year. These partners have made an impact on our education, patient care, research, and community outreach to ensure that VP&S is poised for the next 250 years of successful leadership of medicine.

Scholarship Bequests and Endowment

The 250th Anniversary Scholarship Challenge rallied the community during our landmark year, as our supporters came out in force to provide funding for scholarships. We saw support from friends, alumni, and faculty at the medical center, including several \$1 million gifts and bequests that were especially important in this effort. Contact the Development Office at 212-342-2108 for more information or to make a bequest or a planned gift.

John and Myrna Daniels Professorship of Cardiology

The John and Myrna Daniels Foundation has committed \$2.5 million to establish the John and Myrna Daniels Professorship of Cardiology. This gift was made in honor of Dr. Jeffrey Moses, an internationally recognized interventional cardiologist, and will provide the resources necessary for Columbia to recruit, retain, and support outstanding physicians in interventional cardiology in perpetuity.

The Brown Foundation

The Brown Foundation, established by Bernard Brown and Shirlee Brown, committed \$2 million to VP&S to establish the Shirlee and Bernard Brown Glaucoma Genetics Initiative Fund within the Department of Ophthalmology. The purpose of the fund is to advance the understanding of the genetic pathophysiology of glaucoma and apply this information to the development of new treatments. The fund will support basic science, translational medicine, and clinical research.

Roger M.Y. Wu, MD, and the Wu Legacy

Building on the legacy of their parents, the late Helen and Clyde '56 Wu, Roger Wu, MD, and David Wu, MD, have underlined their parents' commitment to medicine, VP&S, and Columbia's historic ties with China. Their recent gift to complete the endowment of the Wu Family China Center for Health Initiatives will support collaboration in medical research and education between Columbia and Zhejiang University School of Medicine in China. The center fosters joint research activities, conferences, and symposia; medical student exchanges; and visits or temporary appointments of faculty members and research scholars. The funding of the center follows on Dr. and Mrs. Wu's endowment of six professorships and other support given to VP&S. In addition to these acts of philanthropy, Dr. and Mrs. Wu re-established Columbia's relationships with Peking Union Medical College and other Chinese medical schools in the 1990s through the creation of the Wu Fellows Program. The fellowships provided funding for academic physicians/scientists from China to hone their skills at Columbia and other medical schools and laid the groundwork for the Wu Family China Center. "Completing the endowment of the Wu Family China Center for Health Initiatives," says Roger, "is the culmination of our parents' dream of scientific and medical cooperation between China and the United States." Roger and his aunt, Lady Ivy Wu, attended the First Joint Forum of ZJU and Columbia in Hangzhou, China, in October 2017. There, they presented Dr. Chen Zhu, who received an honorary Doctor of Science degree



Chen Zhu receiving the Wu Award in International Understanding

from Columbia in 2016 and is a former Wu Fellow and former Minister of Health of China, with the second Wu Award in International Understanding. The Wu family also has continued to identify scholarships as a top priority, participating in the 250th Anniversary Scholarship Challenge with a contribution of \$1 million. The Wus value and honor their long relationship with Columbia and look forward to the medical and scientific advances borne from this gift and the Wu Family China Center for Health Initiatives.

The Gerstner Family Foundation

In 2008, Louis V. Gerstner Jr. established the Louis V. Gerstner Jr. Scholars Program at VP&S. Designed to cultivate the next generation of leading physician-scientists in medicine and research, the program has named and funded 44 early career investigators as Gerstner Scholars; four of them also have received the Gerstner Merit Award. This year we celebrated the program's 10-year anniversary and its success, including the Gerstner Family Foundation's extended support of the program with a new \$5 million commitment. This gift will enable the Gerstner Scholars Program to continue to flourish, yielding high-impact research and discoveries in myriad clinical

areas, including cancer, cardiovascular disease, respiratory illness, and substance abuse disorders. The Gerstner Merit Award was established in 2014 for an outstanding third-year Gerstner Scholar whose research shows potential but has not yet received an independent investigator award. The Gerstner Merit Award makes scholars' research sustainable over the long term, helping bridge the gap from scientific discovery in the lab to new therapies for patients. Together, the Louis V. Gerstner Jr. Scholars Program and the Gerstner Merit Award have helped drive progress in academic medicine while supporting physician-scientists as they become independent, federally funded researchers.



Lee Goldman with Louis V. Gerstner Jr. celebrating the 10-year anniversary of the Gerstner Scholars Program

To date, in total, the Gerstner Scholars and Merit Awardees have garnered nearly \$100 million in additional funding by leveraging their initial Gerstner grants.

The Louis and Rachel Rudin Foundation

For more than 40 years, Columbia University Irving Medical Center has enjoyed a strong partnership with the Rudin Foundations, thanks to Jack Rudin, who died in December 2016. Since 1975, the medical center has received more than \$25 million in current use and endowed funds from Jack Rudin, the May and Samuel Rudin Family Foundation, and the Louis and Rachel Rudin Foundation to support dozens of programs. The signature initiative—the Rudin Scholars Program—has provided scholarship support to more than 600 students at VP&S, the School of Nursing, the Mailman School of Public Health, the Center for the Study of Society and Medicine, and programs in occupational and physical therapy. In addition, the Rudin Family's foundations also have funded the Rudin Cardiology Fellowship; Jay Meltzer, MD, Fellows Program in Medical Ethics; Michael Cohen Clinical Education Endow-

ment; Samuel Rudin Professorship in Medical Education; Columbia Psychiatry Substance Abuse Fellowship Program at Phoenix House; the IFAP Global Health Program; the Teen to Young Adult Autoimmune Disease Transition Program; Palliative and End of Life Fellowship Program; and other programs. The Rudin Foundations have also joined other donors to provide support to the Paul Marks Scholars Program, the Thomas Q. Morris Symposium on Medical Education, the John Jay Mack Professorship in Clinical Education, and the Glenda Garvey Teaching Academy.

Most recently, the Louis and Rachel Rudin Foundation continued its tradition of scholarship support for medical students by giving \$1 million, which was matched through the 250th Anniversary Scholarship Challenge, to create the endowed Jack Rudin Scholarship Fund.



Rudin Scholars



Crown Awards 2017

The 250th anniversary of VP&S culminated in December with the 2017 Crown Awards gala, held at Lincoln Center. Pictured from left in the photo below are Crown Awards honoree P. Roy Vagelos, Karen Kennedy (gala co-chair), Sarah Billinghamurst Solomon (gala co-chair), honoree Diana Vagelos, Jill Goldman, Cheryl Milstein and Philip Milstein (gala co-chairs), and Lee Goldman, who co-hosted the event. World-renowned soprano Renée Fleming, in the photo at left, gave a special performance.



From left: Misook Doolittle, Paul Lee, and Lee Goldman

Professorship Supports Hospitalist Care

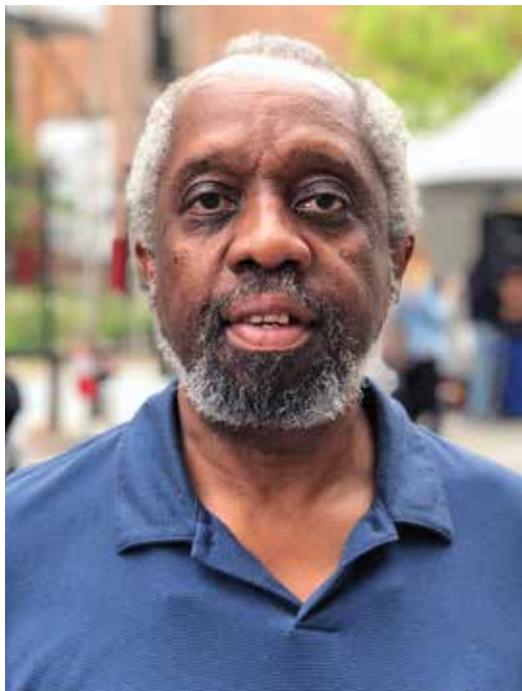
A new professorship will provide permanent support for the hospitalist program in the Department of Medicine, which trains and deploys clinicians who spend the majority of their time caring for hospital inpatients. The Harry C. and Misook Doolittle Professorship of Medicine will be held by Paul Lee, MD, who joined the hospitalist group in the Department of Medicine's Division of General Medicine in 2001 and has served as its medical director since 2003. The professorship is made possible by a \$2.5 million gift from Misook and Harry Doolittle. Misook Doolittle is a fashion industry entrepreneur, and her husband, Harry, is a visual artist. The couple has endowed the professorship specifically in Dr. Lee's honor.

The Avnessians Foundation

The Avnessians Foundation and the Avnessians Family Foundation have committed \$1.5 million for the establishment of an Avnessians Assistant/Associate Professorship of Cardiology. This gift was made in honor of Dr. Susheel Kodali, director of Columbia's Structural Heart & Valve Center, for his outstanding contributions to clinical, education, and research activities related to valvular heart disease.

The Ludwig Family Foundation

The Ludwig Family Foundation supports VP&S research in neurological disease, focusing on Alzheimer's disease and traumatic brain injury. A grant of \$1.2 million is advancing research projects led by Drs. Franck Polleux, Wassim Elyaman, Hynek Wichterle, Steven Kernie, and Richard Mayeux. Says Carol Ludwig, president of the Ludwig Family Foundation: "As a graduate of VP&S and a neurologist, I am pleased to be able to help support the neurology department's efforts in degenerative neurological diseases."



Participants in All of Us

All of Us Precision Medicine Program: Open for Enrollment

Three of the 4,000-plus individuals who have enrolled in the New York City consortium of the NIH All of Us Research Program have this in common: They want to give back in the hopes of improving the health of future generations.

The national effort seeks to enroll 1 million Americans by 2023 into one of the world's largest and most diverse data sets for precision health research. The health data from participants may, over time, identify ways to better treat disease and understand how disease differs from person to person.

In May, hundreds of New Yorkers attended the NYC launch of All of Us at Abyssinian Baptist Church in Harlem, where 105 individuals began the enrollment process for the landmark precision medicine study. Columbia University Irving Medical Center is the lead partner of the local consortium, joining NewYork-Presbyterian Hospital, Weill Cornell Medicine, and Harlem Hospital to form one of several regional networks enrolling participants across the country.

By analyzing DNA from 1 million Americans, All of Us hopes to speed the pace of medical breakthroughs. Researchers believe

this unprecedented volume of data—together with the extensive clinical history and lifestyle habits collected from each participant—will reveal patterns that will enable the creation of new, more precise medical therapies.

All of Us will be about 40 times larger than the well-known Framingham Heart Study, which elucidated major risk factors for heart attack and stroke. The scope of All of Us will provide information about all types of diseases. It's not just about larger numbers, though. All of Us aims to reflect the diversity of the United States. Of the New Yorkers who had enrolled in the New York consortium by early May, 81 percent were from communities typically underrepresented in medical research (because of race, ethnicity, sex, or gender).

"I want us to take advantage [because] for many of these things, we have been left out," said the Rev. Dr. Calvin O. Butts III, pastor of Abyssinian Baptist Church, the oldest African-American Baptist church in New York. At the May launch he related his own bout with cancer and how the work of researchers and physicians led to

the treatment that saved his life. “I don’t want any American not to have that privilege. I am convinced that ‘All of Us’ means all of us. Sign up. It may help you, it may help some of us, it may help your grandchildren.”

It was in that spirit that Edward W. enrolled in the All of Us Research Program. A retired member of the nation’s largest property services union, he enrolled because “I think being a part of a program that could change the face of medicine is a powerful thing. If there’s anything I can do to contribute to the treatment and prevention of disease for myself, my family members, and others, then that’s something that I’m interested in.”

He filled out a series of online surveys of clinical and family history and submitted blood samples that will be used to sequence his genome. His experience as a union organizer also will help the program recruit more volunteers; he has joined the Participant Advisory Board to help spread the word. “Since I was young, it was instilled in me by my mother to help others out. Working for the union, and being a union member in general, that carried over.”

Another participant, Anne H., has always been interested in DNA ancestry tests as a way to fill in the blanks of her family history. Her father’s side is a mystery that begins and ends in Berlin, where her father was raised. He escaped Berlin in the 1930s with a sister when the Nazis took power, but his parents and another sister perished.

She identified All of Us as an opportunity not only to unveil her family history but also to help the next generation—her son, daughter, and five grandchildren. Participants in All of Us have the

option of learning what health information resides within one’s own genome; Anne is unsure what she will decide for herself but thinks the data may be useful for her children and their children. “I think the potential is enormous,” Anne says.

The commitment of Evelyn O. goes back to her birth more than 60 years ago, when she was born in New York-Presbyterian three months premature, weighing a little more than 3 pounds. She spent the first three months of her life in an incubator as doctors tried to figure out why she didn’t move or cry. It was the beginning of a lifelong relationship with Columbia and NYP.

On a recent visit to NYP, Evelyn came across a table where doctors were enrolling volunteers in All of Us. She was intrigued and decided to sign up. “I believe in giving back,” she says. “I got the best care that money could not buy. I cannot complain. That’s why anything I can do to give back, I’m there.”

“We really believe that there is a new kind of medicine coming, a medicine that is informed by what you are like, what’s in your DNA, what’s in your history, to find the best treatment for you,” said David Goldstein, PhD, director of Columbia’s Institute for Genomic Medicine and principal investigator of the All of Us New York City consortium.

“The time is now to transform how we conduct research—with participants as partners—to shed new light on how to stay healthy and manage disease in more personalized ways. This is what we can accomplish through All of Us,” said NIH Director Francis S. Collins, MD, PhD, who spoke at the May launch event in New York City.

To learn more about the program visit www.JoinAllofUs.org.

About the MD Class of 2018

158 MD graduates

47 percent of the graduates were women

12 received MD/PhD degrees

1 graduated from the three-year PhD-to-MD program

9 also received MPH degrees

8 received the first MD/MS biomedical sciences degrees

1 also received an MBA degree

2 also have DDS degrees

1 also received an MS degree in narrative medicine

19 students took an extra year for research

In all, **34** percent of the graduates took extra time for research or a dual degree

8 couples participated in the residency match

32 percent went abroad for summer experiences during their first year, senior electives, and/or scholarly projects, mostly to developing countries

23 percent matched to residencies at Columbia

40 percent matched to residencies in New York City



15 babies were born to students in the class during medical school, and two students had two babies during medical school

24 students got married during medical school, including two in-house couples, and several more got engaged

Surgical Science Returns

Not many surgery departments have a division full of basic scientists, but Columbia has been committed to the concept for years. “We always need a better understanding of what causes diseases, how we can prevent diseases from happening, and how we can treat them better. Those are questions that will be in a surgery department,” says Donna Farber, PhD, the George H. Humphreys II Professor of Surgical Sciences.

Dr. Farber was appointed this year to be chief of the Division of Surgical Sciences in the Department of Surgery. “In order to move forward, you need to do research,” she says. “Sometimes that’s research looking at better ways to do a surgery, or better devices. Other times, such as in transplantation, we want to better understand the immune system so we can tweak it to promote organ and transplant survival.”

Dr. Farber, whose research focuses on immunological memory and tissue immunity, was the sole occupant of the division when she joined the VP&S faculty in 2010. Craig Smith, MD, chair of surgery, has worked over several years to recruit a cadre of new scientists to replace scientists who left the division.

“It is historically challenging for clinical departments, but particularly procedural clinical departments like surgery, to maintain active, basic science research because that’s not what we do every day. But it’s extremely important to the future of what we do,” says Dr. Smith. “The fact that Donna Farber is now taking over the Division of Surgical Sciences is a signal of the real rebirth of that important division that began about 15 years ago.”

Research by the division’s full-time scientists covers a wide spectrum of surgical ideas. For example, Nigel Bunnett, PhD, is uncovering the way chronic pain is transmitted through nerve cells; David Sachs, MD, is developing a colony of pigs whose organs are more compatible for transplantation in humans; and Giovanni Ferrari, PhD, is investigating how cardiovascular diseases affect the physiology of heart valves and vascular cells. This breadth means that collaboration across departments and centers of the University is common, particularly with the Columbia Center for Translational Immunology, which includes Dr. Farber and Dr. Sachs.

The division gives surgeons, who have less time to maintain their own labs, the opportunity to pursue their research questions. “People at Columbia all have interest in research to some degree. That’s why they’re here,” says Dr. Smith. “It’s not enough for them on average to do an operation and go home. They have a desire to come up with new ideas, to push new procedures, to explore the physiological underpinnings of the procedures we already do, or develop a better understanding of the physiology of the body.

“Without a division like surgical sciences, their options are limited to collaborations with basic scientists in other parts of the University; to have those resources within the department makes research that much easier.”



Donna Farber

Dr. Farber plans to apply for NIH grants to organize a training program in surgical sciences for residents and fellows. Dr. Bunnett, the department’s vice chair for research, plans to replicate a program he established a decade ago at UCSF that provides two or more years of funded research for each surgical resident.

Bringing together investigators to connect them with resources is another priority for Dr. Farber. She has set up—and maintained for six years—a research resource through the organ procurement organization Live On New York, through which she has been able to collect tissues from consenting donors for her immunology research. She hopes to further develop it into a biobank for the research community. The Division of Surgical Sciences also has core facilities that researchers in the department can use and offers instruction in grant writing and statistical science.

By re-establishing the division, Dr. Smith says, Columbia “is declaring that science, innovation, research, and investigation are all very important parts of the practice of surgery. Although it’s hard to do, it’s extremely important, and we’re going to show that it’s possible.”

Academy of Clinical Excellence Inducts a New Class

Faculty members in the second class of the VP&S Academy of Clinical Excellence (ACE) were inducted in a May ceremony. The 35 new members join the 119 clinicians who were inducted in the inaugural class in 2017.

ACE honors the accomplishments of faculty members who contribute to the VP&S academic mission by providing high quality, evidence-based, and humanistic patient care.

Once inducted, ACE members work on one of the steering committees that support the work of the academy. All members are full professors and have been at Columbia for five or more years. To be eligible, they must spend more than 50 percent of their time on patient care and training the next generation of clinicians.

This year's ceremony featured the Bill Campbell Champions Symposium, a new

lecture launched through a gift. The speaker was Edward D. Miller, MD, dean/CEO emeritus of Johns Hopkins Medicine and former professor and chair of the Department of Anesthesiology at VP&S, who delivered a lecture on "Balancing the Academic Mission." He discussed the origin of Johns Hopkins' academy of clinical excellence, the first of its kind at an academic medical center and also the model for Columbia's ACE.

Office of Service-Learning Moves Education Into the Community

Community-based education has become increasingly important among the health professions, with growing understanding and acknowledgment of the benefits for both the community and the student.

The new Office of Service-Learning at Columbia University Irving Medical Center coordinates and facilitates community-based training efforts for the four schools on campus and offers students, faculty, and the community service-learning partnerships to improve the health of community members while enhancing the learning of students.

"Service-learning is not voluntarism," explains Anne H. Armstrong-Coben, MD, director of the Office of Service-Learning. "It's about creating reciprocal relations, so that the service and the learning are equally important. We recognize community-based organizations as reciprocal partners; in the methodology of service-learning the community-based organizations become partners in the education process."

Dr. Armstrong-Coben, who is interim senior associate dean for admissions and assistant professor of pediatrics at VP&S, refers to her efforts as "matchmaking": The office identifies not only the needs of the community but also the valuable assets that community-based organizations can bring to the students, strengthening existing community-campus partnerships while also creating new ones.

Students who participate in service-learning provide service in response to community-identified needs, learn about the context in which service is provided, and reflect on the connection among service, their academic coursework, and their roles as citizens. This kind of collaboration provides students with opportunities to perform tasks that demonstrate meaningful applications of their knowledge and skills while gaining better understanding of health issues related to underserved communities and polishing communications with patients.

"It's really important to know who your community is, no matter where you go as a health professional. Knowing the context of your patients' lives, knowing about their community and social determinants, adds to our ability to provide better medical care. The community becomes the teacher, and it is a powerful way to learn," says Dr. Armstrong-Coben.

The Office of Service-Learning participates in programs in the community, including a health fair, career exposure day, and a new partnership with the community-based organization Harlem Grown. In addition, the office will collaborate with the Center for Teaching and Learning to offer training for faculty to extend curricular service-learning and seminars involving community partners.

"I'd love for all students to experience some type of service-learning during their time here, to have service-learning embedded into the curriculum, and for the community to know us as a resource," says Dr. Armstrong-Coben. "The more people know about service-learning, the more students will have the opportunity to experience it."



The Office of Service-Learning sponsored an event in which VP&S students in the Class of 2018 led a health and wellness fair at the Fort Washington Men's Shelter in the Armory.

Program to Raise Diversity in Science Celebrates 15th Anniversary

The Summer Program for Underrepresented Students (SPURS) celebrated its 15th anniversary during the summer of 2017 with one of its largest classes in the program's history: 24 college students from around the country spent two months conducting research in the labs of 23 medical center faculty members.

SPURS was created in 2002 by Andrew Marks, MD, chair of the Department of Physiology & Cellular Biophysics and the Clyde and Helen Wu Professor of Medicine, as a way to increase the number of biomedical researchers drawn from underrepresented and economically disadvantaged groups.

SPURS has provided research opportunities to 236 students. Of the alumni who have graduated from college, 40 percent are pursuing or have received advanced degrees. Three SPURS alumni now hold faculty positions.

A diverse biomedical research workforce is crucial to producing the best science and addressing the medical needs of an increasingly diverse nation, says SPURS co-director Monica Goldklang, MD, assistant professor of medicine. Even though underrepresented students earn 21 percent of undergraduate degrees, they receive only 8.5 percent of the nation's research doctoral degrees. At the faculty level, only 8 percent of research positions are held by African-Americans or Hispanics.

"We're intervening at what we think is a critical time," says SPURS alumnus Michael Holsey, a Columbia graduate student who has been coordinating the program since 2011. Many underrepresented students in college have the potential to become scientists, he says, but for various reasons few reach graduate school.

SPURS helps students in several ways. The opportunity to conduct research is a plus, because graduate schools favor applicants who have research experience beyond the classroom.

"As a low-income student, I don't think I would have had the opportunity to do



Participants in the 2017 SPURS program presented research at a poster session.

laboratory research without this program," says Priscilla Daboni, a 2017 SPURS participant from the University of Chicago, who investigated new drug candidates for treating asthma. "SPURS takes care of room and board [all participants are housed in Columbia University dormitories], and I only had to focus on doing the research."

SPURS is an intense research experience, showing students a path they can take to become a scientist, says SPURS executive director Jeanine D'Armiento, MD, PhD, professor of medicine. "Students tell us that their experience in the lab is eye-opening for them. The research they do is important, but it changes the way they think of themselves and their potential. They realize that they fit in."

For Columbia student Kaylee Wedderburn-Pugh, who worked on a cellular receptor linked to Huntington's disease, time in the lab gave her confidence. "The SPURS program allowed me to be part of a team that engages in cutting-edge translational research. In the program I have learned about lab procedures, engaged in independent research, and mentored students. The

entire experience has reinforced my decision to pursue an MD/PhD."

SPURS students also get the opportunity, through weekly seminars, to meet scientists from a variety of backgrounds. "To know that people who are very successful had to struggle earlier in life was very powerful," says Briana Davis, a SPURS student from North Carolina Central University who spent the summer investigating how the brain integrates taste and hunger. "As a black female student, it made a big impact on me to hear from a successful black researcher that he could keep his identity as a black man and do well. Without this program, I may not have had confidence to apply to Ivy League schools for graduate work."

Dr. Marks remains committed to ensuring the program's future. "Knowing how much the program has meant to so many students is a source of enormous pride and happiness," he says. "Simply put, SPURS provides opportunities that change lives."

SPURS is supported in part by a grant from the NIH and private donations that cover the costs of room and board.

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Bronx, NY

Mary Imogene Bassett Hospital
Cooperstown, NY

Stamford Hospital
Stamford, CT

Helen Hayes Hospital
West Haverstraw, NY

Lawrence Hospital
Bronxville, NY

FACTS & STATISTICS, FY18

MEDICAL SCHOOL ENROLLMENT, FALL 2017

Total medical school enrollment	643
Enrollment of in-state residents	165
Enrollment of international/nonresident students	23
Enrollment of men	325
Enrollment of women	318

ENROLLMENT BY YEAR

	MALE	FEMALE
First-year class	70	80
Second-year class	79	72
Third-year class	91	88
Fourth-year class	85	78
Total enrollment	325	318

MEDICAL SCHOOL ETHNICITIES

Nonresident aliens	23
Hispanic/Latino	79
Black or African-American, non-Hispanic/Latino	64
White, non-Hispanic/Latino	299
Asian, non-Hispanic/Latino	117
Native Hawaiian or other Pacific Islander, non-Hispanic/Latino ...	1
Two or more races, non-Hispanic/Latino	12
Race and/or ethnicity unknown	48

OTHER STUDENTS

MD/PhD students	116
PhD students	393
Other students (PT, OT, Nutrition, Informatics)	475

DEGREES GRANTED, FY18

MD	159
PhD	72
Doctor of physical therapy	82
MS in nutrition	81
MS in occupational therapy	55
Certificate in psychoanalysis	3

APPLICATIONS (ENTERING CLASS 2017)

Number of applicants	8,258
Number of applications considered	7,311
Number of applicants interviewed	1,035
Number of acceptance letters issued	285
Bassett Program applicants	629

FACULTY, 2017-2018 ACADEMIC YEAR

	FULL TIME	PART TIME
Clinical faculty	1,826	2,021
Basic sciences faculty	261	65

FACULTY HONORS

Nobel Prize in Medicine	3
National Academy of Sciences	22
National Academy of Medicine	48
American Academy of Arts and Sciences	26
Howard Hughes Medical Institute	9

FINANCIALS, FY18 (EXCEPT WHERE NOTED)

Budget	\$2.1 billion
Philanthropic support	\$154 million
Endowment	\$1.9 billion
Endowed chairs/professorships	279
NIH research support (FY 2017)	\$438.6 million

PRECISION MEDICINE: Promise (Being) Fulfilled

“

We can offer targeted therapies to home in on particular genetic features of the tumor.”

— Wakenda Tyler, MD



WHAT FINANCIAL FREEDOM MEANS TO TOMORROW'S DOCTORS

Students who before would have found it difficult to attend an Ivy League school now saw it as a possibility.”

— Hilda Hutcherson, MD

RIGHTING A WRONG:

David McDonogh, Denied Degree in 1800s, Receives Posthumous MD

“

By granting the MD degree posthumously to Dr. McDonogh, we add another name to the list of Columbians who have contributed to the VP&S legacy.”

— Lee Goldman, MD

