

Columbia Medicine

Columbia University College of Physicians & Surgeons

2017
Annual Report



WE DON'T JUST PRACTICE MEDICINE.
WE CHANGE IT.

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Going Outside the Four Walls

A community wellness center led by two P&S faculty members will strengthen initiatives in stroke prevention and mental health support. The center continues a longtime P&S tradition of expanding access to health care throughout the city.

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Through the ambitious NIH-funded *All of Us* program, P&S will help enroll 1 million Americans in a large-scale research effort to identify ways to prevent and treat disease based on individual differences in lifestyle, environment, and genetics.

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



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On the Cover

The cover is the second of three 2017 commemorative covers that celebrate the 250th anniversary of Columbia's medical school. This cover recalls the design influences from the middle part of the school's 250 years, from the mid-1800s to the early 1930s. Illustration by Ben Johnston.

2017 Annual Report

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JORG MEYER

P&S: 250 Years Strong

At this year's alumni reunion gala in May, Ron Cohen'81 regaled fellow alumni and guests with his portrayal of Samuel Bard. Dressed in period attire, Dr. Cohen took us back to the 1770s to remind us of the historic beginnings of what is now the College of Physicians & Surgeons. Known then as the King's College medical faculty, P&S has survived mergers, faculty insurrections, wars, and several moves around New York City. That the school—the second medical school established in the Colonies and the first to grant the MD degree—is still here to celebrate its 250-year anniversary is testament to the perseverance of the multiple generations of faculty and administrators who worked hard to raise the bar on medical education, patient care, research, and service to our neighborhood, city, and nation.

The latest achievements in those missions are described in the pages of this year's annual report.

- Stem cell research that is expanding through the Columbia Stem Cell Initiative
- Our many community programs, including a new community wellness center in Manhattanville that not only offers care to Harlem residents but also trains individuals to help their neighbors at risk for stroke or mental illness
- The latest developments in precision medicine and our role in a federal effort to enroll 1 million participants in the *All of Us* program
- The 250th Anniversary Scholarship Challenge and our goal of making medical school at Columbia debt-free for students who otherwise would need to borrow money to become physicians

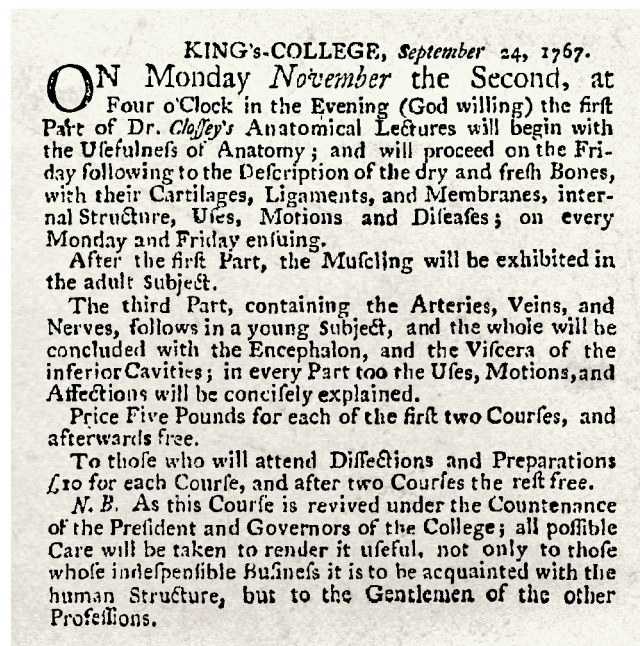
These articles and others not only document our success over the past year, but also celebrate the deep commitments to our missions throughout our history—a history we have been commemorating all year as we near November 2, the 250-year anniversary of the first day of classes at Columbia's medical school. At right is the announcement that ran in the *New York Gazette* in September of 1767.

In 1769, a few years after those initial classes, two men were awarded bachelor's degrees in medicine. Little is known about their careers. When one of those graduates, Robert Tucker, earned an MD degree a year later, he became the first MD recipient in the Colonies. The other 1769 graduate, Samuel Kissam, received his MD in 1771—the second awarded in the Colo-

nies. His family's connection to P&S includes 13 MD graduates between the years of 1771 and 1867.

The first graduation ceremony, in 1769, was an impressive event. Held on May 22 in Trinity Church in lower Manhattan, guests included civilian and military dignitaries as well as Governor Sir Henry Moore. Samuel Bard's speech that day was later published and is remarkable for his call for the graduates to raise the prevailing levels of medical ethics and to keep abreast of medical knowledge, two principles that remain part of the foundation of a P&S education today.

Those first classes offered in November 1767 cost much less than today's tuition, hence the need for a scholarship campaign to ensure that today's graduates pursue the medical careers of their dreams instead of careers that will enable them to pay back hefty loans. That campaign was jump-started by Diana and P. Roy Vagelos'54, who have asked Roy's fellow P&S graduates to help tomorrow's alumni fund their education through scholarships. They also have contributed to the education of our students by being the lead donors for the Roy and Diana Vagelos Education Center, which is now fully occupied and used by our students for classes or studying. The building, with its dazzling views of the Hudson River and the George Washington Bridge, has been popular beyond our wildest expectations and is a fit-





ting legacy to the generosity of Roy and Diana and the many other donors who made the building possible.

Among the materials developed to celebrate the 250 years of medical education at P&S is a graphic suggested by Donald Landry’83, chair of medicine. It is impossible to view the graphic, above, without being awed by the context of our 250 years in civilization. This hit home this year on the Fourth of July, when we celebrated the 241st birthday of our nation. It is humbling to recall that P&S is older than our country and that our founding dean was personal physician to the nation’s first president. We not only have made history with our medical contributions, we also are an important part of history.

As we continue to celebrate our history through special events this year, we also are committed to shaping the future through continuous retooling of our educational programs, growth of our research (our NIH funding increased by 17 percent last year), expansion of patient care programs, and increased engagement with our neighbors in our community and across the city. I invite you to peruse the pages of this report to learn more about the many ways we are making a difference.

With our clinical partner, NewYork-Presbyterian, we also are celebrating the renaming of our shared campus in Washington Heights as the Columbia University Irving Medical

Center, in honor of the commitment, loyalty, and generosity of Florence and Herbert Irving.

We are as proud of our medical school today as the founders must have been when they offered those £5 classes 250 years ago to launch the first generation of American-educated healers. Much has changed in education and patient care since then, but our core values remain unchanged. Our students, classrooms, and clinical facilities may look different, but our commitment to educating physicians and scientists, to caring for patients, to expanding medical knowledge, and to helping our neighbors has not diminished. We can only imagine how academic medicine may evolve over the next 250 years, but we remain confident that our ongoing commitment to excellence will ensure continued success—for our medical school, our medical center, and our graduates.

With best wishes,

Lee Goldman, MD, Dean
lgoldman@columbia.edu

Going Out's² the



Four Walls

Partnerships
Promote
Health Literacy
and Build
Community
Capacity

By Sharon Tregaskis

THINKSTOCK



Olajide Williams, MD, was a neurology resident at Columbia when an annual physical turned his world upside down. “I had just turned 30 years old and I was diagnosed with high blood pressure,” says the Nigerian-born neurologist. “I was fit, healthy. My only risk factor was a family history and being black.”

Now a P&S associate professor of neurology, director of acute stroke services at NewYork-Presbyterian, and co-director of the Center for Stroke Disparities Solutions in New York, Dr. Williams was lucky. His diagnosis came early, he could afford the medical care he needed, and his professional training had given him the health literacy he needed to keep his blood pressure in check: medical compliance, diet changes, exercise, and stress management.

Hypertension, which afflicts nearly one-third of all Americans and is an underlying factor in more than 70 percent of strokes, is a poster child of this country’s racial health disparities. Americans of Hispanic and African descent are more likely to develop hypertension, less likely to be diagnosed early (when treatment is most effective), and less likely to respond fully to the drugs that can manage the condition.

While on rounds at Harlem Hospital Center to evaluate and treat patients who had suffered strokes, Dr. Williams bore daily witness to hypertension’s ravages and its disproportionate insults in Harlem. Among people aged 35 to 45, the incidence of stroke is four times higher in blacks than in whites; of all races, African-Americans have the highest mortality rate from stroke.

And so even as the neurologist garnered millions of dollars in research funding from the NIH to better understand how hypertension and racial disparities conspire to kill African-Americans, Dr. Williams resolved to make prevention—starting with basic health literacy—a cornerstone of his career. He earned a

master’s degree in public health at Columbia’s Mailman School of Public Health, began giving speeches at local churches, and authored “Stroke Diaries: A Guide for Patients and their Families.” And with rapper Doug E. Fresh, he co-founded Hip Hop Public Health, a nonprofit that uses music and media to promote health literacy within economically disadvantaged under-resourced communities and has developed programs such as Hip-Hop Stroke, which is funded by the NIH and supported by the New York State Department of Health.

“I live in Harlem, I raised my children in Harlem, I have worked in Harlem my whole career as a neurologist, and I recognized the painful disparities that plague communities of color,” says Dr. Williams, who performs for schoolchildren, calling himself the Hip Hop Doc and wearing scrubs and an outsized golden chain yet speaking with the hint of a British accent acquired during his own youth at a boarding school in London. “I don’t think that we, as physicians, will be able to realize the type of outcomes that our local communities desperately need if we do not venture out of the four walls of our hospitals.”

Dr. Williams’ community-first approach will be front and center in Columbia’s new Community Wellness Center, slated to open later this year in the Jerome L. Greene Science Center on the University’s new Manhattanville campus. A partnership of the departments of neurology and psychiatry and ColumbiaDoctors—with operating support from the Mortimer B. Zuckerman Mind Brain Behavior Institute—the self-contained center will house two new initiatives: the Community Health Worker Stroke Prevention program, led by Dr. Williams, and Mental Health First Aid, or MHFA, led by Sidney Hankerson, MD, assistant professor of clinical psychiatry.

“There is a huge stigma around mental health in the black community,” says Dr. Hankerson. Dr. Hankerson’s passion for community-based interventions draws on personal experiences and NIH-funded studies focused on reducing race-based health disparities in the United States. The Baptist Church that Dr. Hankerson regularly attended growing up—where his father served as a deacon and his mother played piano for the children’s choir—was a second family to him. “I was raised in Fredericksburg, Va., where my church was a hub of educational, social, and civic engagement. We were a tight-knit community that helped people tackle familial challenges and supported one’s spiritual growth,” says Dr. Hankerson.

After completing undergraduate studies at the University of Virginia, Dr. Hankerson enrolled at Emory University School of Medicine. He did most of his clinical training at Grady Memorial Hospital, a large public hospital system which he calls “the Harlem Hospital of the South.” Fueled by his perception of substandard mental health services at Grady, Dr. Hankerson obtained a dual MD/MBA at Emory to understand how to translate best practices from business into research and clinical care.

Dr. Hankerson came to Columbia in 2009 after receiving a competitive NIMH-funded research fellowship. He studied how community-based interventions could address factors such as



HELP FROM OUR FRIENDS

HELPING PEOPLE IN THE COMMUNITY

The Chapman Perelman Foundation has made gifts of more than \$2.3 million to support programs in the Department of Psychiatry and new projects within the Institute of Genomic Medicine that apply precision medicine technology to improve diagnosis and ultimately treat mental illness. The Chapman Perelman Foundation is continuing support for a program it helped establish in 2014 to provide mental health services to victims of domestic violence in historically underserved communities. Working in tandem with the New York City Mayor’s Office to Combat Domestic Violence, Columbia provides mental health services at the New York City Family Justice Center in the Bronx. The new gift provides support to replicate this program at Family Justice Centers in each of New York’s five boroughs, allowing psychiatry faculty to continue providing comprehensive and integrated care for families affected by domestic violence.



JÖRG MEYER

lack of access to care, financial constraints, stigma, and distrust of health care professionals that contribute to African-Americans' low depression treatment rates. "When I first arrived at Columbia, I attended several community meetings with Dr. Williams, gave free mental health workshops, and talked to numerous community leaders," says Dr. Hankerson.

"I conducted several focus groups with pastors, who described depression as a 'silent killer' in the black community." Indeed, recent data from the Department of Health and Mental Hygiene show that clinical depression is the No. 1 cause of disability in New York City, but many people refuse to seek depression care. "The pastors' insights caused me to pursue their role in mental health care more in-depth."

A landmark national study found that more people contact clergy first for mental health problems compared with psychiatrists, psychologists, or general medical doctors. "Our clergy are trusted," says Dr. Hankerson. And yet, faith communities are often ill-equipped to address the needs of members struggling with depression and other mental health illnesses. "The notion that people of faith don't get depressed or struggle with other mental health problems creates tremendous tension that we have to work through. It's often counter-cultural for us to be talking about mental health in the church, but it's a great opportunity to reach people who need help." For example, Dr. Hankerson found

"It's one thing to provide resources to a community and another thing to help communities build capacity."

high rates of depression (20 percent) via a depression screening study among congregants at three black churches in New York City. The study was the first of its kind, and Dr. Hankerson was invited to the White House last year to discuss the results and his community-based program.

Dr. Hankerson is delivering the eight-hour Mental Health First Aid program, currently housed in Harlem's First Corinthian Baptist Church, in trusted community venues. His program draws on the strong social ties within communities of faith and the credibility of clergy to combat the stigma of mental health troubles and build connections among congregants and health care providers. "The churches have spearheaded the emotional needs of their congregations for years," says Dr. Hankerson.

Mental Health First Aid, which is available in English and Spanish, trains faith leaders—pastors, imams, deacons, and other clergy—and Harlem community members to assess and support someone experiencing a mental health crisis. Participants learn to detect signs and symptoms of depression and other mental illnesses, and the program provides a five-step

A 250-Year Commitment to Community

On May 16, 1769, the medical school now known as Columbia University's College of Physicians & Surgeons celebrated its first commencement. "No less than Life, and its greatest Blessing Health, are to be the Objects of your Attention," the school's dean, Samuel Bard, advised the graduates in his speech that day, "and would you acquit yourselves to your own Consciences, you must spend your Days in arduous Enquiries, after the Means of rendering those of others long and happy."

Language—not to mention capitalization—has changed significantly since those early years of Columbia's medical school, but the commitment to patients has only expanded with the times. Dr. Bard urged the two graduates, who received bachelor of medicine degrees that day, to pursue a life of inquiry, of integrity, and of compassion. He also issued a call for a public hospital. Later the same day, a subscription raised 1,000 pounds to establish New York Hospital, dedicated not only to the care of the city's poorest residents, but also to the study of disease in all its forms and the training of aspiring physicians.

Expansion of Dr. Bard's vision over the years has come in the form of clinics and programs—including many founded by students—that address the population's changing needs. Among the current student-

run clinics are the Columbia-Harlem Homeless Medical Partnership, a 10-year-old program that provides free health services in West Harlem, and the Columbia Student Medical Outreach, or CoSMO, which offers the uninsured in Washington Heights primary health care and access to social workers, health educators, Spanish-language interpreters, and nurses while instilling in students a lifelong commitment to the service of all who are in need.

The Community Wellness Center that will open in the new Jerome L. Greene Science Center on the Manhattanville campus will promote stroke and depression awareness, augmented by the efforts of specially trained health ambassadors. "Ours is not a unique endeavor," says Olajide Williams, MD, co-founding director of the new center. "Community medicine has been a long and deliberate endeavor over many years."

The Ambulatory Care Network—ACN—is just one example of providing care beyond the medical center's boundar-

ies. Established by New York-Presbyterian Hospital nearly 30 years ago to provide health care to the underserved communities of northern Manhattan, the network is composed of 14 primary care practices and more than 50 specialty clinics that care for children and adults by combining the resources of the hospital, the medical center's schools, and the community to enable residents to have the finest care without leaving their neighborhood.

Demand for ACN appointments is high, and new patients sometimes had to wait six to eight weeks to get an appointment. That prompted the ACN's Broadway practice medical director Rachana Gavara, MD, to make timely care a priority, boosting the availability of same-day and walk-in appointments.

Dr. Gavara, assistant professor of obstetrics & gynecology, has a particular interest in patients who are pregnant and have not received any prenatal care. "Initiating prenatal care early on provides an opportunity for early detection of problems during pregnancy and enables early intervention and prevention of complications and poor outcomes," says Dr. Gavara. To speed access for these patients, Dr. Gavara and her colleagues instituted a new policy to see any woman at more than 20 weeks' gestation within a week of her request for an appointment. "It has improved patient satisfaction, relieves the anxiety of the mother, and helps the staff, who are not seeing mothers for the first time late in the pregnancy."

In addition to emphasizing patient care, Dr. Bard early on envisioned the imperative for physicians to tailor their studies of disease to unique manifestations in different populations. "Every Country has its particular Diseases," he declared, "the Varieties of Climate, Exposure, Soil, Situations, Trades, Arts, Manufactures, and even the Character of a People, all Pave the Way to new Complaints and vary the Appearance of those, with which we are already acquainted."

The Irving Institute for Clinical and Translational Research has used part of its \$58.4 million NIH grant to strengthen its commitment to the neighborhood by creating new opportunities to engage community leaders and residents in the design and pursuit of medical research, including precision medicine. Led by José Luchsinger, MD, and co-directors Ana Abraidolanza, PhD, and Rafael Lantigua, MD, and associate director Elizabeth Cohn, RN, PhD, the Institute's Community Engagement Core Resource provides education, training, and off-campus space for health research and promotion activities and links residents to health information and services. "Community-based participation in research allows us to know more about how medical knowledge is generated," says Dr. Luchsinger, who also directs the Center on Aging and Health Disparities in the Division of General Medicine. "It's immensely important for research and for the community we serve."



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Rachana Gavara, MD



Sidney Hankerson, MD

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action plan for connecting people to appropriate support. Dr. Hankerson's team has trained nearly 100 people and scheduled monthly trainings for the remainder of 2017.

Dr. Williams' Community Health Worker Stroke Prevention program has a similar commitment to honoring the ways in which relationships between congregants and their clergy can boost access to health care. Now in its third training block, the program recruits volunteers from local faith communities for a free eight-week course during which they learn about stroke and cardiovascular disease risk factors, screening, and prevention and learn how to do CPR and motivational interviewing. "We train community health workers as resources within the community, to serve as health advocates, linkage to the health system, health educators, and counselors," says Dr. Williams, who plans to extend the program to additional faith communities in Harlem and to predominantly Latino churches in Harlem and Washington Heights. "We provide them with myriad skills required for them to act as the health foot soldiers in their churches." To make good on that promise, the program also helps participants earn New York state certificates that allow them to counsel and enroll fellow New Yorkers into health insurance plans. "It's one thing to provide resources to a community," he says, "and another thing to help communities build capacity."

In addition to offering stroke and mental health awareness programs, the Community Wellness Center will provide free blood pressure readings and cholesterol tests on weekdays and select weekends to all who walk in. Visitors will be given records of their

"It's often counter-cultural for us to be talking about mental health in the church, but it's a great opportunity to reach people who need help."

results plus information on ways to improve their health. Center staff will offer information—in English and Spanish—about free and low-cost clinical resources in the neighborhood and at NewYork-Presbyterian/Columbia University Medical Center.

Perhaps most importantly, the programs housed within the center will address a key and long-standing obstacle preventing access to appropriate health care among African-Americans—that of mistrust of mainstream medical science and health care in general. "We know that people of color—African-Americans and Latinos—are disproportionately affected by chronic medical conditions, such as high blood pressure, diabetes, depression, anxiety, and stroke," says Dr. Hankerson. "This is going to be an amazing opportunity for collaborations, for the development of new partnerships with scientists, physicians, psychologists, and, most importantly, among members of the West Harlem community to really identify how we can provide the best care, delivered in a culturally sensitive way, and how we can positively impact the lives of people in West Harlem." ♦

Elizabeth Chute contributed reporting to this article.



BLOOD BORNE

From Bone Marrow Transplant Discoveries
to Modern-Day Stem Cell Science,
Columbia Investigators Propel Research
to Enhance Patient Care

By Sharon Tregaskis
Photographs by Jörg Meyer



Known as the first responders of the circulatory system, hematopoietic stem cells, or HSCs, lie in wait deep within our bone marrow and leap into action in response to injury or disease. Studying these cells may offer new treatment for cancer and immune system disorders and also help us understand the mechanisms of aging in general.

Emmanuelle Passegué, PhD, has devoted her career to revealing the cellular and molecular processes controlling HSC activity during homeostasis and addressing the changes that culminate in bone marrow malignancies and physiological aging. Using a combination of mouse models and human patient samples, she seeks to reveal the genes and biochemical signals that regulate their optimal function—how they kick-start cell production in the minutes and days after you give blood, for example, and what breaks down as we age, increasing our susceptibility to such conditions as chronic inflammation, anemia, and leukemia. Earlier this year, she celebrated the publication of three groundbreaking discoveries in *Nature* and also accepted an appointment as P&S Alumni Professor of Genetics & Development (in Rehabilitation & Regenerative Medicine) and director of the Columbia Stem Cell Initiative, a collective of research groups whose work runs the gamut from basic and translational research to clinical applications and ethics.

Like any first responder that leaps into action in a time of crisis, HSCs spend a fair amount of time just waiting around.

“Stem cells are deeply embedded in what we do with both regeneration medicine and precision medicine to find novel therapies that are tailored to the need of each patient.”

Professional first responders use those lulls to recuperate and prepare. So do HSCs—by going into a state of quiescence a lot like hibernation. And yet, over time, HSCs seem to accumulate errors. “HSCs self-renew and maintain themselves for life, which makes them one of the few blood cells that truly age,” says Dr. Passegué. “While they efficiently generate all mature blood cells in young individuals, they often fail with age, resulting in degraded blood production characterized by anemia, loss of immune response, and the development of blood cancers.”

Dr. Passegué and her team had a hunch that autophagy—the cellular cleanup and recycling process that earned a Japanese scientist the 2016 Nobel Prize in Physiology or Medicine—plays a part in the signaling process by which HSCs transition between quiescence and activation and maybe even holds the clue to how those aging-related errors accumulate. To test their hypothesis, they compared and analyzed features of HSCs

harvested from older mice with those harvested from younger knockout mice genetically engineered to not use autophagy.

The work—a collaboration of Dr. Passegué and her former colleagues at the University of California San Francisco’s Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research and an independent team at the University of Michigan—showed that autophagy has a previously unknown role as the gatekeeper for the process by which HSCs power down when they are not on duty. The team went on to demonstrate that loss of autophagy allows the accumulation of mitochondria running on overdrive, leading to changes in the epigenetic landscape of the HSC DNA and contributing to many dysfunctions associated with aging in this stem cell population. “This is very much at the front edge of the science being developed in the stem cell field,” says Dr. Passegué, “where we realize that to understand stem cell biology, we have to bridge to the epigenetics with organelle biology and cell metabolism.”

Dr. Passegué’s second *Nature* article reported observations on the mechanism behind leukemia development and drew on her long-standing interest in myeloid progenitor cells, which are more committed cells produced by stem cells that give rise to a restricted type of white blood cells, granulocytes and macrophages in this case. Using immunofluorescent staining of bone sections, the team—comprised of investigators from UCSF, Cambridge University, and the Dana-Farber Cancer Institute—mapped the process of myeloid cell differentiation in situ in the bone marrow cavity and identified a series of chemical signals produced by the bone microenvironment that drive an emergency hematopoietic regeneration response and are transiently activated following an injury but are hijacked during leukemia development. “Leukemia creates a perfect storm where mutations in HSCs cooperate with changes in the bone marrow microenvironment to transform what is normally a very controlled, emergency-stress response pathway into a never stopping mechanism for cancer cell production,” says Dr. Passegué. “This is a fundamental discovery, and we can now start thinking about how to attack this process with drug agents.”

Dr. Passegué’s third *Nature* publication revealed that the lung serves as a reservoir for hematopoietic stem cells and a site for production of platelets, which are essential for blood clotting. “The contribution of the lungs to platelet biogenesis is substantial, accounting for approximately 50 percent of total platelet production or 10 million platelets per hour,” wrote the team, comprised of Dr. Passegué, her former colleagues at UCSF, and collaborators at the University of California, Los Angeles. The discovery—a coup in a field so well tilled that basic discoveries rarely turn up anymore—has implications both for transplant medicine (think of the expansion of the field since cord blood harvest was demonstrated in the 1980s) and basic investigation, as well as treatment of thrombocytopenia, a condition characterized by low platelet counts and inability to stop bleeding.



Throughout her career, Dr. Passegué has toggled between basic and translational investigations, and that emphasis on integrating basic discoveries with their potential for clinical application infuses her vision for the Stem Cell Initiative. “You need the basic laboratory findings to push a treatment in patients,” says Dr. Passegué. “And despite the best understanding you have, you’ll observe something you don’t expect when clinical trials start and you’ll have to go back to the lab to understand it and keep moving forward.” Established in 2008 in the Department of Rehabilitation & Regenerative Medicine, the Stem Cell Initiative is now a stand-alone program with both a stem cell core research facility and a new flow cytometry core facility.

The Stem Cell Initiative is slated to move to a specially designed space in the Black Building in mid-2018, giving Dr. Passegué a busy slate of decisions to make about brick and

mortar, but she has made building the interpersonal connections among initiative members her top priority. An ambitious calendar of invited lectures, faculty seminars, work-in-progress talks given by trainees, an annual off-site scientific retreat, and informal happy hours can further spur the kinds of casual conversations and social connections that launch research collaborations and partnerships. It also provides a fertile ground to recruit the best new talent in the stem cell field to Columbia, which is also one of the key goals of the initiative. Says Dr. Passegué: “What really excited me about coming to Columbia was the possibility to develop and shape the stem cell program of a premier medical institution with such a luminary faculty pool and, of course, an outstanding hospital network.”

Despite the significant responsibilities associated with her own work and her duties to the Stem Cell Initiative, Dr. Passegué also knows she may have an additional role as an ambassador

Emmanuelle
Passegué with
Stem Cell Initiative
researcher
Evgenia V.
Verovskaya

A Long Road to Bone Marrow Transplants

When the eyes and lips of a 2-year-old Baltimore girl started swelling in June 1958, the girl's mother took her to the children's hospital. An anti-histamine reduced the girl's inflammation and the pair returned home. Six weeks later, the child's symptoms had grown far more worrisome: night sweats, vomiting, fatigue, and a persistent, low-grade fever.

This time, the doctors looked more closely, drew blood, and took an X-ray. Acute leukemia, they said. A poor prognosis. A decade earlier, the diagnosis would have been a death sentence. But then a handful of children with acute leukemia—all being treated in Boston—briefly achieved remission in response to a novel drug designed to block the action of folic acid in the production and maturation of blood cells, precisely the process that goes haywire in leukemia. The Baltimore toddler was given a similar regimen, but remission remained elusive. Each subsequent blood test was more ominous than the last and finally doctors proposed what amounted to a Hail Mary pass: Transfer the youngster and her identical twin to an experimental program at Columbia-affiliated Imogene Bassett Hospital in Cooperstown, N.Y., to transplant bone marrow from the healthy girl to her dying sister.

The hospital's physician-in-chief, hematologist E. Donnell Thomas, MD, oversaw their care at Bassett. As a medical student in Boston, Dr. Thomas had been witness to those first chemotherapy trials for pediatric leukemia. After a stint in Germany to fulfill his obligations to the Army Specialized Training Program that had financed his medical degree, he returned to Boston, a crucible for research in hematology, pediatric leukemia, and the emerging Cold War field of radiobiology. He had completed a postdoctoral fellowship investigating the cellular effects of radiation, established his own laboratory as part of Sidney Farber's nascent pediatric cancer institute, and, as chief resident at Peter Bent Brigham Hospital, managed postoperative care for the first human kidney transplant patient, in which a man received whole body radiation to suppress his immune system, then received an organ from his identical twin.

Public anxiety over the hazards of radiation poisoning—and a concomitant quest by physician-sci-

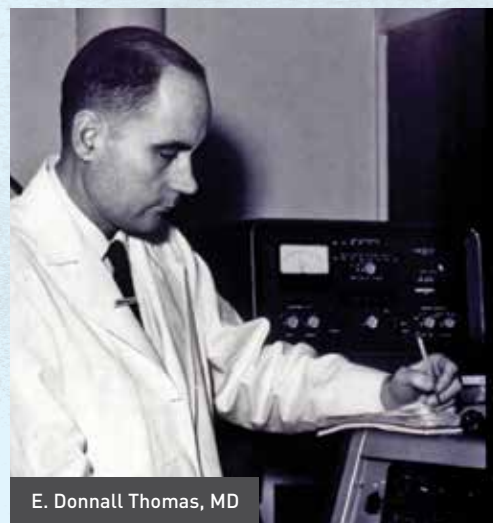
entists for treatments—had been building for more than a decade. Media reports on the Japanese survivors of the atomic bombs dropped on Hiroshima and Nagasaki detailed the devastating effects of radiation on the human body. In 1949, the Soviet Union detonated its first nuclear weapon, and in 1952, the United States tested its first hydrogen bomb. Federally funded scientists raced to find tools for the prevention or treatment of aplastic anemia and leukemia, the most likely diagnoses to afflict survivors of a large-scale nuclear event. Among inbred mice and guinea pigs, at least, bone marrow transplant was the most promising option.

By the time he arrived at Bassett in 1955, Dr. Thomas was intent on unlocking the clinical mechanics of bone marrow transplant in human beings, despite our far more complex and discordant genetic profiles than the lab animals in which the experimental technique had been developed. With fellow Bassett physician Joseph Ferrebee, MD, who was on a quest to refine the emerging field of kidney transplantation, Dr. Thomas acquired a research colony of outbred beagles and assembled a team to investigate why inbred animals tolerated skin, kidney, and bone marrow transplants while outbred animals encountered such complications as rejection and graft-vs.-host disease that made death a certainty. Confident they would solve the riddle, Dr. Thomas and his collaborators simultaneously began refining their protocols for harvest, purification, and storage of human bone marrow, practicing on cadavers, bones removed during surgical procedures, and even one another.

In 1956, the team launched a study funded by the U.S. Public Health Service and the Atomic Energy Commission. The results were published a year later in the *New England Journal of Medicine*. The six trial participants—all with end-stage cancer—received varying doses of radiation, followed by intravenous infusions of marrow from cadaverous, fetal, and living donors. And while

none responded badly to their transplants and a few even showed signs that the grafted marrow was making healthy blood cells, none were cured. The longest-surviving participant gained three months.

“In an atomic age, with reactor accidents, not to mention stupidities with bombs, somebody is going to get more radiation than is good for him,” Dr. Thomas wrote in a discussion of his *NEJM* report. “If infusion of marrow can induce recovery in a mouse or monkey after lethal radiation, one had best be prepared with this form



E. Donnell Thomas, MD

of treatment in man. The leukemic patient who needs radiation and bone marrow and the uremic patient who needs a spare kidney are the people who deserve immediate consideration. From helping them one will be preparing for the atomic disaster of tomorrow, and it is high time one did.”

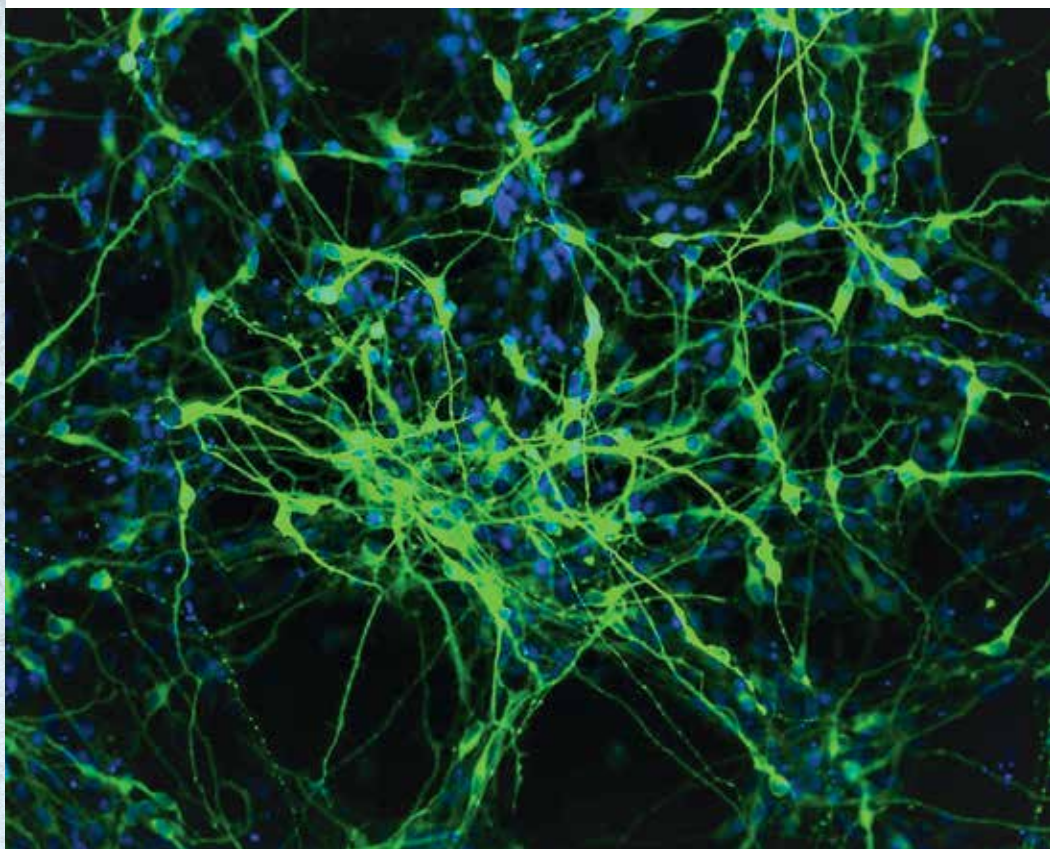
Following the first clinical trial, the little girl from Baltimore entered a specially designed room in Bassett Hospital, where she received total body irradiation to kill every vestige of diseased marrow, then received what doctors hoped would be a life-saving infusion of new marrow from her sister. The child celebrated her third birthday, underwent two cycles of irradiation and transplant, twice achieved remission followed by a relapse, and survived 166 days before leukemia claimed her life.

Immortalized in Dr. Thomas' 1959 report in the *Journal of Clinical Investigation*, the cases of

the girl from Baltimore and another from Florida demonstrated that bone marrow transplantation from a compatible donor was technically feasible and that the procedure could reverse the hematological devastation wrought by high-dose, total body irradiation. A cure for leukemia, however, remained out of reach.

So, too, did insights into the problems of transplantation for human bone marrow recipients without an identical twin. Over the next three decades, spanning his appointment at Columbia and posts in Seattle, Dr. Thomas continued circling from laboratory to clinic and back again. His team refined the protocols for irradiation preceding transplant and methodically unraveled the role of antigens within the blood, establishing the imperative for tissue matching and laying the groundwork for effective histocompatibility analyses in human beings. They developed post-transplant immunosuppression protocols to combat rejection and graft-vs.-host disease and documented that for patients who lived long enough, an effect known as donor-vs.-tumor disease could actually keep errant malignant cells in check, thus maintaining remission. Other scientists would discover that the stem cells that give rise to the components of the circulatory system could be harvested from fetal cord blood, as well as the bone marrow, and the procedure pioneered by Dr. Thomas came to be known as hematopoietic stem cell transplants, a nod to the biological actors who play the starring role in engraftment.

By 1990, when Dr. Thomas was awarded the Nobel Prize in Physiology or Medicine for his work, hematopoietic stem cell transplant was an established clinical treatment for leukemia and aplastic anemia. Today, more than 1 million people have undergone successful bone marrow transplants to treat an ever-increasing array of diagnoses. “In the field of bone marrow transplant, it took us 25 years to get from initial scientific discovery to patients,” says Emmanuelle Passegué, PhD, director of the Columbia Stem Cell Initiative. “And for the first 10 years, bone marrow transplants were risky as we worked out the best procedures. Now it’s so much safer—it’s the only curative approach for many blood cancers—but there was a long path to get there.”



ACHCHHE PAREL

to politicians to champion federal funding for basic and translational research that will help investigators achieve the clinical promise of stem cell research. It is a role for which she seems uniquely prepared after her years in California.

Dr. Passegué was a postdoctoral research fellow at Stanford University when California voters pledged in 2004 to self-fund stem cell research. Storm clouds had been brewing in Washington, D.C., for years, as Republicans took an increasingly hard line against the use of stem cell lines derived from embryonic tissue. The California voters enabled Dr. Passegué and her faculty colleagues at UCSF to continue their work when President George W. Bush issued his first veto in July 2006 to restrict taxpayer-funded research to a short list of existing embryonic stem cells, overriding a 2005 bill to lift restrictions on federal funding for human embryo stem cell research.

Bush-era restrictions eased under President Barack Obama, but with federal funding for basic discovery ever more limited, Dr. Passegué feels a growing sense of responsibility to champion the promise of the work she has pursued since she arrived in the United States in 2001. “Stem cells are deeply embedded in what we do with both regeneration medicine and precision medicine to find novel therapies that are tailored to the need of each patient,” she says. “I think my role now will involve way more advocacy and explaining why it’s so important that we continue to do this research.” ❖

iPSC-derived
dopaminergic
neurons





Columbia Helps Lead Ambitious New Precision Medicine Project

Your genes are vital determinants of your health, but they almost never act alone. Variants or mutations of specific genes might increase the risk of developing Alzheimer's disease, say, or heart disease, but they interact with myriad variables: other seemingly unrelated genes, clinical events such as infections, and environmental and lifestyle dimensions, including stress, diet, and sleep.

The complexity of teasing out the interplay among all these factors is mind-boggling to understand and describe. In 2016, the National Institutes of Health launched an initiative known as *All of Us* to start untangling the cause and effect. Even in this era of big data, it is an ambitious undertaking: Track multiple contributors to health in 1 million Americans from all walks of life over the course of a decade, then crunch the numbers to pinpoint subtle interactions among them. "The results of this initiative will reveal more about our individual differences at all levels and will create the opportunity for new and more effective treatments," says Tom Maniatis, PhD, director of Columbia's Precision Medicine Initiative, a collaboration of all of Columbia University and NewYork-Presbyterian Hospital.

Last July, Columbia, in partnership with Weill Cornell, NewYork-Presbyterian, and Harlem Hospital Center, received a major grant to enroll 150,000 people of the 1 million planned nation-

Getting Personal

By Alla Katsnelson

Illustrations by Joey Guidone

wide. The grant—for \$4 million initially but expected to total \$46.5 million over five years—is significant for the University on many levels, says David Goldstein, PhD, director of Columbia’s Institute for Genomic Medicine and principal investigator for the grant. “Just having a leading role in the country’s signature precision medicine effort is momentous. By participating in this national initiative we can help optimize the way the underlying science of precision medicine develops.”

The project also will have benefits for patients at Columbia and in New York City in general, he says. “It

is completely consistent with the institute’s and Columbia’s vision for bringing genomics as a starting point for precision medicine to the entirety of our patient population—it’s as simple as that.”

Boiled down to its essence, Columbia’s mandate from *All of Us* boasts a deceptively elegant simplicity: Enroll the requisite number of subjects from the New York institutions’ ethnically and economically diverse patient population, obtain their consent and basic information along with some biological samples, and send everything to the program’s national biobank at the Mayo Clinic in Roch-

P&S at 250:

James Wolff, Children’s Cancer Pioneer

James Wolff was a newly minted MD when he started his residency in the nascent hematology/oncology program at Boston Children’s Hospital led by Sidney Farber, MD, and Louis Diamond, MD. It was 1946, and at that time, treatments for acute leukemia—which disproportionately affects children—were nonexistent. Doctors referred to the disease as “a cataclysmic disaster of childhood,” and most youngsters died in a matter of weeks or months.

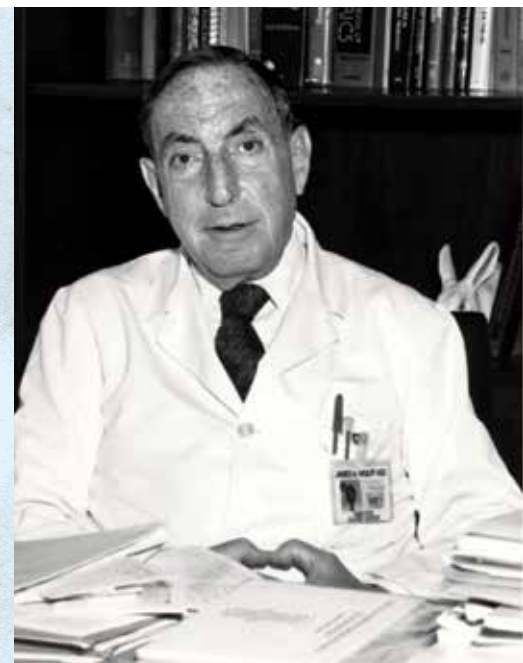
Oncologists had just begun feeling out the possibility of treating cancer with chemotherapy, but most of their early forays were a bust. Then, in 1947, Dr. Farber and Dr. Diamond—Dr. Wolff’s mentor in the residency program—began testing aminopterin, a folic acid antagonist, in children with acute leukemia. The treatment worked, propelling a third of the children in the trial into remission, and in 1948, Dr. Wolff was among the co-authors of a paper published in the *New England Journal of Medicine*, the first paper to show the efficacy of any cancer therapy in children. Shortly thereafter the group tested an even better, less toxic drug called methotrexate.

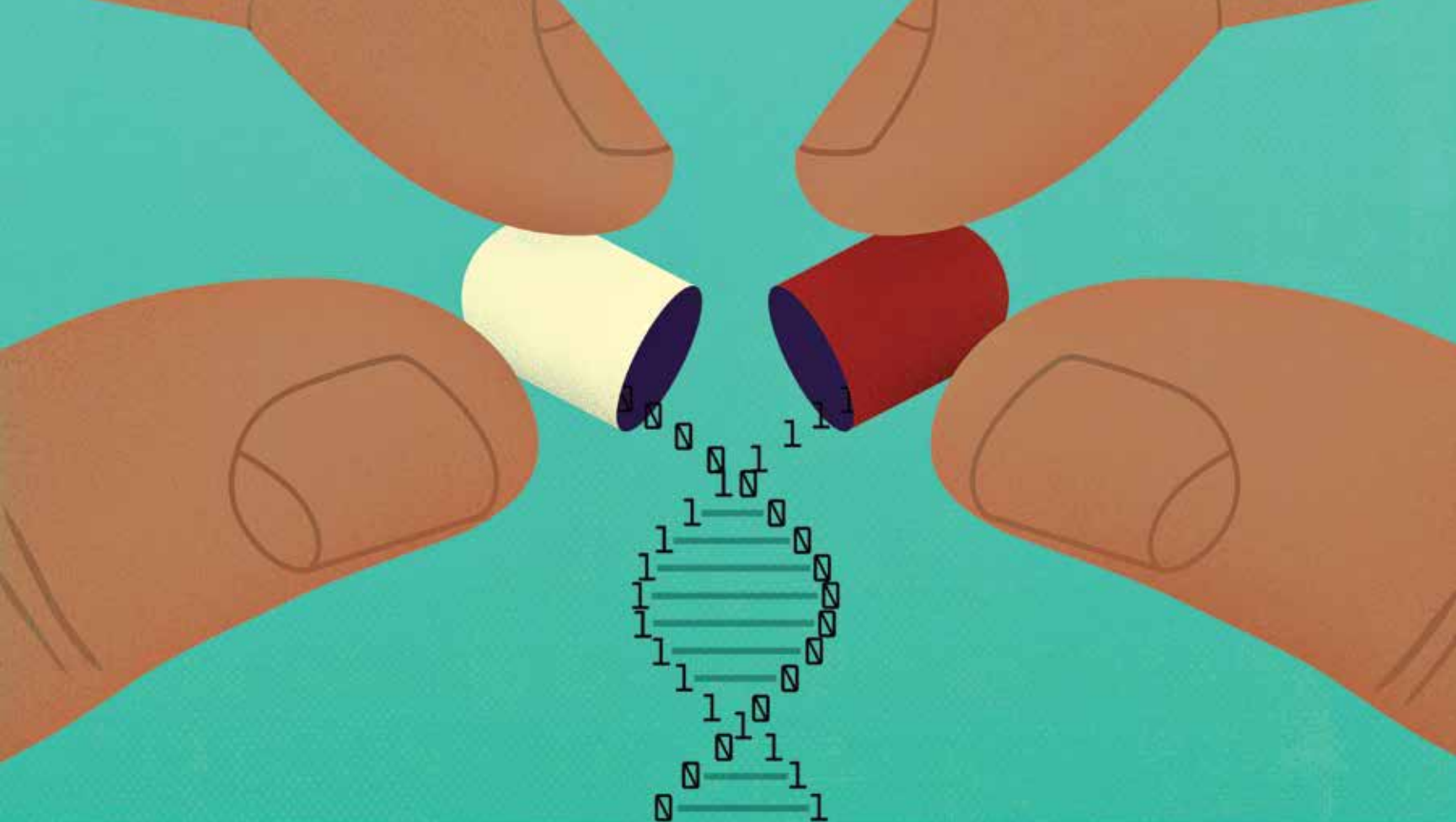
That year, Dr. Wolff finished his training and returned to his native New York City and joined Babies Hospital and P&S. He brought with him the scientific and clinical seeds of a hematological revolution, and they sprouted vigorously in his new professional home. Although large-scale collaborations were rare at the time, Dr. Wolff had a bent toward teamwork. In 1952, he and pediatric surgeon Thomas Santulli, MD, longtime chief of surgery at Columbia, established their Combined Tumor Clinic, one of the first of what is now a patient-care standard at academic medical centers nationwide: regularly scheduled conferences during which radiologists, pathologists, oncologists, surgeons, and other clinicians discuss the details of individual cases to integrate and optimize patient care. (The pair went on to establish a pediatric tumor registry, also one of the first in the world.)

Within a few years, Dr. Wolff, who died in 2012, became one of the eight founding members of the Acute Leukemia Chemotherapy Cooperative Study Group A. At the time, individual hospitals lacked the patient volume to conduct statistically rigorous trials of new therapies. The study

group set out to pool their patients, develop consistent methodologies for delivering therapies, and set criteria for determining treatment. In the mid-60s, Anneliese Sitarz ’54, a trainee of Dr. Wolff’s and longtime professor at P&S, published one of the first reports showing that solid tumors, too, responded to chemotherapy. Soon after, the study group expanded its mission and simplified its name, becoming the Children’s Cancer Study Group, and over the years its members’ joint efforts yielded dramatic improvements in the prognosis for Wilms’ tumor, Hodgkin’s lymphoma, and retinoblastoma. “It was the recognition of coming together and collaborating in a clinical trial group enterprise; that was really how therapy improved,” says Michael Weiner, MD, professor of pediatrics at P&S, who worked with Dr. Wolff in the 1970s.

The results of this coordinated approach have spread far beyond pediatric cancers: Many of the drugs that eventually became mainstay treatments for adult cancer were initially tested by the Children’s Cancer Study Group in pediatric patients. And the approach is still flourishing today. Now known as the Children’s Oncology Group, the study group launched by Dr. Wolff is an international network of more than 200 hospitals, universities, and cancer centers; the network continues to be the main vehicle for centralizing knowledge and clinical trial efforts in pediatric cancer. In the six decades since Dr. Wolff began his training, the five-year survival of pediatric cancer has gone from zero to some 80 percent, and half of all pediatric cancer patients are treated by Children’s Oncology Group-associated clinicians, suggesting that decades of collaboration have paid off.





ester, Minn. Scientists can then endlessly probe the resulting repository. The top-line idea, says Dr. Goldstein, is to combine these data with genomic sequencing to develop a method for state-of-the-art interpretation of everything each individual's genome can reveal. "We don't actually know how to do that interpretation right now," he says. "I'm really excited about taking that on as a challenge as we define Columbia's role in this project."

Investigators also need to create a means for clinicians to provide results to participants, says Wendy Chung, MD, PhD, the Kennedy Family Professor of Pediatrics (in Medicine), who directs the University's clinical genetics program and co-directs the molecular genetics diagnostics lab. "This is our first foray into something on this scale, a big deal for Columbia because we've never done anything on this scale," she says. "We need to help every patient who walks through our doors understand that he or she has the opportunity to be a part of the cures of tomorrow."

Ultimately, the idea is not just for clinicians and researchers to make discoveries and publish papers, but also to engage study participants with the research and help them learn about their health in actionable ways. For example, says Dr. Chung, a password-protected dashboard might allow *All of Us* participants to log in to review their basic health measures, like blood pressure or glucose levels, and assess other aspects of their health gleaned from their genomic and environmental and lifestyle data. "We have to realize that most of health is not happening at the doctor's office. We want people to make daily decisions that are going to sustain their health."

The NIH is still working out how data will be shared with participants, but Dr. Chung says communication must be done in a way that will benefit participants regardless of their economic or educational status. "Some of our underserved communities in New York don't have



HELP FROM OUR FRIENDS

ROY AND DIANA VAGELOS ADVANCE PRECISION MEDICINE

P. Roy Vagelos '54 and Diana Vagelos have given a lead gift of \$34 million to support the Columbia University Precision Medicine Initiative. Their vision and generosity will enable Columbia to build its resources in basic biomedical research to improve our fundamental understanding of diseases. Their gift will support P&S faculty, programs, research, graduate students, equipment, and infrastructure within precision medicine. Faculty support will include start-up grants, bridge funding, and aid in faculty recruitment and retention.

Full Circle

Data Repositories Yield Insights to Fuel Clinical Care

DiGeorge syndrome may be one of the most common genomic disorders you have never heard of. Affecting as many as one in 2,000 babies, the syndrome was first described nearly 60 years ago and spans a cluster of symptoms that can include heart defects, speech delay, intellectual disability, immunodeficiency, and low serum calcium. The assortment of seemingly unrelated health issues that children face can be dizzying for families. About a third of all patients also have congenital renal system malformations that can result in kidney failure.

Over the past six decades, researchers have traced DiGeorge syndrome to deletions within a segment of chromosome 22 that carries some 40 genes and have tied certain hallmarks of the disease, such as cardiac malformations, to specific genes within that stretch of DNA. But the deranged biochemical codes that yield other DiGeorge symptoms have eluded investigators.

In January, Simone Sanna-Cherchi, MD, the Paul Marks Scholar Assistant Professor of Medicine, and his colleagues identified the glitch behind DiGeorge-associated kidney malformations by conducting genomic analyses of 2,666 children born with congenital kidney and urinary tract abnormalities. The study, co-authored by Ali G. Gharavi, MD, the Jay Meltzer, MD, Professor of Nephrology and Hypertension (in Medicine), chief of nephrology, and a member of Columbia's Institute for Genomic Medicine, led the team to a nine-gene region within the DiGeorge stretch on chromosome 22. To home in on the offending glitch, they tested all nine of the genes in both zebrafish and mice. Their results, published in the *New England Journal of Medicine*, revealed that errors in the gene *CRKL* are the main driver of kidney disease among children previously diagnosed with DiGeorge syndrome. Indeed, a full 1 percent of all kidney malformations—including those not previously associated with DiGeorge syndrome—could be traced back to *CRKL*.

Being able to trace kidney malfunction back to that particular stretch of chromosome 22 is life-changing, says Dr. Sanna-Cherchi, especially for children not previously diagnosed with DiGeorge syndrome, which is also associated with symptoms that emerge later in life, including schizophrenia and Parkinson's disease. "So you can see how this knowledge would help patients understand their future diagnostic and disease management options."

Dr. Sanna-Cherchi's study, which mined a global database of pediatric kidney patients, is just one example of the crucial role such repositories are likely to play as the field of precision medicine develops. Investigators at Columbia expect such work will get a major boost as the NIH's signature precision medicine study, *All of Us*, goes online. The massive database will integrate genomic, environmental, and other individual factors to allow researchers to connect the dots among variations that protect our health and those that contribute to illness.

For more than a decade, Columbia investigators have been proving the worth of smaller-scale and more defined databases like the one that led to Dr. Sanna-Cherchi's DiGeorge discovery. Wendy Chung, MD, PhD, the Kennedy Family Professor of Pediatrics (in Medicine), has been a leader in SPARK, a project that aims to build a basic knowledge base about autism by collecting genomic, clinical, and environmental data on 50,000 individuals with the condition. Tom Maniatis, PhD, the Isidore S. Edelman Professor and Chair of Biochemistry & Molecular Biophysics at P&S and co-founder of the New York Genome Center, has worked extensively with the center's ALS Consortium, which brings together multiple academic medical centers, clinicians, scientists, and industry partners to combine clinical and functional genomics with bioinformatics in the study of the mechanisms behind Lou Gehrig's disease. Consortium members have pledged to complete whole genome sequencing and analysis of 3,200 clinical samples in a quest to enhance early diagnosis and effective drug discovery. "Columbia has a leading role in establishing this framework that will apply state-of-the-art clinical and functional genomics together with bioinformatics to study ALS disease mechanisms. This is our best hope for answering questions about this devastating illness," says Dr. Maniatis.



Simone Sanna-Cherchi, MD

JORG MEYER



access to the technology of Silicon Valley, and they don't think about things the same way," she stresses. "We have to make sure we are getting everyone to the table."

Undoubtedly, the success of *All of Us* hinges on recruiting a diverse group of participants that represents the genetic and environmental experiences of the country. But it also relies on creation of a data infrastructure that integrates all participating institutions across the country. Developing that infrastructure is a project in its own right, and last year Columbia received a grant of \$13.7 million to play a central role in launching the NIH's Data and Research Support Center, a collaboration being led by Vanderbilt University.

So far, clinical data for *All of Us* consist of a collection of electronic health records. Eventually, data will include extensive surveys filled out by participants and even data from wearable technologies that track information such as sleep and exercise in real time, says George Hripcsak, MD, the Data and Research Support Center grant's principal investigator at Columbia. Dr. Hripcsak has a lot of practice with enormous databases of health information: He is the principal co-investigator of an international program called OHDSI (Observational Health Data Sciences and Informatics), a network of 60 patient databases worldwide that contain hundreds of millions of patient records. His team developed a platform called OMOP (Observational Medical Outcomes Partnership) to stan-

dardize enormous reams of clinical data within OHDSI, and the NIH initiative will run on OMOP as well.

At first, says Dr. Hripcsak, the clinical and sociomedical data that OMOP stores will be used to probe the demographics of *All of Us* participants to confirm that they are statistically representative of the nation's diversity. But like Dr. Goldstein, Dr. Hripcsak stresses that the magic will really kick in when those data can be combined with

"We need to help every patient who walks through our doors understand that he or she has the opportunity to be a part of the cures of tomorrow."

participants' genome sequences. Imagine that 100 people share the same genomic quirk, but only a small fraction of them get the disease associated with it. "Then we can ask what factors seem to influence whether people who have that genomic characteristic get the disease or not," Dr. Hripcsak says. "Is it your food, your environment, other diseases you have, or drugs you are taking?"

Researchers acknowledge that learning more about "All of Us" may result in more questions than answers at first, but they are convinced that only by looking at the bigger picture will the precision needed for individual health come into focus. ❖



THEN & NOW

A 250-YEAR LEGACY OF TRAINING DOCTORS FOR LIFELONG EDUCATION

By Sharon Tregaskis

The opening of the Roy and Diana Vagelos Education Center at the beginning of the Fall 2016 semester marked the launch of a new era. The 100,000-square-foot, 14-story glass tower at 171st Street and Haven Avenue incorporates technologically advanced classrooms, myriad naturally lit collaboration spaces, and a modern simulation center. “Our new education building will ensure that Columbia continues to train superior doctors and researchers, educated in the latest techniques, as medicine continues to evolve rapidly throughout the 21st century,” said Dean Lee Goldman, MD, when it opened. “The building also will allow us to centralize key activities in a state-of-the-art facility that reflects our commitment to providing world-class instruction and a superb learning environment for students.”

The structure and the activities students now pursue within the Vagelos Education Center are a far cry from the earliest days of what is now the College of Physicians & Surgeons. But the facility exemplifies the vision that has been a cornerstone of medical education at P&S throughout its 250-year history—a commitment to improving teaching methods and creating rigorous curricular standards intended to cultivate a commitment to lifelong discovery necessary in a profession where change is the only constant. “Do not therefore imagine that from this time your studies are to cease,” said the founder of the school, Samuel Bard, when he addressed graduates at the first commencement. “Far from it. You are to be considered as but just entering upon them; and unless your whole lives are one continued series of application and improvement, you will fall short of your duty.”

The medical profession in the 1700s was in serious need of constant improvement. Before Columbia began a medical faculty, New York’s lieutenant governor, himself a physician-scientist, had signed the first significant law of the British province. “No person shall practice as a Physician or surgeon,” the law read, “before he shall first be approved in Physick or surgery and approved or admitted.” At the time, medical practice in New York City was something of a free-for-all with traveling quacks peddling dubious remedies, a scant four dozen self-proclaimed physicians, no licensing body, and no common standard by which to judge the preparation of those who aspired to work in the field. The new law was unenforceable—there being no mechanism to pursue complaints—but it laid the philosophical groundwork for the founding, in August 1767, of a program in medical education at King’s College, later known as Columbia University.

At the school’s inception, students could choose among multiple degrees, from a relatively rudimentary bachelor’s in medicine to the MD. Modeled on the medical courses of study offered at Edinburgh and Oxford, all of



Opposite Page: P&S Class of 1894. Above: P&S Class of 2021.

the degrees required that students attend a full course of lectures—approximately nine months each—on anatomy, surgery, the theory and practice of medicine, chemistry, materia medica (pharmacy), and midwifery, taught by six of the city’s most eminent physicians. To earn an MD, students were also required to demonstrate competence in Latin, attend a second year of lectures, pass two rounds of oral examinations, complete a year of apprenticeship, and author an original research report on “some medical subject.”

Course fees for the program—paid directly to the faculty in the form of tickets for entry to their lectures—exceeded the median annual income at the time and represented only a fraction of the total cost for training, which also included diploma fees, papers and books, and, for students whose families did not reside in the city, room and board. Not surprisingly, few registered to pursue degrees. During the American Revolution, the fledgling school’s facilities at King’s College were commandeered for military activities, so educational programs were suspended.

The institution struggled for several decades to regain its footing after the war, and when the College of Physicians & Surgeons was officially incorporated as a separate, proprietary medical school in 1807, educational standards for the MD were noticeably weakened. While two years of coursework remained a requirement, the time allotted to lectures was cut in half to just four months. Students were permitted to arrange with faculty to participate in anatomical dissection, though there was neither a laboratory nor a clinic dedicated to the activity and body procurement was notoriously conducted under cover of night. They were also permitted to observe clinical work at

the New York Hospital, the Almshouse, or the Lying-In Hospital, but such pursuits were optional and not required as part of a student's education.

The subsequent decades were roiled with faculty infighting, but the college—whose faculty and students had been merged into P&S in 1814—grew in step with the burgeoning city, acquiring new facilities and hopping ever northward up the island of Manhattan. In 1848, Bellevue Hospital was reorganized and became an additional site for student clinical experience. In 1851, the New York state legislature expanded access to cadavers for anatomy instruction by lifting restrictions that had previously allowed dissection only of unclaimed bodies of criminals. In 1880, P&S President Alonzo Clark, an 1835 graduate of the school, oversaw significant improvements to the curriculum and admis-

sions standards. Lectures were expanded to seven months, prerequisites were established, grades introduced, and written exams instituted.

Throughout the late 1800s and early 1900s, P&S continued to expand. The course of study increased to three years in 1888 and four years in 1894. A series of gifts from William H. Vanderbilt and his family spurred construction of a new facility for the college on 10th Avenue and 59th Street, as well as multiple clinics and hospitals in the neighborhood where students were welcomed for demonstrations and hands-on training. Dedicated laboratory space increased and the basic sciences grew in prominence. Mandates for clinical training were instituted, with every student required to serve daily at either the Sloane Hospital or the Vanderbilt Clinic. In 1911, the college embarked on its

A Campaign to Eliminate Student Loans

As part of its 250th anniversary celebration, P&S hopes to raise money to create a permanent endowment for scholarship support, allowing all students with financial need to have that need met by scholarships rather than by loans. Known as the P&S 250th Anniversary Scholarship Challenge for Endowed Financial Aid, the fund was seeded with a \$25 million gift from P. Roy Vagelos⁵⁴ and his wife, Diana.

The commitment to making a medical education affordable stretches back to the 1807 founding of the College of Physicians & Surgeons, before it became part of Columbia. Founder Nicholas Romaine, MD, envisioned a plan to accept one student from each New York state county who would receive free entry to all lectures. The presidents of the state's myriad medical societies were invited to designate recipients who were "of good moral character, of promising talents, and of diligent habits." An 1808 report about the program noted that "a respectable number of young gentlemen, from the interior of the state, are now attending the lectures. These, when they return to their respective homes, we trust, will diffuse a taste for science in medicine, and excite a laudable emulation in their brethren of the profession; and thus contribute to rescue the practice of medicine generally from the hands of ignorance and imposture."

The program lasted just two years before scholarships were eliminated and student fees increased to boost faculty salaries. To make up for the loss, the college frequently offered free supplementary courses open to all students, and alumni were allowed free admission to all courses.

The award of monetary prizes to medical students for best thesis, best exam score, and best clinical report began in the late 1850s. Chief among them was the Harsen Prize, a bequest of Jacob Harsen Jr., an 1829 P&S graduate. Three decades later, P&S began awarding annual grants and fellowships. The first—bestowed in 1887—was the result of a bequest from Alonzo Clark, an 1835 P&S graduate, longtime professor, and former president of P&S who directed his gift to "promoting the discovery of new facts in Medical Science." In 1891, the Alumni Association created three research fellowships; recipients were required to produce a thesis at the end of their terms.

In the early 1900s, P&S tuition spiked by 25 percent. Students petitioned Columbia's trustees to protest the hike, and financial relief followed in the form of several new scholarships. To choose recipients, the faculty formed a scholarship committee to draft regulations, review applications, and recommend awards.

From the first announcement of scholarship applications published in the 1904-1905 catalogue of the medical school, the financial aid program grew with new gifts and support from Columbia University. The Committee on Scholarships received 51 applications for 1907-1908 and awarded aid to 37 medical students. In the mid-1920s, the university also created a loan fund that helped medical students bridge tuition increases.

The preferred protocol for financial aid was to award scholarships for first- and second-year students and to save loans for third- and fourth-year students who would be in a better position to pay back the loans sooner, allowing the funds

to be used to help other students pursue their medical education.

Federally sponsored student loans became widely available after Congress passed the Higher Education Act in 1965, and by 1984, more than 86 percent of students graduated in debt. As medical education costs rose, financial aid expanded in the form of both scholarships and loans. Systems have developed to support students receiving aid. P&S, for example, has a financial planning office that has created an 18-page financial aid handbook to help medical students navigate the process for seeking loans, scholarships, grants, and work study. The office also has a robust program for debt management and financial literacy to assist graduates with navigating the maze of rules around the various loan programs and to assist with integrating student loan repayment in the context of their overall financial planning during postgraduate training.

Today, up to half of all P&S students need financial support—loans and scholarships—to complete their medical education. The 2017 scholarship challenge hopes to enable students with financial need to receive P&S scholarships only rather than a combination of loans and scholarships. This debt reduction program would make P&S more affordable and make it easier for graduates to pursue career options in fields such as primary care, research, and community service. That would ensure P&S's leadership position in medical education for the next 250 years, while changing not only our institution but the landscape of medicine in perpetuity.

— Sharon Tregaskis and Carol Perloff

partnership with Presbyterian Hospital to create what became the Columbia-Presbyterian Medical Center, the first in the nation to embody the concept of a teaching hospital within a multifaceted health services center.

Today, aspiring physicians at P&S complete a four-year curriculum that toggles constantly between theory and hands-on practice in preparation for residency training. With its “study cascade,” a mix of ramps, elevators, stairwells, and open gathering spaces that link lecture halls and classrooms throughout the facility, the Vagelos Education Center is designed to promote that dynamic interplay. The facility also boasts 13,000 square feet of dedicated training rooms in which students practice everything from taking a patient’s medical history to performing a physical exam, all under the tutelage of faculty preceptors. And unlike students in earlier centuries who gained their clinical education in amphitheaters where an impoverished patient exchanged privacy for the price of medical care in front of a large group, today’s students begin their clinical training with computerized, whole-body mannequins and specially trained actors who play the part of “standardized patients.” The specially equipped rooms in which students work with these practice patients feature high-fidelity sound and video recording equipment to enable faculty and students to review a practice encounter in search of opportunities for improvement.

Such features are all part of the latest curricular advance at P&S, an emphasis on coaching, a persistent cycle of practice and feedback intent on cultivating students’ capacity not only to develop specific skills, but also to accept and reflect on input about their performance and seek out additional opportunities for enrichment. As one of 10 schools participating in a five-year pilot study funded by the Association of American Medical Colleges, P&S has the opportunity to test its coaching methods as the path to helping students master 13 core entrustable professional activities, tasks all trainees are expected to perform independently on the first day of residency. “You can’t learn how to do basic procedures overnight or in the last week of medical school; you have to learn what are the basic principles and then practice them over time with some kind of supervision, some kind of assessment, and opportunities for remediation if you need them,” says Jonathan Amiel, MD, associate dean for curricular affairs at P&S and site principal investigator for the pilot study.

“Medical school is a formative period for both the educational and the emotional aspects of becoming a physician, and we aspire to immerse students in optimal learning environments.”

The program pairs first-year students with a coach responsible for teaching their first-year Foundations of Clinical Medicine seminar. Students continue meeting with their coach throughout the remainder of their time at P&S. Says Dr. Amiel, “Our aim is to establish a trusting relationship between the coach and the student so that the student can come to the coach over the course of his or her medical school education with the feedback that they’ve gotten and try to interpret it so that they can create their own short-term and long-term learning plan.”

Such collaborative and supportive approaches to medical education promise a further benefit, according to research published this year in JAMA.



HELP FROM OUR FRIENDS

A SCHOLARSHIP CHALLENGE FOR THE 250TH ANNIVERSARY

P. Roy Vagelos '54 and Diana Vagelos pledged \$25 million in matching funds to kick off the P&S 250th Anniversary Scholarship Challenge. Donors who make gifts designated for endowed scholarships can double their impact by receiving a 1:1 match for gifts of \$50,000 to \$1 million and planned gifts of \$100,000 to \$1 million. With the goal of raising an additional \$25 million for endowed scholarships, this challenge launches an ambitious effort by P&S to eliminate student loans by providing needed financial support through scholarships only, rather than a combination of scholarships plus loans. More than \$10 million toward the goal has been raised to date through the generosity of alumni, faculty, and friends of P&S.

According to a review of existing research, conducted by Lauren Wasson, MD, assistant professor of medicine at P&S, the high rates of burnout and depressive symptoms among medical students compared with their peers in other graduate training programs and the general population can be buffered by features of the medical school learning environment. “Medical school is a formative period for both the educational and the emotional aspects of becoming a physician, and we aspire to immerse students in optimal learning environments,” says Dr. Wasson. “We seek evidence-based ways to cultivate well-being among students during this time and in preparation for the rigorous careers ahead of them.” Among the supportive features Dr. Wasson and her collaborators identified are pass/fail grading, accessible mental health programs, wellness programs that teach stress-reduction skills, group-based faculty advising and mentoring programs, and a curriculum with increased clinical time.

With the move to the Vagelos Education Center, increased emphasis on coaching and clinical skills preparation, and consolidation of student services in the same facility where students spend the most time, P&S continues to seek ways to improve medical education while acknowledging that work remains. Adds the JAMA review’s senior author, Karina W. Davidson, PhD, vice dean for organizational effectiveness, “With so few published studies on the medical school learning environment, there is clearly a need for more rigorous research on an issue that could greatly impact future physicians.” ❖

SCREENINGS AND TREATMENTS

Eye Care on the Go

Columbia ophthalmologists are taking the fight against blindness to the streets with a mobile tele-ophthalmology unit. The unit, which hit the roads in June, will provide free screenings for at least 2,000 people every year at locations in the Bronx, Washington Heights, and Harlem. In



Eye care van

addition to screening for glaucoma, cataracts, macular degeneration, and diabetic retinopathy, the mobile team, under the leadership of Lama Al-Aswad, MD, associate professor of ophthalmology, will assess patients for common risk factors for eye disease, such as diabetes, hypertension, and obesity.

SMA Progress

The first and only effective treatment for spinal muscular atrophy, a neurodegenerative disease that causes progressive muscle wasting, has been approved, thanks to the leadership of several research centers, including the SMA Clinical Research Center at Columbia, directed for many years by Darryl C. De Vivo, MD, the Sidney Carter Professor of Neurology and professor of pediatrics. The

first child in the world to receive the drug, known as nusinersen, was enrolled in a Columbia clinical trial led by Claudia A. Chiriboga, MD, professor of neurology and of pediatrics. A vital clue that led to the drug's development came in 1999 when Umrao Monani, PhD, then a postdoc at Ohio State and now associate

professor of pathology & cell biology (in neurology), discovered that turning on a normally silent gene had the potential to prevent the disease. Dr. Monani also created an SMA mouse model that was crucial to enabling scientists to test the drug in preclinical studies. With an effective treatment for SMA now available, Wendy Chung MD, PhD, the Kennedy Family Professor of Pediatrics (in Medicine), is directing a pilot screening project in seven New York City hospitals to identify SMA cases soon after birth. New work in mice, led by George Z. Mentis, PhD, associate professor of pathology & cell biology and of neurology, was published in *Nature Neuroscience* and showed that SMA may be partly due to abnormalities in the synapses that connect sensory neurons and

motor neurons and also showed that increasing the activity of these synapses can alleviate symptoms of SMA.

Tummy Trouble

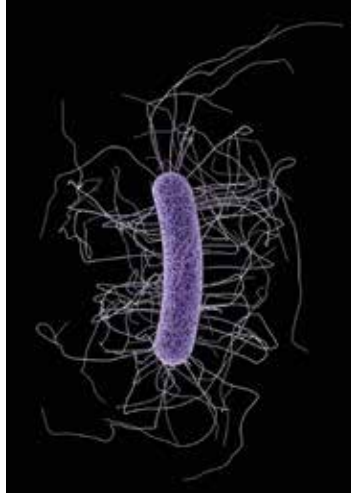
Children with celiac and other gastrointestinal problems now have greater access to treatment with the opening of the Phyllis and Ivan Seidenberg Center for Children's Digestive Health. The center features a multidisciplinary team of specialists who care for children with both simple and complex illnesses. The center, located in the Morgan Stanley Children's Hospital, was made possible by a \$15 million donation from Phyllis and Ivan Seidenberg. "The expertise available in this center is unparalleled," says team leader Joel Lavine, MD, PhD, professor and vice chair of pediatrics, "in terms of quality, access, and interdisciplinary care."

New Blood

Blood transfusions are one of the most common procedures in U.S. hospitals, but new research reveals that older blood could



AMELIA PANICO



CENTERS FOR DISEASE CONTROL AND PREVENTION

pose a threat to hospitalized patients. In a study led by Steven Spitalnik, MD, professor of pathology & cell biology, and Eldad Hod, MD, associate professor of pathology & cell biology, the difference in outcomes between one-week-old and five-week-old blood was negligible, but six-week-old blood released large amounts of iron into recipient bloodstreams. The authors recommend that the FDA lower the maximum blood storage limits from six weeks to five weeks, due to concerns that excessive iron could exacerbate infection.

Crowdsourcing

Some women with endometriosis suffer a wide variety of symptoms, from debilitating menstrual cramps to painful sex, while others experience no pain at all. The breadth of symptoms can lead to under-diagnosis and treatment differences. As part of a broader citizen science project known as Citizen Endo, Noémie Elhadad, PhD, associate professor of biomedical informatics, launched “Phendo,” an iPhone app for women to share their day-to-day experiences. Data collected through the app will be examined for clusters that can develop a temporal picture of endometriosis.

Infection Control

According to a study by Daniel Freedberg, MD, assistant professor of medicine, in *JAMA Internal Medicine*, hospital patients who inhabit a bed previously occupied by someone being treated with antibiotics may be at increased risk for infection with *Clostridium difficile*, the most common cause of diarrhea, even

if they did not receive antibiotics themselves. Antibiotics are a known risk factor for *C. diff* infection, which leads to about 27,000 deaths annually in the United States.

Breathe Easy

Most people with asthma are able to control their symptoms with medications, but 5 percent to 10 percent have persistent symptoms and are more likely to have life-threatening asthma attacks. A new treatment offered by Columbia’s interventional bronchoscopy program is helping many dramatically reduce their steroid use and, in some cases, discontinue steroids completely. Known as bronchial thermoplasty, the treatment works by applying mild heat to the smooth muscle in a patient’s airways, which shrinks the tissue and prevents it from swelling and constricting the airway. Faculty who perform the procedure at CUMC are William Bulman, MD, associate professor of medicine at CUMC; Keith Brenner, MD, assistant professor of medicine at CUMC; and Roger Maxfield, MD, professor of medicine at CUMC.

Respiratory Relief

Pulmonary arterial hypertension, considered a death sentence just a generation ago, is a rare but serious disease that occurs when the walls of the lung’s arteries stiffen and narrow, raising blood

pressure in these arteries. The lungs can be permanently damaged, and the heart must pump harder to push blood through the lung, leading to life-threatening heart failure in children and adults. The Pulmonary Hypertension Comprehensive Care Center at Columbia is one of the first—and among the largest—in the world established to treat the disease. For the past 30 years, the center has been at the forefront of research, including major clinical trials, landmark genetic discoveries, and pioneering treatments such as mechanical support for patients who fail advanced medical therapy. Matthew Bacchetta, MD, associate professor of surgery and the center’s surgical director, is among only a few surgeons in the world who perform surgery for chronic thromboembolic pulmonary hypertension, which happens when thrombi build up in the pulmonary arteries.

Teen Talk

In New York City, young girls with gynecological concerns have a unique program to turn to: the Pediatric and Adolescent Gynecology Program at the Morgan Stanley Children’s Hospital at NewYork-Presbyterian/Columbia. Many gynecologists are not comfortable seeing younger patients and few specialize in the field, says program director Beth W. Rackow, MD, associate professor of obstetrics & gynecology and of pediatrics. The NYP/Columbia program now sees more than 50 new patients each month, providing medical and surgical care for a wide variety of gynecologic conditions.

CANCER

Oncology Care Model

CUMC has joined nearly 200 physician group practices and 17 health insurance companies nationwide in the Center for Medicare & Medicaid Innovation’s Oncology Care Model, a five-year pilot program developed by the CMS Innovation Center and advanced by the Affordable Care Act. The person-centered approach promotes coordination among patient services and encourages practices to lower costs through episode- and performance-based payments that reward high-quality care. “This initiative is a necessary approach to making cancer care as accessible and affordable as possible,” says chief of hematology and oncology Gary K. Schwartz, MD.

Improving Chemo

More than 50 types of soft-tissue sarcomas have been identified. These cancers arise in fat, muscle, nerves, joint linings, blood vessels, and the other tissues that connect, support, and surround various body structures. A multicenter clinical trial by senior author Gary K. Schwartz, MD, chief of hematology and oncology, and published in the *Lancet* has shown that adding olaratumab, a novel monoclonal antibody therapy, to traditional chemotherapy for metastatic sarcomas increases median survival by nearly a year.

Mixed Signals

Cross talk among cells in the stomach sets the stage for gastric tumors, according to research by a multinational team. Timothy C. Wang, MD, the Dorothy L. and Daniel H. Silberberg Professor of Medicine, was senior author of the findings published in *Cancer Cell*.

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The team's mouse studies identified the cascade of chemical signaling that creates the conditions for carcinogenesis within the gastric epithelium. The team also demonstrated that by interrupting the signaling, which involves both acetylcholine and nerve growth factor, tumor growth could be halted, providing a potential new target for treatment and prevention.

Sleeping Beauty

The molecule p53 is a potent cancer-fighting factor. But sometimes, it goes to sleep, which allows tumors to grow unchecked. A research team at the Herbert Irving Comprehensive Cancer Center has implicated a protein called SET, which is often found in excess in cancer cells, in p53 inactivation. By reducing SET levels, the team was able to revive p53 and halt cancer growth. Nature published the full report by Wei Gu, PhD, the Abraham and Mildred Goldstein Professor of Pathology & Cell Biology and in the Institute for Cancer Genetics, and Donglai Wang, PhD, a postdoctoral research scientist in Dr. Gu's lab.

BRCA1

Mutations in the BRCA1 and BRCA2 genes have been linked to breast, ovarian, and fallopian tube cancers. According to a new report, BRCA1 mutations also may be associated with heightened risk for an aggressive type of uterine cancer, called uterine serous carcinoma. Published in JAMA Oncology, the work, led by Catherine A. Shu, MD, assistant professor of medicine, with colleagues at nine academic medical centers, addressed an open question about the role

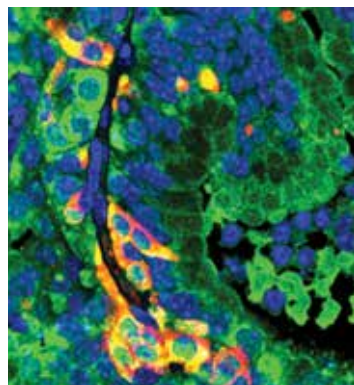
of BRCA in uterine cancer; women with BRCA1 mutations may benefit from prophylactic hysterectomy along with risk-reducing salpingo-oophorectomy.

Web of Life

iCAGES, a computational tool with a user-friendly web interface, can rapidly predict which genes are implicated in an individual's cancer and recommend treatments. The development team, led by Kai Wang, PhD, associate professor of biomedical informatics and director of clinical informatics at the Institute for Genomic Medicine at CUMC, published its work in Genome Medicine.

Key to Resistance

Among people with aggressive prostate cancer, treatment with anti-androgen therapy, the standard of care, may make things worse in some patients. Research in mice reveals that the problem is *SOX11*, a genetic mutation that reprograms tumor cells to resist treatment, according to a Cancer Discovery report co-authored by Cory Abate-Shen, PhD, the Michael and Stella Chernow Professor of Urological Oncology, and Michael M. Shen, PhD, professor of medical sciences. Their work could help identify which patients should avoid anti-androgen therapy and develop new treatments for people with advanced prostate cancer.



HEARTFELT

Bad Medicine

A team of data scientists has discovered eight distinct combinations of medications that can lead to a potentially fatal heart drug interaction. The team, led by Nicholas Tatonetti, PhD, assistant professor of biomedical informatics, developed a novel method for detecting drug interactions and tested it by mining two independent data sets: a government database of reported drug side effects and a university hospital archive of patient records. Among the findings, published in the Journal of the American College of Cardiology, the antibiotic ceftriaxone and heartburn



medication lansoprazole may trigger abnormal heart rhythms and, in rare cases, sudden death.

Best in Class

Pediatric cardiac patients at NYP/Columbia have the lowest risk-adjusted mortality risk in New York state, according to

an analysis of outcomes for patients under age 18 who had surgery from 2010 to 2013 to correct congenital heart defects. Although Columbia had the highest number of cases (1,558), the hospital's adjusted mortality rate was just 2.26. Columbia has long paved the way for advancements in pediatric cardiology care. The first successful pediatric heart transplant was done by Columbia doctors in 1984. Columbia is one of only a few centers in the United States to offer hybrid cardiac surgery—combining conventional surgical methods with catheter-based techniques—for infants and children.

Beyond the CABG Patch

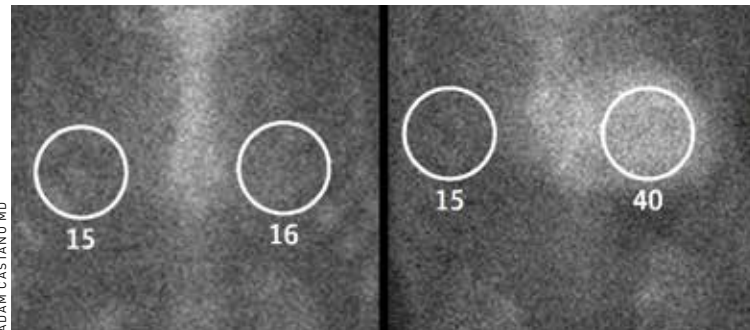
Coronary artery bypass graft surgery, or CABG, has long been the preferred treatment for left main coronary artery disease, in which the artery that supplies oxygen-rich blood to most of the heart muscle is clogged with atherosclerotic plaque. A major international study known as EXCEL (Evaluation of XIENCE versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization), involving 126 medical centers in 17 countries, has found that less-invasive drug-eluting stents are safer and as effective for many patients as bypass surgery. Gregg W. Stone, MD, professor of medicine and director of cardiovascular research and education at the Center for Interventional Vascular Therapy, was first author of the EXCEL report in the New England Journal of Medicine.

PICTURE THIS

Good Image

A condition known as transthyretin-related cardiac amyloidosis, or ATTR-CA, can be detected through imaging—without a biopsy—before it progresses to

ecule known as TRPV6, which is implicated in the disease process. The work, published in *Nature*, reveals that the surface of TRPV6 is lined with negative charges, a configuration that attracts posi-



Tc 99m scan of patient without amyloidosis, left, and with amyloidosis, right

advanced heart failure. The finding in *JAMA Cardiology* emerged from a multicenter study led by Mathew S. Maurer, MD, the Arnold and Arlene Goldstein Professor of Cardiology. “This is a huge advance for patients with ATTR-CA, which is under recognized and often misdiagnosed,” said co-first author Adam Castano, MD, a cardiology fellow at P&S. “Many people with ATTR-CA are frail and elderly, so being able to avoid a biopsy, even when it can be done with a less-invasive catheter-based procedure, is a significant step forward.”

X-ray Vision

Our bodies use dietary calcium to regulate a variety of processes from muscle contractions to brain signaling; dysregulation of that process has been linked to cancer, kidney disease, and Crohn’s disease. Alexander Sobolevsky, PhD, associate professor of biochemistry & molecular biophysics, has captured X-ray crystallography images of a calcium-shuttling mol-

tively charged calcium ions. The work could lead to novel therapies and diagnostic tools for diseases that are caused by a malfunction in calcium absorption.

Big Picture

Using a new lightning-fast camera paired with an electron microscope scientists have captured images of one of the smallest proteins in our cells to be “seen” with a microscope. Science published the images, produced by a team led by structural biologist Filippo Mancina, PhD, associate professor of physiology & cellular biophysics. The protein, called STRA6, sits in the membrane of our cells and is

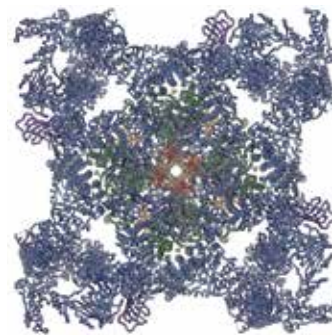


FILIPPO MANCINA LAB

responsible for transporting vitamin A into the cell interior. Vitamin A is essential to all mammals and is particularly important in making the light receptors in our eyes and in the placenta and fetus where it is critical for normal development.

Visual Appeal

Several P&S investigators dedicated their efforts to revealing the unseen, developing new techniques for discovery in the process. A team led by Alexander Sobolevsky, PhD, associate professor of biochemistry & molecular biophysics, obtained the first detailed images of interactions between the AMPA receptor and molecules that regulate chemical signaling in the brain. The findings, published in *Neuron*,



may help elucidate the mechanisms of conditions such as Alzheimer’s and Parkinson’s diseases, epilepsy, and schizophrenia. Using high-resolution electron microscopy, other researchers uncovered new details of the structure and function of an intracellular channel that controls the contraction of skeletal muscle. Andrew R. Marks, MD, the Clyde’56 and Helen Wu Professor of Molecular Cardiology (in Medicine) and professor and chair of physiology & cellular biophysics, led the team, which published its results in *Cell*.

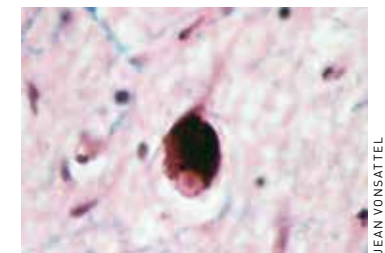
BRAIN HEALTH

Pregnancy and Stroke

Pregnancy-associated stroke occurs in an estimated 34 out of 100,000 women, and doctors have long believed that older women were at greater risk for the condition. A study published in *JAMA Neurology* by Joshua Z. Willey, MD, and Eliza C. Miller, MD, assistant professors of neurology, shows that while the incidence of stroke is rising among all women, younger women are at higher relative risk of pregnancy-associated stroke. Among the causes of pregnancy-associated stroke, preeclampsia develops in about 3 percent to 8 percent of all pregnant women. A second study by the same authors, published in the journal *Stroke*, revealed that stroke risk factors among women with preeclampsia include urinary tract infections, chronic high blood pressure, and clotting or bleeding disorders.

Immune Response

Parkinson’s disease may be caused in part by autoimmunity, according to a study published in *Nature* by scientists at P&S and the La Jolla Institute for Allergy and Immunology. The study, co-led by David Sulzer, PhD, professor of neurobiology, provides the first direct evidence linking a malfunctioning immune system to Parkinson’s disease. The findings could lead to a diagnostic test to identify individu-



JEAN VONSATTEL

2017 Year in Highlights

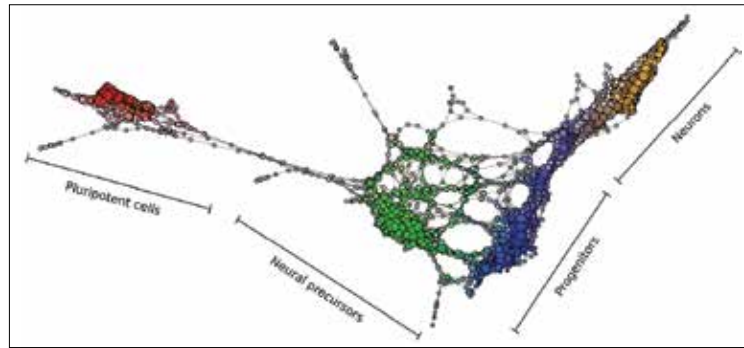
als at risk or in the early stages of the disease and prompt research into immunotherapy approaches to symptom management in more advanced stages of the disease.

Hear, Hear

A team that studies sensory processing in the brains of electric fish has stepped from sea to land. A new study examines how the auditory system cancels out sounds due to our own movements and behavior. By measuring the neural activity of mice during licking behavior, Nathaniel Sawtell, PhD, professor of neuroscience, revealed that mice use the dorsal cochlear nucleus, or DCN, to “tune out” sounds generated by their own behavior. His team’s report, published in *Nature Neuroscience*, sheds light on how the brain focuses attention on behaviorally relevant stimuli and may lead to insights into common hearing disorders such as tinnitus.

Crystal Ball

Columbia computational biologists have created a tool to reconstruct how a cell may differentiate. Rooted in the mathematical field of topology, the algorithm, dubbed single-cell topological data analysis (scTDA), provides a road map that offers detailed insight into how stem cells give rise to specialized cells. scTDA uses the RNA sequences of individual cells to reconstruct their underlying developmental trajectories and capture the progression of different transcriptional programs in time. *Nature Biotechnology* published a report by the team, led by Raul Rabadan, PhD, professor of biomedical informatics (in systems biology), and Tom Maniatis, the Isidore S. Edelman Professor and



Topological representation of four cellular populations during motor neuron differentiation

RABADAN LAB

Chair of Biochemistry & Molecular Biophysics.

Risk Management

Antidepressants are an important treatment for depression, but one with risks to be managed. According to a report in *JAMA Psychiatry*, speech and language disorders were significantly higher among children whose mothers purchased antidepressants at least twice during pregnancy. The study, by a team at P&S and the Mailman School, suggests that the incidence of speech disorders was also higher in offspring of mothers who were diagnosed with depression or other psychiatric disorders but did not take an antidepressant. P&S psychiatry faculty who co-authored the study: Alan Brown, MD; Myrna M. Weissman, PhD; Jay A. Gingrich, MD, PhD; and Andre Sourander, MD. A paper in *Nature Medicine* by Patricia Ducy, associate professor of pathology & cell biology, revealed the mechanism by which antidepressants lead to bone loss and demonstrated that, in mice, beta blockers can avert the damage.

Balancing Act

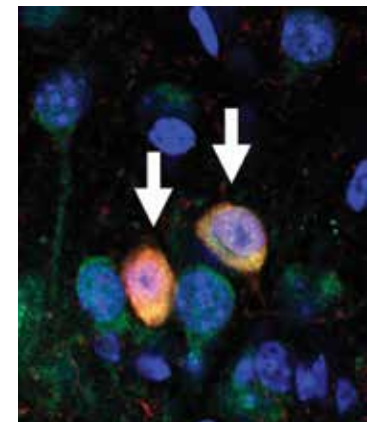
Scientists with Columbia’s Mortimer B. Zuckerman Mind Brain

Behavior Institute have identified a gene that allows neurons that release serotonin to evenly spread their branches throughout the brain. Without this gene, these neuronal branches become entangled, leading to haphazard distribution of serotonin and signs of depression in mice. These observations shed light on how precise neuronal wiring is critical to overall brain health while also revealing a promising new area of focus for studying psychiatric disorders associated with serotonin imbalance, such as depression, bipolar disorder, schizophrenia, and autism. Tom Maniatis, PhD, the Isidore S. Edelman Professor and Chair of Biochemistry & Molecular Biophysics, led the team, which published results in *Science*.

Network Theory

Two new studies offer insight into the genetic and neurological functions of schizophrenia. A *Translational Psychiatry* paper by Catherine Clelland, PhD, assistant professor of pathology & cell biology, reveals that people with a specific genotype may be more receptive to the mood stabilizer valproate than others. The research suggests that people with two copies of the “Val” variant

of the COMT gene, which breaks down dopamine in the brain, will benefit from the elevated levels of proline elicited by valproate. In a paper in *Neuron*, a team led by Jordan Hamm, PhD, a postdoctoral researcher with co-author Joseph Gogos, MD, PhD, professor of physiology & cellular biophysics and of neuroscience, describes how a breakdown in synchronized behavior of a small group of neurons could produce the disordered thinking and perceptions associated with the disease. The research was conducted in two mouse models of the disease: a genetic model (mice carrying a mutation predisposing to schizophrenia in humans) and a pharmacological model (mice



given regular doses of ketamine, an anesthetic that can produce psychotic behavior in humans). The findings support the idea that schizophrenia arises from disruptions in small networks of neurons acting on their own instead of as a coherent group.

Tangled Up

Revelations in neurological functioning may lead to improved treatment and diagno-

sis of patients with Alzheimer's. Research from the lab of Karen Duff, PhD, professor of pathology & cell biology, describes how a toxic protein called tau can spread through the brain, jumping among neurons via the extracellular space that surrounds them. The discovery, reported in *Nature Neuroscience*, suggests that studying the spread of tau may enable doctors to prevent Alzheimer's from developing into severe dementia. Another study, in *Neuron*, indicates that an accumulation of tau causes the spatial disorientation in many Alzheimer's patients. Dr. Duff suspects that disorientation originates in an area of the brain known as the entorhinal cortex, which controls memory and navigation. Although both studies were conducted in mice, further research may yield diagnostic methods using navigation-based cognitive tests and the possibility to treat disorientation with deep-brain stimulation or light-based therapy.

Suicide

Patients discharged from American psychiatric hospitals face a high risk of suicide within 90 days of discharge, according to a study by Mark Olfson, MD, professor of psychiatry and epidemiology, in *JAMA Psychiatry*. Patients with depression had the highest rate of suicide within 90 days of discharge, followed by patients with bipolar disorder, schizophrenia, and other mental disorders. Dr. Olfson's analysis indicates that psychiatric patients remain ill at the time of discharge, highlighting the need for continuity of care and treatment even after patients leave the hospital.

INSIDE INSIGHTS



Hair regrowth after ruxolitinib treatment of a patient with alopecia areata

Good Hair

Seventy-five percent of people with moderate to severe alopecia areata, an autoimmune disease that causes patchy and, less frequently, total hair loss, had significant hair regrowth after treatment with ruxolitinib in a clinical trial overseen by Julian Mackay-Wiggan, MD, associate professor of dermatology and director of the department's Clinical Trials Unit, together with Angela M. Christiano, PhD, the Richard and Mildred Rhodebeck Professor of Dermatology and professor of genetics & development. The study was published in the *Journal of Clinical Investigation/Insight*. By the end of treatment, average hair regrowth was 92 percent. Already approved by the FDA to treat bone marrow malignancies, ruxolitinib is a JAK inhibitor; it interrupts the dominant inflammatory signaling pathways responsible for hair follicle dormancy in alopecia areata.

Kidney Function

For many patients, an initial diagnosis of "acute kidney injury" may have been inaccurate, according to a study co-authored by Jonathan Barasch, MD, PhD, the Samuel W. Lambert Professor of Medicine and professor of pathology & cell biology. Published in the *Journal of the American Society of Nephrology*

and the *Lancet*, the analysis of patient records suggests that the current method of assessing kidney function may be misleading; ongoing studies are underway to identify more accurate biomarkers, including NGAL, which is being evaluated around the world.

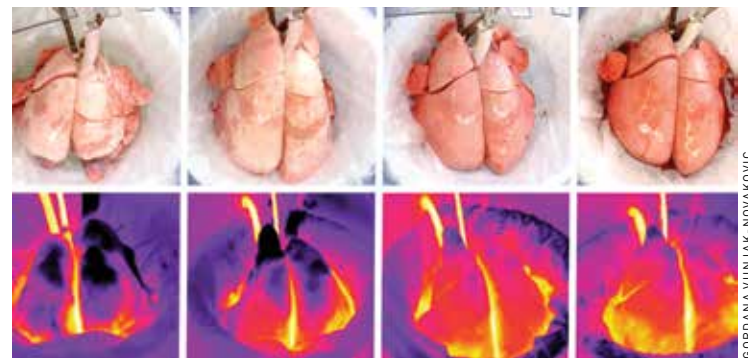
Pulmonary Promise

Breakthroughs in respiratory technology may help tens of thousands of Americans with pulmonary illnesses breathe easier. A new transplantation technique has for the first time maintained a fully functional lung outside the body for several days. Although transplantation is the only definitive treatment for patients with end-stage lung disease, transplant organs are highly perishable. In a study published in *Nature Biomedical Engineering*, researchers detailed the cross-circulation platform that maintains

a donor lung for 36 to 56 hours. The study was led by Gordana Vunjak-Novakovic, PhD, University Professor, the Mikati Foundation Professor of Biomedical Engineering, and professor of medical sciences, and Matthew Bacchetta, MD, associate professor of surgery. The lead authors of the study were John O'Neill (bioengineer) and Brandon Guenthart (surgical fellow). In other research, a tool called a lung organoid, a tiny 3-D structure made of living cells that mimics the features of a real lung, will help identify the pathogens of pulmonary diseases. As outlined in a *Nature Cell Biology* paper, the team's "organ in a dish" allows scientists to replicate models of human diseases, test drugs, and regenerate damaged tissue. The research was led by Hans-Willem Snoeck, PhD, professor of medicine (in microbiology & immunology).

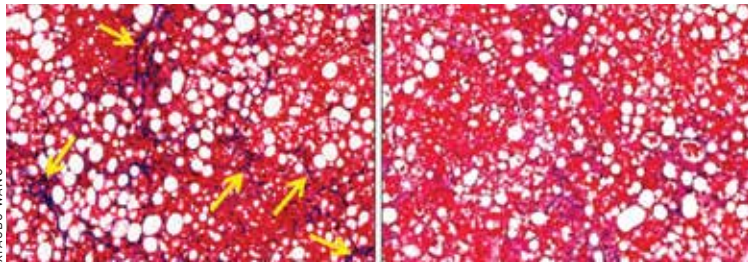
Scar Tissue

Thirty percent of U.S. adults have a benign condition, known as nonalcoholic fatty liver disease, in which excess fat fills the liver. In one in five people with the disease, the liver becomes inflamed and crisscrossed by fibrous scar tissue,



Photographic and thermographic images of injured lungs recovered with extracorporeal cross-circulation

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Mice were fed a diet rich in fat and sugar until they developed nonalcoholic steatohepatitis-like features in their livers. On the left, staining reveals the most important feature of the condition—fibrosis—as dark linear structures (indicated with arrows). On the right, fibrosis reverted when TAZ was silenced in the mice.

and liver cells start dying. The condition, known as nonalcoholic steatohepatitis, increases the risk of liver failure and liver cancer, but no drugs are available to slow or stop the disease. In a paper in *Cell Metabolism*, Xiaobo Wang, PhD, associate research scientist, and Ira Tabas, MD, PhD, the Richard J. Stock Professor of Medicine and professor of pathology & cell biology, identified TAZ, a factor in liver cells that is responsible for initiating fibrosis; by inactivating TAZ in mice, they were able to reverse fibrosis.

Autoimmune Kidney Disease

In a *PLOS Genetics* report, Krzysztof Kiryluk, MD, the Herbert Irving Assistant Professor of Medicine, and colleagues reported new genetic clues to understanding IgA nephropathy, or Berger's disease, an autoimmune kidney disease and a common cause of kidney failure. In a genome-wide scan of 2,633 individuals, the study described two genetic loci with large effects on the abnormal glycosylation of circulating IgA, an inherited risk factor for IgA nephropathy.

The Nose Has It

A study published in the *Journal of Clinical Investigation/Insight* reveals that intranasal vaccination

promotes long-term immunization against both common and novel strains of influenza. The study, led by Donna Farber, PhD, professor of surgical sciences in surgery and in microbiology & immunology, found that mice treated with one brand of intranasal vaccine produced T cells that protect against multiple strains, including those not present in the vaccines. Unlike traditional flu vaccines, which produce antibodies that are often outrun by rapid mutations of the initial virus, intranasal vaccines promote the production of “lung-resident” T cells to protect against multiple viral strains.

Boning Up

A hormone secreted by bone cells can suppress appetite, according to mouse studies conducted by Stavroula Kousteni, PhD, associate professor of physiology & cellular biophysics. The hormone, lipocalin 2, activates neurons in the brain that have been previously linked to appetite suppression. The findings, published in *Nature*, reveal a previously unknown mechanism for regulating the body's energy balance and could lead to new targeted therapies for the treatment of obesity, type 2 diabetes, and other metabolic disorders.

IT'S IN THE GENES

Precision Genomics Lab

The Institute for Genomic Medicine and the Department of Pathology & Cell Biology have launched a Precision Genomics Laboratory to enhance constitutional genomic diagnostics, research, and education. The lab is jointly led by David Goldstein, PhD, director of the Institute for Genomic Medicine, and Kevin Roth, MD, PhD, chair of pathology & cell biology. The lab will combine emerging genomics research with clinically actionable genomics testing to provide patients, families, and physicians with information to help them make health decisions.

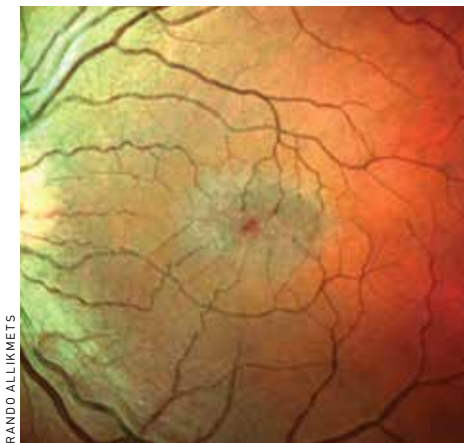
Getting Personal

Wendy Chung, MD, PhD, the Kennedy Family Professor of Pediatrics (in Medicine), launched her program called DISCOVER (short for Diagnosis Initiative: Seeking Care and Opportunities with Vision for Exploration and Research) three years ago. Through the Columbia-based DISCOVER clinic, Dr. Chung and her team diagnose rare diseases using whole exome and whole genome sequencing and provide personalized case management in partnership with a team of specialists.

It's Genetic

P&S scientists revealed genetic clues to an array of human conditions in the past year. In January, *Lancet Neurology* published work by an international team led by David B. Goldstein, PhD, director of the Institute for Genomic Medicine, showing that several genes previously implicated only in rare, severe forms of pediatric epilepsy also

contribute to common forms of the disorder. In March, *Cell Systems* published the identity of a common genetic variant that greatly affects normal brain aging, starting at around age 65, and may modify the risk for neurodegenerative diseases. The study was led by Asa Abeliovich, PhD, professor of pathology & cell biology and of neurology, and Herve Rhinn, PhD, assistant professor of pathology & cell biology; both are members of the Taub Institute for Research on Alzheimer's Disease and the Aging Brain. In April, *Nature Genetics* published clues uncovered by an international team led by Rando Allikmets, PhD, the William and Donna Acquavella Professor of Ophthalmic Sciences, to the genes behind MacTel, a disease of the retina. And



The center of the retina is damaged in MacTel disease.

in May, *Circulation* published a finding that smoking counteracts the effect of a genetic element that normally protects against heart disease. Muredach P. Reilly, MBBCh, the Herbert and Florence Irving Professor of Medicine (in Cardiology), led the study.



HELP FROM OUR FRIENDS

P&S enjoyed a milestone year for philanthropy in 2016-17. The year's largest gifts reflect the generosity of P. Roy Vagelos '54 and Diana Vagelos, who gave a \$34 million lead gift in precision medicine and a \$25 million gift for endowed scholarship support. This report features some of the programs that have been beneficiaries of support from our many friends, and these pages describe other gifts that have made an impact on the research, education, patient care, and outreach missions that have made P&S one of the nation's best medical schools for 250 years.



Cryo-EM

Lynn Shostack and Terry Moore have given \$9 million to enhance and expand a new imaging capability at Columbia known as cryoelectron microscopy. "Cryo-EM" uses electron beams to photograph frozen biological molecules to reveal their structures at the atomic level. A critical tool for precision medicine, Cryo-EM allows researchers to investigate the cellular and molecular mechanisms associated with disease processes and the therapies used to treat them. Ms. Shostack, a member of the CUMC Board of Advisors, has provided major support to the David A. Gardner New Initiatives Fund to advance many cutting-edge technologies at P&S, including PET imaging and the small-animal MRI. Her gifts also have established permanent resources for P&S faculty and trainees through the David A. Gardner Professorship of Cardiology and the G. Lynn Shostack Cardiology Fellowship.



Lynn Shostack and Terry Moore

Jonas Children's Vision Care

When Donald Jonas was diagnosed with a rare genetic condition that would ultimately destroy the cells in his retina and lead to blindness, he and his wife, Barbara, were determined that one day others would not have to face such a devastating loss. It was this experience, coupled with a deep concern for the welfare of children, that led Mr. and Mrs. Jonas to provide a gift to the Department of Ophthalmology to help establish a program aimed at fighting vision problems in children. The initiative, known as Jonas Children's Vision Care, brings together the world-class technological and human expertise at Columbia to provide direct patient care, advocacy, scientific research, and education to fight childhood blindness. The program, which also expands precision ophthalmology initiatives, will be directed by Steven Brooks, MD, the Anne S. Cohen Professor of Pediatric Ophthalmology and

chief of pediatric ophthalmology, and Stephen Tsang, MD, PhD, the Laszlo T. Bito Associate Professor of Ophthalmology and of Pathology & Cell Biology.

"Barbara and Donald Jonas exemplify the philanthropic community," says G.A. (Jack) Cioffi, MD, the Jean and Richard Deems Professor, Edward S. Harkness Professor, and chair of the Department of Ophthalmology. "They realize that they can have a worldwide impact on diseases that have been a direct threat to their family, and they are very smart about how they direct their funds."

The Jonas family joined Columbia faculty and other supporters in January 2017 to launch the new, state-of-the-art program at the NewYork-Presbyterian/Morgan Stanley Children's Hospital and in its home in the Edward S. Harkness Eye Institute.

Witten Outcomes Research Fund

Richard and Lisa Witten have committed \$2 million to the Herbert Irving Comprehensive Cancer Center to support the Center for Cancer Outcomes Research and Evaluation. The gift will strengthen cancer programs across the medical center and help Columbia lead the nation in developing evidence-based approaches to cancer treatment. Cancer outcomes research seeks to provide evidence on the comparative effectiveness, benefits, and harms of treatments in different populations of cancer patients while developing strategies to optimize care for individual patients.

Research priorities of the center, which is directed by Dawn Hershman, MD, address the challenges and opportunities in delivering high-quality care, with a strong focus on racial, ethnic, and socioeconomic disparities. Center investigators also study and learn from the successes and difficulties faced across different cancers, such as breast, ovarian, colon, brain, and, more recently, pediatric cancers and lymphoma.

Outcomes research helps ensure that every patient receives the right treatment, by the right physician, at the right place.



Leonard Tow, founder and chairman of the Tow Foundation, and Emily Tow Jackson, executive director and president

Challenge Grant for ALS Research and Clinical Care

The Tow Foundation awarded a **\$2.05 million**, five-year challenge grant to benefit the Eleanor and Lou Gehrig ALS Center at P&S. With this funding, P&S will support the expansion of clinical services to provide care and access to vital services for ALS patients in the New York metropolitan area. The funding also will support research, including research into the genomics of ALS and opportunities for patients to participate in clinical trials.

Studying the Brain's Relationship to Obesity

The **Russell Berrie Foundation** has pledged \$8.25 million to launch the Obesity Research Initiative at the Naomi Berrie Diabetes Center. The purpose of this initiative is to study the relationships between neurobiology and metabolic disorders, such as obesity and diabetes. The initiative will approach the science of body weight regulation by studying integrated elements of mind, brain, physiology, and metabolism. One goal of the program is to facilitate interactions among Columbia's strong research groups in neuroscience and metabolism. The Berrie Foundation's gift to support this research extends a longstanding philanthropic commitment to Columbia University and the Berrie Center that dates back to the center's establishment at Columbia in 1998.

Rudolph Leibel, MD, the Christopher J. Murphy Memorial Professor of Diabetes Research and co-director of the Berrie Center, and Charles Zuker, PhD, professor of neuroscience and of biochemistry & molecular biophysics, will lead the initiative.

Chan Soon-Shiong Family Professorship

Patrick Soon-Shiong, MD, committed \$4 million to establish the Chan Soon-Shiong Family Professorship in Medicine and provide funds to support research and clinical trials in myelodysplastic syndrome.

The Chan Soon-Shiong Family Foundation was established by Dr. Soon-Shiong and his wife, Michele Chan. The Chan Soon-Shiong Professorship and research gift celebrate the mission of the foundation to fund research that accelerates the potential of immunotherapy as the next generation standard in cancer patients. Azra Raza, MD, professor of medicine and director of the Myelodysplastic Syndrome Center at Columbia, is the inaugural incumbent of the Chan Soon-Shiong Professorship. As a clinician-scientist with an NIH-funded laboratory dedicated to cutting-edge MDS research, Dr. Raza explores the underlying pathology of MDS to seek new therapeutic targets and non-toxic therapies.

Integrative Therapies for Children and Adults with Cancer

Sidney and Helaine Lerner have pledged \$2.5 million to establish the Sid and Helaine Lerner Professorship for Global Integrative Medicine. The professorship will support the leader of Columbia's Integrative Therapies Program, which supplements conventional cancer care with integrative approaches that have been demonstrated to improve health and healing, reduce stress, and minimize pain in cancer patients. The gift pays tribute to several individuals who helped found and establish the Integrative Therapies Program: the Lerner, who established the Carol Ann Resource Center/Integrative Therapies Program for Children with Cancer at Columbia in 1998; director Elena J. Ladas, PhD, who joined the program in 1999 and was recently appointed as the inaugural Lerner Professor; and Michael Weiner, MD, professor of pediatrics and vice chair of development, who, as former chief of the Division of Hematology, Oncology, and Stem Cell Transplantation in the Department of Pediatrics, supported the program from its conception. Upon Dr. Weiner's retirement from Columbia, the chair will be known as the Michael Weiner, MD, Professorship for Global Integrative Medicine.

"We are all humbled by the Lerner family's generous gift and thrilled by Elena's appointment," says Dr. Weiner. "Elena never ceases to amaze me, both in terms of what she has accomplished and, most importantly, her vision for the future. This is an incredible honor that will allow Elena and the program to reach new heights."



MICHAEL DIVITO

Dana Buchman, a member of the CUMC Board of Advisors, and Jeffrey A. Lieberman, the Lawrence C. Kolb Professor of Psychiatry and chair, Department of Psychiatry

The Promise Project

The Promise Project, under the leadership and guidance of CUMC Board of Advisors member Dana Buchman, has continued its support for a sixth year with grants totaling \$1.416 million to Columbia's Promise Program, a pioneering initiative for children with learning disabilities. As part of the Division of Child and Adolescent Psychiatry in Columbia's Department of Psychiatry, the program focuses on the clinical needs of the learning disabilities population and engages in research to

better understand the origins and expressions of learning disorders.

Early diagnosis of and intervention for children with learning disorders are crucial, and the Promise Program helps to identify at-risk children and provide them, their families, caregivers, and educators with appropriate and effective strategies for intervention. Faculty in psychiatry are working on scalable, exportable models for interventions to allow their work to help children elsewhere in the country.

Peter A. & Debby L. Weinberg Family Foundation

In 2010, Debby and Peter Weinberg and their families established the Weinberg Family Cerebral Palsy Center to provide comprehensive, lifetime care to people with cerebral palsy and other neuromuscular conditions, conduct groundbreaking research relating to CP, and educate the medical community, caregivers, and families about supporting and caring for this population. The center, the first of its kind on the

East Coast, sets the standard for transitional, comprehensive, and holistic CP care.

Debby and Peter have built on their commitment to the center by establishing the Weinberg Family Assistant/Associate Professorship for the center's clinical director, a new position that will provide leadership for the center alongside David P. Roye Jr., MD, executive medical director, and will be vital to the center's growth and continued success.

Gilbert Butler

A \$1 million gift from Gilbert Butler has created a permanent endowment to support training of primary care physicians and innovations in medical education within Columbia's Department of Medicine. It is a challenge grant, designed to inspire other donors to make similarly generous contributions, and future donations to the fund may carry naming rights. Mr. Butler asked that the fund be named to honor the memory of Henry S. Lodge, who died this year. The Henry S. Lodge, MD, Primary Care Endowment Fund is a tribute to Dr. Lodge and all he accomplished as a compassionate and intellectually curious physician. At the request of Dr. Lodge's family, his patients, friends, and loved ones have been donating to the fund in his memory.

Pincus Family Foundation

Following the passing of David Pincus in 2011, the Pincus Family Foundation continues to build upon David's legacy of partnership with the IFAP Global Health Program, which encompasses comprehensive, family-centered primary and specialty care, training and education programs that prepare global health leaders and improve health policy, and innovative research designed to bring

evidence-backed interventions directly to children, their families, and communities.

With a recent gift of \$1.3 million, the Pincus Family Foundation has helped to expand IFAP's network with other academic institutions engaged in immigrant and global health research and education, pursuing a mutual goal of improving health outcomes among vulnerable populations.

Jay and Jeanie Schottenstein

A \$1 million gift from Jay and Jeanie Schottenstein has established and endowed the Jay and Jeanie Schottenstein Family Scholars Fund to support two junior investigators, one from the Division of Cardiology and one from the Division of Cardiac Surgery, who will conduct research into cardiac precision medicine.



EVE VAGG

Shelby White, a trustee of the Leon Levy Foundation

Leon Levy Foundation

The Leon Levy Foundation has given a \$3 million gift to renew and expand the scope of the Leon Levy Fellowship Program established in the Department of Psychiatry in 2010. The fellowship has become among the most competitive in the country, bringing some of the brightest and most promising MD/PhDs in the field to train with Columbia faculty mentors. Alumni of the program are among the nation's leading investigators in psychiatry and neuroscience.

Expansion of the program will allow support for the work of young faculty members who are poised to take positions of leadership in their respective disciplines.



Enrollment Begins for *All of Us* Research Program

Columbia has begun enrolling volunteers for *All of Us*, the federal program to enroll 1 million Americans for the NIH-funded Precision Medicine Initiative.

The NIH awarded a five-year grant expected to total \$46.5 million to Columbia, Weill Cornell, NewYork-Presbyterian, and Harlem Hospital to form a regional PMI Cohort Program Healthcare Provider Organization (HPO) to enroll at least 150,000 volunteers by 2021. PMI is a large-scale research effort to improve the ability to prevent and treat disease based on individual differences in lifestyle, environment, and genetics.

The four centers will engage with community organizations throughout New York City to ensure that the volunteers represent the geographic, ethnic, racial, and socioeconomic diversity of the country that the NIH program hopes to achieve through this “patient-powered” project.

“The PMI Cohort Program aligns perfectly with our own precision medicine effort, which we launched in 2015 in partnership with NewYork-Presbyterian and faculty from across Columbia University,” says Lee Goldman, MD, dean of the Faculties of Health Sciences and Medicine and chief executive of CUMC. “This award, in collaboration with NewYork-Presbyterian, Weill Cornell, and our long-standing colleagues at New York City Health + Hospitals/Harlem, will extend our ongoing successes in taking an individualized approach to treating some cancers and rare genetic diseases to a broader range of human illnesses across the ethnically, culturally, and

socioeconomically diverse population we serve. It will also enable us to make sure that research findings benefit our local population and beyond as quickly as possible.”

Adds Tom Maniatis, PhD, director of the Columbia/NewYork-Presbyterian Precision Medicine Initiative: “We are pleased and excited that the NIH has chosen the Columbia/Weill Cornell/NewYork-Presbyterian, and Harlem Hospital collaboration as one of the partners in this ambitious and fundamentally important program. This award is a validation of our commitment to realize the vision of precision medicine, which identifies relationships between genetic, lifestyle, and environmental differences in individuals, and the prevention, diagnosis, and treatment of human diseases.”

“The mission of *All of Us* is simple: to speed up health research,” said the invitation signed by the Columbia PIs, David Goldstein, PhD, director, Institute for Genomic Medicine; Ali Gharavi, MD, the Jay Meltzer, MD, Professor of Nephrology and Hypertension; and George Hripcsak, MD, chair of biomedical informatics. “Together, we will build one of the largest health databases. Researchers will use it to conduct thousands of studies. Their research may lead to the next big medical breakthrough.”

The program is developing features, tools, and resources for the official national launch in late 2017 or early 2018 and will use the early feedback to help *All of Us* succeed.

To learn more and to sign up to participate, visit joinallofus.org.

New York First

P&S has joined other New York state medical schools in recent years to encourage New York lawmakers to fund the New York Fund for Innovation in Research and Scientific Talents—NY FIRST—and the 2017-18 state budget includes \$20 million for academic medical centers. The money will be used to recruit and retain faculty members who have NIH grants.

The deans of the state’s 16 medical schools, through the Associated Medical Schools of New York, called for an investment in what many other states have recognized is a central component of the innovation economy: biomedical research.

NY FIRST focuses investments on the economic development capacities of research laboratories. The investment supports the development

of dozens of additional laboratories throughout the state, each of which employs 10 or more skilled researchers and support staff and generates the intellectual property that leads to new cures, additional funding, and new business opportunities.

The program builds on the previous Faculty Development Program, which yielded a greater than 7 to 1 direct return on the state investment and has helped academic medical centers keep top scientists in New York.

The Faculty Development Program has helped retain or attract 52 scientists in the state since the program began a decade ago. More than 80 percent of the scientists are still doing research, still bringing in grant money, and still creating jobs in New York.

University Professor

Gordana Vunjak-Novakovic, PhD, the Mikati Foundation Professor of Biomedical Engineering, professor of medical sciences at P&S, and director of Columbia's Laboratory for Stem Cells and Tissue Engineering at CUMC, has been appointed a University Professor, Columbia's highest academic honor. The medical center now has five faculty members who are University Professors.

The professorships are granted to members of the faculty in recognition of exceptional scholarly merit and distinguished service to Columbia. Dr. Vunjak-Novakovic has been a pioneer in the engineering of functional human tissue for use in regenerative medicine. With her research team, she has been able to engineer cardiac tissue by culturing stem cells and to grow bone grafts for facial reconstruction surgery. Her discoveries have led to new approaches for treating injuries and complex diseases and have supported the development and evaluation of therapeutic drugs.

Dr. Vunjak-Novakovic completed her PhD degree in chemical engineering at the University of Belgrade and relocated to the United States after receiving a Fulbright Fellowship. She is the founder of three public-



spirited biotechnology companies, the first woman engineer to deliver the Director's Lecture at the National Institutes of Health, and the first of Columbia's female faculty members to be elected to the National Academy of Engineering.

Other CUMC University Professors: Richard Axel, neuroscience, biochemistry & molecular biophysics, and pathology & cell biology; Wayne Hendrickson, biochemistry & molecular biophysics and physiology & cellular biophysics; Eric R. Kandel, neuroscience and physiology & cellular biophysics; and Wafaa El-Sadr, epidemiology and medicine.



AMELIA PANICO

About the Class of 2017, Largest in P&S History

170 MD graduates

51 percent of the graduates are women

19 also received PhD degrees

3 were graduates of the three-year PhD-to-MD program

2 also received MPH degrees

3 also received MBA degrees

2 also have DDS degrees

1 also received an MS degree in narrative medicine

30 students took an extra year for research

35 percent of the graduates took extra time for research or a dual degree

12 graduates participated in the residency match as couples

19 percent went abroad for senior electives or scholarly projects, mostly to developing countries

16 percent matched to residencies at Columbia

36 percent matched to residencies in New York City

12 babies were born to students in the class during medical school, and three students had two children during medical school

26 students got married during medical school and 12 more got engaged

Diversity Alliance Honors Students, Residents, Faculty

Students, residents, and faculty gathered in November 2016 for the Kenneth A. Forde Diversity Alliance’s third annual symposium and reception to celebrate the achievements of the group. Four individuals received awards in recognition of their contributions to promoting diversity at CUMC:

- Julia Iyasere, MD, assistant professor of medicine at CUMC, received the Faculty Diversity Award.
- Christopher Gonzalez, MD, a resident in medicine at P&S, received the Resident Diversity Award.
- Two students in the Class of 2019, Naralys Batista and Christopher Travis, received Medical Student Diversity Awards.

The evening included a tribute to the alliance’s namesake, Kenneth A. Forde, MD, the José M. Ferrer Professor Emeritus of Clinical Surgery. P&S Alumni Association president Kathie-Ann Joseph, MD, led the tribute. Dean Lee Goldman, MD, announced a new scholarship established in Dr. Forde’s honor. The Kenneth A. Forde Scholarship will be provided on the basis of need and merit and cover four years of tuition at P&S.

Dr. Forde has received numerous awards for his contributions to clinical practice, research, teaching, and leadership, including the 2015 Distinguished Service Medal of the College of Physicians & Surgeons. He is a member of the CUMC Board of Advisors, a trustee of Columbia University, and a trustee of NewYork-Presbyterian Hospital.

The evening’s program, sponsored by the Office of Diversity and Multicultural Affairs and the P&S Alumni Association, included a poster ses-



AMELIA PANICO

Posing at the Diversity Alliance event are, from left, Diversity and Multicultural Affairs Senior Associate Dean Hilda Hutcherson, Christopher Travis, Naralys Batista, Ken Forde, Julia Iyasere, Christopher Gonzalez, and P&S Dean Lee Goldman.

sion of research conducted by students of BALS0—the Black and Latino Student Organization at P&S—as well as musical performances by several P&S students.

The alliance was established in 2014 to recruit and retain a diverse community, provide networking events, foster and maintain a supportive environment, raise awareness about diversity, support pipeline programs, and provide career and leadership development through mentoring.

The newest pipeline program is the Gerald E. Thomson Undergraduate Pre-Medical Program, which will pair premed students at Columbia, Barnard, and City University with mentors and provide career exposure and development (through lectures, workshops, and networking opportunities) and practical experience (through clinical shadowing, medical school class visits, and volunteer opportunities). The program is named for Dr. Thomson, the Samuel Lambert and Robert Sonneborn Professor Emeritus of Medicine, who received the inaugural Kenneth A. Forde Diversity Alliance Lifetime Achievement Award in 2015. Dr. Thomson joined the P&S faculty in 1970 and served in a variety of capacities, including senior associate dean and head of the Office of Minority Affairs.

Academy of Clinical Excellence Welcomes First Class

The new Academy of Clinical Excellence welcomed its first members when 119 P&S clinicians were named to the academy’s first class in May 2017. ACE was launched to laud the achievements of faculty members who contribute to the P&S academic mission largely through high-quality, evidence-based, and humanistic patient care. Inductees are full professors and have been at Columbia for five or more years. All devote more than 50 percent of their time to patient care and training the next generation of clinicians.

“The idea of recognizing and rewarding people for outstanding performance helps shape other people’s behavior and helps them aspire to that pinnacle of excellence and that’s what

we’re hoping the academy will do,” says James McKiernan, MD, chair of ACE and a member of the inaugural class. He also chairs the Department of Urology and is the John K. Latimer Professor of Urology.

At the induction ceremony, Kenneth A. Forde, the José M. Ferrer Professor Emeritus of Clinical Surgery, a Columbia University trustee, and a NewYork-Presbyterian trustee, said those who most inspired him throughout his career were “exemplary practitioners of the art of medicine.”

He added that today’s clinicians face many challenges that can distract them from patient care, but he noted a resurgence in clinical values evident in the medical school curriculum, which teaches lifelong learning, respect for cultural

differences, and ways to help patients and their families cope with death and dying.

“Academies such as this have a bright future as long as the patient remains central to the vision of academic medicine,” Dr. Forde said.

In addition to recognizing clinical faculty, ACE launched a discussion series for clinical faculty. Joseph Tenenbaum, MD, the Edgar M. Leifer Professor of Medicine and a member of ACE’s inaugural class, presented “What I’ve Learned: The Importance of Clinical Excellence” at the first session in April. Dr. Tenenbaum talked about his experiences as a mentor and a mentee. He fondly recalled all that he learned from his late mentor, Edgar M. Leifer, PhD, MD, a physician he described as “the leading internal medicine clinician of his day.”

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David Brenner, PhD, DSc

Center for the Study of Society
and Medicine and Center on
Medicine as a Profession
David J. Rothman, PhD

Columbia Stem Cell Initiative
Emmanuelle Passegué, PhD

Columbia Translational
Neuroscience Initiative
Serge E. Przedborski, MD, PhD

Institute for Cancer Genetics
Riccardo Dalla-Favera, MD

Institute of Comparative Medicine
Brian Karolewski, VMD, PhD

Institute for Genomic Medicine
David B. Goldstein, PhD

Institute of Human Nutrition
Richard J. Deckelbaum, MD

Herbert Irving Comprehensive
Cancer Center
Stephen G. Emerson, MD, PhD

Irving Institute for Clinical and
Translational Research
Muredach P. Reilly, MBBCh

Kavli Institute for Brain Science
Eric Kandel, MD

Gertrude H. Sergievsky Center
Richard Mayeux, MD

Taub Institute for Research
on Alzheimer's Disease and
the Aging Brain
Richard Mayeux, MD
Michael L. Shelanski, MD, PhD

Clyde and Helen Wu Center
for Molecular Cardiology
Andrew Marks, MD

P&S Hospital Affiliations

New York-Presbyterian Hospital
New York, NY

New York State Psychiatric Institute
New York, NY

Harlem Hospital
New York, NY

James A. Peters Veterans
Administration Hospital
Bronx, NY

Mary Imogene Bassett Hospital
Cooperstown, NY

Stamford Hospital
Stamford, CT

Helen Hayes Hospital
West Haverstraw, NY

Lawrence Hospital
Bronxville, NY

FACTS & STATISTICS, FY17

MEDICAL SCHOOL ENROLLMENT, FALL 2016

Total medical school enrollment	660
Enrollment of international/nonresident students	24
Enrollment of in-state residents	193
Enrollment of men	331
Enrollment of women	329

ENROLLMENT BY YEAR

	MALE	FEMALE
First-Year Class	79	72
Second-Year Class	83	81
Third-Year Class	84	88
Fourth-Year Class	85	88
Total Enrollment	331	329

MEDICAL SCHOOL ETHNICITIES

Nonresident aliens	24
Hispanic/Latino	70
Black or African-American, non-Hispanic/Latino.....	62
White, non-Hispanic/Latino	307
Asian, non-Hispanic/Latino.....	121
Native Hawaiian or other Pacific Islander, non-Hispanic/Latino....	1
Two or more races, non-Hispanic/Latino	9
Race and/or ethnicity unknown.....	66

OTHER STUDENTS

MD/PhD students	118
PhD students	394
Other students (PT, OT, Nutrition, Informatics)	512

DEGREES GRANTED, FY17

MD	170
PhD	66
Doctor of physical therapy.....	63
MS in nutrition	82
MS in occupational therapy	54
Certificate in psychoanalysis.....	4

APPLICATIONS (ENTERING CLASS 2016)

Number of applicants	8,047
Number of applications considered.....	7,243
Number of applicants interviewed.....	1,009
Number of acceptance letters issued.....	327
Bassett Program applications.....	864

FACULTY, 2016-2017 ACADEMIC YEAR

	FULL TIME	PART TIME
Clinical faculty	1,826	1,994
Basic sciences faculty	269	42

FACULTY HONORS

Nobel Prize in Medicine	2
National Academy of Sciences	19
National Academy of Medicine	48
American Academy of Arts and Sciences	25
Howard Hughes Medical Institute	9

FINANCIALS, FY17 (except where noted)

Budget	\$1.9 billion
Philanthropic support	\$388 million
Endowment	\$1.8 billion
Endowed chairs/professorships	261
NIH research support (FY 2016)	\$406.3 million



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A New Look on 168th Street

Projects in various stages of completion and planning will provide new looks for the Alumni Auditorium, its lobby, and the adjoining Black Building lobby and first floor.

Renovation of the interior of the Alumni Auditorium was completed over the summer of 2017 and is now in use for classes and events. New auditorium seats with tablet arms and electrical outlets were installed, and the carpet was replaced. The renovation also included improved lighting and a new audiovisual system.

Demolition of the auditorium's lobby continued through the summer, and a new lobby and façade are expected to be completed by next summer. The ceiling of the lobby will be raised to create an open and larger lobby. Construction of the new glass façade will begin next spring. When complete, the auditorium will connect to the lobby of the P&S building.

A design is being conceived for a project that would transform the lobby and first floor of the Black Building into a new destination for students, faculty, and staff. Amenities planned include a lactation room, a large café, and additional electrical outlets for the community to use while lounging in the lobby and café spaces.

