EINSTEIN
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BREAKING THE CHAINS OF ADDICTION

Einstein-Montefiore Doctors Confront America’s Opioid Epidemic
in this issue

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Cover illustration: Chris Gash
A Message from the Dean

Probing the molecules and cells that make life possible is a major focus at Einstein. Thanks to our connection with Montefiore, we also broaden our horizons to study the interactions among the people who make a treatment program run. In our cover story, “Breaking the Chains of Addiction,” we describe how department of medicine clinicians at Einstein and Montefiore are exploring ways to bring patients and medication together. Dr. Julia Arnsten works with an especially hard-to-treat, appointment-shy population: patients with HIV who are addicted to opioids. She proposes giving them their HIV antiretrovirals when they come in for the methadone that treats their addiction. Likewise, Dr. Chinazo Cunningham gives opioid-addicted heroin users the methadone-like drug buprenorphine when they come in to exchange drug needles.

This issue of the magazine also spotlights two physician-scientists, Drs. Ana Maria Cuervo and Robert Michler. Dr. Cuervo, a professor of developmental and molecular biology, is an expert in autophagy, an essential process in which cells digest damaged molecules and proteins. She and other researchers have established connections between autophagy failure and many human disorders, including cancer, diabetes and Alzheimer’s disease. Dr. Michler, a professor and the chair of cardiovascular and thoracic surgery, is a clinical investigator who pioneered minimally invasive and robotic surgery in heart patients and repairs hearts around the world. His expertise spans multiple specialties, including complex cardiac surgery, heart transplantation, valve repair surgery and ventricular reconstruction for congestive heart failure.

Never have I been more proud to be associated with Einstein and Montefiore. We are well into our second year as official partners, and our relationship grows stronger by the day. May it continue to strengthen, so that both of our institutions can bring even better healthcare to those in need.
Governor Cuomo Addresses Healthcare Rally

In a speech last February to an overflow audience at Einstein, New York governor Andrew Cuomo stressed that repeal of the Affordable Care Act would imperil healthcare, jobs and funding. The event was sponsored by 1199SEIU (Service Employees International Union), the nation’s largest healthcare union. The governor was joined by Steven M. Safyer, M.D. ’82, president and CEO of Montefiore Medicine; George Gresham, president of 1199SEIU; and others.

A crowd of about 1,000 people from Einstein and Montefiore filled the Mary and Karl Robbins Auditorium and spilled into the nearby Lubin Dining Hall, which was equipped with a video feed.

In his opening remarks, Dr. Safyer said that healthcare in the Bronx and across New York is endangered by possible repeal of the Affordable Care Act. Dr. Safyer voiced strong support for Governor Cuomo, who has vowed to defend the act. “Everyone in this room is concerned about the future of the world, the country and certainly our state, and the governor is standing up for what’s right,” he said.

“We will not allow our healthcare to be thrown into crisis when we can least afford it,” said Mr. Gresham, who outlined the threats to jobs and healthcare and described how union leadership is responding.

The capacity crowd greeted Governor Cuomo with a standing ovation and raised posters that read, “Standing with Governor Cuomo to Save NY’s Healthcare.”

“Three million New Yorkers are now insured under the Affordable Care Act,” said the governor. “That is one in every six who would lose their insurance—and we’re not going to let that happen. You demand and you deserve quality healthcare,” he added, noting that Montefiore is not only a “beautiful” healthcare institution but provides 31,000 jobs. “You think Montefiore is great now; you ain’t seen nothing yet,” he said. “The State of New York is going to invest another $50 million in Montefiore and the workforce here because we believe in you. We’re going to be stronger than ever.”

Other speakers were Kenneth Raske, president of the Greater New York Hospital Association; Jeff Klein, state senator and the leader of the Independent Democratic Conference; and Bronx borough president Ruben Diaz Jr.
A screening of *Call Me Kuchu.*
Several Einstein students had fellowships in Ugandan hospitals, where they witnessed homophobia toward patients—leading them to bring the 2012 film *Call Me Kuchu* and co-director Malika Zouhali-Worrall to Einstein. “Kuchu” is a Swahili label for homosexuals; in Uganda, homosexuality is highly stigmatized, as it is in many parts of the world. The hour-and-a-half documentary explores the struggles of the LGBT community in Uganda, focusing in part on the 2011 murder of LGBT activist David Kato. After the screening, Ms. Zouhali-Worrall described the making of the movie and answered questions.

Other 2016 Global Health Center events included:
**Guest speaker Donald McNeil, Jr., global health reporter for the New York Times.** Mr. McNeil specializes in “plagues and pestilences,” as he put it. In his speech, “Sex, Albino Murders, Drone Strikes, Tightwad Superpowers and the Battle for Global Health—Plus Zika,” he described what his assignments abroad have taught him. Doctors should “always ask patients if they’re seeing another practitioner,” he advised, because local caregivers often prescribe purging—so oral medications never reach their target. He noted that some patients may have fears that keep them from taking vital treatment. One religious group, for example, insisted that polio vaccinations would cause infertility because the box was marked “sterile.” Mr. McNeil also gave examples illustrating different levels of understanding that students may encounter. One woman thought she got sleeping sickness because she hadn’t borne enough children. In a Zika-affected country, a pregnant woman said, “God will make his head grow,” when an ultrasound scan showed that her baby had a small head. The message: medical students thinking of working in poor countries should expect the unexpected.

**Global health faculty meet-and-greet.** Global Health Center co-director Louis M. Weiss, M.D., M.P.H., and other faculty members met with about 50 first-year M.D. students...
to describe the global research projects they’re involved with as well as the clinical, public health and research opportunities available to students. Dr. Weiss is a professor of pathology and of medicine at Einstein and an attending physician in infectious diseases at Montefiore.

**Student-to-student panel discussion.** Second-year med students who had traveled to Asia, Africa, South America and the Caribbean shared their experiences with first-year students. “While traveling in the Indian Himalayas, I experienced my first true exposure to forms of non-Western medicine, specifically from Tibetan and Ayurvedic practitioners,” said Chase Moon, Class of 2019.

“Patients used the prescriptions and medications that these healers provided but also wanted the help of ‘Western’ medicine—a good reminder that a physician should always be open-minded about what will best meet the goals of the patient.”

**Photo exhibit.** Einstein’s “Main Street” showcased student photos of places they traveled to and people they met.

The Global Health Center ended 2016 with an all-day conference on ethical and logistical issues in global health. Thought leaders from around the world shared their views, and attendees met new colleagues and got ideas for ways to improve programs.

1. Donald McNeil, Jr., global health reporter, the New York Times.
3. Family Time by Damien Jackson. Lake Atitlan, Guatemala. A Mayan girl helps her mother with the laundry.
5. A Day at the Monastery by Jason Matakas. Himachal Pradesh, India. The Buddhist shrine is the main temple of the Sarabhai Monastery.
6. La Sonrisa de la Llama by Teresa Longo. Cusco, Peru. Llamas were integral to the Incans and remain important today.
2016 Ceremonies

Ph.D. Student Ceremonies
Sponsored by the Graduate Programs in Biomedical Sciences

JUNE 16, 2016
The Qualification Jubilation
Each year, the graduate division and the Einstein Alumni Association honor third-year Ph.D. and M.D./Ph.D. grad students who’ve received master of science degrees and are candidates for doctoral degrees. This year’s celebration, known as the Qualification Jubilation, honored 33 students. Victoria H. Freedman, Ph.D., associate dean for graduate programs, and Allen M. Spiegel, M.D., Einstein’s Marilyn and Stanley M. Katz Dean, offered opening remarks. Barbara K. Birshtein, Ph.D., professor of cell biology, scientific director for the training and educational grants office and director of training grant support programs, was chosen by the students to deliver the keynote address.

SEPTEMBER 21, 2016
The Declaration Celebration
The annual Declaration Celebration marks the end of a first-year grad student’s rotations through several laboratories and the beginning of thesis work in his or her lab of choice. The research culminates in Ph.D. degrees. This year, 34 Einstein students declared new “lab homes.” Keynote speaker Kamran Khodakhah, Ph.D., professor and chair of the Dominick P. Purpura Department of Neuroscience, reminded students that earning a Ph.D. requires dedication and hard work.
Medical Student Ceremonies
Sponsored by the Einstein Alumni Association

AUGUST 17, 2016
The White Coat Ceremony
At this annual event, an Einstein alumnus “cloaks” each first-year medical student in a physician's white coat donated by the Einstein Alumni Association. The white coat symbolizes the responsibilities that await the future physicians and the humanistic values and scientific excellence they will need. This year’s event brought together the 183 members of the Class of 2020, faculty and special guests. Speakers included Yaron Tomer, M.D., professor and chair of medicine at Einstein and Montefiore, and Janina Galler, M.D. ’72, the president of the Alumni Association’s board of governors. Some alumni had the privilege of cloaking family members.

SEPTEMBER 20, 2016
Scrubs Day
First-year Einstein medical students receive sets of scrubs in the fall from the Alumni Association to mark the start of the Gross Anatomy course. Students also learned who would be in their lab groups.

SEPTEMBER 21, 2016
The Stethoscope Ceremony
The Stethoscope Ceremony introduces new Einstein students to a critical diagnostic tool. Keynote speakers this year were Evelyne Albrecht Schwaber, M.D. ’59, who received the 2012 Dominick P. Purpura Distinguished Alumnus/Alumna Award, and Martin N. Cohen, M.D., professor of medicine.
Our Website Is a Winner

Einstein magazine’s online edition is now the award-winning online edition! In October, the winter/spring 2016 Einstein magazine won a 2016 Folio design award for the best online publication among nonprofits with fewer than six issues a year. The online edition also won an honorable mention in the Association of American Medical Colleges’ 2017 awards. Einstein’s online edition includes hyperlinks, videos, animations and infographics that aren’t in the print magazine. It’s also searchable and allows readers to leave comments. Digital editions differ from the print layouts, but readers still know they’re looking at Einstein magazine. Our graphics staff accomplished the near-impossible by making the online edition readable on computers, tablets and phones. To see the prizewinning edition for yourself—on the device of your choice—visit magazine.einstein.yu.edu/winterspring-2016/.

Westchester in the Bronx

Ever wonder why the Bronx business district south of our campus is called Westchester Square? In 1654, Thomas Pell of Connecticut bought most of the eastern half of the modern Bronx from Native Americans living there (although the Dutch also laid claim to the land). He then invited 16 families to form the village of Westchester near what is now Westchester Square. Between 1683 and 1714, the village was the seat of Westchester County. It became part of the Bronx in the second half of the nineteenth century.

The towns in 1788 of what was then part of Westchester County but now belongs to the Bronx.
Lab Chat

David Shechter, Ph.D., studies what he calls “the biochemistry of epigenetic information,” i.e., non-DNA molecules that influence gene expression, such as methyl groups and the histone proteins that package DNA to form chromatin. Dr. Shechter graduated from Cornell University, earned his Ph.D. from the Columbia College of Physicians and Surgeons and did his postdoctoral research at Rockefeller University. He came to Einstein in 2009 and is an associate professor of biochemistry.

What do you like about science?
Designing experiments is one of my favorite aspects of research. There’s also the thrill of discovery and the joy of having your hypothesis proven wrong.

Wrong?
There’s an Isaac Asimov quote, “The most exciting phrase in science is not ‘Eureka’ but ‘That’s funny...’” Of course I’m always happy when our data support our hypothesis. But getting results inconsistent with your hypothesis—something “funny” and totally unexpected—can lead to a new discovery. When I’m interviewing prospective Ph.D. or M.D./Ph.D. students I tell them, “If you don’t wake up occasionally in the middle of the night thinking about an interpretation for an experiment you’ve done or a new idea for an experiment, then you’re in the wrong field.” Science is a crazy, not-very-lucrative career, and the thrill of discovery is the major reward.

What’s the focus of your research?
We do several things—I’d get bored doing just one. We study a class of enzymes called protein arginine methyl transferases (PRMTs), which transfer methyl groups onto cellular proteins, including the histones that bind to DNA to form chromatin. Overexpression of PRMTs has been linked to cancer. Our basic biochemistry and research on the frog *Xenopus laevis* has shown how PRMT-5 can function to cause cellular changes. We’re currently bringing our basic findings in the frog into human cancer studies.

We also study proteins called histone chaperones, which attach to those histone proteins not bound to DNA and escort them throughout the cell. The gene that codes for one of those histone chaperones, *Npm1*, is the most frequently mutated gene in acute myeloid leukemia, and we’ve gained some unique insights into its function.

Where do you do your best thinking?
In the lab—I love hearing the sounds and seeing people working. People have this idea that scientists are always alone. But people talk all the time in an open lab, so it’s actually a very social job.

What do you like most about Einstein?
There’s a strong collaborative environment here, and my own research has certainly benefited from it.

Do you have any hobbies?
I really like to cook. In the lab you have to be precise and accurate, but not when you’re cooking. I love going to a restaurant, ordering something interesting and then trying to duplicate it at home. I’m pretty good at it. I also do photography, but my 14-year-old daughter, the oldest of our three kids, decided she wants to be a wedding photographer and took my camera.

Any chance that your kids will become scientists?
They all love coming to the lab, although none of them seems interested in a scientific career. But you never know where kids will go. After all, my dad taught social studies and my mother taught art.
Twelve Professors Get Tenure

Congratulations to 12 newly tenured professors:

Chinazo O. Cunningham, M.D., M.S.  
professor of medicine

Jean M. Hebert, Ph.D.  
professor of neuroscience

Marla J. Keller, M.D.  
professor of medicine

Adam Kohn, Ph.D.  
professor of neuroscience

Fernando Macian-Juan, M.D., Ph.D.  
professor of pathology

Melissa D. McKee, M.D.  
professor of family and social medicine

Laura Santambrogio, M.D., Ph.D.  
professor of pathology

Nicholas E. S. Sibinga, M.D.  
professor of medicine

Yaron Tomer, M.D.  
professor of medicine

Joe Verghese, M.B.B.S.  
professor of neurology

Amit K. Verma, M.B.B.S.  
professor of medicine

Xiaonan (Nan) Xue, Ph.D.  
professor of epidemiology & population health

The Pharmacist Is IN

Einstein employees, faculty members and students enrolled in certain Montefiore insurance plans can now pick up prescriptions at the new campus ScriptCenter on the first floor of the Gruss Magnetic Resonance Research Center, just past the Student Café.

This pharmacist-stocked kiosk is loaded daily with prescriptions filled at Montefiore. Prescription orders received at the Montefiore Outpatient Pharmacy by 11 a.m. (Monday through Friday) will be ready for pickup at the ScriptCenter after 2 p.m. the same day. You’ll be notified once your prescription has arrived at the ScriptCenter. The kiosk will also offer ibuprofen, cough drops and other over-the-counter items for purchase. For more information, visit www.scriptcenter.com.
Congratulations!

Sean C. Lucan, M.D., M.P.H., M.S., has been named a 2016 Fellow of the National Academy of Medicine. He is an associate professor in the department of family and social medicine at Einstein and an attending physician at Montefiore.

Liise-anne Pirofski, M.D., was named a fellow of the American Association for the Advancement of Science in 2016. She is a professor of medicine, chief of the division of infectious diseases, a professor of microbiology & immunology and the Selma and Dr. Jacques Mitrani Chair in Biomedical Research at Einstein and Montefiore.

Welcome!

In March, Jonathan E. Alpert, M.D., Ph.D., joined Einstein and Montefiore as a professor and university chair of the department of psychiatry and behavioral sciences. He also assumed the Dorothy and Marty Silverman Chair in Psychiatry at Einstein. He succeeds T. Byram Karasu, M.D., who led the department for nearly 25 years.

Dr. Alpert previously served as vice chair for clinical services in psychiatry at Massachusetts General Hospital (MGH), where he led the behavioral health executive committee. He directed the depression clinical and research programs at MGH and was the first recipient of the Joyce R. Tedlow Chair in the field of depression studies at Harvard Medical School.

Dr. Alpert has written more than 200 publications on topics including pharmacological and other innovative approaches to treatment-resistant major depressive disorder; depressive subtypes and biomarkers; drug metabolism and drug interactions; ethical issues in the design and conduct of human studies; behavioral health integration; and medical education.

He has received numerous awards for teaching, mentorship and clinical excellence, serves on the board of the National Network of Depression Centers and is a distinguished fellow of the American Psychiatric Association.

Dr. Alpert received his M.D. from the Yale University School of Medicine and his Ph.D. in behavioral pharmacology from the University of Cambridge, United Kingdom, where he was a Marshall Scholar. He completed residencies at Harvard-Boston Children’s Hospital (pediatrics) and at Harvard-McLean Hospital (psychiatry) before joining the Harvard-MGH psychiatry faculty in 1992.

Einstein, Meet TED

Congratulations to Nir Barzilai, M.D., who in November became the first Einstein faculty member to give a TEDMED talk. His theme was “What if a drug that targets the process of aging could help us live longer, higher-quality lives?” A video of his talk will soon be posted online. Dr. Barzilai is a professor of medicine and of genetics, the Ingeborg and Ira Leon Rennert Chair in Aging Research, the director of the Institute for Aging Research at Einstein and an attending physician in medicine at Montefiore.
Choosing a career can be a daunting exercise for high school students. Hands-on experience and counseling can help enormously, and that’s why Einstein students established the Einstein Science High School Mentoring Program (EiSci) three years ago. Some 25 medical and graduate student volunteers organize events aimed at getting Bronx high schoolers interested in science- and healthcare-based careers.

“EiSci’s mission is to improve the academic and future career prospects of Bronx public high school students through mentoring and by exposing them at a young age to careers in science and medicine,” says Barbara K. Birshtein, Ph.D., a professor of cell biology who works with the EiSci volunteers. Dr. Birshtein is also the director of training grant support programs and scientific director in the training and educational grants office at Einstein.

The EiSci program currently partners with Pelham Lab High School, Renaissance High School and Schuylerville Prep. EiSci outreach members meet with the teens twice a month after school. They also organize workshops at Einstein where students can experience introductory-level science and medicine and are encouraged to ask questions.

Engaging Students

Last year, EiSci sponsored the Biomedical Science Careers Student Exploration Day, which welcomed tenth graders from the three high schools. The event began in Einstein’s Education Center, where Libusha Kelly, Ph.D., an assistant professor of systems & computational biology and of microbiology & immunology, shared her career path with the visitors. Then came tours of various core facilities that aid Einstein researchers in their work. The day concluded with a Q&A session and a talk about clinical research.

“It’s about helping students who show interest in science and medicine to acquire essential skills,” says third-year Ph.D. student Leah Guthrie, co-organizer of the event and co-founder of EiSci.

This year, the EiSci team hopes to add two new partners: Herbert H. Lehman High School and Bronx River High School.

EiSci: Targeting Teens Who Like Science
Behind the Scenes: Research Technicians

Einstein’s 148 research technicians rarely publish papers or appear in the media, but they are the guardians of laboratory productivity and research quality. Their responsibilities include assisting with assays, placing orders, keeping track of reagent and equipment expenses and training lab members in experimental procedures.

“Research technicians are essential for lab life,” says Teresa V. Bowman, Ph.D., an assistant professor of developmental and molecular biology and of medicine. “They’re the ones who understand all the techniques of a lab, maintain colonies and supplies and know whom to contact to get anything done. They are the glue that can provide continuity through many generations of trainees.”

Most research technicians hold bachelor’s degrees in the biological sciences and have at least some prior lab experience. Some come straight from undergraduate training to gain a few years of research experience before progressing to the next phase of their careers, which might include medical school, graduate school or a different research role.

One such person is Mia McKinstry (pictured below), a research technician in Dr. Bowman’s lab, who joined Einstein after finishing her undergraduate studies and had worked as an undergraduate research assistant. With medical school on the horizon for next fall, McKinstry wanted to gain more basic science research experience first.

“Even though technicians are not the main drivers or idea-bringers in experimental research, it is exciting to know that we are helping push the research forward,” says Ms. McKinstry.

“I enjoy being at the bench. Combining that with the stimulation of learning about the biological processes your lab is trying to understand makes the job a good balance of physical and mental work.”

Glasses for Guatemala

While at Boston College in 2012, second-year medical student Garred Greenberg had an idea. His mother’s church group distributed recycled prescription eyeglasses to economically disadvantaged Guatemalans. “It was a low-cost, low-tech service, yet it had a profound impact on people’s lives,” he observed recently. “What if we could bump up the volume?”

Mr. Greenberg and his sister Megan translated their idea into action, and “Glasses for Guatemala” (G4G) was born.

Later in 2012, Mr. Greenberg packed up 900 pairs of recycled eyeglasses provided by a local Lions Club and headed to Guatemala City. He stayed at the home of the secretary general of the Consejo Ecumenico (CE), a Christian service group, and his wife, a CE coordinator, in the nearby city of Chimaltenango. From there the eyewear went out to Guatemala City, Chimaltenango and the city of Quetzaltenango. More trips followed, and to date G4G has delivered 8,500 pairs of eyeglasses, supplied mostly by the Lions Club. To learn more, visit www.glassesforguatemala.com.

Wanted: Your Opinion

What did you like about this issue of Einstein magazine? Was there anything you didn’t like? What topics should we cover next? Tell us by taking our survey at www.einstein.yu.edu/r/winter-spring-survey-2017.
In Memoriam

We acknowledge with regret and appreciation the passing of the following Einstein faculty members. We honor and respect their memories and extend our deepest condolences to their families, former colleagues and friends.

Samuel A. Levine, M.D.

Dr. Samuel Levine passed away on July 16, 2016, at age 88. Dr. Levine was an associate professor emeritus of physical medicine and rehabilitation at Einstein and founding clinical director of the Lubin Rehabilitation Center (now at Montefiore/Wakefield) of the Jack D. Weiler Hospital (now known as the Einstein-Weiler Hospital), a division of Montefiore.

Dr. Levine was on the Einstein faculty from 1967 until he retired in 1993 and was board-certified in physical medicine and rehabilitation. He earned his M.D. degree from New York University School of Medicine. He then completed an internship at Maimonides Hospital (now Maimonides Medical Center), an assistant residency in medicine at Montefiore Hospital and a senior residency in medicine at Kingsbridge Veterans Administration Hospital, followed by a fellowship in the office of vocational rehabilitation, physical medicine and rehabilitation at Montefiore. He served on many committees and was a member of the American Academy of Physical Medicine and Rehabilitation and other professional medical associations.

Thomas K. Aldrich, M.D.

Dr. Thomas Aldrich died on September 5, 2016, at age 65, after a long battle with cancer. He was a professor of medicine and director of the pulmonary/critical care training program at Einstein and director of the pulmonary function laboratory at Montefiore.

Dr. Aldrich received his M.D. degree from the University of Minnesota. He completed his residency training at the University of California, Irvine, followed by fellowships at the University of Virginia and the University of Pennsylvania. He joined Einstein-Montefiore in 1982 and was division chief in pulmonary medicine from 1994 to 2007. He was also a member of the Montefiore Institutional Review Board.

Board-certified in internal medicine and clinical care medicine, Dr. Aldrich had a productive clinical research career, with a recent focus on the pulmonary physiology of the World Trade Center 9/11 cohort. He received numerous awards, including the ALA-Trudeau Scholar Award and the New York State Lung Association Amberson Award, and held five patents in oximetry.

Norman Bank, M.D.

Dr. Norman Bank, a professor emeritus of medicine, died on September 17, 2016. He was 90 years old.

Dr. Bank received his medical degree with honors from the Columbia College of Physicians and Surgeons in 1953. After more than a decade at New York University School of Medicine he came to Einstein, where he rose to the rank of professor of medicine. From 1971 to 2008 he was chief of the division of nephrology at Montefiore Medical Center.

He served as the president of the New York Society of Nephrology in 1972 and also was on several committees at the National Institutes of Health. His laboratory made numerous discoveries about kidney function in health and disease for which he received awards, among them the Distinguished Service Award from the National Kidney Foundation and the Service Award from the American Society of Nephrology.

Bertrand Bell, M.D.

Dr. Bertrand Bell, a distinguished professor emeritus of medicine and of family and social medicine at Einstein, passed away on October 4, 2016, at age 86.

Dr. Bell earned his medical degree from what is now the University at Buffalo School of Medicine and Biomedical Sciences. After a captainship
in the Air Force Medical Service, he completed his residency in internal medicine at Jacobi Hospital and a fellowship in gastrointestinal medicine at Bellevue Hospital. For the next four years, he was in private practice and chief of staff at Calvary Hospital. He then returned to Jacobi, rising to the position of director of ambulatory care.

He joined the Einstein faculty in 1966 and mentored many Einstein students completing rotations in ambulatory care. Dr. Bell led a New York State–established panel that became known as the Bell Commission, which recommended limiting residents’ duty hours to 80 a week. He also championed window guards in apartment buildings, seat belts in taxis and improved training in emergency medicine.

Olga Blumenfeld, Ph.D.

Dr. Olga Blumenfeld, a professor emerita of biochemistry, passed away on October 31, 2016, at age 93. She was renowned for her work in human blood group matching.

Born in Poland in 1923, Dr. Blumenfeld escaped to the United States in 1942, where she studied biochemistry at City College. She completed her master’s degree at the University of Colorado and her Ph.D. at New York University.

Dr. Blumenfeld came to Einstein in 1960 as a postdoc working with Drs. Paul Gallop and Sam Seifter. She joined the Einstein faculty in 1962 and rose to the rank of professor in 1972. Many of her publications deal with the molecular basis for genomic diversification of a red cell family of glycoproteins called glycophorins. Her Blood Group Antigen Gene Mutation Database is still in use today. Working with her colleague Helen M. Ranney, M.D., she was among the first to detect the unusual hemoglobin known as HbA1c—the biomarker that has transformed the way diabetes is diagnosed, treated and prevented. Dr. Blumenfeld also chaired a committee on women’s rights at Einstein.

Harold Nitowsky, M.D.

Dr. Harold Nitowsky, a clinical professor emeritus of obstetrics & gynecology and women’s health and of pediatrics, as well as a professor emeritus of genetics, died on November 12, 2016. He was 91.

After earning his medical degree from New York University School of Medicine, he completed his internship at Mount Sinai Hospital in New York and his residency in pediatrics at the University of Colorado Medical Center. During his postdoctoral fellowship in biophysics and pediatrics there, he earned a master’s degree in biophysics. He then served as a surgeon in the Public Health Service’s Communicable Disease Center.

Dr. Nitowsky arrived in the Bronx in 1967 from the Johns Hopkins School of Medicine. At Einstein, he founded and directed the Genetic Counseling Program, which included a mobile unit dubbed “Operation Gene Screen,” which screened for Tay-Sachs disease.

He also directed the genetics research center and the division of genetics in the department of pediatrics and the division of reproductive genetics in the department of obstetrics & gynecology and women’s health.

David Hamerman, M.D.

Dr. David Hamerman, a distinguished professor emeritus of medicine at Einstein and a founding faculty member, died on December 25, 2016. He was 91 years old.

Dr. Hamerman arrived at Einstein in 1955 as a junior member in the department of medicine. He rose through the ranks and pursued a productive career in rheumatology research, developing expertise in the metabolism of hyaluronate, now used as an injectable treatment for arthritic knees. He also assumed important leadership roles, beginning with his appointment as director of Einstein’s rheumatology division. In 1968, Dr. Hamerman became chair of the newly designated academic department of medicine at Montefiore.

After stepping down in 1979, he developed and led the geriatrics division and in 1992 became director of Einstein’s Jack and Pearl Resnick Gerontology Center. His textbook Geriatric Bioscience: The Link Between Aging and Disease (American Society for Clinical Investigation) was published in 2007.
Einstein Research Leads to New Drug for Hard-to-Treat Lymphomas

In March, Japan became the first country to approve a lymphoma drug developed through research at Albert Einstein College of Medicine. This also marks the first time that an Einstein-licensed drug has been approved for patient use.

The new oral drug, called Mundesine®, was conceived at Einstein and synthesized at Victoria University of Wellington, New Zealand. It uses an enzyme-inhibition technology developed by Vern Schramm, Ph.D., professor and Ruth Merns Chair in Biochemistry, to treat patients with a type of lymphoma called peripheral T-cell lymphoma (PTCL)—a group of aggressive diseases in which patients’ T cells have become cancerous and that accounts for 10 to 15 percent of all cases of non-Hodgkin’s lymphomas.

PTCLs are rare in the U.S. but more common in Asia, Africa and the Caribbean, possibly due to exposure to viruses such as Epstein-Barr virus and the human T-cell leukemia virus.

Mundesine has been specifically approved for patients whose PTCL has relapsed (recurred) or is refractory (resistant to treatment). Until now, few effective treatments were available for these PTCL conditions. PTCL patients who relapse following chemotherapy currently live an average of only six more months. Mundesine’s approval in Japan was based on 19 clinical trials.

“This drug is the first of a novel class of drugs we’ve designed that has received approval,” says Dr. Schramm. “Patients with relapsed or refractory PTCL have been thought to have untreatable cancers, and this approval is an important step in providing them with further treatment opportunities. It’s the culmination of our biomedical goal here at Einstein, which is to transfer new scientific discoveries into better lives for patients.”

Dr. Schramm’s pioneering work involves creating molecules called transition-state analogs that block key enzymes from functioning. His findings have led to powerful new strategies for treating cancer, antibiotic resistance and autoimmune diseases. In the case of PTCL, Dr. Schramm’s goal was to inhibit the enzyme purine nucleoside phosphorylase (PNP). When PNP is blocked, the PTCL cancer cells are killed.

To counteract PNP, Dr. Schramm and his colleagues first decoded PNP’s fleeting “transition state”—a structure that forms for less than a billionth of a second when an enzyme converts one chemical into another. The next step was to design a chemical closely resembling PNP’s transition-state structure. That chemical, forodesine hydrochloride, was later formulated into Mundesine. It powerfully inhibits PNP by binding to the PNP molecules in PTCL patients’ T cells and not letting go.
Your Years Are Numbered…

It may not be possible to extend the human life span beyond the ages already attained by the oldest people on record, Einstein scientists reported last October in *Nature*.

Since the 19th century, average life expectancy has risen almost continuously thanks to improvements in public health and other areas. On average, for example, U.S. babies born today can expect to live to nearly age 79 compared with an average life expectancy of only 47 for Americans born in 1900. Since the 1970s, the maximum duration of life—the age to which the oldest people live—has also risen. But the Einstein researchers found that this upward arc for maximal life span has a ceiling—and we’ve already touched it.

“Demographers as well as biologists have contended there is no reason to think that the ongoing increase in maximum life span will end soon,” says senior author Jan Vijg, Ph.D., a professor and chair of genetics, the Lola and Saul Kramer Chair in Molecular Genetics and a professor of ophthalmology and visual sciences at Einstein. “But our data strongly suggest that it has already been attained.”

When Dr. Vijg and colleagues looked at survival improvements since 1900 for people age 100 and above, they found that gains in survival peaked at around 100 and then declined rapidly, regardless of the year people were born. “This finding indicates diminishing gains in reducing late-life mortality and a possible limit to human life span,” says Dr. Vijg.

Using maximum-reported-age-at-death data, the Einstein researchers put the average maximum human life span at 115 years—a calculation allowing for record-oldest individuals occasionally living fewer or more than 115 years. (Jeanne Calment—the French woman who died in 1997 at age 122, after living longer than any person in recorded history—was a statistical outlier, they concluded.) The researchers calculated that the probability in a given year of seeing one person live to 125 anywhere in the world is less than one in 10,000.

…But Last Ones Can Be Golden

The final years of an exceptionally long life could well be healthy ones, Einstein researchers reported last summer in the *Journal of the American Geriatrics Society*.

“Most people struggle with an ever-increasing burden of disease and disability as they age,” says study leader Nir Barzilai, M.D., a professor of medicine and of genetics at Einstein and director of Einstein’s Institute for Aging Research. “But we found that those who live exceptionally long lives have the additional benefit of shorter periods of illness—sometimes just weeks or months—before death.”

Dr. Barzilai and colleagues looked at the health status of centenarians and near-centenarians enrolled in two ongoing studies: the Longevity Genes Project and the New England Centenarian Study. Both studies also included non-centenarian comparison groups.

The long-lived participants in these two studies proved markedly similar with respect to major illness: Compared to the younger groups, their onset of major age-related disease was delayed, with serious illness compressed into a few years very late in life. The findings contradict the notion that the older people get, the sicker they become and the greater the cost of taking care of them.

Dr. Barzilai is also the Ingeborg and Ira Leon Rennert Chair in Aging Research and an attending physician in endocrinology at Montefiore.
Frequent soccer-ball heading is a common and under-recognized cause of concussion symptoms, according to a study of players led by Einstein researchers and published last February in *Neurology*. The findings run counter to earlier soccer studies suggesting that concussion injuries mainly result from inadvertent head impacts such as collisions with other players.

“Our study suggests that you don’t need an overt collision to warrant concern,” says study leader Michael L. Lipton, M.D., Ph.D., professor of radiology and of psychiatry and behavioral sciences at Einstein and director of MRI Services at Montefiore.

Dr. Lipton and his colleagues asked 222 adult male and female amateur soccer players to fill out online questionnaires on their soccer-related activities during the previous two weeks, including details about heading and other unintentional head impacts and any resulting headaches, pain and dizziness as well as more-severe symptoms.

Approximately 35 percent of the participants reported one unintentional head impact, and 16 percent reported more than one such impact. The median number of headings during the two-week reporting period for all respondents was 40.5. Twenty percent of the participants reported experiencing moderate to very severe concussion symptoms. Although these symptoms were more strongly connected with unintentional head impacts, heading was shown to be an independent risk factor for concussion symptoms.

Players who headed the most were the most susceptible to concussion. “Our findings certainly indicate that heading is more than just a ‘subconcussive’ impact, and that heading-related concussions are common,” says Dr. Lipton. “We need to give people who have these injuries proper care and prevent multiple head impacts, which are particularly dangerous.”

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**Gunning for Chikungunya**

Alphaviruses include important human pathogens such as encephalitic viruses and Chikungunya virus (CHIKV)—a mosquito-borne alphavirus that recently caused large epidemics worldwide, including in the Americas.

In a study published online last December in *PLOS Pathogens*, Margaret Kiellian, Ph.D., and Maria Gaudalupe Martinez, Ph.D., describe for the first time how alphavirus is transmitted from cell to cell during infection. Long cellular extensions from an infected cell contact uninfected neighboring cells and then release alphavirus particles, effectively shielding viruses from neutralizing host antibodies.

Drs. Martinez and Kiellian found that the alphavirus structural proteins alone induce host cells to form these extensions, which preferentially target uninfected cells.

The findings could influence efforts now under way to develop vaccines against CHIKV. Dr. Kiellian is a professor of cell biology and the Samuel H. Golding Chair in Microbiology. Dr. Martinez is an associate in the department of cell biology.
“Protective” Mechanism Could Underlie Brain Disease

To stay healthy, neurons must prevent protein aggregates and defective organelles such as mitochondria from accumulating inside them. We now know that an animal species has found a solution to its neuronal trash problem—one that might also be present in humans and lead to neurodegenerative disease if it becomes dysfunctional.

Researchers studying the roundworm *C. elegans* have discovered that neurons in adult worms possess a previously unrecognized garbage-removal mechanism: The neurons expel large (4-micron diameter) membrane-bound vesicles (dubbed “exophers”) that are filled with clumped protein and damaged cellular organelles, including mitochondria. The findings are described in a paper published in February in *Nature*. One of the paper’s senior authors is David H. Hall, Ph.D., professor in the Dominick P. Purpura Department of Neuroscience.

The researchers observed that inhibiting other avenues of protein degradation—autophagy and proteasomal digestion, for example—enhanced exopher production. And when roundworm neurons were induced to express high levels of neurotoxic huntingtin protein, they produced significantly more exophers than did neurons in control worms. Inducing neurons to express another toxic protein (amyloid-forming human Alzheimer’s disease fragment) yielded similar results.

Significantly, neurons stressed by toxic proteins seem to function better after they generate exophers. For example, several strains of roundworm express altered proteins that progressively impair touch sensation. At midlife in these strains, the touch sensitivity of a particular touch-detector neuron was enhanced in worms that produced exophers earlier in their lives compared with worms that had not.

After discovering that exophers can also expel mitochondria, the researchers found they could trigger exopher production by stressing, damaging or otherwise impairing mitochondrial quality. For example, increased production of neuronal exophers was observed in roundworm strains in which either of two genes involved in mitochondrial maintenance was rendered defective.

What is the fate of exophers and their trash after neurons jettison them? Data supported by electron microscopy suggested that at least some of the material is degraded by neighboring cells of the worm’s hypodermis (the cell layer that secretes its outer cuticle layer). But a portion of the exopher material entered the worm’s body cavity and was scavenged by distant cells. If human neurons possess the equivalent of exophers, the researchers note, then this transfer of potentially toxic material could have implications for neurological disease.

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Recent findings indicate that mammalian neurons can expel protein aggregates associated with Alzheimer’s, Parkinson’s and prion disease. Once outside the neuron, these aggregates can be taken up by other cells—possibly the way disease damage spreads in the brain. “We propose that exophers are components of a conserved mechanism that constitutes a fundamental, but formerly unrecognized, branch of neuronal proteostasis [protein homeostasis] and mitochondrial quality control, which, when dysfunctional or diminished with age, might actively contribute to pathogenesis in human neurodegenerative disease and brain aging,” the researchers conclude.

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Einstein scientists received more than $160 million in research funding from the National Institutes of Health (NIH) during the federal fiscal year 2016. Here are highlights of grants received between July 1, 2016, and December 31, 2016.

**Smartphones vs. Alzheimer’s**

The NIH has awarded Einstein and Pennsylvania State University researchers a five-year, $12.2 million grant to continue studies on the aging brain, Alzheimer’s disease and other dementias. Scientists at the Einstein Aging Study will conduct the research in collaboration with experts at Pennsylvania State University. Their studies will enroll seniors who will be equipped with smartphones on which they’ll answer questions testing their thinking ability—an effort to measure the cognitive changes that precede the onset of dementia.

“We will also look at those risk factors for cognitive decline that can be corrected, including stress, pain, vascular disease and poor sleep,” says Richard B. Lipton, M.D., co-principal investigator on the grant and the Edwin S. Lowe Chair in Neurology at Einstein, and vice chair of neurology at Einstein and Montefiore.

**Improving Outcomes for Patients with HIV**

Einstein and Montefiore, in collaboration with the City University of New York, have received a $9.4 million grant from the NIH to lead research in Central Africa to improve clinical care and health outcomes for patients with HIV. The ongoing, five-country observational study, called Central Africa International Epidemiologic Databases to Evaluate AIDS, involves more than 50,000 HIV-positive children and adults taking antiretroviral therapy.

“Over the next five years, we will use our high-quality data to address scientific clinical and healthcare delivery questions that will inform care in Central Africa and beyond,” says principal investigator Kathryn Anastos, M.D., a professor of medicine, of epidemiology & population health and of obstetrics & gynecology and women’s health at Einstein and an attending physician in general internal medicine at Montefiore.
Congenital Heart Disease
The NIH has awarded Bernice E. Morrow, Ph.D., and collaborators at the Children’s Hospital of Philadelphia a five-year, $7.5 million grant to study the genetics of congenital heart abnormalities.

Congenital heart disease affects four of every thousand live births, with most cases due to unknown causes. Dr. Morrow studies the genetics of a rare syndrome usually referred to as 22q11.2 deletion syndrome (22q11.2DS), in which affected individuals are missing a portion of chromosome 22.

Approximately 60 percent of patients with 22q11.2DS, also known as DiGeorge syndrome and velocardiofacial syndrome, have congenital heart disease, mostly of the conotruncal type (i.e., malformations of the cardiac outflow tract), which includes aortic arch anomalies. Dr. Morrow is professor and director of the division of translational genetics in the department of genetics and the Sidney L. and Miriam K. Olson Chair in Cardiology.

Studying Developmental Disabilities
The NIH has awarded Einstein a five-year, $6 million grant that creates a new research program at the Rose F. Kennedy Intellectual and Developmental Disabilities Research Center (IDDRC). The program focuses on 22q11.2 deletion syndrome (22q11.2DS), described at left.

“The grant will provide critical support for dozens of ongoing studies in intellectual and developmental disabilities at Einstein,” says co-principal investigator Steven U. Walkley, D.V.M., Ph.D., director of the IDDRC and a professor in the Dominick P. Purpura Department of Neuroscience and the departments of pathology and of neurology. The grant’s other co-principal investigator is Sophie Molholm, Ph.D., an associate professor of pediatrics and of neuroscience and the Muriel and Harold Block Faculty Scholar in Mental Illness and co-director of the IDDRC.

Better Asthma Care for Children
Marina Reznik, M.D., M.S., an attending pediatrician in the department of pediatrics at Children’s Hospital at Montefiore and associate professor of pediatrics at Einstein, has been awarded a $4.2 million grant from the NIH to launch a five-year study to help healthcare providers adhere to national asthma-management guidelines and improve clinical outcomes for children with asthma.

“Asthma disproportionately affects low-income, minority children living in inner cities such as the Bronx,” says Dr. Reznik.

Using her NIH grant, Dr. Reznik is leading a clinical trial at 20 Montefiore Medical Group outpatient sites to find out why national asthma-management guidelines aren’t being used. The goal is to improve clinical outcomes for children ages two to 12 with persistent or uncontrolled asthma.
Major NIH Research Awards (cont’d.)

The human gut microbiome is a promising target for dietary changes and treatments to combat type 2 diabetes—especially in groups, such as the Hispanic/Latino population, that disproportionately develop the disease.

**Gut Microbiomes and Diabetes Risk**

Einstein researchers have received a five-year, $3.9 million NIH grant to investigate the role of the gut microbiome in the development of type 2 diabetes among Hispanics/Latinos, the fastest-growing segment of the U.S. population.

Einstein investigators on the grant are Robert C. Kaplan, Ph.D., professor in the department of epidemiology & population health; and Robert D. Burk, M.D., professor in the departments of pediatrics, microbiology & immunology, obstetrics & gynecology and women’s health and epidemiology & population health.

The human gut microbiome is composed of billions of bacteria and other microbes found in the intestines. It is a promising target for dietary changes and treatments to combat type 2 diabetes—especially in groups, such as the Hispanic/Latino population, that disproportionately develop the disease.

**Tuberculosis and HIV Co-infection**

Tuberculosis (TB) is the leading cause of death worldwide among people infected with HIV. But no current test can reliably show when latent (inactive) TB infections in people with HIV start progressing to active—and potentially fatal—TB disease. An Einstein researcher has received a five-year, $3.7 million NIH grant to identify biomarkers that signal an increase in activity by *Mycobacterium tuberculosis*, the bacterium that causes TB, in people with HIV.

“While infection with HIV or TB is usually manageable, the combination of the two diseases is particularly deadly,” says the study’s principal investigator, Jacqueline M. Achkar, M.D., M.S., an associate professor of medicine and of microbiology & immunology at Einstein and an attending physician in medicine at Montefiore.
Curbing Childhood Tooth Decay and Obesity

Einstein and Montefiore researchers have received a five-year $3.7 million grant from the NIH to test a new intervention to improve the health outcomes of children of South Asian immigrants. They are the fastest-growing immigrant community in the United States.

Community health workers, who will also be South Asian women, will visit nearly 400 mothers with newborns in the Bronx and greater New York to help them learn healthy feeding practices and improve oral hygiene for their children.

“We’ve found that many new mothers bottle-feed more frequently and delay weaning to a later age than is optimal,” says Alison Karasz, Ph.D., an associate professor of family and social medicine at Einstein and principal investigator on the project. The project’s co-principal investigator is Karen A. Bonuck, Ph.D., a professor of family and social medicine, of obstetrics & gynecology and women’s health and of pediatrics at Einstein.

Preventing and Controlling Diabetes

The NIH has awarded researchers at Einstein and Montefiore a five-year, $2.9 million grant to launch a new center, one of only eight in the country, for diabetes translational research. The center will serve as a collaborative hub for investigators conducting studies on prediabetes, diabetes and its complications.

The two principal investigators on the grant are Elizabeth A. Walker, Ph.D., R.N., a professor of medicine and of epidemiology & population health at Einstein, and Judith Wylie-Rosett, Ed.D., R.D., a professor and division head of health promotion and nutrition research in the department of epidemiology & population health, the Arfan Foundation Chair in Social Medicine and a professor of medicine at Einstein.

The center’s overall goal is to improve the health of people who have diabetes or are at risk for developing it.

Cancer Immunotherapy

Two Einstein co-investigators were awarded a five-year, $2.6 million NIH grant to make immunotherapy agents that more effectively treat a variety of cancers while causing far fewer side effects than current immunotherapies.

The two investigators are Steven C. Almo, Ph.D., a professor and chair of biochemistry, a professor of physiology & biophysics and the Wollowick Family Foundation Chair at Einstein; and Chandan Guha, M.B.B.S., Ph.D., a professor of radiation oncology, of pathology and of urology at Einstein and vice chair of radiation oncology at Einstein and the Montefiore Einstein Center for Cancer Care.

The Einstein researchers have developed a novel immunotherapy strategy for directing T cells to attack specific types of cancer while also modulating their behavior. This strategy allows them to rev up T-cell activity to attack cancer cells or suppress their activity in situations where immunotherapy is aimed at treating autoimmune diseases.
Pediatric Ethics: Protecting the Interests of Children

Alan R. Fleischman, M.D. '70
Professor of Clinical Pediatrics
Professor of Clinical Epidemiology & Population Health
Senior Associate, Montefiore Einstein Center for Bioethics
Albert Einstein College of Medicine
Attending Physician in Neonatal-Perinatal Medicine
Children's Hospital at Montefiore

"Children Are Special" is the title of the first chapter of Pediatric Ethics, and it sums up the attitude of the author, who says he’s never met a newborn he didn’t like. Children are special also because, unlike adults, they can’t always verbalize their wishes and therefore can’t direct their own healthcare. Someone else must make decisions that may have long-term consequences for their lives.

Dr. Fleischman—a pediatrician, neonatologist, father and grandfather—sees the child as a complete person, which informs his take on some of medicine’s most painful situations: What is the obstetrician’s obligation when a pregnant woman whose membranes have ruptured refuses a cesarean section that could save her child’s life? When should a child be removed from life support? If the parents request it, should a doctor deceive a dying child by saying that a treatment has been successful?

Pediatric ethics “seeks to define parental and clinician obligations to children and most importantly attempts to protect the interests of children,” says Dr. Fleischman, who has been untangling ethical issues since he joined the faculty at Einstein and Montefiore in 1975 as a young assistant professor and later on as a professor of pediatrics and director of the division of neonatology. In this book, Dr. Fleischman covers ethical issues in caring for children, including a comprehensive chapter on research on children—an area in which he has particular expertise, having served on two Health and Human Services advisory committees and as an advisor on an Institute of Medicine committee on the subject.

Dr. Fleischman dedicates Pediatric Ethics to “countless patients and their families who have allowed me into their lives during times of serious illness and great distress.” Healthcare professionals and families with the authority and responsibility to make complex decisions for sick children will profit from the discussions in the book. And the children they care for will benefit from wiser and more thoughtful decisions made on their behalf.

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Do cell phones cause cancer? Do vaccines cause autism? Will genetically modified foods modify us? What you read and hear might make you think so.

In *Getting Risk Right: Understanding the Science of Elusive Health Risks*, Dr. Kabat is the calm voice of reason, explaining how scientific studies get distorted en route to the newspaper, radio, Internet or TV screen—and how we, the audience, aid and abet the distortions.

Alarming news often has only a tenuous connection to evidence or logic, says Dr. Kabat. Reporters and the scientists they quote may, for example, overlook missing data or make weak connections. In the 1950s, statisticians pointed out that sales of silk stockings were highly correlated with cigarette consumption. Does buying silk stockings induce you to smoke? Of course not.

And people on the receiving end of the news tend to pay a lot of attention to things that pose little risk because they sound true and rouse our fear of disease and death. We fail to notice that people aren’t dropping like flies or that reports of a hazard are often followed by “corrections” finding the hazard doesn’t exist.

Dr. Kabat proposes an antidote: “We need to promote a model of what science is and how it operates at its best.” He lays out the basics and offers advice on recognizing faulty conclusions. In emphasizing the importance of addressing risks scientifically, he describes highly publicized cases (cell phones and cancer, the HPV virus and cancer, endocrine disruptors, a Chinese weight-loss herb that damaged kidneys) and whether the accompanying risk assessments were valid or bogus.

He ends with a dose of reality. “Research that uncovers new knowledge involves the painstaking process of formulating a hypothesis, obtaining meaningful data, ruling out artifacts and overcoming biases, comparing results from different research groups, and considering and excluding alternative explanations,” he says. Scientists must be willing to modify or reject a hypothesis if it conflicts with the evidence. In fact, they must accept that their work may turn out to be of no consequence at all.

As for the public, it’s our responsibility to develop a healthy skepticism when confronted by the latest scare story.
Last summer, for the first time ever, the U.S. Surgeon General sent a letter to every physician in the country. The subject wasn’t heart disease or cancer, or even the Zika virus menace. It was America’s opioid epidemic.

“Since 1999, opioid overdose deaths have quadrupled and opioid prescriptions have increased markedly—almost enough for every adult in America to have a bottle of pills,” wrote Surgeon General Vivek H. Murthy, M.D., M.B.A. “Yet the amount of pain reported by Americans has not changed. Now, nearly two million people in America have a prescription opioid use disorder, contributing to increased heroin use and the spread of HIV and hepatitis C.”

Many experts trace the roots of today’s opioid epidemic to the Vietnam War, from which thousands of soldiers returned addicted to heroin. So the government cracked down on opioids, both legal and illegal. Research in the late 1980s indicated that patients with chronic pain were suffering unnecessarily and could benefit from newly formulated prescription opioids that seemed to pose little risk of addiction or abuse.

“When I was in medical school some 15 years ago, we were taught to aggressively treat people with pain,” says addiction medicine specialist Joanna L. Starrels, M.D., M.S., who is an associate professor of medicine at Einstein and an attending physician in general internal medicine at Montefiore. “The message was, ‘Be supportive of your patients and don’t worry about addiction.’”

The conclusions drawn regarding
the addiction potential of prescription opioids turned out to be deeply flawed. But it was too late. America was already hooked.

“It’s so rare to see a cause of death increase in the U.S.,” said former Centers for Disease Control and Prevention director Thomas R. Frieden, M.D., last December. “Since 2000, more than 300,000 people have died of opiates, and we have yet to see big decreases anywhere.” (See the “Deadly Opioid Statistics” sidebar on page 32 for highlights from a CDC report issued that month.) Also in December, a survey released by the Washington Post–Kaiser Family Foundation found that one-third of Americans who have taken prescription opioids for at least two months report becoming addicted to or physically dependent on the painkillers.

While physicians around the country now scramble to prevent and treat opioid misuse, at least one region was prepared: the Bronx. “Opioid dependence and related deaths have been high in the Bronx for decades and are now even higher,” says Julia H. Arnsten, M.D., M.P.H., a professor of medicine, of epidemiology & population health and of psychiatry and behavioral sciences at Einstein and chief of the Einstein-Montefiore division of general internal medicine in the department of medicine. “Sadly, the rest of the country is now catching up.”

With Dr. Arnsten in the lead, Montefiore has established one of the nation’s foremost clinical, research and training programs in addiction medicine. Its key elements are highlighted below.

**Double trouble: Opioid misuse and HIV infection**

Since HAART (highly active antiretroviral therapy) was introduced in the mid-1990s for treating HIV infection, most but not all patients have readily embraced these lifesaving medications.
Among the holdouts were patients struggling with opioid misuse. Their addiction makes it difficult to follow doctors’ orders or discourages them from seeking healthcare in the first place.

Dr. Arnsten was among the first researchers to study how best to care for this doubly marginalized population of opioid-addicted, HIV-positive people. She found the solution in the tuberculosis field, where clinicians discovered they could cure patients by directly handing them their medications day after day. In 2004, Dr. Arnsten brought this approach—called “directly observed therapy” (DOT)—to substance abuse clinics.

“People with opioid addictions tend to avoid any contact with the healthcare system but do visit clinics for their regular doses of methadone,” she says. “So, the idea was that when they came in, we’d also give them antiretrovirals to make sure they received proper HIV care.” This novel use of DOT proved successful, significantly reducing the viral loads of HIV-positive methadone users and increasing their counts of CD4 immune cells. Dr. Arnsten’s study showed that chronic medical care could be effectively integrated into substance abuse care, which had previously focused solely on addiction.

Dr. Arnsten has also urged the healthcare community to integrate substance abuse treatment into conventional clinical practice.

“Primary care providers can be reluctant to tackle opioid abuse,” she says. “They’re worried they’ll attract patients who will be disruptive and demanding and unpredictable. But substance abusers are already in their practices. The patients are just not telling their doctors about their addictions—and not getting treatment. Such care doesn’t need to be offered in a separate setting. That’s an important message for states that have few resources for dealing with the growing problem of substance abuse.”

Dr. Arnsten’s most important contribution to addiction medicine may be a training program she developed at Montefiore. She realized early in her career that she’d need help from other experts in her field. But addiction medicine specialists were few and far between, not just at Montefiore but around the nation. The solution, she realized, was to develop her own local specialists—a goal she realized through a National Institutes of Health (NIH)
grant that she won in 2002.

The NIH grant allowed Dr. Arnsten to create the first-of-its-kind Clinical Addiction Research and Education (CARE) program, based at Montefiore. CARE includes two components: a two-year fellowship that prepares physicians to conduct research and deliver clinical care in addiction medicine, culminating in a master’s degree issued by Einstein; and an inpatient and outpatient training program in substance abuse diagnosis and treatment for residents in internal medicine, family medicine and psychiatry. Thus far, about 15 fellows have trained under CARE, many of whom have remained at Montefiore and launched their own NIH-funded studies. In addition, some 600 residents have rotated through the program, expanding the ranks of addiction medicine specialists nationwide.

Mitigating prescription opioid abuse

Dr. Starrels, one of Dr. Arnsten’s protégés, started her research career a decade ago by studying how primary care providers were prescribing opioids for chronic pain. At the time, prescription opioid misuse was a relatively minor problem, but a looming epidemic was evident to those who bothered looking.

Providers were “pretty lax” in prescribing these drugs, Dr. Starrels found. “Few doctors were monitoring patients for opioid misuse. They based their suspicions on patient characteristics such as race rather than on actual risk factors, such as a personal or family history of addiction or mental health problems.”

Next, Dr. Starrels used an NIH career development award to study tools for reducing opioid addiction and overdose in treating chronic pain. One such tool—the opioid treatment agreement

Dr. Starrels, one of Dr. Arnsten’s protégés, started her research career a decade ago by studying how primary care providers were prescribing opioids for chronic pain.
“Few doctors were monitoring patients for opioid misuse. They based their suspicions on patient characteristics such as race rather than on actual risk factors, such as a personal or family history of addiction or mental health problems.”

(OTA) between doctor and patient—defines treatment and monitoring plans and conditions for terminating opioid use. She concluded that OTAs should be used from the beginning with all patients rather than waiting until things go wrong. Her study of urine drug testing for patients prescribed opioids for chronic pain found that interpreting the results is more complicated than many physicians realize.

Today, Dr. Starrels is examining prescription opioid use in patients with HIV. Now that they are living longer, people with HIV are experiencing painful problems associated with aging, such as osteoarthritis. Unfortunately, antiviral therapy can worsen their misery by causing peripheral neuropathy (damage to nerves in the feet and lower legs). Opioids are commonly prescribed to alleviate their chronic neuropathy pain.

“We know that patients using illicit drugs such as heroin are less likely to adhere to HIV treatment,” says Dr. Starrels, who served as a core expert for the CDC 2016 opioid prescribing guidelines. “We don’t know if taking prescription opioids similarly interferes with HIV therapy. If it does, then we have to pay more attention to how we prescribe opioid drugs to people with HIV and how we monitor people with HIV for misuse.”

In an NIH-funded study, Dr. Starrels will follow 250 individuals with HIV and chronic pain, including patients who use prescription opioids (intermittently and long-term), those who don’t use these drugs at all and those with and without a history of opioid misuse.

“Like all primary care physicians, HIV providers are overburdened,” Dr. Starrels acknowledges. “We often don’t have the time, the resources or the training to perform the long laundry list of things for ensuring that these medications are used safely. But given what we now know about the risks of these medications, it would be reckless to continue prescribing opioids the way we’ve been doing.”

Supporting people on society’s margins
After two decades on the front lines of the Bronx opioid wars, Chinazo O. Cunningham, M.D., M.S., a professor of medicine and of family and social medicine at Einstein and associate chief of the division of general internal medicine at Montefiore, has mixed feelings about the new concern over drug addiction.

“Now, with addiction spreading from cities to rural and suburban areas, from the poor to the affluent and from minorities to whites, the outcry is loud,” she wrote in an April 2016 post on The Doctor’s Tablet, an Einstein blog. “Suddenly, we must do more...It’s about time that we finally recognize that drug addiction is a medical problem that requires medical treatment, not punishment. It is unfortunate that our path to this realization has been so bittersweet—and so long in coming.”
Deadly Opioid Statistics

Last December, the Centers for Disease Control and Prevention issued a sobering report on deaths due to America’s opioid epidemic (“Increases in Drug and Opioid Overdose Deaths—United States, 2000–2014”). Among the findings:

From 2000 through 2014, the death rate from drug overdoses in the United States increased by about 140 percent. In addition, the 2000 through 2014 period saw a... increase in the rate of overdose deaths involving opioids (opioid pain relievers and heroin).

Since 1999, opioid pain reliever prescribing has quadrupled and has increased in parallel with overdose deaths involving the most commonly used opioid pain relievers.*

Opioid overdose deaths increased by a significant 14 percent from 2013 to 2014 (from 7.9 per 100,000 in 2013 to 9.0 per 100,000 in 2014), driven in part by sharp increases in overdose death rates from heroin and illicitly manufactured fentanyl, a synthetic opioid.

Past misuse of prescription opioids is the strongest risk factor for starting on and using heroin.

The report concluded that efforts to prevent opioid-dependent people from overdosing should involve expanding access to naloxone (a safe and effective antidote for all opioid-related overdoses) and increasing access to medication-assisted treatment in combination with behavioral therapies.

*Oxycodone (e.g., Percocet, Percodan and OxyContin) and hydrocodone (e.g., Vicodin) are the most commonly prescribed opioids.
The medical treatment for addiction to heroin and prescription pain relievers has relied mainly on methadone—a less-addictive opioid, used for decades, that doesn’t produce the “high” that others do. Taking methadone as maintenance therapy reduces people’s use of drugs they’ve been misusing as well as their craving for those drugs. But since the early days of her career, Dr. Cunningham has championed the use of a methadone alternative called buprenorphine, introduced in 2002. Like methadone, the opioid buprenorphine blocks cravings for other opioids and helps relieve pain. But according to Dr. Cunningham, buprenorphine carries a lower risk of overdose than methadone, making it appropriate for office- and community-based treatment. Fears of misuse, however, have limited its availability.

Illicit use of buprenorphine occurs, Dr. Cunningham acknowledges, mainly because the drug is difficult to obtain legally. And those using buprenorphine illicitly are self-treating their withdrawal symptoms or addiction rather than taking it to get high, she says.

Convinced of buprenorphine’s value, Dr. Cunningham began developing and testing new ways to expand the drug’s use to nonmedical settings such as syringe-exchange programs. This approach, she has found, improves people’s access to opioid addiction treatment, enhances health outcomes and reduces behaviors that spread HIV infection among injection drug users. She has also shown that buprenorphine is safe and effective when delivered in primary care settings, even by physicians with little training in addiction medicine.

“It’s about time that we finally recognize that drug addiction is a medical problem that requires medical treatment, not punishment. It is unfortunate that our path to this realization has been so bittersweet—and so long in coming.”

Dr. Cunningham has championed buprenorphine as an alternative to methadone.
addiction,” Dr. Cunningham wrote in a Huffington Post blog.

Thanks in part to her efforts, the New York City Department of Health and Mental Hygiene and the American Society of Addiction Medicine have recently amended their buprenorphine treatment guidelines to expand the drug’s availability.

Dr. Cunningham’s latest project: developing a “live” database of all prescription opioid use within the Montefiore system, with the goal of more fully understanding how these drugs are used, how clinicians can prevent opioid misuse and how opioid use is related to clinical outcomes.

“One challenge in tackling these issues is that the field is fractured,” says the researcher, whose work is supported by an NIH midcareer investigator award. “Addiction treatment historically has been what psychiatrists do. And then there’s pain management, which is what primary care doctors and some subspecialists do. There’s been little communication between those who prescribe these medicines and those who must deal with the unintended consequences. This database will provide a foundation for better understanding what the problems are and how we can address them.”

Dr. Cunningham is also using the NIH award to develop a standardized approach to mentoring junior investigators in addiction medicine, with a focus on minorities and women, who have been underrepresented in the field.

**Breaking the cycle of drug use and incarceration**

One might imagine that incarceration would help opioid users, forcing them to kick their habit by going “cold turkey.” But that’s wishful thinking, addiction medicine specialists say. Studies show that up to 75 percent of people with opioid addictions relapse within three months of release, increasing the likelihood they’ll find themselves back behind bars. Compounding the problem: Few prisons provide addiction treatment, and newly released inmates often shun health services of any kind.

How to break the cycle of drug use and incarceration?

One possible solution, devised by Aaron D. Fox, M.D, M.S., an associate professor of medicine at Einstein, is to reach out to ex-inmates before the ink on their release papers is dry. Studies show that drug users are at highest risk of relapse and deadly overdose in the two weeks immediately after release.

Dr. Fox, a CARE alumnus, first looked at the problem from the inmates’ perspective. Through lengthy interviews soon after prison release, he learned that forced abstinence from drugs in prison may turn former inmates against subsequent treatment with methadone or buprenorphine.
“Individuals who’d been taking methadone or buprenorphine in the community could no longer take those medications in prison—causing them to experience painful withdrawal,” says Dr. Fox. “Now that they’re out of prison, these former inmates don’t want to go back on those medications for fear of having to go through withdrawal again should they miss a dose or be reincarcerated.” He reported his findings last year in the *Journal of Substance Abuse Treatment*.

Many former inmates felt that entering treatment would be a step backward or a sign of failure, reflecting the social stigma often associated with substance abuse care. Others didn’t know that buprenorphine can be dispensed for take-home use, sparing them the stigma and inconvenience of regular substance abuse clinic visits. And many drug users said that since they hadn’t misused drugs for months, they had no need for maintenance medications on release from prison. “Basically, there was a lot of confusion about drug treatment in general and buprenorphine use in particular,” he says.

Dr. Fox’s interviews led him to recommend using peer mentors—formerly incarcerated drug users who have used buprenorphine—to broach the idea of drug treatment with newly released inmates.

“The hope is that the mentors can dispel some of the myths about treatment, help these individuals navigate the healthcare system and get them into our clinic for care,” says Dr. Fox, who is co-director of the Bronx Transitions Clinic, a collaboration between Montefiore and the Osborne Association, a community-based organization that provides reentry services and outpatient drug treatment to former inmates.

“Ideally,” says Dr. Fox, “we would want the mentors to meet people right at the prison door. We’re also looking into ways to get information to inmates about the program while they’re still inside.”

His intervention strategy, called Buprenorphine Facilitated Access and Supportive Treatment (BUP-FAST), will be tested in an NIH-funded study of 72 newly released inmates who’ll be randomly assigned to receive intensive peer mentoring or a simple referral to a substance abuse clinic.

“The primary goal of BUP-FAST is to get people to show up for treatment,” says Dr. Fox. “But we’ll also look at whether we can reduce the rates of relapse, overdose, recidivism and reincarceration.”
Addiction to opioids and cigarettes

Opioid misuse is clearly bad for your health. But surprisingly, cigarettes pose an even greater health threat to people who misuse drugs.

“Of the patients we see in our opioid treatment programs, up to three-quarters of them are dying from smoking-related illnesses, such as pneumonia, heart disease and cancer,” says Shadi Nahvi, M.D., M.S., an associate professor of medicine and of psychiatry and behavioral sciences at Einstein and an attending physician in internal medicine at Montefiore. In a 2006 survey, Montefiore researchers found that 83 percent of patients in its substance abuse clinics were current smokers—five times the rate in the overall New York City population. Researchers have found many reasons why opioid use and smoking are so intertwined. Some evidence suggests that nicotine triggers the same reward centers in the brain as opioids, so substance abusers may simply be balancing one addiction with another. Social factors, such as hanging out with peers who smoke, probably also encourage people to light up.

While the majority of people who misuse opioids smoke, most of them would like to shake the habit. Nearly half of the smokers in the Montefiore survey were thinking about quitting in the next six months, and an additional 22 percent were immediately ready to quit (within the next month) and had made a serious attempt to quit within the previous month.

Drug abuse treatment programs traditionally ignore smoking, assuming that smoking cessation efforts might jeopardize drug treatment and that patients have little interest in quitting.

Dr. Nahvi is having none of that. Several years ago, she tested whether varenicline (Chantix), a prescription drug that reduces cravings and decreases the pleasurable effects of tobacco products, might help reduce cigarette use among opioid-dependent smokers. It stood to reason that varenicline—the most effective stand-alone smoking cessation drug—would work well in this population, but no one knew for certain. “The original trials that led to the drug’s approval by the FDA excluded people with substance use disorders,” says Dr. Nahvi, another CARE alumna. Her study found that about 10 percent of the patients who took varenicline were able to quit, compared to none of the controls receiving a placebo. The results were promising, but the 10 percent quit rate fell far below varenicline’s 40 percent success rate in the general population.
Dr. Nahvi suspected that treatment adherence might be an issue and launched a follow-up study taking advantage of the clinics’ robust patient support infrastructure. “We wanted to see if adding short-term adherence support—essentially handing people their doses of varenicline several times a week—would help,” she explains. “And it did. The success rate nearly doubled, to 19 percent.”

Dr. Nahvi was recently awarded a five-year, $3.4 million NIH grant to study whether extended adherence support can be even more successful in getting people in opioid treatment programs to stop smoking.

**Ending opioid addiction**

“I know solving this problem will not be easy,” Surgeon General Murthy concluded in his letter to the nation’s physicians. “We often struggle to balance reducing our patients’ pain with increasing their risk of opioid addiction. But, as clinicians, we have the unique power to help end this epidemic.”

The Surgeon General proposed building “a national movement of clinicians” to accomplish three things:

- educate ourselves to treat pain safely and effectively;
- screen our patients for opioid use disorder and help them obtain evidence-based treatment; and
- shape the public view of addiction by talking about and treating it as a chronic illness, not a moral failure.

“As cynical as times may seem,” he wrote, “the public still looks to our profession for hope during difficult moments. This is one of those times.”

“**We often struggle to balance reducing our patients’ pain with increasing their risk of opioid addiction. But, as clinicians, we have the unique power to help end this epidemic.**”

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Dr. Arnsten leads a discussion about protecting the confidentiality of patients participating in research projects.
“JUNK” SCIENCE
One Scientist’s Quest to Understand Cellular Housekeeping, Aging and Age-Related Diseases
BY GARY GOLDENBERG
While growing up in Spain, Ana Maria Cuervo, M.D., Ph.D., often heard her mother say, “In a clean house, everything works better.” This sage advice would become the guiding principle of her scientific career.

Dr. Cuervo is a physician-scientist who specializes in autophagy—from the Greek words “auto” and “phagein,” meaning “self-devouring.” Essentially, autophagy is a fancy term for cellular waste management. Almost every type of cell in the human body uses a variety of strategies to degrade and recycle old, mutated or otherwise damaged proteins and other molecules so that cells’ interiors remain spic-and-span.

Autophagy was discovered in the 1960s, but the biomedical community paid little attention at first. After all, who cares about the trash as long as it’s discarded regularly? But over time, researchers realized that good cellular housekeeping is not just for neat freaks but also maintains health by preventing defective proteins from accumulating inside cells. What’s more, since autophagy slows down with age—one of Dr. Cuervo’s major discoveries—therapies to enhance autophagy may help prevent or reverse a range of age-related diseases and perhaps slow the aging process itself.

Autophagy is finally basking in the limelight. In October, the Japanese scientist Yoshinori Ohsumi was awarded the 2016 Nobel Prize in Physiology or Medicine for his pioneering studies of the genes and mechanisms that underlie this vital process.

“The honor recognizes our field of autophagy and how basic research—Dr. Ohsumi studies yeast genes—can have a transforming impact on biomedical science,” says Dr. Cuervo, a professor of developmental and molecular biology, of anatomy and structural biology and of medicine; co-director of the Institute for Aging Research; and the Robert and Renée Belfer Chair for the Study of Neurodegenerative Diseases at Einstein.

“The discovery of the autophagy genes in yeast has allowed researchers including me to establish connections between autophagy failure and many human disorders, including cancer, diabetes and Alzheimer’s disease,” she says. “Academic and industry labs are now developing drugs that target those genes, with the goal of curing those diseases by modulating autophagy.”

Early honors
Dr. Cuervo won recognition early in her career for dispelling the notion that lysosomes—the cells’ enzyme-filled recycling centers—degrade proteins at random. She and her mentor (the late J. Fred Dice of Tufts University School of Medicine) discovered that this recycling effort is actually quite selective and identified the molecular machinery that drives the process, which they dubbed chaperone-mediated autophagy (CMA). It involves specialized proteins that guide, or “chaperone,” old and damaged proteins to the lysosomes for digestion.

“CMA makes sure your proteins behave—kind of like the old-fashioned chaperone who escorted you and your boyfriend to the movies,” says Dr. Cuervo. “And if the proteins don’t behave, CMA eliminates them from the cell.” Those findings were published in the journal Science in 1996, a coup for such a young scientist.
Since joining the Einstein faculty in 2001, Dr. Cuervo has made several other major discoveries in the field:

- Autophagy is impaired in several age-related diseases such as Parkinson’s and Alzheimer’s diseases
- A newly recognized type of autophagy—lipophagy—helps cells burn fat to obtain energy
- Different autophagic pathways collaborate and compensate for one another when one of them fails
- Autophagy coordinates glucose and lipid metabolism
- Cancer cells are “addicted” to CMA for survival, and blocking CMA can shrink tumors and prevent metastasis
- Preventing age-related decline in the CMA of mouse livers keeps those organs functioning and healthy into old age

The making of a scientist

Most parents are thrilled to hear that their child is applying to medical school. Ana Maria Cuervo’s were dumbfounded. “You remember that you faint when you see blood?” her mother reportedly asked. “That was true,” admits Dr. Cuervo, who was born in Barcelona and raised in Valencia. She applied anyway, reasoning that medical school was the best path to a career in research, her ultimate destination. She had little company. “Just
three of us in our class of 300 at the University of Valencia were interested in research,” she recalls. “They were my best friends, and one of them became my husband [Fernando Macian-Juan, M.D., Ph.D., now a professor of pathology at Einstein].”

Dr. Cuervo grew accustomed to the sight of blood, but her days at the bedside only reinforced her plans to do research. “It was shocking,” she says. “I am very empathic, and the first thing they taught us in medical school was that you cannot be, or you will be suffering with all your patients.” She also came to realize that she had less interest in learning how things are done in medicine and more in discovering how they could be done better.

After graduating from medical school in 1990, she set her sights on a doctorate in biochemistry and molecular biology and looked for a lab studying the biology of aging. “During my rotation in geriatrics, I realized that almost nothing could be done for older people other than helping manage their symptoms,” she explains. “It was the most depressing thing I had ever seen.”

Dr. Cuervo was initially directed to a lab at the Instituto de Investigaciones Citológicas, also in Valencia, which focused on the role of mitochondria (the cell’s powerhouses) in aging. As fate would have it, the principal investigator was absent the day of her visit, so she was sent to the office of Erwin Knecht, a lysosome specialist.

Dr. Knecht invited her to join his team, but it wasn’t the warmest of welcomes. When his lab switched its emphasis to proteasomes—supposedly the next big thing in protein degradation—she was told to stick with lysosomes. “Dr. Knecht had never before had an M.D. in his lab and wasn’t sure if I was going to continue a career in science,” she says. “That was hard for me. All the cool things were happening in proteasomes.”

By 1993, Dr. Cuervo published her first paper on lysosomes, the one demonstrating the selective nature of autophagy. The budding scientist’s next break came shortly thereafter, thanks to Spain’s custom of closing down most workplaces, labs included, for the long summer holiday.

Instead of taking time off, Dr. Cuervo ventured to Tufts to work with Dr. Dice, an acquaintance of Dr. Knecht’s and a fellow autophagist. One summer morphed into two and then into three. Then, Ph.D. degree in hand, she crossed the Atlantic one more time to join the Dice lab as a postdoc in 1994, despite warnings from colleagues that autophagy was a career dead end.

It almost was—for another reason. Soon after Dr. Cuervo arrived at Tufts, Dr. Dice began losing his eyesight from complications of diabetes and offered to find his protégé a spot in another lab. She declined, even as the lab shrank and its funding dwindled. For six years, the...
In mouse brain cells, fat deposits (green) have accumulated because a type of autophagy called lipophagy has failed to metabolize them.

**FINDING THAT CMA NATURALLY DECLINES WITH AGE OPENED A NEW PERSPECTIVE ON THE BIOLOGY OF AGING.**

two collaborated, she from the lab, he from home, leading to their discovery of CMA and their groundbreaking finding in 2000 that CMA naturally declines with age in mammals, opening a whole new perspective on the biology of aging.

Thanks in part to Dr. Cuervo’s own contributions, lysosomes were becoming “cool.”

**A fountain of youth?**

After relocating to Einstein, Dr. Cuervo discovered why CMA declines with age: As animals get older, a receptor on the lysosomal membrane known as LAMP-2A—which helps pull chaperone-delivered proteins into the lysosome for digestion—progressively disappears.

To see whether this CMA decline could be halted, Dr. Cuervo designed a transgenic mouse model in which the age-related decrease in LAMP-2A was prevented. The results, published in *Nature Medicine* in 2008, showed that the transgenic mice maintained CMA activity until advanced ages. And compared with “normal” aging animals, the aged transgenic mice had less intracellular accumulation of damaged proteins and improved liver function—the first evidence in mammals that preventing the age-related decline in autophagy slows cellular aging and preserves organ function.

Dr. Cuervo’s work has since expanded into neurodegenerative disorders, and
she and her collaborators have found
evidence that CMA is impaired in
Parkinson’s and Alzheimer’s diseases.

“Healthy older individuals can lose,
say, 50 percent of their ability to recycle
materials and they’ll still do reasonably
well,” says Dr. Cuervo, whose words
tumble out by the dozens as she enthusi-
astically discusses her favorite topic.

“But problems can arise for people who
produce mutant proteins—as in some
forms of Alzheimer’s disease—but whose
efficiency at getting rid of those proteins
decreases significantly. This leads mutant
proteins to accumulate even as their rate
of production stays the same, ultimately
contributing to neurological problems.”

Studies suggest that other intracel-
lar stressors that affect older people—
the elevated blood glucose of type 2
diabetes and abnormally high lipid levels
of atherosclerosis, for example—simi-
larly overwhelm the cells’ ability to clear
them.

While autophagic aging may be
inevitable, the good news is that it may
be treatable. A study led by Dr. Cuervo’s
husband, Dr. Macian-Juan, found that
centenarians have naturally robust
autophagy, which presumably contrib-
utes to their longevity. “If we can deter-
mine the genes that are responsible for
their youthful autophagy, we might be
able to mimic this effect with drugs or
other therapies,” says Dr. Cuervo.

Dr. Cuervo’s research team is already
testing autophagy-boosting drugs, which
have shown promise in animal models.
In the meantime, people of any age can
take measures to keep their autophagy
humming along. “Basically, follow your
grandmother’s advice: eat a balanced
diet, get enough sleep and exercise,”
she says. “Each of these activates
autophagy.”

**Autophagy and cancer**

Venturing even farther afield, Dr.
Cuervo’s team is also investigating
autophagy’s role in cancer, which affects
primarily older people.

“As you age, the decline in
autophagy’s efficiency makes your
cells—particularly your DNA—more
vulnerable to damage,” she explains.

“And this increases the possibility of
a normal cell transforming into a bad
cell—a cancer cell.” Recently, Dr.
Cuervo found that autophagy plays yet
another role in cancer: Cells ramp up
their CMA when they become malig-
nant. Of 17 types of tumor cells that
her lab analyzed, CMA was enhanced
in almost every one. When the research-
ers blocked CMA, the tumors shrunk,
Dr. Cuervo reported in a 2011 paper in
*Science Translational Medicine*.

“Since cancer cells have such a high
rate of growth, they need a huge amount
of nutrients, which they get through
efficient recycling of their components,”
she notes. “This would also explain why
cancer cells can be so resistant to che-
motherapy. Chemo aims to cause damage
to the cancer cells. But because their
CMA is so good, cancer cells can handle
that damage very well. It’s as if they’re
saying, ‘Bring it on!’”

In one of her many studies funded
by the National Institutes of Health, Dr.
Cuervo is attempting to find out how
cancer cells activate CMA. “The CMA
activation we see in cancer cells is what
we’d like to achieve in normal cells,”
she says.

“I’m not claiming that ‘fixing’
autophagy will be a cure-all, but it may
do a lot,” says Dr. Cuervo. “Autophagy
is a fundamental mechanism in the cell.
And if the cell is cleaning up after itself,
other things in the body will start to
function more efficiently.”

Which is essentially what her mother
said all those years ago. E
Dr. Michler is the Samuel I. Belkin Endowed Chair; surgeon-in-chief, chairman and professor of surgery and cardiothoracic and vascular surgery; and co-director of the Montefiore Einstein Center for Heart and Vascular Care. He is an internationally renowned cardiothoracic surgeon and researcher, with expertise in multiple specialties, including complex cardiac surgery, heart transplantation, valve repair surgery, ventricular reconstruction for congestive heart failure and minimally invasive cardiac surgery. Dr. Michler was one of the first to perform minimally invasive and robotic surgery in heart patients. His pivotal work in robotics led to approval by the Food and Drug Administration of this advanced technology for mitral valve repair and coronary artery bypass surgery. He is a National Institutes of Health investigator with more than 10 years of NIH funding and joined the faculty of Einstein and Montefiore in 2005.

Heart disease doesn’t seem to elicit the same fear as cancer. Why? Probably because we have a better understanding of heart disease and how to treat it compared to cancer. People feel that cancer is a death sentence despite the fact that more men and women die each year of heart disease than all types of cancer combined. Cancer is often a lingering illness whereas heart disease is often considered curable. But while coronary artery disease, the most common form of heart disease, can be extremely well treated with bypass surgery or by inserting stents, it is a chronic illness that can recur.

Could more be done to prevent heart disease? That’s the Holy Grail, of course. We have a responsibility to encourage people, especially those at higher risk, to avoid behaviors that might lead to or accelerate heart disease. The challenge is keeping those at risk on a steady course of prevention therapies. Many people find it too difficult to change bad habits. We know many of the genetic factors that predispose people to heart disease, but we don’t yet understand the individual epigenetic factors that control the expression of those genes and affect disease outcomes. While we can offer recommendations for large segments of the population, we cannot yet alter a person’s genes or their expression. One day, we hope to offer individual patients specific preventive measures.

What kinds of clinical trials are being conducted in surgery and cardiovascular surgery at Montefiore? We have about 30 ongoing trials, including studies of stent implantation, bariatric surgery, atrial fibrillation, reflux disease, infection control during pediatric surgery and neuro-protection for patients undergoing valve replacement, to give just a few examples. Our work through my NIH award has led us to make specific recommendations regarding the treatments of ischemic mitral regurgitation, atrial fibrillation and the use of mechanical circulatory assistance for heart failure. This work has resulted in four articles in the New England Journal of Medicine in the last two years.

What about stem cell therapy for heart disease? We’re conducting a clinical trial looking at whether injections of mesenchymal stem cells—cells that give rise to blood, bone, cartilage and other tissues—can regenerate heart muscle in heart failure patients being sustained by mechanical-assist devices. This is a limited patient population, and the therapy could one day apply to the many patients who have lost segments of heart muscle—due to coronary artery disease, heart attacks or congenital abnormalities—and are at risk for heart failure. To me, this is the most exciting area of clinical investigation in our field.
In recent years, Montefiore has been involved in several large multicenter trials. What attracts federal funding agencies and industry to this institution? First and foremost, it is our faculty. We are solid investigators with a track record of excellence in the field of cardiovascular disease. Second, our patient community is a particularly fertile ground for clinical research because of its rich diversity. We often see untreated and more advanced disease, which of course is more challenging to treat. What we learn here can be generalized to many other communities, not only around the country but around the world.

How are you promoting closer ties between researchers at Einstein and clinicians at Montefiore? We have had many successful collaborations over the 10 years I’ve been on the faculty, and my goal is to strengthen and amplify them. We welcome inquiries from basic science investigators and host research meetings to discuss opportunities. Most importantly, both clinicians and scientists need to reach out and build bridges. We’ve been working in many ways to build our research infrastructure. On the clinical side, we recruited a biostatistician and several research nurses to support clinical trials. We created a research open house, where faculty members can share their studies with one another and the broader research community. We also won a coveted NIH T32 grant, which prepares pre- and postdoctoral fellows to conduct cancer research. This T32 grant is being used to train surgeons to conduct research into the microenvironment of tumors.

Are there unique or unusual cardiovascular health issues in the Bronx? We see more advanced disease here, and this affects all areas, not just cardiovascular disease. People of lower socioeconomic status are less likely to seek medical attention when disease is in its early stages, perhaps out of fear, uncertainty about where to go and whom to see or cost concerns. We must encourage people to seek medical care when they feel unwell and come in for specific screening tests, especially for heart disease and cancer. Often, patients’ first interaction with the healthcare system is the emergency room, when they can no longer tolerate discomfort or pain or they have an acute event. This is undesirable on many levels, beginning with the unnecessary suffering. And the longer they wait to have a disease diagnosed or treated, the lower the likelihood of having a cure or a good outcome.

How do you reach these people? You have to convince them that the healthcare system—and specifically Montefiore—is a welcoming place for them and their families. Whether you’re a recent immigrant or a Wall Street banker, we’re going to take extraordinary care of you.

There are many choices for heart care around the region. Why go to Montefiore? The simple answer is that there is no better hospital. We achieve extraordinary results in surgery while also being convenient for people who live in the Bronx and Westchester. But it goes well beyond that. There’s no condition that can’t be treated by our experts here at Montefiore, whether that’s an asthma attack or complex heart failure.

What’s the status of Heart Care International, the charitable organization you and your wife founded? We are in our 22nd year. We’ve now treated close to 1,500 children and young adults with heart surgery and an additional 500 with medical treatment. It has been a wonderful source of goodwill and humanitarian aid, and a great educational experience. We’ve taken faculty, residents and medical students from Einstein and other institutions to countries in Central and South America. They have opportunities to see and treat unusually complicated cases as well as diseases no longer common here in the United States, such as rheumatic heart disease.

For me personally, Heart Care International is the expression of everything that I stand for as a physician. Heart Care International represents access to healthcare for those with no hope for care, the care is free and our singular mission is educating and training host country medical professionals.

What about developing countries now confronting the “curse” of affluence in the form of chronic diseases, including heart disease? If we can help these countries keep up with training and education, we will have a chance to help humanity. It is a dilemma that demands more research and better understanding of the problem, which underscores what we at Einstein and Montefiore are all about: We are a socially responsible institution that thinks long and deep about our place—not just in the local community but in the world at large. I am very proud to be part of it.
On October 31, more than 130 Women’s Division members and friends gathered at the Harmonie Club in Manhattan for the division’s annual “Cards for a Cause” event. The Halloween-themed afternoon featured lunch, shopping, mah-jong and canasta while raising funds for cancer research.

In her welcoming remarks, Women’s Division president Carol Roaman highlighted recent national news about Einstein and Montefiore that exemplified the world-class research and patient care they offer. She spoke about the McDonald twins, separated in October at Montefiore by a multidisciplinary team of physicians led by Einstein and Montefiore’s James T. Goodrich, M.D., Ph.D., an expert in craniopagus surgery, and Oren Tepper, M.D., a renowned plastic and reconstructive surgeon and the director of the craniofacial surgery program. The surgeons shared 3-D imaging models with the group; the guests then saw a video that explained the groundbreaking 28-hour procedure.

Ms. Roaman and executive vice presidents Jackie Harris and Helen Radin served as event co-chairs, alongside honorary chair Andrea Stark.

To join the Einstein Women’s Division’s initiative to support research on women’s and men’s cancers, or to learn more about the Women’s Division, please contact Mary Anna Smith at 718.920.6036 or maryanna.smith@einstein.yu.edu.
Montefiore and Einstein in Florida 2017

In February, Einstein and Montefiore presented three consecutive days of educational events for friends and supporters in the Palm Beach community. More than 300 people attended the gatherings, hosted by the Einstein and Montefiore Trustees.

The first event, a kickoff luncheon at the Palm Beach Country Club, was hosted by Einstein Trustees Marilyn and Stanley M. Katz. Marilyn Katz welcomed Stephen M. Safyer, M.D., president and CEO of Montefiore Medicine; Allen M. Spiegel, M.D., Einstein’s Marilyn and Stanley M. Katz Dean; and the many Einstein and Montefiore Trustees. Kamran Khodakhah, Ph.D., chair of the Dominick P. Purpura Department of Neuroscience, gave a presentation, “The Brain: The Essence of Our Being.” The afternoon concluded with a lively question-and-answer session.

The next evening, Einstein Trustee Karen Mandelbaum and her husband, David, hosted cocktails in their home in Jupiter. Steven C. Almo, Ph.D., the Wollowick Family Foundation Chair in Immunology and director of Einstein’s Macromolecular Therapeutics Development Facility, gave a presentation, “New Strategies for Immunotherapy: Releasing the Power Within.”

The weekend concluded with a sunset reception at the beachfront home of Montefiore Trustee Melissa Ceriale and her husband, John. This event included a presentation by Evan S. Garfein, M.D., chief of the division of plastic and reconstructive surgery at Montefiore and associate professor of both surgery and otorhinolaryngology at Einstein, “Conjoined Twins: Uniting Clinical Excellence and Innovation.”

1. Dean Allen M. Spiegel with Einstein Trustees Marilyn and Stanley M. Katz, and Steven M. Safyer, M.D., president and CEO, Montefiore Medicine.
2. David Mandelbaum and Einstein Trustee Karen Mandelbaum.
3. Melissa Ceriale, Montefiore Trustee, and Etonella Christlieb.
Evan Charney, M.D. ’60, writes: “Hello, fellow alumni of ’60. I am happily retired with my wife, Jane, in Falmouth, MA, and enjoying life as a printmaker (evansart.smugmug.com). If you find yourself on Cape Cod, please get in contact!”

David Shultz, M.D. ’63, recently celebrated his 55th anniversary with his wife, Monique. They have two children, Mitchell and Charles, and five grandchildren. Dr. Schultz, an ophthalmologist, practiced in Northridge, CA, and taught at the Jules Stein Eye Institute. He had a heart transplant in 2013 and retired in June 2015. His practice passed to his son Mitchell, who has been developing a national reputation in ophthalmology. Charles is a tax attorney who advises high-income Citibank private clients. Dr. Schultz’ eldest granddaughter, Shaina, spent a year in Israel and is now attending Washington University. Her sister Nicole is now in Israel and will attend the University of Michigan.

Alan Rockoff, M.D. ’72, reports that his second book, Act Like a Doctor, Think Like a Patient: Teaching Patient-Focused Medicine, has just been published by Medical Education Press. The book is based on his experiences teaching senior medical students at the Tufts University School of Medicine in Boston for 35 years. It focuses on the need for medical providers to know not just how to diagnose and treat disease, but how to personalize medicine by understanding illness and treatment through the eyes of their patients. His book is available online through Amazon and Barnes and Noble.

Joan Heller-Brown, Ph.D. ’74, is the 2017 recipient of the Otto Krayer Award in Pharmacology, given by the American Society for Pharmacology and Experimental Therapeutics. This award commemorates the enduring legacy of Dr. Krayer’s ethical behavior, commitment to teaching, high standards of scientific scholarship, promotion of interdisciplinary research to reveal the actions of chemicals and support of younger scientists. The award recognizes Dr. Heller-Brown’s studies of G-protein-coupled receptors and her scientific scholarship and strong commitment to teaching and mentoring younger scientists.

Jeff Gilbert, M.D. ’75, retired from Montefiore in October 2013. He was the founder of the STD Center for Excellence and served as its medical director for 21 years. He spent most of his 38 years in practice in the Bronx, 33 in the field of sexually transmitted diseases. He held appointments at Einstein in the departments of medicine and ob-gyn. Dr. Gilbert enjoyed more than three decades of teaching medical students, residents, fellows, nurse practitioners, physician assistants and attendings at the STD Center. Since leaving Montefiore, he has been the medical director of sexually transmitted infections (STIs) at BioReference Laboratories, an Opko Health Company. He is currently involved with a major STI project in the Dominican Republic directed by staff members at the Columbia University College of Physicians and Surgeons. He is also the author of a popular children’s book, Milton’s Moment (www.miltonsmoment.com), and is a recognized Hudson River driftwood artist (www.driftymaster.com).

Ann Landowne, M.D. ’75, writes: “After practicing psychiatry for 20 years, I took a break and attended rabbinical school at Hebrew Union College–Jewish Institute of Religion, graduating in 2011. I’m currently serving as the rabbi at Temple Beth-El in Geneva, NY, and working as a child psychiatrist at Hillside Children’s Center, a residential treatment center near Rochester, NY.”
My husband, Geoffrey Stein, died suddenly while jogging in 2012. My four children and I miss him very much. I just had the honor of officiating at my son Joseph’s wedding to Fiamma Varoli, in Sovicille, Italy.”

William Breitbart, M.D. ’78, is the Jimmie C. Holland Chair in Psychiatric Oncology and chief of the psychiatry service in the department of psychiatry and behavioral sciences at the Memorial Sloan Kettering Cancer Center in New York. He received the 2017 American Cancer Society Trish Greene Quality of Life Research Award. Dr. Breitbart is a past president of the Academy of Psychosomatic Medicine and of the International Psycho-oncology Society. He has edited or written 12 textbooks, including Psycho-oncology (first, second and third editions); the treatment manuals for Meaning-Centered Group Psychotherapy in Advanced Cancer Patients and Individual Meaning-Centered Psychotherapy for Advanced Cancer Patients; and his newest textbook, Meaning-Centered Psychotherapy in the Cancer Setting (Oxford University Press). Dr. Breitbart is editor-in-chief of Cambridge University Press’ international palliative-care journal, Palliative & Supportive Care. He and his wife, Rachel, recently celebrated their 30th wedding anniversary and live on the Upper East Side of Manhattan. Their son Sam, 25, graduated from Yeshiva University’s Cardozo Law School and is an associate at the Sherman Sterling law firm. Dr. Breitbart’s e-mail is breitbaw@mskcc.org, and he is eager to hear from his fellow classmates and Einstein alumni.

1980s

Vickie Mabry-Height, M.D. ’81, recently published White Coat Secrets, in which “Dr. Vickie, M.D.,” shares an extraordinarily personal account of her career spanning more than 30 years in medicine. She grew up in the Jim Crow cotton fields of North Carolina, survived the inner-city ghettos of Brooklyn, NY, and persevered to rise in the medical field as both a practitioner and an entrepreneur. In the book she explores the issues of racism, sexism, health disparities and injustices that still plague the medical field today.
She also details her passion for giving back to the community and helping improve care for patients around the globe. Told from the perspective of a female doctor of color, her story is meant to empower aspiring healthcare practitioners. Dr. Mabry-Height is board-certified in internal medicine. She received a master’s in public health with an emphasis in environmental and occupational toxicology from the University of California at Los Angeles, followed by a Leadership Fellowship in healthcare at the University of California at San Francisco. She is a fellow of the American College of Physicians and received a congressional award for community service.

Joel Cohen, M.D. ’83, tells us that after 29 years as an Einstein faculty member in the department of neurology, he has left Einstein to join the staff of Shaare Zedek Medical Center in Jerusalem to help develop its new stroke service. “My wife, Pearl, and our four children—Tova, Natan, Meir and Sara—joined me in moving to Israel in September 2016,” he writes. “The 37 years I spent at Einstein since becoming a medical student in 1979 have been filled with a multitude of wonderful personal and professional experiences, which I will always treasure.”

2000s

Andrew Chertoff, M.D. ’05, was promoted to associate residency director of the department of emergency medicine for Einstein at Jacobi and Montefiore Medical Centers. Previously, he was a residency site director and assistant residency director within the department. He graduated from the Jacobi/Montefiore emergency medicine residency program.

Stanley K. Frencher, M.D. ’06, received the Herbert W. Nickens Faculty Fellowship at the 2016 Association of American Medical Colleges’ annual meeting in Seattle. The award recognizes an outstanding junior faculty member who demonstrates leadership potential in resolving inequity in medical education and healthcare; is working to address the educational, societal and healthcare needs of racial and ethnic minorities in the United States; and is committed to a career in academic medicine. The honoree receives a $15,000 grant that funds a project to support racial and ethnic minorities.

Michael Jones, M.D. ’08, was promoted to residency director of the department of emergency medicine for Einstein at Jacobi and Montefiore Medical Centers, effective July 1, 2017. Dr. Jones, a graduate of the Jacobi/Montefiore residency program, has served as the department of emergency medicine’s associate residency director for the past five years.

Jeremy Mazurek, M.D. ’08, tells us that, after completing fellowship training in cardiovascular diseases, advanced heart failure/cardiac transplantation and pulmonary hypertension at the Hospital of the University of Pennsylvania in June 2016, he joined the faculty of that university as an assistant professor of clinical medicine in the advanced heart failure/transplant and pulmonary hypertension programs.

IN MEMORIAM

We acknowledge with sadness the passing of the following Einstein alumni. We honor their memories and extend our deepest condolences to their families and friends.

Michael E. Goldstein ’59
Kurt Link ’61
Anne Elayne Bernstein ’62
Herman Bruch ’62
Donald Goldmacher ’67
Leora Bella Sachs ’76
“I feel empowered and deeply grateful for the scholarship that’s allowing me to achieve all that is possible with an Einstein education.”

– Hope Miodownik, Class of 2019

Give to the Einstein Alumni Association Annual Fund

The Einstein Alumni Association Annual Fund provides scholarships to help gifted Einstein students like Hope realize their dreams of a career in medicine. The fund also supports programs to enhance student life at Einstein. To contribute online, go to www.einstein.yu.edu/alumni, then click “Support Einstein.” Designate your gift or pledge to “Alumni Association Annual Fund.” Contributions from non-alumni are welcome.

For more information, please contact the Office of Alumni Relations at 718.430.2013 or alumni@einstein.yu.edu.
EINSTEIN’S FIRST DORMITORY

Sixty years ago—before the high-rise student housing on Eastchester Road existed—Einstein’s earliest students lived closer to the heart of campus: off the courtyard in what’s now known as the Harold and Muriel Block Building.

The photo above shows Dean Marcus D. Kogel, M.D., and professor of microbiology & immunology Edward J. Hehre, M.D., surveying the site, on which construction began in 1956. More than 1,000 people—including Samuel Belkin, Ph.D., president of Yeshiva University; New York senator Jacob Javits; and New York City mayor Robert Wagner—attended the new dormitory’s dedication in October 1957. The building was named after the late Abraham Mazer, a philanthropist who was also a College of Medicine founder and Yeshiva trustee. Some 300 students moved into the Abraham Mazer Residence Hall soon thereafter.

When the Eastchester Road apartments were completed in 1973, the Mazer building was reconfigured to house administrative offices. In 2012, one of the high-rise student housing buildings was renamed in honor of Abraham Mazer, and the former Mazer building became the Harold and Muriel Block Building in honor of Muriel Block’s major bequest to Einstein.

Today, the Block Building is home to the Block Institute for Clinical and Translational Research, the Global Health Center, the Montefiore Einstein Center for Bioethics, the department of family and social medicine and the department of epidemiology & population health’s division of biostatistics, among others.
Be part of the Einstein legacy: Help us transform human health.

For over 60 years, Albert Einstein College of Medicine has been a leader in advanced medical research and patient care. You can help continue the standard of excellence for which Einstein is renowned. Make a legacy gift to the College of Medicine today and join the Walking with Einstein legacy society.

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– earn a valuable income-tax deduction

To learn more about the benefits of making a legacy gift to Einstein, visit www.einstein.yu.edu/r/plannedgiving or contact: Al Seminsky, Executive Director of Development, at 718.430.2412
Most cancer deaths result from breakaway tumor cells that spread, or metastasize, to distant organs. Prime suspects are hypoxic (oxygen-deprived) cells that overexpress genes involved in cancer-cell invasion and metastasis. A study by Einstein researchers, published last year in *IntraVital*, offered unprecedented insights into their behavior. After designing a red fluorescent protein that turns on under low-oxygen conditions, the researchers used it to label breast cancer cells, and—using multiphoton microscopy—compared hypoxic and “normoxic” tumor cells (labeled with green fluorescent protein) at single-cell resolution in live breast xenograft tumors (human tumor cells growing in mice). To metastasize, tumor cells must first degrade collagen and other substances outside the cell to reach nearby blood vessels. This image shows the increased activity of hypoxic cancer cells in tumors. The bright white spot on the red (hypoxic) cell shows it was actively degrading collagen. The work was done in Einstein’s Gruss Lipper Biophotonics Center. The paper’s lead author was Yarong Wang, M.S., an associate in the department of anatomy and structural biology; senior author John S. Condeelis, Ph.D., is a professor and co-chair of the department.