The Defect Detectives: Obesity, Diabetes and the Hunt for the Glitches That Cause Them
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Comes to Academic Medicine

Montefiore
Mavens of Medicine

Top Stories

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Cover illustration: Chris Gash
A Message from the Dean

Earlier this year, Parsa Mirhaji, director of clinical research informatics at Einstein and Montefiore, traveled to Washington, DC, to take part in President Obama’s Precision Medicine Initiative Summit at the White House. Healthcare leaders from across the country met to begin integrating biological, clinical, environmental and administrative data to fuel research innovations and improve care.

In this issue of Einstein magazine, “Big Data Comes to Academic Medicine” describes how Dr. Mirhaji and his colleagues are building an Einstein-Montefiore infrastructure that will allow findings from research studies and patient encounters to flow into a “semantic data lake.” From there, those findings can inform clinical decision-making, personalize therapies, define community health needs and more.

About 15 years ago, the Diabetes Prevention Program (DPP) trial revealed several effective measures for staving off type 2 diabetes: a lifestyle intervention that involved exercise and modest weight loss, and taking the insulin-sensitizing drug metformin. As director of the National Institute of Diabetes and Digestive and Kidney Diseases, which supported the DPP, I had the honor of bringing this news to the public. In the ensuing years, despite education efforts, the nation continued to gain weight, and type 2 diabetes rates continued to rise.

Perhaps stronger medicine is needed. In our cover story, “The Defect Detectives,” five scientists at the Einstein-Mount Sinai Diabetes Research Center take us on a guided tour of their work. Their surprising conclusion is that strategies should shift upstream, to the brain—and that the best approach to obesity and type 2 diabetes may be to treat them as brain disorders. Their studies will get a boost from Einstein’s new Brain Science Initiative as it moves forward.

The “Collegial Life” section describes U.S. Surgeon General Vivek Murthy’s visit to Einstein-Montefiore to highlight the opioid abuse epidemic devastating the United States. Addiction too is increasingly viewed as a brain disorder, one that Einstein, with its outstanding neuroscience research, and Montefiore, given the patient population it serves, are in a unique position to address.

ALLEN M. SPIEGEL, M.D.
The Marilyn and Stanley M. Katz Dean
Albert Einstein College of Medicine
Executive Vice President, Chief Academic Officer
Montefiore Medicine
Vivek Murthy, M.D., M.B.A., the U.S. surgeon general, spoke about the opioid drug crisis to an overflow audience on June 30 in Einstein’s Judith and Meshulam Riklis Auditorium. He noted that most people who misuse opioids obtain them from physicians via legally written prescriptions, usually for pain relief. “By sharpening our prescribing practices,” he said, “we can turn the tide.”

Opioid drugs include oxycodone (such as OxyContin) and hydrocodone (such as Vicodin). From 1999 to 2014, overdoses of prescription opioids caused more than 165,000 deaths in the United States. People who misuse opioids are also 40 times more likely than others to use heroin, placing them at risk of infection from HIV and hepatitis B and C viruses.

Einstein-Montefiore was Dr. Murthy’s eighth stop on his national tour, dubbed the “Turn the Tide” campaign, in which he speaks to clinicians about addiction to prescription painkillers. Joining him at Einstein were New York City First Lady Chirlane McCray, who leads the city’s efforts on mental health and substance misuse; Herminia Palacio, M.D., M.P.H., deputy mayor for health and human services; Mary Bassett, M.D., M.P.H., commissioner of the New York City Department of Health and Mental Hygiene; and Leonard Gill, a patient in long-term recovery and a peer educator.

**Action Plan**

The panel discussed ways clinicians can combat opioid misuse and overdose, starting with identifying patients at risk.

“A shadow of shame hangs over opioid addiction,” said Dr. Bassett. She urged doctors to “ask patients in a non-judgmental way if they use opioids, just as you ask about alcohol intake.”

Other tactics include making naloxone (for emergency treatment of a drug overdose) more available, connecting patients to treatment and helping patients understand both the benefits and the dangers of opioids.

“With the nation’s second-largest opioid treatment program, Montefiore has been fully engaged in working to stem the opioid crisis and provide the best care to people struggling with addiction,” said meeting host Lynn Richmond, N.P., executive vice president of Montefiore Health and chief strategy officer. “Our approach is to care for the whole patient, from the medical issues to the emotional, social, legal and financial.”

Healthcare professionals nationwide who prescribe opioids will soon receive a letter from Dr. Murthy urging them to intensify their efforts to combat the country’s opioid epidemic.
Meet Me on Main Street

What was once a dark hallway and warren of rooms on the ground floor of the Leo Forchheimer Medical Science Building has for two years now been called “Main Street”—a bright, well-traveled thoroughfare and destination at the heart of the Jack and Pearl Resnick Campus. It’s home to the Einstein Café (check out the panini press!) and the site of numerous events.

Positive Exposure. On a truly rare day—February 29, 2016—Main Street’s long wall was lined with photos of people living with rare genetic disorders. Through his not-for-profit organization Positive Exposure, photographer Rick Guidotti addresses myths and misperceptions about these individuals. The award-winning former fashion photographer challenges accepted definitions of beauty and aims to help people with these serious disorders feel better about themselves. The photos were part of the Rose F. Kennedy Intellectual and Developmental Disabilities Research Center (IDDRC)’s fourth annual Rare Disease Day celebration for students, faculty and guests. The day also included lectures and a film screening.

Leading the proceedings was IDDRC director Steven U. Walkley, D.V.M., Ph.D., a professor in the Dominick P. Purpura Department of Neuroscience, the department of pathology and the Saul R. Korey Department of Neurology. Other organizers included Frederick J. Kaskel, M.D., Ph.D., a professor of pediatrics (nephrology) and chief of the division of pediatric nephrology at Einstein and Montefiore; and Robert W. Marion, M.D., a professor of pediatrics (genetics), chief of the division of pediatric genetics and a professor of obstetrics & gynecology and women’s health.

Posters, Posters, Posters. The Einstein community got a close-up view of the work of its Clinical Research Training Program (CRTP) graduates at a poster exhibit on Main Street in December. More than a dozen posters were displayed, covering a range of clinical research topics, including factors associated with longevity, health outcomes of antiretroviral therapy in formerly incarcerated HIV-positive patients and clinical effects of the antibiotic azithromycin in asthmatic children. “Scientists from various medical specialties and subspecialties rub shoulders with each other in the CRTP,” notes former program director Ellie E. Schoenbaum, M.D. “The posters showed the synergy between healthcare services at Montefiore and patient-oriented, translational research at Einstein.”

In March, a crowd of medical students, deans, faculty and staff gathered on Main Street for this year’s exhibit of more than three dozen medical student posters. “It’s a tremendous opportunity for Einstein’s medical students to present the research and community projects they’ve been working on with..."
faculty members at Einstein-Montefiore, at other institutions across the nation and all over the world,” says Dr. Schoenbaum, who is now director of medical student research. “The exhibit affords the students a way to have meaningful conversations with colleagues about their projects.” Dr. Schoenbaum is also a professor of epidemiology & population health, of medicine (infectious diseases) and of obstetrics & gynecology and women’s health.

**Doctors Without Borders.** Main Street was the setting in May for a reception and photo exhibit sponsored by Doctors Without Borders (also known as Médecins Sans Frontières, or MSF). The exhibit, “Because Tomorrow Needs Her,” captured the challenges women face in getting urgently needed care in four countries. Videos focusing on childbirth in Burundi, sexual health in Haiti, HIV in Malawi and family violence in Papua New Guinea played on the back wall of the open seating area.

“The realities of women’s health are not discussed enough,” said Melissa Pracht, a digital content editor at MSF who helped create the videos and exhibit. “I want you bright medical professionals to take these issues and make them top priority.” Also on hand was Patricia Kahn, Ph.D. ’81, who is now a medical editor at MSF and who was impressed with our airy new event space.

Part two of the MSF presentation took place later in the month and also made use of Main Street for a reception. Among those attending were Einstein-Montefiore physicians Lisa Nathan, M.D., an assistant professor of obstetrics & gynecology and women’s health, and Darin A. Portnoy, M.D., M.P.H., an associate professor of family and social medicine. Dr. Nathan also directs the department’s Women’s Global Health program and has worked on fistula-repair initiatives in Africa; she now focuses on maternal morbidity and mortality prevention. Dr. Portnoy has worked with MSF since 1997 in Central Asia, Central America and Africa and was previously president of MSF-USA’s board of directors. After the reception, they took part in a panel discussion in the Mary and Karl Robbins Auditorium on women’s healthcare worldwide.

Einstein’s Global Health Center sponsored both events.

Clockwise from top: Medical students’ posters attracted interest; a street scene from Haiti at the Doctors Without Borders reception; and 18-year-old Alena Galan, who was born with mucopolysaccharidosis type VI, signing a copy of her book, *Differences Are Blessings*, on Rare Disease Day. Facing page: photographer Rick Guidotti discusses the meaning of beauty on Rare Disease Day.
Education Update

Competency Criteria
Television’s Dr. House—a brilliant diagnostician who is stunningly deficient in people skills—probably wouldn’t be admitted to medical school today.

Bedside manner and an array of other abilities are now being factored into medical school admissions decisions, thanks to a new Association of American Medical Colleges (AAMC) initiative. The AAMC has endorsed an admissions policy that considers an applicant’s leadership ability, communication skills, commitment to service, maturity and compassion as well as grades. The Class of 2019 is the first group to be admitted to Einstein based on these “competency-based admissions” (CBA) criteria.

“To be successful physicians, medical students need to do more than just meet requirements on a checklist,” says Noreen Kerrigan, M.P.A., associate dean of admissions. She and other members of Einstein’s admissions committee wrote a report on their experiences developing and implementing the new standards, which was published in Medical Education Online early this year.

Einstein will track CBA students as they move through their medical education, residencies and career choices.

Brainstorming for Curriculum Reform
Think outside the box. Dream big. Imagine new ways for Einstein to give graduates every advantage in the ever-changing world of medicine. Thoughts such as these were on the minds of some 130 faculty, students, community members and guest speakers at Einstein’s first Thought Leaders Conference on curriculum reform, held earlier this year in the Education Center and Robbins Auditorium.

Responding to a call from the AAMC and other organizations, medical schools across the country are redesigning their curricula. “Graduates need to be ready to face a flood of new scientific information, constant advances in technology, continual restructurings of healthcare delivery and financing and changes in society,” said Martha S. Grayson, M.D. ’79, Einstein’s senior associate dean for medical education.

The Thought Leaders Conference kicked off the Einstein initiative. “Medical education needs to be aligned with what’s happening in the healthcare environment, and its overarching goal should be to improve health outcomes,” said keynote speaker Maryellen E. Gusic, M.D., president of the Academic Pediatric Association and a past chief medical education officer at the AAMC. In her view, an effective education program:

- emphasizes competencies (see box);
- stimulates students to inquire and innovate;
- strives to meet different learning needs;
- assesses learning outcomes; and
- encourages students to develop professional values, actions and aspirations.

Einstein’s Seven Competencies
The College of Medicine expects its graduates to demonstrate competency in these areas:

- Healer
- Scientist
- Advocate
- Educator
- Colleague
- Role model
- Lifelong learner
Dr. Grayson followed with a presentation on engagement as the heart of the process. Next came “vision presentations” by faculty members and students. “We had 42 presentations and published 93 proposals,” notes Dr. Grayson. Topics ranged from curricular themes and the structure of a medical school curriculum to teaching methods and effective assessments. Working groups from the Curricular Design Executive Committee are now reviewing the proposals generated at the conference. Curricular updates will occur over four years, beginning in the fall of 2017 with the class of 2021.

**Match Day 2016**

“On Match Day, students feel an enormous anticipation,” says Stephen G. Baum, M.D., senior associate dean for students at Einstein. “The envelopes they receive hold their futures. The good news is our students do very well in the match, and this year is no exception. It’s a day to toast their achievements and future careers as practicing physicians.”

Eighty-eight of the 197 Einstein M.D. and M.D.-Ph.D. students who matched will enter primary care specialties: 48 matched to internal medicine (#1), 31 to pediatrics (#2) and 9 to family medicine (#7). Rounding out the top 10 matched specialties this year were: emergency medicine (16 students), surgery (14), psychiatry (13), anesthesiology (11), radiology—diagnostic (9), neurology (6) and orthopedics (6). This year saw an uptick in matches to surgery and psychiatry. Close to a quarter of Einstein’s graduating students will stay in the Einstein community, joining Montefiore or an affiliated hospital.

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Dr. Safyer Is a Top Influencer

Steven M. Safyer, M.D., president and CEO of Montefiore Medicine, was named a top leader on Modern Healthcare magazine’s list of the “50 Most Influential Physician Executives & Leaders.” Dr. Safyer rose in the ranks to number 13, up from number 36 in 2015. This was the eighth consecutive year that he was named to this list of medical executive leaders.

Dr. Safyer graduated from Einstein with the class of 1982 and has worked at Montefiore since then. An internist in the department of medicine, throughout his career he has been a leader in advancing Montefiore as an innovative and equitable healthcare system. Since being appointed president and CEO in 2008, Dr. Safyer has increased Montefiore’s care-management capabilities, with an emphasis on innovation and population health. Modern Healthcare also named Dr. Safyer as one of the “100 Most Influential People.”

Welcome

Edward M. Wolin, M.D., has been recruited as director of the neuroendocrine tumor program at the Montefiore Einstein Center for Cancer Care. Previously, Dr. Wolin directed the neuroendocrine and gastrointestinal tumor program at the Markey Comprehensive Cancer Center of the University of Kentucky, where he was also director of clinical research. Dr. Wolin is internationally recognized for his research in treating neuroendocrine tumors. These include rare malignancies such as carcinoid, insulinoma and gastrinoma, which often produce hormones. Dr. Wolin brings a robust portfolio of clinical trials with a recent focus on drugs targeted to receptors on the surface of this family of cancer cells.

Anniversary of Note

10th: In 2006, Einstein became the only medical institution in the Northeast to serve as a research site for the Hispanic Community Health Study. The principal investigator (PI) was Sylvia Wassertheil-Smoller, Ph.D., now Distinguished University Professor Emerita of epidemiology & population health. Robert C. Kaplan, Ph.D., a professor of epidemiology & population health and the Dorothy and William Manealoff Foundation and Molly Rosen Chair in Social Medicine, became PI of the study in 2008.
Where are you from and how did you become interested in science? I’m from Queens and just always liked biology. My parents encouraged me, though they worked in other fields—my father in shipping, my mother as a secretary. I took a fabulous developmental biology course in college and got hooked when I saw chick embryos in the lab. You could watch them develop by opening a piece of the shell.

Why Einstein for your Ph.D.? I got a really good, warm feeling. I sensed they wanted me. It felt like home.

You had a scary interaction with a centrifuge…. Yes, as a Ph.D. student, I blew up an ultracentrifuge. It was spinning at high speed when it began to rattle and shake like an off-balance washing machine, the loudest sound you can imagine. There was smoke and a metallic smell. I was ready to quit, but the lab director was supportive—“Not your fault,” he said. It turned out that a rotor arm had blown off. His handling of the incident kept me in the program and made me the mentor I am today.

Are there ultracentrifuges in your lab now? We have regular centrifuges that run at much lower speeds.

How was it being a young working mother? As a postdoc, I was pregnant with my daughter, and my son was an infant. I’d drag the stroller to the chair’s office, and she would watch him while I went into the lab. But mostly, people asked “Why are you having children?” and said it would mess up my career.

Why do you focus on VCFS? A week after I joined Raju Kucherlapati’s lab, we saw a little girl with VCFS at Montefiore. I felt an immediate connection to her and knew I wanted to dedicate my career to finding the genes for the disorder.

Do you have any hobbies? I play tennis—not competitively, strictly for fun and friendship. And on the court, you forget your problems.

Did either of your children follow you into medical research? No, they both decided to go into finance, because they wanted to be different from their parents. My husband is a dentist.

Do you have advice for Einstein students? If you believe what you’re doing really is for you, stick with it. Perseverance is super-important. It helps to have a good mentor. You can also get advice from your committee members. Finally, make friends everywhere. They’ll help you through the hard times and celebrate with you when things go well.
In May, 13 paintings by artist Arthur Lidov were hung in the department of anatomy and structural biology in the Forchheimer Building. Mr. Lidov (1917−1990) was a painter, illustrator, muralist, sculptor and inventor with a special talent for portraying the human body, often in imaginative ways. His work appeared in major magazines of his day (such as Life, Time, Fortune and the Saturday Evening Post), was exhibited in top venues (the Art Institute of Chicago, the National Academy of Art, the Museum of Modern Art and more) and appeared on book covers. In 1964, the College of Medicine engaged Mr. Lidov as a judge for its fifth annual art exhibit, featuring 150 entries by faculty, staff and students. The event cemented a relationship that would last beyond Mr. Lidov’s death in 1990, when his widow donated a number of his works, particularly those with medical themes, to Einstein. The paintings on these pages are representative of his style and of the artworks displayed on campus.
See more Lidov paintings online
magazine.einstein.yu.edu

In Memoriam

Ronald L. Nagel, M.D.

Dr. Ronald Nagel, a professor emeritus of medicine (hematology) and of physiology & biophysics, passed away on April 16. Dr. Nagel had retired from his position as chief of the division of hematology at Einstein and Montefiore in 2008 due to illness.

Dr. Nagel was born in Chile in 1936 to a mother proud of her Spanish and Araucanian Indian heritage. His father had emigrated to Chile from Bratislava, the capital of Slovakia, ahead of the Holocaust. Dr. Nagel attended medical school in Chile, graduated in 1960 and did three years of postgraduate training as a resident in medicine and as a student of physics and mathematics at the University of Chile. During those years he published a number of papers, including two letters to Nature that touched on population studies that would form part of his later career.

He came to the United States as a National Institutes of Health international postdoctoral fellow and joined the laboratory of Helen Ranney, M.D., with whom he published a number of papers on hemoglobin-haptoglobin interactions. He then worked with Dr. Ranney and fellow trainee Robert M. Bookchin, M.D., on mutant hemoglobins. In his 45-year career at Einstein, Dr. Nagel held numerous leadership roles, published more than 300 peer-reviewed papers and was author or co-author of five scientific books on hemoglobin and two volumes of poetry.
Einstein scientists have developed a technology allowing them to “see” single molecules of messenger RNA as they are translated into proteins in living mammalian cells. The findings, which may shed light on neurological diseases and cancer, were published online in May in Science.

“Genome-wide studies show that translation controls protein abundance in cells—important to every single function that cells carry out,” says Robert H. Singer, Ph.D., the paper’s senior author, co-chair of anatomy and structural biology and co-director of the Gruss Lipper Biophotonics Center at Einstein. “Using this technology, we can finally learn how translation is regulated and gain insights into diseases that occur when translation is faulty.” Dr. Singer also is co-director of the EGL Charitable Foundation Integrated Imaging Program and holds the Harold and Muriel Block Chair in Anatomy and Structural Biology.

Protein production starts in the cell nucleus, when protein-making information encoded in a gene’s DNA is transcribed into molecules of messenger RNA (mRNA). In the next step, called translation, the mRNA molecules hook up with molecular structures called ribosomes. Using mRNA as their blueprint, the ribosomes generate proteins by linking amino acids.

Researchers Visualize Proteins Being Born

The scientists made a surprising finding in mouse neurons, where mRNA translation into protein was found to occur in “bursts”—a phenomenon never before possible to observe. “Bursts of translation activity may be the best way for neurons to control the amount and location of protein production—and neurological disease may result from neurons’ inability to control that bursting,” says Dr. Singer.

“So our findings may have implications for intellectual disorders such as fragile X syndrome, which seem to involve too much protein production, and for neurodegenerative disorders such as Alzheimer’s, in which clumps of beta-amyloid protein may block neuron-to-neuron signaling at synapses.”

Another surprising observation occurred in cancer cells, where the researchers noted a striking inability to regulate the translation of mRNA. Instead, mRNA translation was continuous. Since proteins play crucial roles in controlling cell division, the uncontrolled translation of certain proteins may lead to certain types of cancer.

“With our technology, researchers can now study disease-causing protein aberrations at a basic level that was never possible before,” says Dr. Singer, also a professor in the department of cell biology and in the Dominick P. Purpura Department of Neuroscience.
Headlines about America’s worsening drug epidemic have focused on deaths from opioids—heroin and prescription painkillers such as OxyContin. But overdose deaths have also soared among the millions of Americans using benzodiazepine drugs, a class of sedatives that includes Xanax, Valium and Klonopin, according to a study led by researchers at Einstein, Montefiore Health System and the Perelman School of Medicine at the University of Pennsylvania. Their findings appeared in February in the American Journal of Public Health.

“We found that the death rate from overdoses involving benzodiazepines has increased more than fourfold since 1996—a public health problem that has gone under the radar,” says lead author Marcus A. Bachhuber, M.D., M.S., an assistant professor of medicine (general internal medicine) at Einstein and an attending physician in internal medicine at Montefiore. “Overdoses from benzodiazepines have increased at a much faster rate than prescriptions for the drugs, indicating that people have been taking them in a riskier way over time.”

An estimated one in 20 U.S. adults fills a benzodiazepine prescription during the course of a year. The drugs are prescribed for conditions including anxiety, mood disorders and insomnia.

In 2013, benzodiazepine overdoses accounted for 31 percent of the nearly 23,000 deaths from prescription drug overdoses in the United States. But little was known about the national trends in benzodiazepine prescribing or in fatalities from the drugs. To find out, the researchers examined data for the years 1996–2013 from two sources: the federally sponsored Medical Expenditure Panel Survey and multiple-cause-of-death data from the Centers for Disease Control and Prevention.

Their analysis revealed that the number of adults purchasing benzodiazepines by prescription increased by 67 percent over the 18-year period, from 8.1 million in 1996 to 13.5 million in 2013. For those obtaining benzodiazepine prescriptions, the average quantity filled during the year more than doubled between 1996 and 2013. Crucially, the overdose death rate over the 18-year period increased from 0.58 deaths per 100,000 adults in 1996 to 3.14 deaths per 100,000 adults in 2013, a more than fourfold increase.

Overall, the rate of overdose deaths from benzodiazepines has leveled off since 2010. But for a few groups—adults ages 65 and over, blacks and Hispanics—the rate of overdose deaths after 2010 has continued to rise.

“We found that the death rate from overdoses involving benzodiazepines has increased more than fourfold since 1996—a public health problem that has gone under the radar.”

“The greater quantity of benzodiazepines prescribed to patients suggests a higher daily dose or more days of treatment, either of which could increase the risk of fatal overdose,” says senior author Joanna L. Starrels, M.D., M.S., an associate professor of medicine (general internal medicine) at Einstein and an attending physician in internal medicine at Montefiore.

Dr. Starrels also offers two other possible reasons for the spike in benzodiazepine deaths. “People at high risk for fatal overdose may be obtaining diverted benzodiazepines [i.e., not from medical providers], and we know that combining benzodiazepines with alcohol or drugs—including opioid painkillers—can lead to fatal overdoses,” she says. She notes that opioid prescribing has increased rapidly during most of the period covered in her study and that opioids are involved in 75 percent of overdose deaths involving benzodiazepines.
Alzheimer’s disease is the most common cause of dementia in older people. It occurs when amyloid precursor protein (APP) undergoes two sequential enzymatic cleavages, forming smaller clumps called amyloid-beta peptides that accumulate between neurons in the brain.

Luciano D’Adamio, M.D., Ph.D., a professor of microbiology & immunology at Einstein, has received a five-year, $3.6 million grant from the National Institutes of Health (NIH) to continue his research into how APP is processed in the brain.

Genetic evidence suggests that aberrant processing of APP may contribute to Alzheimer’s disease. The protein is first cleaved by the enzyme beta-secretase 1 (BACE1). Some people—those possessing a variant of APP for which processing by BACE1 is reduced—are protected from developing Alzheimer’s disease and from experiencing normal age-dependent cognitive decline. And mutations in genes that regulate APP processing are known to cause familial dementias. Yet little is known about the physiological relevance of APP processing or of APP itself.

Although best known for its involvement in Alzheimer’s, APP also plays a key role in synaptic transmission—that is, conveying neural impulses across synapses. The NIH grant will allow Dr. D’Adamio to analyze the role of APP (and of APLP2, a member of the APP protein family) in synaptic transmission and to investigate the molecular mechanisms that underlie it.

Horwitz Prize: Dr. Emmons and the Worm

The Einstein community gathered in the Mary and Karl Robbins Auditorium on February 29 for the 10th annual Marshall S. Horwitz Faculty Prize memorial lecture, given this year by prize recipient Scott W. Emmons, Ph.D., a professor of genetics and in the Dominick P. Purpura Department of Neuroscience, and the Siegfried Ullmann Chair in Molecular Genetics. He was honored for his innovative work in connectomics, which describes how nervous system synapses are connected.

Dr. Emmons’ lecture described his effort, over the past three decades, to map the Caenorhabditis elegans worm’s neural connections. He discovered in the early 2000s that the male worm will abandon a meal to seek mates. His findings served as a launch pad for investigations into male behavior, including copulation. In 2012, he and his team submitted a map of the wiring for the nervous system governing mating behavior in the adult male worm for publication in the journal Science. The manuscript was not only accepted but received the American Association for the Advancement of Science’s Newcomb Cleveland Prize for the most outstanding research article in Science that year.
Einstein researchers have solved a mystery surrounding the development of hematopoietic stem cells in utero. Their study, published in *Science*, was directed by Paul S. Frenette, M.D., a professor of medicine and of cell biology and the chair and director of the Ruth L. and David S. Gottesman Institute for Stem Cell and Regenerative Medicine Research.

Researchers have long known that fetal hematopoietic stem cells (HSCs)—which give rise to adult blood cells—migrate during development from the dorsal aorta and placenta to the fetal liver and from there to the bone marrow. The *Science* article describes for the first time the conditions that promote HSC proliferation in the fetal liver.

Dr. Frenette collaborated with Aviv Bergman, Ph.D., a professor and founding chair of systems & computational biology. In experiments involving mice, the researchers found evidence that pericytes (contractile cells that wrap around capillaries and venules) associate with the liver's portal vessels to form a niche, or microenvironment, that promotes HSC proliferation in the fetal liver.

This rapid expansion of HSCs contrasts sharply with their quiescence when HSCs later reside in bone marrow. The findings suggest that the expansion of HSCs during fetal development is governed by fractal geometries (repeating patterns that display at every scale) associated with the growing surface area of the portal vessel niche. Insights into this niche may lead to new ways of cultivating stem cells for transplantation.
Dr. Cuervo Gives Harvey Society Lecture

Einstein’s Ana Maria Cuervo, M.D., Ph.D., delivered “Selective Autophagy: The Ultimate Recycling for a Long and Healthy Life” at the Harvey Society lecture series on March 17. Dr. Cuervo is a renowned expert on autophagy—the mechanism by which cells digest and recycle internal products. She has found that impaired autophagy is associated with aging and with age-related disorders, including Huntington’s disease and Parkinson’s disease.

The Harvey Society was founded in 1905; it sponsors seven lectures annually that are presented at Rockefeller University in New York. The series is considered one of the nation’s most distinguished forums for scientific discourse and has a long-standing tradition of featuring leaders in their respective biomedical fields from around the world.

Dr. Cuervo was selected from more than 100 researchers to present her findings. With her selection, she joins a group of elite scientists, including many Nobel laureates, who have received the honor. Dr. Cuervo is a professor of developmental and molecular biology, of anatomy and structural biology and of medicine (gastroenterology & liver diseases) at Einstein. She also is the co-director of the Einstein Institute for Aging Research and holds the Robert and Renée Belfer Chair for the Study of Neurodegenerative Diseases.

New Chair

Einstein has named Kamran Khodakhah, Ph.D., as chair of the Dominick P. Purpura Department of Neuroscience. He has been interim chair since 2013.

Dr. Khodakhah will be a leader of the Brain Science Initiative, which will reinvest in and reinvigorate brain research at Einstein and Montefiore. The initiative will spur a range of investigations led by researchers from clinical and basic science departments at the institutions. Research programs will focus on fundamental neuroscience and a wide range of diseases, from autism and neurodegenerative disorders to addiction and obesity.

Searches are now under way for chairs of neurosurgery and of psychiatry and behavioral sciences. These chairs are expected to play important roles in this initiative, which will include establishing a Montefiore Einstein Center of Excellence in Neuroscience.

“These are exciting times for brain research,” says Dr. Khodakhah. “Einstein has a long and storied history in neuroscience excellence and is home to a cadre of internationally recognized leaders in the field. I look forward to expanding our department, fostering collaborations among basic science, translational and clinical investigators and departments and building Einstein and Montefiore into a preeminent center for brain research.”

Dr. Khodakhah, who also holds a Harold and Muriel Block Chair in Neuroscience, joined the Einstein faculty in 2001 as an assistant professor of neuroscience. He became a full professor in 2007 and later received appointments in the Saul R. Korey Department of Neurology and the department of psychiatry and behavioral sciences, where he is now vice chair of research.

The Khodakhah laboratory studies the role of two brain regions, the cerebellum and basal ganglia, in motor coordination and movement disorders such as ataxia (uncoordinated movement) and dystonia (involuntary muscle contraction). He and his colleagues combine basic science and clinical approaches, including behavioral studies, electrophysiology, genetics and optogenetics. Dr. Khodakhah received his first independent research grant from the NIH in 2001 and has been continuously funded since then.

An active member of the scientific community, Dr. Khodakhah has chaired or been on the roster of six different NIH study sections. He has been on grant review boards for the Wellcome Trust (U.K.), the Italian Teleton Foundation, the Japan Science and Technology Agency, the Dystonia Medical Research Foundation and the Agence Nationale de la Recherche (France), among others.

In 2007, Dr. Khodakhah received Einstein’s LaDonne H. Schulman Excellence in Teaching Award.
On March 21, the Graduate Program in Biomedical Sciences held the 20th annual Julius Marmur Symposium, honoring excellence in graduate student research. It also honors the memory of its namesake, Julius Marmur, Ph.D., who was an Einstein faculty member for 33 years until his death in 1996. Dr. Marmur is remembered today as one of the founding fathers of molecular biology. Victoria H. Freedman, Ph.D., associate dean for graduate programs in biomedical sciences, reminisced about her days working in his laboratory as a rotation student during her first year of graduate training at Einstein. “He was an excellent teacher who brought a 20th-century understanding of molecular biology to students, and he was very supportive, always encouraging us to aim for higher scientific goals,” said Dr. Freedman.

Marmur award winners are decided by an independent committee of faculty members who haven’t personally worked with the students. This year, four outstanding graduate students received recognition for their research contributions.

**Dachuan Zhang, Ph.D.**, was recognized for his work on neutrophil aging, conducted in the laboratory of Paul S. Frenette, M.D. “Winning this award has made me confident to pursue biomedical research further,” he noted. “And it will help me demonstrate my research capabilities when I apply for jobs and funding opportunities.”

**Veronika Miskolci, Ph.D.**, used biosensors to study the roles of signaling molecules known as Rho GTPases in immune cells. She worked under the guidance of Dianne Cox, Ph.D., and Louis Hodgson, Ph.D. “I’ve loved being a Ph.D. student at Einstein,” she said. “Being selected for this award has made me a part of my school and Dr. Marmur’s legacy.”

**Philip Campbell, Ph.D.**, a graduate student and Medical Scientist Training Program candidate in the laboratory of Florence L. Marlow, Ph.D., studied zebrafish development. “This award has provided me a platform for sharing my research with a wider audience,” he said. “Julius Marmur made noteworthy contributions to his field, and I’m inspired to do so in my area of research.”

**Fanny Cazettes, Ph.D.**, worked in the laboratory of José Luis Peña, M.D., Ph.D., on how the brain handles sensory uncertainty. She defended her thesis recently and described winning the award as “the best way to end a Ph.D. It’s recognition of my years of hard work. Women are highly underrepresented in computational neuroscience, so it’s particularly validating for me.”

“What makes the Marmur symposium extra-special is that, in addition to the awardees, other graduate students also present their thesis research at a poster session held later in the day,” said Dr. Freedman. “Students from all years participate, even the first-years. It’s a great opportunity for them to showcase their accomplishments.”

Mildred Marmur, Dr. Marmur’s widow, commented, “If Julius were around, he’d be thrilled to know that the Einstein community is keeping his legacy alive in such a wonderful way.”
More than one third of American adults—some 78 million people—are obese, and about 28 million have type 2 diabetes, which is usually associated with excess weight. Both problems persist despite numerous efforts aimed primarily at treating their “downstream” effects (e.g., liposuction to remove fat and type 2 diabetes drugs to alter insulin output by the pancreas).

Research by Einstein scientists suggests that treatment strategies should instead shift to the ultimate *upstream* target—the brain—since obesity and type 2 diabetes increasingly appear to be brain disorders. The Einstein research builds on decades of studies showing that the brain—the hypothalamus in particular—controls food intake and metabolism.

In 1940, Northwestern University Medical School’s A. W. Hetherington and S. W. Ranson published a classic paper in which they made lesions in the midregion of the hypothalamus of 22 rats. All but one of the rats increased their food intake and became obese. In a second landmark paper, in 1951, B. K. Anand and J. R. Brobeck of Yale University reported that lesions in a different part of the hypothalamus had the opposite effect: rats stopped eating and died of starvation.

These two studies, along with later research, have firmly established that the hypothalamus—an almond-sized portion of the brain—plays the central role in regulating both metabolism and weight.
What if a pill could mimic the positive effects of gastric bypass surgery and avoid the negative ones? Sounds far-fetched, but research into this intriguing idea is well under way in the laboratory of Streamson C. Chua, Jr., M.D., Ph.D., a professor in the department of medicine (endocrinology) and in the Dominick P. Purpura Department of Neuroscience.

Throughout his career, Dr. Chua has concentrated largely on the genetics of obesity and diabetes and on leptin (the “satiety hormone”). Gastric bypass didn’t cross his mind until a colleague studying its physiological effects sought his help regarding a protein called fibroblast growth factor 19, or FGF19.

Throughout his career, Dr. Chua has concentrated largely on the genetics of obesity and diabetes and on leptin (the “satiety hormone”). Gastric bypass didn’t cross his mind until a colleague studying its physiological effects sought his help regarding a protein called fibroblast growth factor 19, or FGF19.

Dr. Chua’s colleague wanted to know what FGF19 is doing. “Everyone thought that FGF19 mainly works...”

But we now know that many more players get into the act as well.

When and how much we eat, how much we weigh and even whether we’ll develop type 2 diabetes depend on an extraordinarily complex web of interactions involving not only the hypothalamus but also the stomach, small intestine, pancreas, liver, blood, adipose (fat) tissue and even other parts of the brain, including the ventral tegmental area (part of the midbrain). To perform its finely calibrated job of controlling body weight and metabolism, the hypothalamus integrates messages from these other parts of the body and responds with its own directives (in the form of hormones, neurotransmitters and activated signaling pathways) that control how much we eat and how much energy we expend.

Molecule by molecule, Einstein scientists are trying to understand how the body controls its weight—and what goes wrong when this finely tuned regulatory mechanism breaks down. Their detective work has revealed several molecular glitches—in the hypothalamus and elsewhere—that lead to weight gain and elevated glucose levels that occur in type 2 diabetes. Repair of those glitches may lead to treatments for obesity and diabetes that target the root causes of these problems.

**COULD A PILL MIMIC GASTRIC BYPASS?**

Gastric bypass surgery has helped countless people shed excess pounds and control type 2 diabetes. But this operation—which shrinks the size of the stomach and reroutes nutrients to the lower intestine—is far from perfect. Many patients eventually regain much of their lost weight, and the surgery itself has a sobering mortality rate, with about one out of every 200 patients dying from it.
peripherally, in the liver and in brown fat,” says Dr. Chua. “But some evidence suggested it might also be affecting the hypothalamus,” the brain’s appetite-control center.

Dr. Chua found in mouse studies that the brain responds when FGF19 is administered in the peripheral circulation. He next injected FGF19 directly into the hypothalamus of genetically obese mice and of mice fed a high-fat diet. In both cases, the injected protein caused weight loss by selectively stimulating a signaling pathway called ERK1/2 and thereby silencing AGRP neurons (which promote feeding and insulin secretion). The FGF19-treated obese mice also exhibited several healthy signs—improvements in glucose tolerance and insulin sensitivity along with decreases in both insulin and glucose levels, as Dr. Chua reported in 2013 in *Molecular Metabolism*. FGF19 would seem to be an ideal
weight-loss drug. But unfortunately, it causes liver cells to proliferate. So over the last two years, Dr. Chua has been trying to identify peptides (small chains of amino acids) that duplicate FGF19’s actions.

Working in collaboration with the Danish pharmaceutical company Novo Nordisk, he has already identified several promising drugs that bind to FGF19-related receptors on AGRP neurons and silence their activity. Dr. Chua now plans to test these peptides in obese mice and glucose-intolerant mice to see if the peptides work as predicted in reducing blood-glucose and insulin levels.

As the pounds accumulate, the brain becomes less sensitive to leptin’s “stop eating” message.

YOUNG-HWAN JO, PH.D.

A SMALL BUNDLE OF BRAIN CELLS HAS A BIG EFFECT ON APPETITE

Leptin is called the “satiety hormone” because it plays a key role in curbing appetite. Fat cells that have grown suitably plump synthesize leptin and release it into the bloodstream. The hormone travels to the brain’s hypothalamus—telling us, in effect, “You’ve had enough food, so step away from the table.”

But for reasons not fully understood, leptin’s communication with the brain starts breaking down when people gain excess weight. As the pounds accumulate, the brain becomes less sensitive to leptin’s “stop eating” message.
Being overweight somehow disrupts this highly orchestrated interaction among different POMC neurons.

With support from a five-year, $1.82 million grant from the National Institute of Diabetes and Digestive and Kidney Diseases, Young-Hwan Jo, Ph.D., is trying to determine why for so many people leptin no longer works, the body's energy balance breaks down and obesity results. Leptin has a special affinity for a bundle of hypothalamic neurons called the arcuate nucleus (ARC), which is crucially important for maintaining a neutral energy balance (in which energy intake equals energy expenditure). Within the ARC are thousands of proopiomelanocortin (POMC) neurons sprouting numerous leptin receptors.

These POMC neurons were long thought to be identical. But recent studies by Dr. Jo and others have found at least two distinct types. “We hypothesize that the different types of POMC neurons have different functions and that their interplay regulates energy balance,” says Dr. Jo, an assistant professor of medicine (endocrinology) and of molecular pharmacology. “In response to leptin and other signaling molecules, the different POMC neurons interact to release hormones needed to suppress appetite.”

Leptin molecules activate leptin receptors on POMC neurons, causing them to release melanocortin peptides as well as neurotransmitters that powerfully inhibit food intake. “The different types of POMC neurons seem to maintain energy balance by coordinating the release of these appetite-suppressing chemicals,” says Dr. Jo. “We propose that being overweight somehow disrupts this highly orchestrated interaction among different POMC neurons.”

Dr. Jo’s work has already revealed one possible glitch. Leptin, it turns out, not only turns on POMC neurons and their anti-appetite message; it also fine-tunes POMC activity by either (1) causing other neurons to release GABA (the central nervous system’s main inhibitory transmitter) onto POMC neurons or (2) preventing those neurons from releasing GABA. Whether leptin inhibits or activates GABA’s release onto POMC neurons depends, in turn, on signals from nutrients.

In a study in 2015 in *Nature Communications*, Dr. Jo and colleagues showed that glucose levels in the blood influence leptin’s action in releasing GABA. When glucose levels are high (as might occur following a meal), leptin...
inhibits GABA release from neurons (meaning that the POMC neurons’ “stop eating” message is unimpeded). Conversely, at low blood-glucose levels, leptin stimulates GABA release—in effect curbing POMC neuron activity and encouraging eating when blood sugar is low. But more interesting was what happened in mice that had been fed a high-fat diet for three weeks.

“We assumed that elevated body weight in these mice would make leptin inhibit GABA release onto POMC neurons, allowing their ‘stop eating’ message to be broadcast,” says Dr. Jo. “But we made the unexpected finding that the high-fat diet actually prompted leptin to enhance GABA release, which paradoxically may reduce leptin’s appetite-suppressing effects in obese animals. This finding may explain the energy-balance breakdown that occurs when people become overweight.”

Dr. Jo’s further research into POMC neurons may lead to strategies for helping their “stop eating” message prevail over signaling molecules trying to squelch it.

EXPLORING THE BRAIN-GLUCOSE CONNECTION
Diabetes by definition involves abnormally high glucose levels in the blood. Those high levels eventually damage tissues, leading to the serious complications related to diabetes. While we tend to associate elevated blood
glucose with too much dietary sugar and other carbohydrates, the main source of hyperglycemia in type 2 diabetes is actually excessive *endogenous* glucose production—chiefly by the liver, which produces, stores and secretes glucose into the bloodstream.

Over the past decade, professor of medicine Meredith A. Hawkins, M.D., and her Einstein colleagues have shown that the hypothalamus plays a key role in regulating blood-glucose balance in healthy people. The researchers found that when the hypothalamus detects certain nutrients and hormones in the blood, potassium channels in the hypothalamus become activated; these activated channels send a signal via the vagus nerve that tells the liver to dampen its output of glucose to the bloodstream.

Dr. Hawkins, who is associate director of the Einstein−Mount Sinai Diabetes Research Center (DRC) and director of Einstein's Global Diabetes Institute, recently investigated whether this glucose-regulatory mechanism is defective in people with diabetes, which could help account for their abnormally high blood-glucose levels.

“Despite all the medications available for lowering blood-glucose levels, half of patients with type 2 diabetes are not able to achieve adequate blood-sugar control,” she notes. “Given the role of the hypothalamus in controlling blood glucose in healthy individuals, we looked at whether this control mechanism is impaired in people with diabetes. If so, then therapies could possibly be developed to restore the brain’s regulation of blood-glucose levels.”

To two groups of people—seven healthy individuals and eight with moderately to poorly controlled type 2 diabetes—Dr. Hawkins and her team administered oral diazoxide, a drug that activates potassium channels in the hypothalamus. (Diazoxide is used clinically to inhibit the pancreas from secreting excessive amounts of insulin; in this experiment, the researchers controlled insulin secretion by the pancreas to ensure that any change in blood-glucose levels would occur only through diazoxide’s effect on the brain.)

Several hours after diazoxide was given, blood tests showed that the drug had significantly lowered the glucose output of the healthy participants’ livers by an average of 27 percent—showing that the “activated potassium-channel

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**DIABETES CAUSES BREAKDOWN IN BLOOD-GLUCOSE BALANCE**

**A. HYPOTHALAMUS**
Nutrients and hormones in blood activate potassium channels in the hypothalamus, sending a signal via the vagus nerve directing the liver to dampen its glucose output.

**B. LIVER**
Several hours later, glucose output by the livers of healthy people had fallen significantly. But the drug had no effect on blood-glucose levels of participants with diabetes, indicating a breakdown in brain-liver communication allowing the liver to release glucose unabated.
Little is known about how atypical antipsychotic drugs (APDs) disrupt the body’s metabolism, and even less about how to prevent the problem.

GARY J. SCHWARTZ, PH.D.

Second-generation antipsychotic drugs—brands including Abilify, Risperdal, Seroquel and Zyprexa—debuted in the 1990s. They help millions of Americans cope with psychiatric disorders such as schizophrenia, depression and anxiety. But these medications (sometimes referred to as atypical antipsychotic drugs, or APDs) also cause adverse metabolic side effects, including weight gain and increased risk for type 2 diabetes.

Little is known about how APDs disrupt the body’s metabolism, and even less about how to prevent the problem. Gary J. Schwartz, Ph.D., a professor of medicine (endocrinology) and of neuroscience, is among a handful of researchers trying to find some answers, thanks to a three-year, $2.5 million grant from the Department of Defense.

Schizophrenia and several other psychiatric illnesses are characterized by an overabundance of the neurotransmitter dopamine in the central nervous system. APDs work by countering this dopamine excess. They do so in part by blocking two types of dopamine receptors (called DR2 and DR3) that dopamine activates.

The problem, says Dr. Schwartz, is that DR2 and DR3 are also found outside the brain—most importantly, on insulin-secreting beta cells of the pancreas. Studies by Dr. Schwartz and colleagues at Columbia University Medical Center suggest that APDs disrupt these DR2 and DR3 receptors, triggering uncontrolled release of insulin from beta cells and leading to weight gain.

Dr. Schwartz is trying to disentangle the relative “contributions”
that pancreatic beta cells’ DR2 and DR3 receptors make to APD-induced metabolic problems. He is also teasing out the relative importance of DR2 and DR3 receptors in causing these problems. To do so, he and his colleagues are developing “knockout” mice with pancreases lacking either DR2 or DR3 as well as novel antipsychotic compounds that specifically target either DR2 or DR3 receptors, but not both.

“We hope this work will lead to new antipsychotics with fewer metabolic side effects, which in turn would improve treatment compliance,” says Dr. Schwartz. The findings, he adds, may also reveal new strategies for treating overeating, weight gain and impaired glucose tolerance.

The Defense Department has a keen interest in the topic. Several hundred thousand veterans currently take APDs for post-traumatic stress disorder. Their prevalence of metabolic problems is more than twice that of the general population.

“We hope this work will lead to new antipsychotics with fewer metabolic side effects, which in turn would improve treatment compliance.”
ANOTHER REASON TO AVOID STRESS
It’s well known that stress contributes to many health problems, from headaches to hypertension; it also appears to play a role in obesity and diabetes. It’s not the stress we associate with a tight deadline at work, but rather intracellular stress caused mainly by nutrient overload. Recent studies show that intracellular stress can trigger damaging inflammatory responses inside neurons of the hypothalamus.

Dongsheng Cai, M.D., Ph.D., a professor of molecular pharmacology, was one of the first researchers to connect hypothalamic inflammation to metabolic dysfunction. Studies had shown that overeating can chronically inflame certain peripheral tissues and lead to insulin resistance—an early step in type 2 diabetes. About a decade ago, Dr. Cai reasoned that something similar might be happening in the hypothalamus.

Hundreds of molecules play a role in inflammation, so deciding on possible culprits wasn’t easy. Dr. Cai hypothesized—correctly, it turns out—that a protein complex called nuclear factor κB (NF-κB) was a prime suspect. “Many molecules are involved in intracellular inflammation, but NF-κB sits at the center of this regulatory map,” he explains.

In studies funded by the National Institute of Diabetes and Digestive and Kidney Diseases, he found
that the NF-κB inflammatory signaling pathway is present in the hypothalamic neurons of mice, and that a high-fat diet turns it on. He then showed that interrupting this pathway—by knocking out the gene for IKKβ, an enzyme that activates NF-κB—suppresses inflammation in hypothalamic neurons and also stops the animals from overeating and becoming obese or diabetic.

In other mouse experiments, Dr. Cai found yet another way that a high-fat diet triggers the inflammatory NF-κB signaling pathway: by stressing the endoplasmic reticulum (ER)—a membranous structure involved in protein and lipid transport—within hypothalamic neurons. Injecting the ER stress inhibitor tauroursodeoxycholic acid into the cerebral ventricles of mice on a high-fat diet suppressed their appetite and reduced their degree of obesity.

Today, Dr. Cai is exploring how to apply these findings clinically.

“We have a number of ideas for selectively blocking this pathway in the hypothalamus using peptides,” he says.

In a fascinating related study involving mice, Dr. Cai recently investigated whether aging might cause weight gain and diabetes through its effects on the hypothalamus. He found that aging— independent of a high-fat diet—does indeed trigger inflammation within neurons of the hypothalamus by activating the NF-κB pathway. Dr. Cai was able to extend the life span of mice by interrupting this pathway.

Together, these discoveries point to an entirely new approach for controlling metabolic disorders as well as certain aging-related health problems.

PRIORITY ON BRAIN RESEARCH AT EINSTEIN
The efforts of these and other Einstein researchers have clearly shown that obesity and diabetes can be viewed as brain disorders. Progress in identifying the specific molecular defects and neuronal signaling pathways involved is already shedding light on potential new therapeutic strategies. Yet much remains to be learned about the complex metabolic integration that controls glucose metabolism and energy balance in the body.

“Studies focusing on the brain—and on discrete components of the hypothalamic signaling network in particular—may soon get a boost here, thanks to the strategic plan that Einstein announced in June,” says Jeffrey E. Pessin, Ph.D., DRC director and the Judy R. and Alfred A. Rosenberg Professorial Chair in Diabetes Research. The plan’s six priority research areas include the Brain Science Initiative as well as “obesity and metabolic disorders,” including diabetes.
These days, you would be hard-pressed to find a bank, supermarket or retailer that still relies on paper records for transactions. But remarkably, one in five physicians still doesn’t use electronic medical records (EMRs), and almost half of those using EMRs don’t use these systems to their fullest, according to the U.S. Department of Health and Human Services.

A similar disconnect can even be found in academic medicine. “Most healthcare data are stored in silos, with separate and incompatible systems for patient records, clinical research findings, genomic data and so on,” says Parsa Mirhaji, M.D., Ph.D., director of clinical research informatics at Einstein and Montefiore and a research associate professor of systems & computational biology at Einstein. “This is true within institutions and between institutions. We’re not making full use of our biomedical data, and this greatly hinders discovery and innovation.”

But with the advent of informatics—using computer systems to create, store, manipulate and share information—things are changing quickly. Leading academic medical centers have started building the infrastructure that allows findings from each research study and patient encounter to be systematically captured, assessed and—most importantly—used to improve patient care.

To support such an effort at Einstein and Montefiore, Dr. Mirhaji is creating a “semantic data lake”—an integrated reservoir that collects all data flowing into the two institutions, with links to a wide variety of outside resources, from PharmGKB (a databank of how variations in human genetics lead to variations in drug responses) to UMLS (the National Institute of Health’s Unified Medical Language System) to OMIM (the Online Mendelian Inheritance in Man, a continuously updated catalogue of human genes and genetic disorders and traits).

The semantic data lake’s purpose is not just to gather data. It also defines, contextualizes, annotates, characterizes and indexes data—the “semantic” aspect of the data lake. Providing context and meaning to each bit of data should help investigators in several ways, allowing them to make new connections between genomic data and clinical phenomena, link environmental exposures to diseases, develop “smart” applications for clinical decision-making, create personalized therapies and assess community health needs in real time, to cite a few examples.
Stopping Respiratory Distress from Starting

Big Data’s potential is already evident in several places around Montefiore. One is the division of critical-care medicine, which uses the power of clinical research informatics to redefine the treatment of acute respiratory failure (ARF), a common type of organ failure in the hospital associated with high mortality and loss of function.

ARF usually affects critically ill patients suffering from acute illnesses such as pneumonia or from chronic health conditions. It’s difficult to predict which lung patients will develop ARF and when they’ll develop it. All too often, clinicians are left to deal with ARF after it culminates in respiratory distress, when supportive therapy on a mechanical ventilator must be started immediately. A 2010 study of older patients with ARF on mechanical ventilation in intensive care units in the U.S., published in the *Journal of the American Medical Association*, found that 30 percent of patients die within six months.

“There’s no single sign or symptom that announces the onset of ARF in its early phases,” says Michelle Ng Gong, M.D., a professor of medicine (critical care) and of epidemiology & population health at Einstein and director of critical-care research at Montefiore. “Rather, there’s usually a subtle pattern of abnormalities, none of which on its own is enough to raise a red flag until very late in the course of the illness.”

Try as they might, even the most experienced physicians have a hard time discerning these patterns. But an informatics tool called predictive analytics shows promise for doing so.

Several years ago, Dr. Gong and her colleagues started scouring the EMRs of thousands of patients who ultimately needed mechanical ventilation (the most intensive supportive therapy for ARF). The goal: to find clinical patterns that might predict the onset of lung failure. The researchers identified 44 key clinical variables—including heart rate, oxygen saturation and hemoglobin levels—which were inserted into a prediction model called APPROVE (for Accurate Prediction of Prolonged Ventilation score). A retrospective validation study involving more than 34,000 patients showed that APPROVE was better than most existing tools at predicting the onset of ARF.

As a practical matter, clinicians would be overwhelmed trying to monitor and analyze dozens of constantly changing clinical variables involving the patients they care for. So APPROVE is being incorporated into Montefiore’s EMR system, where its algorithm will run silently in the background, periodically analyzing each patient’s clinical data for early warning signs of ARF.

“We have an awful lot of data on our patients,” says Dr. Gong. “APPROVE will make those data more transparent and help make clinicians more aware of changing, and potentially dangerous,
situations. APPROVE won’t capture everyone—some patients are in respiratory distress the minute they present in the emergency department. But in a hospital that has more than 600 inpatients, it allows our critical-care team to focus our attention on those patients who seem to be at highest risk.”

The companion to the APPROVE early warning system is PROOFcheck (Prevention of Organ Failure checklist). Once APPROVE signals that a patient is at risk for ARF, the EMR will present clinicians with a customized list of best practices for limiting lung injury in that patient. The team is now running a clinical trial, funded by the National Heart, Lung, and Blood Institute, that will test whether using PROOFcheck improves clinical outcomes. Dr. Mirhaji’s semantic data lake provides the Big Data platform allowing models such as APPROVE and PROOFcheck to be developed and integrated into the healthcare delivery process.

The PROOFcheck clinical trial will also collect feedback—drawn from physicians and clinical records—to learn what happens after the checklist is generated. The checklists are recommendations rather than instructions. The goal is to learn whether clinicians follow the checklist and if not why not, so the system can continuously learn from these clinical interactions.

Dr. Gong’s primary motivation is to save lives, but her work may also save money. “Care is extremely expensive in the ICU [intensive care unit], where ARF is treated,” says Dr. Gong. “ICU patients with ARF tend to have the longest stays and often need to be readmitted to the hospital after they’re discharged. If we can prevent just a few of these patients from progressing to ARF, we could dramatically improve their outcomes and reduce hospitalization costs for both the patient and the hospital.”

**Cardiogenetics: Too Much Information**

By linking several heart conditions to specific genetic defects, cardiology was among the first medical subspecialties to tap the potential of modern genetics. Today, for example, when a young patient is suspected of having a potentially fatal arrhythmia called long QT syndrome, testing 16 different genes will usually find a telltale genetic variant in

**TRY AS THEY MIGHT, EVEN THE MOST EXPERIENCED PHYSICIANS HAVE A HARD TIME DISCERNING THESE PATTERNS.**

Thomas V. McDonald, M.D., in his lab.
one of them—confirming the diagnosis and informing treatment.

“We’ll find a clinically important variant in about 75 percent of patients with long QT,” says Thomas V. McDonald, M.D., a professor of medicine (cardiology) and of molecular pharmacology and co-director of the Montefiore Einstein Center for CardioGenetics. “The challenge is determining the cause of the syndrome in the other 25 percent.”

Clues sometimes arise through expanded testing that involves sequencing a patient’s exome. This subset of the genome consists of DNA segments that code for proteins (i.e., our 20,000 or so genes). “When we’ve done this on a research basis, we’ve found up to 800,000 variants—changes from what is considered the normal exome—in a single patient. That will sometimes lead us to a well-known deleterious mutation. But most of the time, we don’t know if the genetic variants have anything to do with the patient’s condition,” says Dr. McDonald.

The exome accounts for just 1.5 percent of the genome. If exome sequencing doesn’t reveal genes that influence disease, the next step—looking for variants in the whole genome and its three billion base pairs—is even more daunting. The whole genome encompasses the vast majority of our DNA that does not code for genes but that can affect our health.

In 2008, to provide an overview of all human genetic variation, the 1000 Genomes Project began sequencing the whole genomes of 1,000 people around the globe. After the sequencing of 2,500 individual genomes was completed last year, the project found that the average person has 3.5 million to 5 million variants from what is considered a “normal” genome.

“What’s needed are bioinformatics and analytics systems that can sift through all the relevant data, try to make sense of them and then deliver a report directly to the patient’s electronic medical record,” says Dr. McDonald. “And you’d want this to be fully automated, so that the clinician simply has to draw a blood sample, send it to the lab and wait for the magic to happen.
This is just in my mind at this stage, but I think we'll get there.”

Dr. McDonald is working with Dr. Mirhaji and the software giant Microsoft to bake this precision-medicine approach into an app available at the point of care—not only for cardiongenetics but also for other specialties such as pediatrics and cancer.

**Big Data for a Big Region**

Einstein’s and Montefiore’s Big Data initiatives extend well beyond the Bronx. Both institutions participate in the New York City Clinical Data Research Network (NYCCDRN), which is linking clinical researchers throughout the city in an effort to conduct health-outcomes studies more efficiently and at lower cost. In just its first year, the NYCCDRN has already gathered clinical data on more than four million patients, a number expected to reach six million by next year. This mammoth network will give researchers access to larger and more-diverse study populations.

NYCCDRN and its 10 sister networks around the country make up PCORnet—the National Patient-Centered Clinical Research Network. One of PCORnet’s aims is to foster research into some of the 7,000 rare diseases that collectively affect more than 25 million Americans.

PCORnet will also help in the study of common diseases, which often require patient enrollments far beyond the scope of a single medical center. For PCORnet’s first research project, the nation’s 11 CDRNs are participating in a study of heart disease patients to compare the safety and effectiveness of low- and high-dose aspirin for preventing heart attack and stroke. Doctors have prescribed aspirin to such patients for decades, but the ideal dose still isn’t known.

**PARSA MIRHAJI’S LONG JOURNEY:**

**FROM IRAN TO TEXAS TO THE BRONX**

It’s hard to imagine anyone more qualified than Dr. Mirhaji to lead Einstein’s and Montefiore’s Big Data initiatives. A native of Iran, Dr. Mirhaji first became interested in computers while studying medicine at Tehran University, starting in the late 1980s. At the time, finding a computer to connect to medical databases outside the insular republic was nearly impossible. With nowhere to turn for technical support, he taught himself Unix, an early operating system for computer networks, and built the necessary Internet connections on his own. Dozens of faculty members and hundreds of medical students came to rely on his electronic links to the outside world.

Dr. Mirhaji’s prowess with computer networks piqued the interest of university researchers, who asked him to create the infrastructure for linking clinical databases on thousands of patients spread over several hospitals.

In 2001, Dr. Mirhaji relocated from Tehran to the University of Texas Health Science Center in Houston for a fellowship in cardiology. The attacks of 9/11 soon followed, changing the course of his career. With his background in data networks and data analytics, Dr. Mirhaji developed Houston’s first public health preparedness network, which received the Department of Health and Human Service’s “Best Practice in Public Health Award” in 2002. He later received several grants to build a bioterrorism surveillance network for Houston and Harris County, TX.

No bioterror attacks hit Texas, but Dr. Mirhaji’s informatics infrastructure would serve another purpose: providing the foundation for the state’s surveillance system for natural disasters, which proved invaluable during Hurricane Katrina. “We built a system literally overnight that Houston’s health department used to support evacuees coming from New Orleans and to determine how they were faring in the various shelters,” he says. Dr. Mirhaji went on to create a surveillance system for the Harris County, TX, health department to monitor schools for outbreaks of avian flu.

Dr. Mirhaji’s success in informatics effectively ended his ambition to become a cardiologist. “Clinical life is rewarding, but there’s an engineer in me,” says Dr. Mirhaji, who completed a doctorate in health informatics at the University of Texas in 2009. “I’m still working on clinical problems, just on a much larger scale. You should have seen the people inside the shelters after Katrina. It was awful, and no one else was in a position to help them.”

In 2012, Dr. Mirhaji moved north to be closer to his extended family and to lead Einstein’s and Montefiore’s forays into health informatics.

**A Visit to the White House**

Thanks to his work at Einstein and Montefiore, Dr. Mirhaji was invited to participate in President Obama’s Precision Medicine Initiative Summit, held at the White House on February 25, 2016. The summit brought together healthcare leaders from across the country to begin integrating biological, clinical, environmental and administrative data to spawn research innovations and improve the delivery of care.
Have you always wanted to work on cancer?
I was very interested in sports, and my initial goal was to do orthopedics and sports medicine. That led me to surgery and then to cardiac surgery, because of the world-class surgeons at Columbia, including Robert Michler [now chair of surgery at Einstein and Montefiore]. In the middle of my residency, I had an epiphany that while cardiac surgery was amazing, I also had a passion for research, and I wasn’t compelled by the questions needing to be answered in cardiology. Eventually, I realized that oncology was the best match for my skills as a surgeon and a researcher.

Were there any other influences on your decision?
My grandmother was diagnosed with pancreatic cancer when I was a freshman in college. She went from this vibrant woman to a frail skeleton of a person within six months. Seeing how someone could deteriorate so quickly had a tremendous impact on me.

Why did you broaden your cancer focus beyond surgery?
That can be summed up by a quote from the 18th-century surgeon John Hunter: “Surgery is like an armed savage who attempts to get back by force what a civilized man would get by stratagem.” Surgery, with few exceptions—and particularly for solid tumors—is the only modality we have that can cure cancer, although that may soon change with immunotherapy. But while surgery is a powerful tool, it is also traumatic for the patient. Anyone who thinks that we can fix all cancers mechanically is being arrogant and simplistic. We need other strategies.
We’re 45 years and billions of dollars into the “War on Cancer.” Is that investment paying off? It really hasn’t been a war but rather a very long thesis on the disease. Slowly, we’ve been learning about the pathways that lead to cancer and how to manipulate those pathways to eradicate, or at least control, the disease. We’ve made progress against the most common cancers—colon, lung, breast and prostate—and overall, there are fewer deaths due to cancer now than there were 15 years ago.

What brought you from the NCI to Einstein and Montefiore? The NCI’s intramural research program is a wonderful place, where your patients are a hallway away from your laboratory. It’s ideal for taking ideas from the clinic to the lab and back again in the form of new therapies. But the program is relatively small. After 14 years, I began to realize that to have a bigger impact, I needed to be on a different stage, such as an academic medical center. With perfect timing, Steven Safyer [president and CEO, Montefiore Medicine] and Allen Spiegel [dean of Einstein] offered me an exciting opportunity to help lead the effort to bridge cancer research at Einstein with the clinical capabilities at Montefiore.

What are some examples of those bridges? One is the collaboration between John Condeelis, an Einstein basic scientist, and Joseph Sparano, a clinical researcher in oncology at Einstein and Montefiore. Dr. Condeelis studies the factors in the tumor microenvironment that promote the spread of breast cancer. Dr. Sparano brings in-depth knowledge of agents that might be able to target those mechanisms, plus extensive experience in carrying out clinical trials to evaluate therapies for breast cancer and other malignancies.

Another example is my work with Lakshmi Rajdev, a medical oncologist at Einstein and Montefiore. Dr. Rajdev asked me if we could treat neuroendocrine tumors more effectively by taking advantage of the discovery that the mTOR pathway plays an important role in these malignancies. Using a transgenic mouse model of neuroendocrine tumors—developed at the NCI and refined here—we tested an agent that can hit two different targets within the mTOR pathway. We’ve since shown that this treatment is more effective than single-agent therapy in this model, and we now have approval for an NCI-sponsored clinical trial.

Any examples related to immunotherapy? Yes, several. For instance, we have a pilot study in which we’ll take T cells from a patient with a solid tumor and transform them in the lab. We’ll “infect” the T cells with a retrovirus carrying the gene for an artificial T-cell antigen receptor. This means that the gene is designed to express a receptor on T cells that recognizes and binds to an antigen on the patient’s tumor called NY-ESO-1. These engineered T cells will be expanded in number and then returned to patients, providing a personalized therapy for their cancer. NY-ESO-1 is expressed in about 30 percent of solid tumors, so this approach could have wide application.

This modified T-cell antigen receptor was developed at the NCI. But we now have the infrastructure here at Einstein that will allow our talented scientists—such as Ulrich Steidl, Amit Verma and Chandan Guha—to identify new targets and develop new antigen receptors. This Einstein-Montefiore collaboration will allow us to ask and answer questions at the cutting edge of immunotherapy.

What changes have you implemented regarding cancer care at Montefiore? One change was to get away from the traditional cancer-care model—where a patient goes from one physician to the next—and instead have patients engage all their providers in a single program. This relieves patients, and maybe even their primary care doctors, of the burden of coordinating cancer care. We’ve also improved our ability to conduct clinical trials by expanding our patient population. In the years I’ve been here, Montefiore has grown from three hospitals in the Bronx into a health network encompassing 11 hospitals with various levels of affiliation in the Bronx and in Westchester, Rockland and Orange Counties.
It’s a pleasure to see so many happy people in one place at one time,” said Edward R. Burns, M.D. ’76, Einstein’s executive dean, at Einstein’s 58th commencement. The event took place May 25 in New York at Lincoln Center’s David Geffen Hall.

Allen M. Spiegel, M.D., the Marilyn and Stanley M. Katz Dean, distributed the alumni and faculty awards (see facing page) and then introduced the commencement speaker—Einstein’s own Susan Band Horwitz, Ph.D., the distinguished professor of molecular pharmacology who discovered the mechanism of action of the anticancer drug paclitaxel (Taxol). Dr. Horwitz shared homespun wisdom with the graduates. “Every morning when I walk through the lobby of the Forchheimer Building, I see the words ‘Science at the Heart of Medicine,’” she said. “That motto sets me up for the day, because I know that progress in treating serious disease will come from a greater understanding of human physiology and chemistry.”

Dr. Horwitz is a fan of the simple question. “The right simple question can often produce meaningful results,” she said. In her case, the question was “How does Taxol kill tumor cells?” Pursuing the answer became her life’s work, and today this extract of the Pacific yew has helped more than a million people with ovarian, breast and lung cancer. She has received many honors for her discovery, including the Rose C. Falkenstein Chair in Cancer Research at Einstein and membership in the National Academy of Sciences and the National Academy of Medicine.

Dr. Horwitz concluded her address by reminding the audience not to forget the “heart” part of the Einstein motto. “It’s important to listen to students, patients, colleagues and children with genuine interest and concern,” she said. “Great advances in technology can never replace empathy between humans or within a community.”
FACULTY AWARDS

Irene Blanco, M.D. ’04, M.S. ’10
Samuel M. Rosen Award for Outstanding Teaching–Basic Science

Mimoza Meholli, M.D.
Samuel M. Rosen Award for Outstanding Teaching–Clinical

Joshua D. Nosanchuk, M.D.
Harry Eagle Award for Outstanding Basic Science Teaching

Lawrence J. Brandt, M.D.
Harry Eagle Award for Outstanding Clinical Teaching

GRADUATE CLOSE-UPS

Ryan White, Ph.D. ’16
Dr. White, originally from Greensboro, NC, will always appreciate the sense of community he found at Einstein. “When I came to interview, it was clear that the students were all good friends both in and outside the lab, and I had the joy of seeing many ‘beer-hour’ or lunch-break talks turn into fruitful collaborations spanning departments,” he says. Dr. White is bringing this collegiality to his new research position at Rockefeller University, where he studies how replication machinery copes with DNA lesions and how defects in DNA-repair proteins affect replication. Elucidating these basic mechanisms will contribute to a better understanding of genetic defects underlying certain types of bone marrow failure.

Joy Goldstein, M.D. ’16
For Dr. Goldstein, who came to Einstein from nearby West Hempstead, NY, the sense of community at Einstein included support from an Alumni Association scholarship, which freed her to follow her passions and interests. As she begins her residency in pediatrics at Children’s Hospital Los Angeles, Dr. Goldstein looks forward to working with her young patients and their families. “I’m grateful to have had the opportunity to learn from some amazing mentors and excited to put the great clinical training that I got at Einstein into practice,” she says.

ALUMNI AWARDS

Alfredo A. Sadun, M.D. ’78, Ph.D. ’76
Dominick P. Purpura Distinguished Alumnus Award

Sue Wickner, Ph.D. ’74
Distinguished Ph.D. Alumna Award

Gail Solomon, M.D. ’62
Distinguished Alumnus/Clinical Practitioner Award

FACULTY AWARDS

Irene Blanco, M.D. ’04, M.S. ’10
Samuel M. Rosen Award for Outstanding Teaching–Basic Science

Mimoza Meholli, M.D.
Samuel M. Rosen Award for Outstanding Teaching–Clinical

Joshua D. Nosanchuk, M.D.
Harry Eagle Award for Outstanding Basic Science Teaching

Lawrence J. Brandt, M.D.
Harry Eagle Award for Outstanding Clinical Teaching

Robert W. Marion, M.D. ’79
Lifetime Achievement Award for Excellence in Teaching

Harris Goldstein, M.D. ’80
Lifetime Service Award

Stephen G. Baum, M.D.
Honorary Alumnus Award

Neil Flomenbaum, M.D. ’73
Lifetime Achievement Award

Dianne Cox, Ph.D.
LaDonne H. Schulman Award for Excellence in Teaching

Richard G. Gorlick, M.D.
Saul R. Korey Award in Translational Science and Medicine

Top, jubilant graduates; bottom, before the ceremony, from left: Einstein’s Dean Spiegel and Edward R. Burns, M.D. ’76, executive dean; Steven M. Safyer, M.D. ’82, president and CEO of Montefiore Medicine; and Philip O. Ozuah, M.D., Ph.D., executive vice president and chief operating officer at Montefiore Medicine.
Reunion 2016: Honoring the Class of 1966

This year’s Einstein reunion drew alumni from 10 classes (graduation years ending in 1 or 6), including the milestone 50th Anniversary Class of 1966.

Tuesday, May 24
ALUMNI DAY ON CAMPUS
The alumni gathered on Einstein’s Jack and Pearl Resnick Campus to catch up, remember their medical-school days and take part in Einstein Alumni Association activities. On the itinerary: a campus tour, an alumni-faculty luncheon in the Lubin Dining Hall and a symposium in the Price Center/Block Research Pavilion’s LeFrak Auditorium. The symposium featured a discussion of “the new Einstein” led by Edward R. Burns, M.D. ’76, executive dean, and presentations on timely medical issues by Einstein faculty members Liïse-anne Pirofski, M.D. ’82, and Joe Verghese, M.B.B.S.

GALA REUNION DINNER
Members of the milestone anniversary class were guests of honor at the Gala Reunion Dinner, which was held for all 10 reunion classes at Manhattan’s Grand Hyatt New York Hotel and hosted by the Alumni Association. During the dinner, class representatives took to the podium to share memories of their Einstein years.

Speaking for the Class of 1966 was Ruth E. K. Stein, M.D. ’66, recipient of the Alumni Association’s 2015 Lifetime Achievement Award. “Our class predated broad-spectrum antibiotics and the AIDS, Ebola and Zika epidemics, and we had only just begun to understand the role of DNA and RNA. Epigenetics and personalized medicine were not yet on the horizon,” Dr. Stein recalled. She is a professor of pediatrics at Einstein, associate director and director of research training for the developmental-behavioral pediatrics training program at Einstein and Montefiore and director of academic affairs for the Children’s Evaluation and Rehabilitation Center and the division of developmental medicine.

Stephanie A. Green, M.D. ’81, a pediatrician whose father, the late Ernst R. Jaffé, M.D., was Einstein’s first chief of hematology, represented her class. “Thirty-five years ago, I walked across the stage at my graduation from Einstein to receive my medical degree. My father hooded me and gave me a congratulatory kiss,” Dr. Green
Einstein Then and Now...

CLASS OF 1966

Class size (entering) | Women | Men | Age range | U.S. states represented | Countries represented | Faculty | M.D. | M.D./Ph.D. |
---|---|---|---|---|---|---|---|---|
93 | 14 | 79 | 19–28 | 9 | 3 | 87 | 0 |

CLASS OF 2016

Class size | Women | Men | Age range | U.S. states represented | Countries represented | Faculty | M.D. | M.D./Ph.D. |
---|---|---|---|---|---|---|---|---|
183 | 85 | 98 | 21–34 | 25 | 32 | ~2,000 | 170 | 13 |
recounted. She then asked her classmates to “take a moment and remember that special day when you were officially called ‘Doctor.’”

Today, she noted, “we each practice in our own specialty world but we are all doctors, and we are even more connected because of our time at Einstein.”

**Wednesday, May 25**

**COMMENCEMENT DAY**

The festivities continued with an Alumni Association–sponsored luncheon for members of the Class of 1966, held at a Manhattan restaurant.

Members of the Class of 1966 led other reunion celebrants in marching at Commencement. As they entered Lincoln Center’s David Geffen Hall, the honorees were greeted with applause by the assembled dignitaries, guests and new graduates.

“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

HELP US TRANSFORM THE FUTURE OF MEDICINE

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.
The Einstein Professional & Leadership (P&L) Division hosted its 2016 Golf & Tennis Tournament and Dinner on June 27, at the Westchester Country Club in Rye, NY. This year’s honoree was Carol M. Joseph, a noted real estate attorney and a former partner in the New York law firm Blank Rome LLP. The event benefited Einstein’s Center for Experimental Therapeutics, which advances Einstein investigators’ most promising research on innovative treatments for cancer, diabetes, heart disease and other health problems.

Dean Spiegel and Martin (Marty) Luskin, Professional & Leadership Division chair, welcomed the assembled division members and guests, and Mr. Luskin then presented the 2016 Albert Einstein Humanitarian Award to Ms. Joseph. “Carol is committed to making life better for people everywhere and truly exemplifies the professional excellence and humanistic values of Albert Einstein and of the Einstein professional community.”

Helping advance Einstein research on innovative treatments for cancer, diabetes, heart disease and other health problems.
“I have always enjoyed learning about and supporting organizations that have substantial impact,” said Ms. Joseph, who is active in a number of philanthropic causes, including global human rights, affordable housing and education for children with learning disabilities. “It’s been exciting to meet researchers at Einstein and Montefiore and to learn about their work, which will affect human health throughout the world and help educate the next generation of scientific leaders.”

In another program highlight, Greg Gonzalez, the P&L Division’s incoming chair, presented a ceremonial gavel to Mr. Luskin, whose term ended in June. The gavel was a token of appreciation for Mr. Luskin’s leadership and his service to Einstein.

Division executive board members Peter Bernstein and Raymond S. Cohen co-chaired the event. Mr. Luskin and Mr. Gonzalez, division vice chair, served as journal co-chairs with executive board members Neil A. Clark and Jeffrey A. Fiedler; Jack M. Somer, executive board member, and Marc Altheim served as tennis co-chairs; Peter E. Zinman, division vice chair, and Marlon Bustos, executive board member, were the auction co-chairs.

The Golf & Tennis Tournament and Dinner, the P&L Division’s major annual fundraiser, celebrates a 55-year tradition of philanthropic leadership and collaboration among business leaders committed to advancing Einstein’s mission to improve human health.
Spirit of Achievement Luncheon
Benefits Cancer Research

The Einstein Women’s Division hosted its 62nd annual Spirit of Achievement Luncheon on May 17, at the Rainbow Room in Manhattan.

The honorees included legendary music industry executive and producer Clive Davis; Sharmila K. Makhija, M.D., M.B.A., an expert on cancer prevention and gynecologic cancers, and professor and university chair of obstetrics & gynecology and women’s health at Einstein and Montefiore; and Danielle Weisberg and Carly Zakin, co-founders and CEOs of theSkimm, a popular current events e-newsletter for young professional women.

Ruth L. Gottesman, Ed.D., a trustee of Einstein and Montefiore, received the Lizette H. Sarnoff Award for Volunteer Service, the Women’s Division’s highest honor.

Jill Martin, a contributor to NBC’s Today show and a past Spirit honoree, served as the afternoon’s emcee.

Women’s Division president Carol Roaman spearheaded the event with executive board members and luncheon co-chairs Mindy Feinberg, Jackie Harris and Andrea Stark.

Proceeds from the luncheon benefited the Women’s Division’s initiative to support Einstein-Montefiore research on ovarian, breast, cervical, uterine, prostate, lung and pancreatic cancers and leukemia.

Spirited Tributes
Steven M. Safyer, M.D., ’82, president and CEO of Montefiore Medicine, presented Dr. Makhija with her Spirit award. In her remarks, Dr. Makhija, who holds the Chella and Moise Safra Chair in Obstetrics & Gynecology and Women’s Health at Einstein, stressed the importance of women’s health issues and of Montefiore’s outreach to women in underserved communities. She also shared a video showing how Einstein is training the next generation of highly skilled ob/gyn physicians.
Ms. Zakin and Ms. Weisberg explained how technology is changing the way we receive news and how the new generation of entrepreneurs is embracing philanthropy.

Allen M. Spiegel, M.D., Einstein’s Marilyn and Stanley M. Katz Dean, introduced Dr. Gottesman as a woman “whose dedication and service to Einstein has set a new standard.” Dr. Gottesman’s affiliation with Einstein spans nearly 50 years. She holds the titles of board chair emerita, professor emerita of pediatrics and founding director of the Fisher Landau Center for the Treatment of Learning Disabilities. In accepting her award, she called the College of Medicine “a beacon of light” and praised the Einstein community’s “spirit of cooperation, compassion and collaboration.”

Dr. Safyer introduced Mr. Davis, highlighting his role in galvanizing the music industry’s early support for AIDS/HIV awareness and research. Mr. Davis, in turn, expressed his admiration for the researchers at Einstein-Montefiore who are working to combat major health problems.

Visit our video-enhanced online edition at [magazine.einstein.yu.edu](http://magazine.einstein.yu.edu)
Members and friends of Einstein Emerging Leaders (EEL) gathered for an evening of cocktails and conversation at the Norwood Club in Manhattan on February 29. Billed as a “leap-year fundraising party,” the event benefited the Montefiore Einstein Children’s Evaluation and Rehabilitation Center (CERC). Guests also brought boxes of diapers to be distributed to CERC families.

Danielle Segal, EEL executive chair, welcomed the attendees and introduced guest speaker Anne P. Murphy, Ph.D., an associate professor of clinical pediatrics at Einstein and Montefiore. Dr. Murphy directs the Center for Babies, Toddlers and Families and the Early Childhood Center and serves as clinical director of CERC.

Dr. Murphy discussed a clinical trial she is conducting with Einstein’s department of family and social medicine in collaboration with the New School University’s Center for Attachment Research. The randomized controlled study is funded by the Health Resources and Services Administration to test the effectiveness of the group attachment-based intervention. This intensive parent-child treatment is aimed at helping parents who were abused as children break the intergenerational cycle of abuse and neglect, and create positive social-emotional and developmental outcomes for their own children.

Also attending was Theodore A. Kastner, M.D., director of CERC, co-director of the Rose F. Kennedy Intellectual and Developmental Disabilities Research Center and chief of the division of developmental medicine (pediatrics) at Einstein and at the Children’s Hospital at Montefiore. Dr. Kastner holds the Ruth L. Gottesman Chair in Developmental Pediatrics at Einstein.

Einstein Emerging Leaders are philanthropic New York City professionals committed to advancing Einstein’s mission to improve human health. EEL hosts a variety of educational programs, volunteer activities and fundraising events throughout the year. To learn more, please contact Eve Marsan at eve.marsan@einstein.yu.edu.
Montefiore and Einstein in Florida 2016

Einstein and Montefiore presented educational events for friends and supporters in the Palm Beach community. Allen M. Spiegel, M.D., Einstein’s Marilyn and Stanley M. Katz Dean; Steven M. Safyer, M.D., president and CEO, Montefiore Medicine; and David A. Tanner, chairperson, Montefiore Medicine Board of Trustees, spoke at a welcome reception and dinner at the Boca Raton Resort & Club on February 19.

The next day, a medical symposium on healthy aging featured Montefiore-Einstein speakers: Jessica L. Zwerling, M.D., who discussed Alzheimer’s disease; Robert E. Michler, M.D., heart health; Mark P. Schoenberg, M.D., urology; and Scott Wetzler, Ph.D., behavioral sciences. Dean Spiegel spoke about science in the news; Dr. Safyer gave the program’s opening and closing remarks.

Einstein Trustee Benjamin J. Winter and his wife, Susan, and Montefiore Medicine Trustee Melissa Ceriale and her husband, John, co-hosted a reception at the Ceriales’ home in Palm Beach.

The series concluded with a luncheon and panel discussion, “How Genetics Is Revolutionizing Medical Diagnosis, Prevention and Treatment,” hosted by Einstein Trustees Marilyn and Stanley M. Katz at the Palm Beach Country Club. Dr. Safyer and Dean Spiegel joined Susan D. Klugman, M.D., director of reproductive genetics and a professor of clinical obstetrics & gynecology and women’s health at Einstein and Montefiore, in leading a lively discussion.
1950s

Don Kline, M.D. ’59, writes, “I am proofing my fifth and latest novel, Waltzing Matilda. My fourth book, The 1880s Cattle Drive Murder, was published earlier this year. When not writing, I am painting, using oil, acrylic and watercolor. I’m getting ready to plant a vegetable garden, and trying to relearn the guitar and banjo and learn the keyboard and clarinet. Who ever said retirement was easy?”

1960s

Phillip Frost, M.D. ’61, received the 2016 Sand in My Shoes Award from the Greater Miami Chamber of Commerce for his outstanding community service and contributions to the south Florida community. In 2015, he gave a presentation, “Building a Pharmaceutical Company with Practical Solutions to Making Better Drugs,” to the University of Padua’s department of molecular medicine in Padua, Italy. Dr. Frost received the Einstein Alumni Association’s Dominick P. Purpura Distinguished Alumnus Award in 2014. That year, he also received the Ellis Island Medal of Honor. The medal, bestowed by the National Ethnic Coalition of Organizations, recognizes immigrants and their children for their contributions to America; about 100 medalists are chosen each year.

Kenneth Schiffer, M.D. ’61, writes, “I have had the pleasure of practicing primary care pediatrics with two of my children, each of whom is a graduate of Einstein: Michelle Schiffer Merer, M.D. ’90, who is married to David Merer, M.D. ’90, and Todd Jay Schiffer, M.D. ’93. My loving wife of 54 years, Marcia, a Barnard graduate, has run our pediatric office since its inception and is utterly central to our pediatric practice.”

Michael S. Olstein, M.D. ’65, writes: “I retired in 2015, the year I celebrated my 75th birthday and 50 years of practicing medicine. After graduating from Einstein, I did my internship at Maimonides Medical Center in Brooklyn. Then the Public Health Service sent me to Boston, where I practiced adult medicine at a community health center, did my ophthalmology residency and worked as an emergency room doctor at a busy hospital. In 1971, I opened my solo ophthalmology practice in Medford, MA. I practiced there for 44 years and also served on the faculty of the Tufts University School of Medicine. Shortly before I retired, two of my patients, both in their 90s, reminded me that in addition to caring for their children and grandchildren, I had cared for their parents! I feel fortunate to have been able to work when solo private practice was still viable. I am deeply grateful to Einstein for the superb education and training I received there. I grew up in the Bronx and can remember visiting the site where the new medical school was being built. That same medical school provided me with the foundation of knowledge that let me feel confident and comfortable taking care of my patients.”

1970s

Diane E. Stover, M.D. ’70, reports, “I am happy to announce that my daughter, Dana, has started a fellowship in infectious diseases at Yale. She plans to do epidemiologic work within the public health field.”

Janina R. Galler, M.D. ’72, received the Leon Eisenberg Award in Child Psychiatry on May 11, at the Harvard Faculty Club in Cambridge, MA. The award honors contributions to the fields of child mental health and development and of ethics, and it is given annually by the division of developmental medicine at Boston Children’s Hospital (BCH). As part of the award presentation, she delivered the sixth annual Ludwik S. Szymanski, M.D., Lecture in Mental Health, Developmental Disabilities and Ethics, “The Legacy of Childhood Malnutrition: Effects on Brain and Behavior Across Generations,” during
the BCH department of psychiatry’s grand rounds. Dr. Galler is director of the Barbados Nutrition Study and a psychiatrist in the Massachusetts General Hospital’s Chester M. Pierce, M.D., Division of Global Psychiatry. She currently serves as president of the Einstein Alumni Association.

Peter Rottwein, M.D. ’75, reports: “After 17 years at Oregon Health & Science University in Portland, OR, including the last 10 as chair of the department of biochemistry and molecular biology, I took a new position. Since September 2014, I have been part of Texas Tech University Health Sciences Center in El Paso, a new medical university and the fourth institution in the Texas Tech University system. There I am vice president for research and associate dean for research at the Paul L. Foster School of Medicine, and serve as chair of the department of biomedical sciences. Lots of jobs, lots of challenges, but exciting opportunities and great fun.”

Lyda Tymiak Lindell, M.D. ’76, recently sold her ophthalmology practice (which she’d had for 30 years) and medical spa in Palm Harbor, FL. She is active in community and philanthropic organizations and serves on the board of the Humane Society and on the dean’s advisory board of the University of South Florida’s College of Arts and Sciences.

Sam Moskowitz, M.D. ’76, writes: “I have added a third fellowship to my title. I am now Sam Moskowitz, F.A.C.P., F.A.C.G. and, most recently, A.G.A.F. (Fellow of the American Gastroenterological Association). I founded the Association for Orthodox Jewish Gastroenterologists 15 years ago; it has members from all over the world, including Europe, Israel and Australia. We meet annually as part of Digestive Diseases Week and hold our own meetings to network among ourselves. This year the meeting was in San Diego; it conflicted with my 40th reunion alumni"

Three Generations of Einstein Excellence

“I have your back” is more than just a catch phrase to Einstein alumni. Dr. Sterling J. Haidt, Class of 1970—a retired vitreoretinal surgeon, founder of Northern California Retinal Vitreous Associates and an adjunct clinical associate professor of ophthalmology at Stanford University Medical School—recently went to Dr. Dimitriy Kondrashov, Class of 2000, a spinal surgeon at St. Mary’s Medical Center in San Francisco, seeking relief from stenosis complicated by scoliosis.

Dr. Kondrashov obliged his fellow alum by performing a five-level spinal fusion at St. Mary’s Spine Center, using the only robot designed for spinal surgery. Dr. Eric Holden, Class of 2011, Dr. Kondrashov’s fellow, assisted. “I am doing well and almost pain-free,” Dr. Haidt reports. To express his gratitude, he made a gift to the Einstein Alumni Association in Dr. Kondrashov’s honor.
dinner. I am a founding partner in the Brooklyn Surgery Center, a new multispecialty surgery center in Brooklyn, NY. It includes gastroenterology, orthopedics, podiatry, pain management and IVF, with other specialties coming on board.”

Miriam Gutmann Sava, M.D. ’76, writes: “I share office space with my son, Aryeh Sava, Ph.D., a licensed clinical child and adolescent psychologist. We are collaborating on a number of shared clinical cases and it’s really been exciting—he even occasionally asks for my advice now! I continue to supervise child psychiatry residents year-round. My daughter is married and has four children; she also lives in Chicago, and we just celebrated our oldest grandchild’s bat mitzvah. My youngest, Dani, an Einstein graduate (Daniel Sava, M.D. ’14), is finishing his first year in physical medicine and rehabilitation at Johns Hopkins.”

1980s

Max Shapiro, M.D. ’84, writes, “I have two sons in medical school!”

Joseph R. Maldonado, Jr., M.D. ’85, M.Sc., M.B.A., Dip. E.B.H.C., reports: “I completed my term as president of the Medical Society of the State of New York and have been appointed the new president of the Medical Educational Scientific Foundation. Last year, I found a missing link in my lifelong genealogical research, which connects my family’s roots to Sephardic Jews expelled from the Iberian peninsula during the Inquisition. On Yom Hashoah 2016, I made a return to Orthodox Judaism. My next task is to find the ancestral links to eight exact genetic Y chromosomal-matching Ashkenazi Jews in Eastern Europe!” Dr. Maldonado can be reached at joe.maldonadojr@yahoo.com.

Lori Feldman-Winter, M.D. ’86, is a professor of pediatrics at the Cooper Medical School of Rowan University in Camden, NJ, and co-course director for the Scholars’ Workshop, a four-year course at this new medical school. Dr. Feldman-Winter also serves as a consultant for the CHAMPS project, a breastfeeding initiative funded by the W. K. Kellogg Foundation, and is a member of American Academy of Pediatrics’ task force on sudden infant death syndrome. Her husband, Jonathan, is president of the New Jersey Dermatological Society. Her daughter Rebecca graduated from Columbia University’s School of Engineering, received a master’s degree in mechanical engineering from the University of Pennsylvania and is now pursuing a Ph.D. at Drexel University in Philadelphia. Her daughter Sarah, a magna cum laude graduate of the University of Michigan, is a first-year student at the University of Pennsylvania’s School of Veterinary Medicine.

Maryirene Ilchert-Flynn, M.D. ’86, has been in private practice on Staten Island, NY, since 1992, specializing in sports medicine. She became a police surgeon for the New York Police Department in 2009 and notes, “Currently, I am the only female police surgeon!” She adds, “Tony and I have been married for 33 years. We have three beautiful children. Kathleen, 26, graduated from Fairfield University in Connecticut with a bachelor’s degree in English and a business law minor. She works at Glocap Search, a firm specializing in the financial sector, based in New York City. Kelly, 21, a junior at Lafayette College in Pennsylvania, is a chemical engineering major and a starting player for its Division I volleyball team. Sean, 15, is a freshman at Holy Cross High School in Queens, NY. Already 6 feet 5 inches tall, he loves sports and plays basketball and volleyball.”

Paul Quartararo, M.D. ’86, has served as chief medical director for the New York Life Insurance Company since 2013, and is active in the American Academy of Insurance Medicine. He writes: “Carol and I recently celebrated our 30th wedding anniversary. Much of our recreation comes from ballroom dancing. Our first-born daughter, Catherine E. Quartararo, Ph.D. ’13, was married the week before Reunion. Our other two daughters have completed college; one is independent and the second is almost there!”

1990s

Panayiotis Andreou Ellinas, M.D. ’91, M.P.H., resigned from the U.S. Army Medical Corps Reserves and is now practicing industrial/occupational medicine. He writes, “I made a fresh start for my whole family in what is probably America’s most wonderful and best-kept secret of a small town: Edwardsville, IL.”

Ronald Lubetsky, M.D. ’91, recently celebrated 14 years as medical director of the ProCare Health Center in North Miami Beach, FL, and 10 years as medical director of Broward
Physician Therapy in Hollywood, FL. He is a fellow at the Arizona Center for Integrative Medicine and is working on a book.

**Hugh Bases, M.D. ’94,** is a developmental-behavioral pediatrician at the New York University School of Medicine and serves as program director for its developmental-behavioral fellowship program. He writes, “My daughter, Rachel, is heading to college this fall, and my son, Ben, will be starting the 10th grade. My wife, Randi Asher (Ferkauf, Psy.D. ’96), is in private practice as a clinical psychologist on Manhattan’s Upper West Side.”

**2000s**

**Henry Rascoff, M.D. ’01,** and his partner, Katherine Noble, M.D., recently co-launched Sound Beach Pediatrics, a private practice in Stamford, CT. He writes, “Our motto is ‘Health, Family, Community.’ Our goal is to serve both privately insured and Medicaid patients.”

**Savita Srivastava, M.D. ’01,** writes, “I enjoy being a gastroenterologist in the University of Virginia Physicians Group, in Charlottesville, and am honored to participate in the American Gastroenterological Association’s Future Leaders program. I have a son, Neil, 5, and a daughter, Nayla, 4.”

**Matthew Dombrow, M.D. ’06,** completed a residency in ophthalmology at the University of Medicine and Dentistry of New Jersey (now a part of the Rutgers School of Biomedical and Health Sciences) and a fellowship in retina at Yale Medical School. He reports, “I am now in private practice in the New Haven area of Connecticut. I married my wife, Melissa, during my fourth year of medical school. We have two daughters: Leah, age 6, and Alexa, age 3.”

**Shahrooz Eshaghian, M.D. ’06,** is an attending physician in the division of hematology & oncology at Cedars-Sinai Medical Center in Los Angeles, and a clinical instructor at the David Geffen School of Medicine at the University of California, Los Angeles (UCLA). After completing his internship and residency in internal medicine at Cedars-Sinai in 2009, Dr. Eshaghian did a three-year fellowship in hematology & oncology at UCLA Medical Center, serving as chief fellow in 2011–12. He was named a Super Doctor Southern California Rising Star in 2013, 2014 and 2015.

**Adam Friedman, M.D. ’06, F.A.A.D.,** reports: “After serving for five years as the director of dermatologic research and as associate residency program director in the division of dermatology at Einstein, I was recruited to be the founding residency program director and director of translational research in the department of dermatology at the George Washington University School of Medicine & Health Sciences in Washington, DC. During my time at Einstein, I published more than 100 manuscripts and two textbooks, and was awarded multiple patents, culminating in the formation of Nano BioMed, Inc.,” a company specializing in nanoparticle-based drug therapies.

**2010s**

**Vijay Kotecha, M.D. ’14,** has completed his second year of residency in internal medicine at the University of California, San Francisco. He writes, “I continue to see a few Einstein alums around the hospital on a regular basis: internal medicine interns Saate Shakil, M.D. ’15, and Nick Iverson, M.D. ’15, and general surgery resident Key Nguyen, M.D. ’14. My plans after residency remain uncertain, though I likely will work in some capacity in general medicine and health systems improvement. Happy to reconnect with any Einstein folks who find themselves in the Bay Area!”

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**ON THE WEB**

www.einstein.yu.edu/alumni

For news about Reunion 2017 and other upcoming alumni programs and events, please visit our website.
“From nine to five, I’m a numbers guy,” says Damien Jackson, director of student finance at Einstein. But put a camera in his hand and his inner visual artist emerges.

“Photography allows me to express myself,” explains Jackson. “I’m really an introvert, but my photographs let me give my opinion of things and show you what I think is beautiful.”

He started taking pictures eight years ago, after moving from Atlanta to New York following a divorce. His daughter and son, now 9 and 10, were toddlers at the time, and he wanted a photographic record of their growth and development. Although he travels to Atlanta to see them every six weeks, Jackson is always surprised by how much they’ve grown. “It’s shocking to see how different they are each time,” he says.

Jackson liked taking his children’s pictures so much that he soon broadened his scope and began photographing places and people he encountered. Although he attends occasional photography workshops, Jackson is mainly self-taught. “I just take the camera and go,” he says with a laugh. Moreover, while he thinks technical training can be useful, he believes obsessing over things such as aperture size, shutter speed and exposure times can inhibit creativity. “You
have to make sure that you continue to do whatever made you pick up a camera in the first place,” he says.

Jackson is especially interested in travel photography and what he calls “environmental portrait photography”—taking photos of people where they live, work or play that say something about their personalities. “Candid is what I aim for,” he says. “I want you to ‘get’ who this person really is.”

Jackson and his girlfriend recently traveled to South Africa, where he photographed rugged coastlines, animals, school children—and some grim reminders of apartheid, including signs above the entrance to the Apartheid Museum reading “Blankes” (whites) and “Nie-Blankes” (nonwhites).

Back home in New York, Jackson does portrait shoots on commission and has a long-running project under way called “Faces of Fisk,” a compilation of images of people who’ve graduated from the historically black Nashville university since its founding in 1866. Fisk boasts many prominent graduates, including civil rights activist W. E. B. Du Bois and poet Nikki Giovanni. A 1997 graduate himself, Jackson started working on “Faces of Fisk” several years ago, for the school’s 150th anniversary next year. His goal is to capture 1,866 images of Fisk grads, exhibit the photos in galleries and turn them into a book.

Taking pictures that capture a person’s essence and his day job helping Einstein students fund their studies both involve making positive connections, says Jackson. “I enjoy interacting with students and letting them know we’re here to help,” he says. “And when it comes to taking your portrait, I want to figure out who you are.”

ON THE WEB
www.nedariphoto.photoshelter.com

SCIENCE AT THE HEART OF MEDICINE 55
It wasn’t until 1961 that Rose and Joseph P. Kennedy revealed to the public that their daughter Rosemary was intellectually disabled. That same year, their son President John F. Kennedy asked the National Institutes of Health to create the National Institute of Child Health and Development. The NICHD established 10 centers around the country for treating people with intellectual and developmental disabilities—one of those centers at Einstein.

Fifty years ago, on May 1, 1966, ground was broken for the Rose F. Kennedy Center for Research in Mental Retardation and Human Development, a nine-story building in the Jacobi Hospital complex. Those attending the ceremony included Mrs. Kennedy and her son Robert F. Kennedy (at center in the photo above).

The federal government funded 75 percent of the center’s cost. Other contributors included the Joseph P. Kennedy, Jr., Foundation, the estate of Louis and Ida Katz and the family of Siegfried Ullmann.

Today, the Kennedy Building (earlier this year renamed the Rose F. Kennedy Center for Research in Intellectual Disabilities and Human Development) houses the offices of the NICHD-funded program known as the Intellectual and Developmental Disabilities Research Center (IDDRC); Einstein’s Dominick P. Purpura Department of Neuroscience and Saul R. Korey Department of Neurology; and three shared “core” research facilities.

The Children’s Evaluation and Rehabilitation Center (CERC), now relocated to the nearby Van Etten Building, remains an integral part of the IDDRC. CERC offers clinical services to children (and adults) with intellectual and developmental disabilities and conducts clinical research.
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Joining the circulatory systems of an old and a young animal is called heterochronic parabiosis. Here we see a cross-section of the small intestine of a young mouse that was parabiosed to an old mouse for two months. Postdoctoral research fellow Tahmineh Tabrizian, M.D., Ph.D., has found that factors in old-mouse blood “age” intestinal stem cells in young mice by impairing their ability to proliferate. (The stem-cell damage can’t be seen in this low-magnification image.) The next step in Dr. Tabrizian’s research: Identify the stem-cell aging factors present in old blood and see whether targeting those factors (using neutralizing antibodies, for example) helps rejuvenate stem cells in old mice and, ultimately, in old people. Dr. Tabrizian’s mentor is Derek M. Huffman, Ph.D., an assistant professor of molecular pharmacology and of medicine (endocrinology).