A SMALL FISH WITH A WHALE OF AN IMPACT

ZEBRAFISH
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ON THE COVER:
Zebrafish genes have a great deal to tell us about human diseases and developmental biology. Research technician KathyAnn Lee helps keep operations bubbling along in the laboratory of Florence Marlow, Ph.D. For more about zebrafish research at Einstein, see page 24.
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A Message from the Dean

Nathan Myhrvold, former chief technology officer for Microsoft, in “Even Genius Needs a Benefactor” (Scientific American, February 2016), makes a compelling case for government support of basic research. Fortunately, the increased federal budget allocation for NIH in 2016 shows that Congress and the president agree at least on this point. This issue of Einstein highlights examples of important basic research, as well as ways in which it is being translated to address medical needs.

In our cover story, “Zebrafish: A Small Fish with a Whale of an Impact,” we spotlight three researchers—Florence Marlow, Teresa Bowman and Ertugrul Ozbudak—whose zebrafish work is yielding valuable information about infertility, acute myeloid leukemia, congenital spinal defects and other conditions. The zebrafish’s fast reproductive cycle, transparency and genetic parallels with humans make it an excellent model organism for research.

“Healing All Wounds” exemplifies how Einstein basic research holds considerable promise for Montefiore clinical care. In Montefiore’s state-of-the-art Wound Healing Program, physicians are treating ulcers, bedsores and other wounds with unprecedented success. Approaching from the basic science angle is David Sharp in Einstein’s department of physiology & biophysics. When his research team deactivated an enzyme called fidgetin, wounds healed twice as fast as normal. The next step is to develop a therapy based on these findings, which would then be clinically assessed at Montefiore—translational medicine at its best.

This issue also spotlights physician-scientist Joe Verghese, a 2001 graduate of Einstein’s Clinical Research Training Program. His background in neurophysiology, aging and dementia places him, as he puts it, “in an ideal position to build bridges between Einstein’s rich aging-related research in neurology and Montefiore’s extensive clinical services in geriatrics.” Joe is doing exactly that: he directs the Montefiore Einstein Center for the Aging Brain and leads our integrated divisions of cognitive & motor aging (neurology) and of geriatrics.

He and others in this issue of Einstein magazine show how our collaboration with Montefiore enhances our missions of research excellence, outstanding education and improved human health.

Allen M. Spiegel, M.D.
The Marilyn and Stanley M. Katz Dean
“pipeline program” that brings underprivileged students to Einstein has received a new name and a major grant renewal.

The Bronx Science and Health Opportunities Partnership (BxSHOP) has been renamed the Bronx Health Opportunities Partnership–Einstein (Bronx HOPE) in memory of Hope Spano, an administrator in the department of family and social medicine who was passionately committed to BxSHOP. She was also the administrator of Einstein’s Hispanic Center of Excellence and its Bronx Center to Reduce and Eliminate Ethnic and Racial Health Disparities. Ms. Spano died in September 2014 from colon cancer at age 52.

Bronx HOPE is directed by Alvin H. Strelnick, M.D., assistant dean for community engagement and the department’s division chief of community health. It serves students who are economically and educationally disadvantaged and come from groups underrepresented in medicine. The partnership—a broad network of Bronx-based educational institutions and community agencies—offers a pathway to training in science, medicine and healthcare for middle and high schoolers, undergraduates and postbaccalaureate students. Some 350 students participate in structured programs each year, and 1,000 to 2,000 students, parents, teachers and counselors attend events sponsored by the partnering institutions. The department also won a renewal grant from the federal Health Resources Services Administration through its Health Careers Opportunity Program. Over three years, nearly $2 million will be distributed to help continue and expand Bronx HOPE and other programs.

“Hope Spano was a devoted and inspiring mentor for students, and a staunch supporter of faculty and staff from Einstein, Montefiore and our collaborating institutions,” says Dr. Strelnick. “She set high standards and helped others live up to them. The new ‘Bronx HOPE’ name was chosen by a unanimous vote of our partners, all of whom knew and loved her. This renewed federal funding is a strong vote of confidence that will allow us to carry on Hope’s legacy.”
Images of Global Health

Over the last year, the Global Health Fellowship Program has sent almost 100 students around the world to learn about health systems in other countries. Last November, the long wall of Einstein’s “Main Street” in the Forchheimer Medical Science Building became a photo gallery that captured their experiences in images and words, a sampling of which appears on these two pages.

A committee of students curated the show, “Global Vision: The Einstein Community Abroad.” The director of the fellowship program is Jill Raufman, M.S., M.P.H.

The ER Stock
Ryan Arams

Nuevo Hospital San Roque, Córdoba, Argentina

The medicine cabinet in the emergency room at Nuevo Hospital San Roque in Córdoba, Argentina, contains many little vials of most drugs anyone would need. Public hospitals are staffed with doctors and other healthcare professionals but are lacking in resources.

Health Education
Hope Feldman

Murinzi, Uganda

Immaculate, the woman on the right (holding a computer), is the psychiatric nurse at Kisoro District Hospital. She meets monthly with villagers to discuss health topics and to offer support. Here, she is showing a video of a child undergoing a crude tonsillectomy: the gapfura (or tonsil-scraping) procedure. As the people in the audience react with horror at the scene shown in the video, Immaculate concludes by urging them to keep their children away from this dangerous procedure.
Still Life with Gourds
Elia Rackovsky
Caminito, Barrio La Boca, Buenos Aires, Argentina

More than just an energizing herbal tea, mate (mah-tay) is a Latin American ritual that brings families together and tightens the bonds of friendship. It is as important as a handshake—or hug—in closing a business deal. Sweetened with sugar and sipped from a gourd through a metal straw, one drink is traditionally passed from person to person within a group. These silver-adorned gourds were for sale by their craftsman in the Caminito street market.

To Work for the People Is to Decide with the People!
Mara Phelan
Cange, Haiti

This photo was part of an image campaign created by our Social Medicine course. The goal: to raise awareness about the failure of reconstruction efforts following the 2010 earthquake. Please visit us on Facebook at Travay pou pèp la, se deside ak pèp la.

Doctors in Training
Marlis Gnirke
Village of Mane, Spiti Valley, Himachal Pradesh (Indian Himalayas)

This was my spunky little friend from one of the villages where we set up clinics. She had been one of our last patients that day, so after clinic we played clapping games and took selfies on my phone. She quadruple-checked that we both had hearts. I’ll always have this memory—it was such a special feeling to connect beyond the boundaries of language and culture.

The Hike-In Clinic
Ben Scoblionko
Himachal Pradesh Region, Northern India

After hours of weaving and winding through the Himalayan mountains in northern India, we came upon a small clinic perched on the side of the narrow road overlooking the coursing river. The concrete walls were worn from dust storms and blizzards. Inside, the rusty frame of the only patient table sagged from decades of use, springs nearly brushing the dusty floor. This one-room clinic serves the local shepherds and farmers of the region.
The White Coat Ceremony

Every August, first-year Einstein medical students take part in the White Coat Ceremony, also known as “On Becoming a Physician.” An Einstein alumnus “cloaks” each student in a physician’s white coat provided by the Einstein Alumni Association. The white coat symbolizes the responsibilities that await the future physicians—and the humanistic values and scientific excellence that will serve as guiding principles.

At the 2015 ceremony, Joshua D. Nosanchuk, M.D., assistant dean for student affairs, welcomed the assembled Class of 2019, faculty and guests. Stephen G. Baum, M.D., senior associate dean for students, introduced Judy L. Aschner, M.D., the keynote speaker, who shared an inspirational anecdote from her days as a pediatric resident to illustrate the rewards and challenges ahead for the newest class of Einstein students. Dr. Aschner is a professor and the Michael I. Cohen, M.D., University Chair of Pediatrics at Einstein and physician-in-chief and chair of pediatrics at the Children’s Hospital at Montefiore.

Janina R. Galler, M.D. ’72, president of the Einstein Alumni Association board of governors, and Allison B. Ludwig, M.D. ’04, assistant dean for student affairs, also offered their insights.

The Stethoscope Ceremony

At this annual rite of passage, first-year Einstein medical students each receive a special gift from the Einstein Alumni Association: a stethoscope. This critical diagnostic tool is a reminder that it’s important to listen to patients. The keynote speakers at the 2015

Stethoscope Ceremony were Evelyne Albrecht Schwaber, M.D. ’59, recipient of the 2012 Dominick P. Purpura Distinguished Alumnus/a Award and an internationally renowned authority on clinical listening, and Martin N. Cohen, M.D., a professor of medicine (cardiology) at Einstein and an attending physician at Montefiore.

The Class of 2019 also heard from Felise B. Milan, M.D. ’88, director of the Introduction to Clinical Medicine (ICM) program; Martha S. Grayson, M.D. ’79, senior associate dean for medical education; Mimi McEvoy, N.P., M.A., co-director of the ICM program; and Janina Galler, M.D. ’72.
Scrubs Day
Each year, the Einstein Alumni Association ensures that every first-year medical student starts the Gross Anatomy course with a brand-new set of scrubs. Scrubs Day for the Class of 2019 featured remarks by Todd R. Olson, Ph.D., professor emeritus of anatomy and structural biology, and Harris Goldstein, M.D. ’80, associate dean for scientific resources, the Charles Michael Chair in Autoimmune Diseases, professor of pediatrics (allergy and immunology) and director of the Einstein Montefiore Center for AIDS Research. Dr. Goldstein started this Einstein tradition several years ago.

Other speakers were Raja Flores, M.D. ’92, professor and chair of thoracic surgery at Mount Sinai Medical Center, representing the Einstein Alumni Association board; Janina Galler, M.D. ’72; and Sherry A. Downie, Ph.D., a professor of clinical anatomy and structural biology and of clinical physical medicine and rehabilitation at Einstein.

Choosing the lab that best fits your interests and temperament is critical to your career.

The Declaration Celebration
The Declaration Celebration marks the transition of second-year Ph.D. and third-year M.D./Ph.D. students from graduate school coursework to their own work as laboratory researchers.

“Choosing the laboratory that best fits your interests and temperament is critical to your career path,” said Victoria H. Freedman, Ph.D., associate dean for graduate programs in the biomedical sciences, at this year’s fifth annual event. “There will be ebullience at an exciting result and despair when things aren’t going your way. The support of your mentor and lab colleagues will steer you through the difficult days.”

Libusha Kelly, Ph.D., assistant professor of systems & computational biology and of microbiology & immunology, encouraged students to look to their mentors for advice, not answers. “Always keep an elevator pitch ready,” she added. “Communicating your work in a concise and compelling manner is a skill that all scientists should develop.”

The young investigators each received backpacks containing a coffee mug and other items, including The Beginner’s Guide to Winning the Nobel Prize by Peter Doherty.
Welcome

Yaron Tomer, M.D.

Dr. Tomer, a leading endocrinology researcher and clinician, has joined Einstein-Montefiore as professor and university chair of the department of medicine. Dr. Tomer was previously at the Icahn School of Medicine at Mount Sinai, where he served as vice chair for research; division chief of endocrinology, diabetes and bone disease; and the Lillian and Henry M. Stratton Professor of Molecular Medicine. As endocrinology division chief, he expanded the clinical and research operations in endocrinology, including the creation of centers for diabetes, pituitary and adrenal disorders and the medical management of obesity.

Dr. Tomer is the author of more than 170 manuscripts and book chapters and has served on the editorial boards of several journals, including Endocrinology, the Journal of Clinical Endocrinology & Metabolism, Autoimmune Reviews and Thyroid. He is a member of the American Society for Clinical Investigation, and a fellow of the American College of Physicians as well as the American College of Endocrinology. He is the recipient of several national awards, including the American Thyroid Association’s highest honor, the Van Meter Award.

Balazs Halmos, M.D., M.S.

Dr. Halmos has joined Einstein-Montefiore as director of the thoracic oncology program and of clinical cancer genetics and a professor of clinical medicine. Dr. Halmos completed his clinical and laboratory research training in hematology/oncology at Beth Israel Deaconess Medical Center/Harvard Medical School. He was director of thoracic medical oncology at Columbia University Medical Center before coming to Einstein-Montefiore.

Dr. Halmos is an authority on managing lung and gastroesophageal cancers and thymomas. His clinical and laboratory research efforts focus on developing agents for treating thoracic malignancies and the genomic basis for drug resistance. He’ll inaugurate a program for obtaining genomic information from tumor specimens and tying this information to patient care.

Military Salute for Dr. Moadel-Robblee

Faculty members usually recommend students for accolades. In a notable about-face, an Einstein student has honored a faculty member.

At the 2015 Staff Service Recognition ceremony, Alyson B. Moadel-Robblee, Ph.D., an associate professor of clinical epidemiology & population health and of clinical medicine at Einstein and Montefiore, received a first-for-Einstein award. Colonel Mary Lynch Westmoreland from the U.S. Department of Defense’s Office of Employer Support of the Guard and Reserve presented Dr. Moadel-Robblee with its Patriot Award, which is given to supervisors or managers who have supported a Reserve service member or his or her family during the service member’s deployment. Staff member Damaris Santiago-Singer, who serves with the Air Force National Guard, had recommended the unsuspecting Dr. Moadel-Robblee for the award.

“Damaris wrote a compelling letter about the support Dr. Moadel-Robblee provided over a lengthy period and noted that her mentor’s example also helped her to excel during her service to the Air Force,” Col. Lynch Westmoreland said.

From left, Col. Mary Lynch Westmoreland; Alyson B. Moadel-Robblee, Ph.D.; and Damaris Santiago-Singer.
Lab Chat

Myles Akabas, M.D., Ph.D., is trying to develop novel antimalarial drugs, based on the parasites’ Achilles’ heel: They can’t synthesize the purines needed for making DNA and RNA. So they rely on a parasite protein called PfENT1 to transport purines from the host red blood cells. Dr. Akabas has developed a high-throughput assay to identify inhibitors of the PfENT1 transporter. He is a professor in the departments of physiology & biophysics and of medicine and in the Dominick P. Purpura Department of Neuroscience, and director of Einstein’s Medical Scientist Training Program (MSTP).

How did you come to Einstein?
I was an MSTP student here in the deep, dark past, from 1977 to 1983. Then I went to Columbia for an internship and residency in internal medicine. I was on the Columbia faculty for 15 years. Einstein recruited me back here in 2000, and I became MSTP director in 2004.

What do you like about directing the MSTP?
The students are a wonderful and dedicated group. They undergo a separate admissions process that identifies people who really want to be physician-scientists. I greatly enjoy teaching them and overseeing their development over the eight years that it takes to complete the MSTP.

When did you first want to be a scientist?
From as long ago as I can remember. My father, a CPA, had a client who owned a newsstand in Brooklyn, and he’d go there once a month to do the books. He came back with magazines—*Scientific American* for me; *Mad* magazine for my brother, who became a lawyer. I vividly recall reading those *Scientific Americans* in middle school and wanting to be a scientist.

Were you into sports as a kid?
At Scarsdale High I played soccer and lacrosse and wrestled during junior year. The wrestling team had no one in the 180-pound weight class that year, and forfeiting meant losing five points. I weighed only 170, but the coach knew I was a good athlete and asked me to try out. Even if I lost, we’d lose only three points provided I didn’t get pinned. So my goal that season was to not get pinned.

Did you pursue sports in college?
I went to Cornell and played lacrosse on the freshman team, and played on the varsity team my sophomore year, when I detached the collateral ligaments in my thumb during practice. That ended my college lacrosse career—and the team went on to win the NCAA championships the following two years. But the injury was also a blessing in disguise.

How so?
At the time my college grade point average was only 3.3, and MSTP programs don’t say, “Let’s admit this guy for our lacrosse team.” My grades improved greatly after I could no longer play lacrosse.

Do you have any hobbies?
My favorite thing to do is hike in the mountains—day hiking and backpacking. The Rockies are my favorite place. My wife and three children and I spend most of our summer vacations hiking and backpacking through Colorado, the Tetons and Mount Rainier, and up into Canada to the Banff and Jasper National Parks. We carry everything with us: three to five days’ worth of food, tents, sleeping bags, a stove, gas for cooking and bear spray to scare away grizzlies, which luckily we’ve never had to use. It’s a lot of fun to get out in the woods—no cell phone, no Internet, beautiful scenery.
Simulation training has long been used in the military and in the automotive and airline industries. Einstein is now making simulations an integral part of student education, particularly in obstetrics/gynecology.

Practice scenarios are supervised by faculty members and feature lifelike mannequins and computers to replicate doctor-patient encounters. Trainees can hone their communication and technical skills in a safe, supportive environment before setting foot in an actual examination or delivery room.

Most training takes place at the Montefiore Einstein Center for Innovation in Simulation (MECIS), housed in newly renovated quarters in Einstein’s Van Etten Building. The 2,460-square-foot center occupies a suite of spaces appointed to look like real clinical settings.

Dena Goffman, M.D. ’01, spearheads ob/gyn “simu” training at Einstein-Montefiore. An associate professor of clinical obstetrics & gynecology and women’s health (maternal and fetal medicine), she directs the Montefiore Quality, Patient Safety and Simulation Program (QPSSP).

Dr. Goffman launched Einstein-Montefiore’s first simulation training for ob/gyn team members in 2010. QPSSP has since expanded to include monthly team training for attendings, residents, nurses, midwives, physician assistants, fellows, anesthesiologists and neonatal unit staff, and a two-day summer “boot camp” for interns.

Using an anatomically correct model, Staci Pollack, M.D., M.S. (left), guides third-year students as they practice the proper way to insert a speculum and perform a Pap smear.
Preparing for New Challenges

Encouraged by the success of Dr. Goffman’s “simu” training, Staci Pollack, M.D., M.S., director of undergraduate ob/gyn medical education, created a training program to prepare third-year medical students for their ob/gyn rotation. The program was launched in 2015 with members of the Class of 2017 as its first users.

“Thanks to support from staff at the MECIS and clinical skills center, and the involvement of many ob/gyn faculty members, we were able to mobilize the resources to provide our students with a baseline of practical experience that allows them to approach their clinical learning on the wards with confidence,” says Dr. Pollack, who is an associate professor of clinical ob/gyn at Einstein and an attending physician in reproductive endocrinology at Montefiore.

Delivering Results

“The ob/gyn team must be ready to spring into action at the first sign of maternal or fetal distress,” notes Dr. Goffman.

She is assessing the simulation program’s impact. Her study of 71 obstetrical attendings and residents found that simulation training helped them better manage shoulder dystocia (when the baby’s shoulders get stuck behind the mother’s pubic bone).

In a randomized study of 30 third-years, those receiving simulation training took part in more deliveries during their clerkship rotations than members of a control group whose only pre-rotation training was a PowerPoint presentation.

“Our program prepares clinicians to manage medical emergencies with consummate skill and seamless collaboration,” she says.
In Memoriam

Oliver W. Sacks, M.D.

Dr. Oliver Sacks, the eminent neurologist and author, died of cancer on August 30, 2015. He was 82.

Perhaps you noticed the ladders leaning against the side of the Anne and Isidore Falk Recreation Center. Maybe you spotted hoses going up to the roof. What on earth is going on?

Earth actually has a lot to do with it. Einstein engineers have covered the flat roof with a membrane and a five-inch “nutrient layer” (dirt) and planted native wetland grasses and other plants. This “green roof” will absorb storm water and backwash pumped up from the Falk pool and Jacuzzi, says Salvatore P. Ciampo, senior director of facilities management at Einstein. “The goal is to minimize surge in the sewer system, which wasn’t built for the development that exists now,” he says. It’s a major reason that the New York City Department of Environmental Protection was eager to support the project as part of its Green Infrastructure Grant Program. The Falk roof is the only known green roof to be irrigated using water from a swimming pool. (What about the chlorine? “This water has less chlorine than the water on our coastline where these wetland plants usually grow,” says Mr. Ciampo.)

The green roof will also reduce the Falk’s energy bill in summer by blocking the sun and by cooling through water evaporation.

The innovative roof is expected to be sustainable, cost-effective and attractive to look down upon from the surrounding residence halls, labs and office buildings, says Mr. Ciampo.

Among Dr. Sacks’ other books are Migraine, Musicophilia, A Leg to Stand On, Seeing Voices and the best-selling The Man Who Mistook His Wife for a Hat. (See “A Look Back,” page 56.)

Dr. Sacks was diagnosed with a rare ocular melanoma in 2006. He was treated at Memorial Sloan Kettering Cancer Center by his former Einstein protégé David H. Abramson, M.D. ’69, to whom he dedicated his book The Mind’s Eye.

Realizing he wasn’t suited for basic research, Dr. Sacks focused on chronically ill patients at nearby Beth Abraham Hospital. As the Einstein neurology website notes, “His weekly case conferences became the highlight of the medical students’ neurology rotations.”

In 1967, he offered the drug L-DOPA to postencephalitic patients who had been languishing at Beth Abraham since the 1918 influenza pandemic. He described the drug’s startling if temporary benefits in his 1973 book Awakenings. Actor Robin Williams portrayed him in the Oscar-nominated film of the same name.
Milford Fulop, M.D.

Einstein distinguished university professor emeritus of medicine Dr. Milford Fulop passed away on November 26, 2015, at the age of 88.

Dr. Fulop completed an internal medicine residency at Columbia-Presbyterian Medical Center and in 1955 was recruited to the new Albert Einstein College of Medicine to develop the medicine residency program at Bronx Municipal Hospital Center (later renamed Jacobi Medical Center). He went on to become a professor and the Gertrude and David Feinson Chair in Medicine. He also served as vice chair and director of medicine at Jacobi.

He received numerous awards, including Einstein’s Lifetime Achievement Award for Excellence in Clinical Teaching and the Silver Anniversary Honorary Alumnus Award of Einstein’s first graduating class.

Dr. Fulop carried out animal studies of renal excretion of bilirubin and phosphate, and human studies of acid-base disturbances. He retired in 2010 after 55 years on the Einstein faculty.

John Arras, Ph.D.

Dr. John Arras, one of the original faculty members of the certificate program in bioethics, died on March 9, 2015, at the age of 69.

Dr. Arras’ research interests were physician-assisted suicide, rationing of medical care and social disparities in health conditions and care. In 1981, while on leave as chair of the philosophy department at the University of Redlands in California, he was appointed to the clinical staff of Montefiore as a philosopher. He went on to serve as an associate professor of bioethics at Einstein from 1981 to 1995.

Professor Arras later taught biomedical ethics, philosophy and public health sciences at the University of Virginia, served on the Presidential Commission for the Study of Bioethical Issues and was a founding member of the ethics advisory board of the Centers for Disease Control and Prevention.

Yasuhiro Taketomo, M.D.

Dr. Yasuhiro Taketomo, a clinical professor emeritus of psychiatry and department member for more than 45 years, died on October 14, 2015, at the age of 94.

A graduate of Osaka University in Japan, Dr. Taketomo came to Einstein early in his career (1970) and never left. He became an attending physician at Montefiore and the Jack D. Weiler Hospital in 1976, and head of the transcultural psychiatry component of the Research Fellowship Progressive in Einstein’s department of psychiatry in 1988. In addition to writing articles for professional journals, he was a contributing author of two books, The World Biennial of Psychiatry and Psychotherapy and Psychoanalysis and the Nuclear Threat: Clinical and Theoretical Studies. With a colleague, he edited another book, The Japanese and Life-Threatening Illness, Loss and Grief. Upon retiring, he became a private-practice psychiatrist who helped patients with many conditions, including attention deficit disorder, bipolar disorder, depression, insomnia and schizophrenia.

Laurence Finberg, M.D.

Dr. Laurence Finberg, a pediatrician and scientist known for contributing to the management of salt/water balance in children, died on January 22, 2016, at the age of 92.

Dr. Finberg began his career in academic pediatrics at Johns Hopkins Medical School. In 1963 he became chair of pediatrics at Montefiore Hospital and professor of pediatrics at Einstein, where he remained for nearly two decades. He later served as chair of pediatrics and dean of the School of Medicine at SUNY Downstate in Brooklyn. After he retired from SUNY, he taught pediatrics at the Stanford and University of California–San Francisco medical schools.

Dr. Finberg wrote many original papers and two books on fluid and electrolyte abnormalities in children, and became an international authority on dehydration and rehydration in infants. He was also an expert in diagnosing and treating lead poisoning in children and promoted the idea of testing the environment rather than waiting to find high lead levels in children. He served as president of the American Board of Pediatrics and chair of the American Academy of Pediatrics’ committees on nutrition and environmental hazards.
**Skipping Chemotherapy**

A clinical trial involving more than 10,000 early-stage breast cancer patients found that women scoring low on a gene test for cancer recurrence can limit their post-surgery/radiation treatment to hormonal therapy without the need for chemotherapy. Five years after beginning treatment, these patients had less than a 1 percent risk of their cancer recurring at a distant site. The leader of the study was Joseph A. Sparano, M.D., a professor of medicine and of obstetrics & gynecology and women’s health at Einstein, and the results were published in September in the *New England Journal of Medicine* (NEJM).

The study illustrates how genetic information is transforming cancer care and could change the way breast cancer is currently treated: Guidelines now recommend erring on the side of caution and treating most early-stage breast cancer patients aggressively, using both hormonal therapy and chemotherapy together with surgery.

“The current treatment approach ensures that most women with high-risk cancers get treated, but it also means that most women with low-risk disease are overtreated and unnecessarily exposed to potentially toxic therapies,” says Dr. Sparano, also vice chair of medical oncology at the Montefiore Einstein Center for Cancer Care and associate director of clinical research at the Albert Einstein Cancer Center. “The compelling results of this study show that women with a low likelihood of cancer recurrence based on this test can effectively be treated without chemotherapy.”

The trial recruited the 10,253 eligible early-stage breast cancer patients at 900 sites worldwide. The women were representative of more than 100,000 of the 231,000 women diagnosed with breast cancer each year in the United States. They had invasive breast cancer, meaning cancer cells from inside milk ducts had penetrated nearby tissue but were still contained within the breast.

At the start of the trial, tumor tissue from each participant was tested using the Onco*type* DX assay. This test analyzes the expression levels of 21 breast tumor genes and comes up with a “recurrence score” ranging from 1 to 100, with a low score associated with a low risk for recurrent cancer.

The findings published in the *NEJM* article involved a subset of 1,626 patients whose recurrence scores were between 0 and 10. They all were treated with hormonal therapy alone without chemotherapy.

After five years of treatment with just hormonal therapy (i.e., no chemotherapy following initial surgery/radiation), fewer than 1 percent of the women had experienced a recurrence of cancer beyond the breast, and only 1.3 percent had a recurrence of the cancer anywhere.

Future findings from the ongoing TAILORx trial will pertain to the larger group of participants with mid-range cancer recurrence scores (from 11 to 25) on the Onco*type* DX test.
Einstein and Montefiore scientists found that feeling stressed increases the likelihood that elderly people will develop mild cognitive impairment—often a prelude to full-blown Alzheimer’s disease. Highly stressed participants were more than twice as likely to become impaired as those who were not. Stress is treatable, so the results suggest that detecting and treating stress in older people might help delay or even prevent the onset of Alzheimer’s. The findings were published online last December in *Alzheimer Disease & Associated Disorders*.

Each year 470,000 Americans are diagnosed with Alzheimer’s dementia. Many of them first experience mild cognitive impairment. This study looked at the connection between chronic stress and “amnestic mild cognitive impairment” (aMCI), the most common type of MCI, which is characterized primarily by memory loss.

“Our study provides strong evidence that perceived stress increases the likelihood that an older person will develop aMCI,” says Richard B. Lipton, M.D., senior author of the study, vice chair of neurology at Einstein and Montefiore; professor of neurology, of psychiatry and behavioral sciences, and of epidemiology & population health, and the Edwin S. Lowe Chair in Neurology at Einstein; an attending physician in neurology at Montefiore; and director of the Montefiore Headache Center.

The researchers studied data collected from 507 people enrolled in the Einstein Aging Study (EAS), a community-based cohort of older adults. Since 1993, the EAS has systematically recruited adults ages 70 and over who live in Bronx County, NY. Participants undergo annual assessments that include clinical evaluations, a neuropsychological battery of tests, psychosocial measures, a medical history, assessments of daily-living activities and reports of memory and other cognitive complaints.

Starting in 2005, the EAS began assessing stress using the Perceived Stress Scale (PSS). This widely used 14-item measure of psychological stress was designed to be sensitive to chronic stress perceived over the previous month. PSS scores range from 0 to 56, with higher scores indicating greater perceived stress.

All 507 enrollees were free of aMCI or dementia at their initial PSS assessments and later underwent at least one annual follow-up evaluation. They were followed for an average of 3.6 years.

Seventy-one of the 507 participants were diagnosed with aMCI during the study. The greater the participants’ stress level, the greater their risk for developing aMCI. Participants in the highest-stress quintile were nearly 2.5 times more likely to develop aMCI than were people in the remaining four quintiles combined.
Microbiome Implicated in Sickle Cell Disease

Using antibiotics to deplete the body’s microbiome may prevent acute sickle cell crisis and could offer the first effective strategy for warding off the long-term complications of sickle cell disease (SCD), such as organ failure, according to a study by scientists at Einstein and Montefiore. The findings were published last September in Nature.

People with sickle cell disease have an inherited gene mutation that leads to abnormal hemoglobin, causing red cells to take on a sickle shape and become less flexible. The sickled red cells tend to clog small vessels—impeding blood flow and preventing oxygen from reaching tissues. The Einstein study was led by Paul S. Frenette, M.D., a professor of medicine and of cell biology and chair and director of Einstein’s Ruth L. and David S. Gottesman Institute for Stem Cell and Regenerative Medicine Research. Dr. Frenette reported in 2002 that SCD vessel blockages occur when sickled red cells bind to white cells called neutrophils that have adhered to the vessel walls.

“This earlier work indicated that some neutrophils appear to be inert while others appear overly active in promoting inflammation—which is useful for attacking microbes but causes neutrophils to capture sickled red cells inside vessels,” Dr. Frenette says.

In this study, Dr. Frenette’s lab found that neutrophils became more active as they aged in the circulation. The researchers traced these “aging” signals to chemicals produced by the body’s microbiome, which cross the intestinal barrier and enter the bloodstream, generating the aged neutrophils that contribute to SCD. “Since the body’s microbiota seem to ‘educate’ neutrophils to age,” says Dr. Frenette, “we realized that purging those microbes through use of antibiotics might help against SCD.”

Dr. Frenette’s team found that SCD mice possessed five times as many aged neutrophils as healthy control mice. When the researchers depleted the microbiota of SCD mice using antibiotics, they observed a striking reduction in neutrophils. Moreover, the antibiotics appeared to prevent sickle cell crisis: interactions between neutrophils and red cells were markedly reduced, resulting in improved local blood flow and greatly improved survival of these mice.

In addition, “The spleen enlargement and liver damage were significantly reduced in the microbiota-depleted animals,” Dr. Frenette notes.
Immunotherapy Zaps Lethal Ebola Strains

Researchers at Einstein and the U.S. Army Medical Research Institute of Infectious Disease (USAMRIID) have engineered the first antibodies that can potently neutralize the two deadliest strains of the virus that causes Ebola hemorrhagic fever. The findings, made in mice, are a significant step toward immunotherapies that are effective against all strains of Ebola virus that cause human disease. The study was published in January in *Scientific Reports*.

“A broadly effective immunotherapy for Ebola virus would be a tremendous advance, since it’s impossible to predict which strain of the virus will cause the next outbreak,” says study co-leader Jonathan R. Lai, Ph.D., an associate professor of biochemistry at Einstein. The other study co-leader is John M. Dye, Ph.D., branch chief of viral immunology at USAMRIID.

Zaire Ebola virus (EBOV) was responsible for the 2014 Ebola outbreak in West Africa, the largest in history. The second-most pathogenic strain of Ebola virus is Sudan Ebola virus (SUDV), which has been responsible for large outbreaks in the past.

Although a Zaire-specific vaccine is in clinical trials, no vaccine has yet been approved for preventing infection from any strain of Ebola virus.

In previous work, Dr. Lai and his colleagues used a technique called synthetic antibody engineering to create the first antibodies against SUDV. Those antibodies were designed to bind to SUDV’s surface glycoprotein, which the virus uses to gain entry into host cells. Since SUDV’s glycoprotein shares just 55 percent of the amino acid sequences found in EBOV’s glycoprotein, antibodies against SUDV do not neutralize EBOV.

In the current study, Dr. Lai’s team engineered “bispecific” antibodies that contain key glycoprotein-binding sequences from both the EBOV and SUDV antibodies. The bispecific antibodies effectively neutralized both EBOV and SUDV in tissue-culture studies. In addition, the antibodies provided high levels of protection for mice that had been exposed to lethal doses of either of the viruses.

If the new immunotherapy proves safe and effective for people, it might best be suited for preventing local outbreaks from getting out of hand.

The bispecific antibodies must still be tested in larger animals and in humans to show that they’re effective. If the new immunotherapy proves safe and effective for people, says Dr. Lai, it might best be suited for preventing local outbreaks from getting out of hand, as happened in the recent West African Ebola virus epidemic. “It’s also possible,” he notes, “that a therapy like this could be used prophylactically, to protect health workers or family members who come into contact with Ebola virus patients.”

Dr. Lai has now broadened his approach to Ebola virus therapy. He is developing antibodies and antibody cocktails aimed at neutralizing the three most dangerous Ebola virus species (Zaire, Sudan and Bundibugyo), as well as Marburg virus, a deadly pathogen closely related to Ebola virus.
Monitoring the Placenta

The placenta's health is crucial to the health of both fetus and mother. Abnormalities in placental structure or function cause pregnancy complications, including preterm birth, miscarriage, stillbirth and preeclampsia. S. Zev Williams, M.D., Ph.D., has received a five-year, $3.8 million grant to develop methods for noninvasively monitoring placental function so that problems can be detected early and treated.

The research is premised on the fact that changes in the expression of coding and noncoding genes reflect the functional state of an organ, and those changes in gene expression can be detected by assessing that organ’s transcriptome (the identity and concentration of all its RNA molecules—mRNA as well as noncoding types, including tRNA, rRNA and microRNA).

Dr. Williams’ laboratory, in collaboration with Thomas Tuschl, Ph.D., at Rockefeller University and the Howard Hughes Medical Institute, has developed an RNA sequencing method for profiling placental microRNAs found in the mother’s blood. His project will advance this technology to permit noninvasive monitoring of the placental transcriptome using both maternal blood and urine. Ideally, this work will result in a noninvasive tool for gaining insights into the processes underlying pregnancy-related diseases and indicate when therapeutic interventions are needed. Dr. Williams is an assistant professor of obstetrics & gynecology and women’s health and of genetics and director of the Program for Early and Recurrent Pregnancy Loss at Einstein and Montefiore.

Testing a New Autism Therapy

Up to 90 percent of children with autism spectrum disorders (ASD) have “sensitivity issues”—they’re too sensitive or not sensitive enough to their environment, or are not able to integrate sensory information in an orderly way. Such problems impair ASD children’s school performance and social opportunities as well as their long-term outcomes. Sophie Molholm, Ph.D., and her research partners have been awarded a five-year, $3.18 million NIH grant to better understand the brain processes responsible for these sensitivity issues and to test the effectiveness of Sensory Integration Treatment (SIT), a noninvasive intervention for treating sensory symptoms in ASD. The testing will involve 180 children ages 6 to 8-1/2 who have ASD and sensory issues. They will be randomized to receive either 10 weeks of SIT, 10 weeks of a commonly used behavioral intervention (Discrete Trial Training) or no treatment. Outcome assessment will involve behavioral and electrophysiological measures taken at baseline, immediately after treatment and at 12 weeks following treatment. The team will evaluate SIT’s impact on functional skills and autism severity and look for possible neurological mechanisms through which this intervention may work. Dr. Molholm is an associate professor in the department of pediatrics and in the Dominick P. Purpura Department of Neuroscience, the Muriel and Harold Block Faculty Scholar in Mental Illness, director of the Sheryl and Daniel R. Tishman Cognitive Neurophysiology Laboratory and associate director of the Rose F. Kennedy Intellectual and Developmental Disabilities Research Center.

Opioid Use and HIV

The dramatic increase in misuse, addiction and overdose of prescription opioid (PO) analgesics stems largely from providers prescribing POs for chronic pain. That puts people living with HIV at particular risk for PO misuse, since they suffer disproportionately from chronic pain and from substance use and mental health disorders. Joanna L. Starrels, M.D., M.S., has been awarded a four-year, $2.3 million grant to study how PO use influences the health outcomes of people living with HIV and chronic pain, 250 of whom will be followed over a 12-month...
period. The main goals of her research are to gather evidence that can help guide the clinical management of patients living with HIV and chronic pain and to improve the health of these patients. Dr. Starrels is an associate professor of medicine at Einstein and an attending physician in internal medicine at Montefiore.

Longer-Lasting Transplants
Over the past several decades, patients suffering from end-stage organ failure have greatly benefited from donated kidneys, hearts and other organs. Unfortunately, graft vascular disease (GVD) limits the long-term effectiveness of almost all donated organs—even when immunosuppressant drugs are used. In GVD, lesions consisting of smooth muscle cells and extracellular matrix develop within the intima (innermost layer) of vessels of the donated organ. No therapies have yet proven effective in preventing or reversing GVD. As they accumulate, GVD lesions restrict blood flow and lead to organ failure. Nicholas E. S. Sibinga, M.D., has been awarded a four-year, $2.1 million grant to study the role that a cellular growth factor called colony stimulating factor-1 (CSF-1) plays in GVD. In previous studies involving mice, Dr. Sibinga, in collaboration with E. Richard Stanley, Ph.D., a professor of developmental and molecular biology at Einstein, has shown that the absence of CSF-1 either in tissue recipients or in donor tissue significantly limits the size of GVD lesions. Now he will investigate whether inhibiting CSF-1 could be a treatment strategy for minimizing GVD and prolonging the function of transplanted organs. Dr. Sibinga is an associate professor of medicine and of developmental and molecular biology and an attending physician at the Montefiore Einstein Center for Heart and Vascular Care.

Lab-Made Donor Blood
People with sickle cell disease and other chronic anemia conditions typically receive transfusion therapy over many years. But for patients of Asian and African backgrounds, finding compatible donors can be difficult: The high degree of genetic diversity in their blood-group antigens means they tend to have rare blood groups, yet most blood donors are whites and of European ancestry whose blood-group antigens are much less diverse. Over time, the difficulty of finding well-matched donors for these patients causes a high incidence of alloimmunization (unwanted immune response following transfusion of genetically different blood cells). Eric E. Bouhassira, Ph.D., has received a four-year, $2 million grant to develop methods for the laboratory production of red blood cells that people with rare blood groups can use safely. One part of the project involves a panel of six donors with rare blood types. From skin cells of these individuals, Dr. Bouhassira and his colleagues at the New York Blood Center will generate induced pluripotent stem cells that will be made to differentiate into hematopoietic stem cells and then into red cells that lack the antigens responsible for causing immune reactions. The goal is to produce “universally safe” red cells in sufficient quantity for use in the production of reagent red blood cells and eventually for lifesaving transfusion therapy. The first people to receive such cells would be patients with sickle cell disease who have no other treatment options. Dr. Bouhassira is a professor of cell biology and of medicine and the Ingeborg and Ira Leon Rennert Professor of Stem Cell Biology and Regenerative Medicine.

Exploring the Interactome
For any organism, the network of molecular interactions that occur intra-cellularly, intercellularly and between its cells and their external environment is known as its interactome. Little is known about interactions involving the one-third of proteins that human cells secrete or that are present on their surfaces (e.g., cell-surface receptors). These proteins detect environmental and other cues critical to both normal physiology and disease, including autoimmune disease, infectious diseases and cancer. Steven C. Almo, Ph.D., has been awarded a three-year, $1.9 million grant to map the “ecto-interactome”—the entire set of interactions involving secreted and cell-surface proteins—using two high-throughput platforms now being optimized. This
mapping effort could both increase our understanding of basic biology and lead to novel strategies for treating a wide range of human diseases. Dr. Almo is a professor and chair of biochemistry, a professor of physiology & biophysics, the Wollowick Family Foundation Chair and director of the Einstein Macromolecular Therapeutics Development Facility.

The Doors of Visual Perception
Elyse S. Sussman, Ph.D., and Adam Kohn, Ph.D., have been awarded a three-year, $1.7 million grant to study how visual adaptation contributes to visual perception. Visual adaptation is a widespread process in which recent visual inputs dramatically influence brain activity and perception. However, adaptation's function in vision is poorly understood. Based on preliminary data, the researchers hypothesize that adaptation may be a form of predictive coding that “educates” perception by taking special notice of new or unexpected events while discounting expected ones. They will test this hypothesis by conducting research involving human electroencephalography (monitoring and recording electrical activity in the brain), monkey neurophysiology and computer modeling. These studies may reveal how the visual circuits of the brain influence perception—knowledge needed for treating people with visual-processing deficits and for developing prosthetic devices for aiding vision. Dr. Sussman is a professor of neuroscience and of otorhinolaryngology–head & neck surgery. Dr. Kohn is an associate professor of neuroscience and of ophthalmology and visual sciences.

Treating Infections in Children
The U.S. Department of Health and Human Services’ Agency for Healthcare Research and Quality recently awarded Michael L. Rinke, M.D., Ph.D., a three-year, $1.3 million grant to study healthcare-associated infections (HAIs) in children receiving ambulatory care. Information on HAIs among children in ambulatory settings is scarcer than similar information for children treated in hospitals. Dr. Rinke will use the New York City Clinical Data Research Network—a comprehensive repository of healthcare data from five pediatric healthcare systems—to identify incidence rates, risk factors, patient outcomes and costs for three pediatric ambulatory HAIs, along with ways to track them using computerized data. The three HAIs he will track are central-line–associated bloodstream infections, catheter-associated urinary tract infections and surgical site infections in ambulatory pediatric patients. The project’s goals are to focus attention on the safety of pediatric ambulatory patients and reduce HAIs among young patients. Dr. Rinke is an assistant professor of pediatrics at Einstein, and the medical director of pediatric quality and a hospitalist at the Children’s Hospital at Montefiore.

Halting HIV Assembly
More than 35 million individuals worldwide are living with HIV, and drug resistance to various available treatments is prevalent because of the virus’ extremely high mutation rate. The National Institute of General Medical Sciences has awarded Ganjam V. Kalpana, Ph.D., nearly $1.3 million over four years to study potential drug targets for HIV and develop inhibitors for these targets. More specifically, she and her laboratory team are focused on inhibiting the early stages of HIV virus assembly, which is the process by which the viral components are assembled together inside the cell to form infectious virus particles. The researchers have found that disrupting the interaction between the HIV protein integrase and the host protein integrase interactor 1 (INI1) can vastly reduce the ability of HIV to assemble its viral machinery, thereby preventing HIV replication inside human cells. Dr. Kalpana and her team plan to build on these findings to shed new light on the mechanisms involved in early virus particle formation. Dr. Kalpana is a professor of genetics and of microbiology & immunology and the Mark Trauner Faculty Scholar in Neuro-oncology.
New Chairs

Biochemistry

Steven C. Almo, Ph.D., an internationally recognized leader in the field of structural biology, has been named chair of the department of biochemistry at Einstein. Dr. Almo is a professor of biochemistry and of physiology & biophysics and holds the Wollowick Family Foundation Chair. Dr. Almo will assume the chair left vacant by Vern Schramm, Ph.D., who led the biochemistry department for 28 years. Dr. Schramm will return to his lab full time.

Dr. Almo joined Einstein in 1992 and has been an active member of the Albert Einstein Cancer Center since 1996. In 2007, he became the director of Einstein’s Macromolecular Therapeutics Development Facility, a shared facility that provides expertise for developing and optimizing protein-based therapeutics and supports high-throughput automated development, analysis and production of proteins.

His laboratory determines the shapes and structures of proteins to better understand their function and advance the development of therapeutics. His work on enzyme function is offering insights into the gut microbiome’s contributions to human health, providing new chemical processes for industry and expanding understanding of critical environmental issues such as global nutrient cycles and how complex microbial communities evolve. His research on molecular mechanisms involved in immunity are leading to novel immunotherapy strategies and compounds for treating infectious diseases, autoimmune diseases and cancers.

Dr. Almo received his first major independent research grant in 1993 and since then has been continuously funded as a principal investigator by the NIH. His research is currently supported by two major NIH grants with annual funding totaling approximately $6.8 million.

To learn about Dr. Almo’s most recent grant, which will support his work in mapping the “ectointeractome” (the entire set of interactions involving secreted and cell-surface proteins), see page 19.

Molecular Pharmacology

Jonathan M. Backer, M.D., an internationally acclaimed molecular pharmacologist and sought-after mentor to promising young scientists, will chair the department of molecular pharmacology at Einstein. Dr. Backer is a professor of molecular pharmacology and of biochemistry and the William S. Lasdon Chair in Pharmacology. The department’s prior co-chairs were Susan B. Horwitz, Ph.D., and Charles S. Rubin, Ph.D.

Dr. Backer will step down from his position as director of the Belfer Institute for Advanced Biomedical Studies, which integrates all postdoctoral training programs at Einstein. Anne R. Bresnick, Ph.D., will succeed him.

Dr. Backer joined the Einstein faculty in 1993 as an assistant professor of molecular pharmacology, was promoted to professor in 2002 and was named director of the Belfer Institute in 2008.

His research focuses on a group of enzymes called phosphoinositide (PI) 3-kinases. These enzymes sense when certain cell-surface receptors receive signals and then relay those signals into the cell. This makes the PI 3-kinases important regulators of key cellular processes such as proliferation, motility, apoptosis, vesicular trafficking and insulin signaling. Mutations that activate PI 3-kinases are linked to the genesis and spread of several types of human cancers. Dr. Backer studies the molecular mechanisms that regulate PI 3-kinase activity and the role of PI 3-kinases in the aberrant intracellular signaling involved in diabetes, cancer and aging. His work is supported by an NIH program project grant, two NIH R01 grants, an Innovation Award from the American Diabetes Association and the Department of Defense’s Prostate Cancer Research Program.

Drs. Horwitz and Rubin will return to their research full-time.
Depression in late life has long been a neglected area of mental health. Most older adults aren’t depressed. But those who are depressed often don’t receive adequate treatment—due in part to the varied and sometimes overlapping causes of late-life depression such as social stress, physical illness and disability. And depression in old age can be hard to treat even when it is properly diagnosed.

Dr. Kennedy shines a light on the growing problem in this practical guide for physicians, psychologists, social workers and other caregivers. The author, who directs the fellowship training program in geriatric psychiatry at Montefiore, backs up his clinical recommendations with current research.

As the baby boomer generation ages, depression among adults ages 60 and over will become more prevalent. Disturbingly, this trend is occurring as fewer practitioners are choosing to specialize in geriatrics. On the upside, Dr. Kennedy posits that the complex nature of depression in the elderly offers multiple avenues for creative therapeutic approaches supported by scientific evidence. One example is collaborative care involving a team of practitioners in which a depression-care manager coordinates interventions to combat depression. The growing problem of depression in older adults can also serve, he says, as a catalyst for much-needed changes in public health policy.

The book ends with Dr. Kennedy challenging health professionals to take the lead in advocating for better mental health care for our aging population.


Excerpt from Chapter 1:
The Problem of Depression in Late Life

Depressive disorders are emerging as a leading cause of disability for older adults, soon to be second only to heart disease. By 2030, major depressive disorder is expected to be the second leading cause of disability worldwide after HIV and AIDS and the number one cause of disability in the developed nations. As a result, the public health imperative to reduce late-life disability and to compress morbidity into the very end of the lifespan is immense.
Riddles in Accountable Healthcare

Eran Y. Bellin, M.D.
Professor of Clinical Epidemiology & Population Health
Albert Einstein College of Medicine
Vice President, Clinical Information Technology Research and Development
Emerging Health Information Technology Group
Montefiore

What makes a hospital excellent—a low mortality rate, convenient parking, great food, a stellar reputation? Is there a right size for a healthcare system? Does visiting your doctor after hospital discharge prevent readmission—or cause it?

Why is my hospital doing better than yours in all of the measured categories, but overall yours looks better?

Questions form the framework for Dr. Bellin's inquiry into how we assess healthcare: by gathering statistics, measuring illness, defining health and healing, describing patients and much more. Such parameters are critical in tracking outcomes and delivering the best future care.

Dr. Bellin is an experienced clinician well qualified to tackle the issues raised by “accountable healthcare”: Montefiore’s Emerging Health Information Technology Group guards nearly two decades’ worth of the health system’s electronic medical records from 2.4 million patients. Internal medicine residents at Montefiore and members of Einstein’s Clinical Research Training Program learn how to use the data to improve healthcare and patient outcomes.

Though nearly a decade old, the concept of accountable healthcare still raises thorny questions—and more than half of Dr. Bellin’s chapter titles are questions, which he answers with statistics, technology, common sense and examples.

The book is clearly written and should be readily understood by students, professionals and general readers alike. One exception: the section for data geeks and statisticians labeled “For those mathematically and R-programming inclined.”


Excerpt from Chapter 28:
How Can [Children] Be Getting Fatter When a Higher Percentage Is Losing Weight?

When studying a school health population of children younger than age 14, Montefiore came across an interesting paradox. Between school years 2012 and 2013, we noted that a higher percentage of overweight children reduced their weight to normal than the percentage of normal-weight children who became overweight. Yet, overall the overweight percentage of the population increased. Question: How could both be true? [Answer: There were three times as many normal-weight children as overweight children at the start of the study. So the sheer number of normal-weight children who became overweight exceeded the number of overweight kids who reduced their weight to normal, resulting in a net gain of overweight kids.]
ZEBRAPFISH
A SMALL FISH WITH A WHALE OF AN IMPACT
BY CASSANDRA WILLYARD
On a lab bench in an Einstein laboratory, the tiny one-day-old fish embryo, barely visible to the naked eye, basks and occasionally twitches in the warm water of a petri dish. Move over fruit flies, roundworms, rats and mice: There’s a new animal model in town, and it’s making a big splash at Einstein and in laboratories around the world. It hails from the Ganges River and its name is *Danio rerio*—more commonly known as the zebrafish.

George Streisinger, a molecular biologist at the University of Oregon as well as a fish hobbyist, began developing the zebrafish as an animal model in the 1970s. Today, thousands of researchers worldwide rely on these tiny swimmers for help in better understanding vertebrate development and human disease.

Zebrafish offer key advantages over other model organisms. They’re vertebrates, so they resemble us more closely than do fruit flies or roundworms. They are easily maintained and are prolific breeders, with each female laying 200 to 300 eggs daily. Embryos hatch just three days after fertilization. (Mice, by contrast, have a three-week gestation period and cost much more than zebrafish to feed and house.)

Zebrafish eggs are fertilized outside the mother, making the embryos easily accessible for study. But the real beauty of zebrafish is that their eggs and embryos are transparent, so researchers can watch organs develop in real time. Their embryonic development is remarkably similar to ours, with one big exception: Zebrafish develop much faster.

“In just 24 hours, zebrafish embryos have developed all their organs, including a brain and a heart—equivalent to the first month of human embryonic development,” says zebrafish researcher Florence L. Marlow, Ph.D., an associate professor in the department of developmental and molecular biology and in the Dominick P. Purpura Department of Neuroscience.

About 70 percent of human genes have zebrafish counterparts, and mutation studies involving zebrafish have yielded crucial genetic information. Zebrafish mutations can readily be induced by adding mutagens to aquarium water (traditionally directed at the germ cells of adults) or by using CRISPR/Cas9 (the recently developed gene-editing technique) to cause targeted mutations in embryos.

After mutations are induced in the germline (eggs and sperm), the effects can be evaluated by crossing males and females carrying the same mutation and examining their progeny for changes in appearance, behavior or physiology. Sequencing the genomes of fish exhibiting such phenotypic differences reveals the affected gene. And by knowing the
phenotype and that gene’s human counterpart, researchers can find the human gene’s normal function.

Zebrafish mutants exhibiting phenotypes that mimic human diseases have allowed researchers to pinpoint the genetic and cellular defects responsible for a number of diseases, including Duchenne muscular dystrophy and hereditary spastic paraplegia. And as a bonus, testing different drugs on zebrafish disease models can yield treatments for their human counterparts.

Dr. Marlow and two Einstein colleagues (see following pages) use zebrafish to study vertebrate development. They primarily study zebrafish larvae, the free-swimming and most advanced embryo stage. Their research may reveal strategies for combating human health problems such as infertility, cancer and congenital spinal disorders.

FLORENCE L. MARLOW, Ph.D.: CELL POLARITY
The cells that give rise to zebrafish eggs might look perfectly symmetrical. But closer scrutiny with a microscope shows that these cells, known as oocytes, are asymmetric on the inside. Scientists first noticed oocyte polarity more than a century ago when they spotted a clump of organelles and proteins on one side of the cell. This structure is the Balbiani body—an aggregate of organelles including endoplasmic reticulum, golgi and mitochondria. It is found in the oocytes of all animals, from fruit flies to fish to humans.

Dr. Marlow has long been fascinated by oogenesis, the process by which an oocyte becomes a fully functional egg and, eventually, an embryo. The oocyte’s polarity seems to play a crucial role in transforming oocytes into eggs and then into embryos with the proper developmental blueprint.

In earlier research, she discovered that a gene called bucky ball assembles the Balbiani body, which is essential for generating polarity in vertebrate oocytes. She observed that zebrafish carrying bucky ball mutations produced oocytes with no polarity and no Balbiani bodies—which proved disastrous. “The mutant mothers produce eggs,” she says, “but those eggs can’t develop into embryos.”
Before their own genomes kick in, the embryos of zebrafish and other vertebrates rely exclusively on maternal gene products (RNAs and proteins) for their early development. These gene products are either made by the developing oocyte or imported into the oocyte (typically via the maternal bloodstream or from nearby follicle somatic cells). Genes that provide essential maternal functions during oogenesis and embryonic development are “maternal-effects genes.” Dr. Marlow had shown that bucky ball is a maternal-effect gene, vital for assembling the Balbiani body and creating oocyte polarity. Did its influence on cell polarity extend to the early zebrafish embryo as well?

To find out, Dr. Marlow identified other proteins that bind to Bucky ball protein. She then looked at where in zebrafish embryos those proteins were produced, and induced gene mutations to assess the functions of these proteins. The Bucky ball–binding proteins turned up in neurons and in cartilage-forming cells in the jaw, where they were found to play important roles. Both cell types share a key trait with oocytes: polarity. Neurons, for example, are visibly asymmetrical, with thick cell bodies and long, skinny protrusions that send and receive information. “They have to be polarized so that they can function,” Dr. Marlow says.

While polarity depends on bucky ball, it also requires trafficking—the process that enables molecules to travel inside a cell. All cells have cellular transport systems, but polarized cells depend especially on trafficking to ensure that proteins, RNA and other cargo arrive and are produced in the right place at the right time.

“When an egg cell can’t traffic goods, you get abnormal embryos,” Dr. Marlow says. In neurons, “you get neurodegenerative diseases. And aberrant trafficking in cartilage-forming jaw cells causes abnormal growth and malformation of the head and facial bones.”

Dr. Marlow has collaborated with Einstein’s Robert H. Singer, Ph.D., to develop a technique to observe trafficking in a zebrafish embryo. (Dr. Singer is professor, co-chair and the Harold and Muriel Block Chair of anatomy and structural biology, a professor of cell biology and of neuroscience, and co-director of Einstein’s Gruss Lipper Biophotonics Center and of its EGL Charitable Foundation Integrated Imaging Program.)

She brings up a movie of a zebrafish neuron on her computer. A bright green dot travels from the right side of the screen to the left. That dot is messenger RNA tagged with a fluorescent protein, and it’s traveling from the neuron nucleus through the cytoplasm en route to a nearby synapse. “Nobody has seen this in a live vertebrate animal before,” she notes.

Using this imaging technique, Dr. Marlow hopes to better understand the factors that regulate trafficking. Improved understanding of how this process works in fish—and what happens when it doesn’t—may provide insights into infertility as well as neurodegenerative diseases such as Alzheimer’s, Parkinson’s and Huntington’s diseases and hereditary spastic paraplegia.

**TERESA BOWMAN, Ph.D.: EXPLORING THE SPLICEOSOME**

After they’re transcribed from genes but before being translated into proteins, many vertebrate messenger RNA molecules (mRNAs) undergo splicing: noncoding mRNA regions (introns) are removed, and the flanking coding regions (exons) are bound together. This mRNA splicing and binding is carried out by spliceosomes—giant, complex molecular machines found in the nucleus and composed of small nuclear RNAs and protein complexes. Spliceosomes help regulate gene

An image from Dr. Bowman’s lab of an early zebrafish embryo (36 hours postfertilization). Blood vessels are stained red and blood cells are stained green.
expression and increase mRNA diversity. And for unknown reasons, they can cause cancer when defective. Zebrafish may reveal why.

About four years ago, researchers studying patients with myelodysplastic syndrome (MDS)—often a precursor to acute myeloid leukemia (AML)—noticed that MDS patients often had mutations affecting their spliceosome components. “This was quite unexpected—no one had thought that spliceosome mutations could potentially lead to cancer,” says Teresa V. Bowman, Ph.D., an assistant professor of developmental and molecular biology and of medicine (oncology) and a member of the Ruth L. and David S. Gottesman Institute for Stem Cell and Regenerative Medicine Research at Einstein. “Many labs are now trying to figure out why—and ours is too, using zebrafish as our in vivo model system.”

Spliceosomes contain many proteins encoded by different genes. Dr. Bowman and her team have focused on one spliceosome gene in particular, called SF3B1. It is the most frequently mutated gene in MDS, affecting as many as 60 percent of MDS patients. Single-point mutations in an SF3B1 allele somehow lead to defective hematopoietic (blood-forming) stem cells, which in turn results in anemia, neutropenia and the other blood abnormalities that characterize MDS.

“Because of where they’re located in the gene and its corresponding protein, it’s unclear how the mutations are changing the protein’s function,” says Dr. Bowman. “Zebrafish have that same gene, and we’re studying how a somewhat different sf3b1 mutation—a loss-of-function mutation—affects the blood system in zebrafish embryos, whose blood systems fully develop in just 24 hours. What we find may lead to strategies for correcting the hematopoietic problems that afflict MDS patients.”

While the mutant zebrafish embryos and MDS patients don’t have precisely the same mutations in that gene, they do exhibit some of the same blood abnormalities, including anemia and neutropenia (an abnormally low number of neutrophils). “We’ve observed striking similarities in the blood-cell defects and gene-expression changes that occur...”
thereby reversing anemia. Her lab has already found that the anti-inflammatory steroid dexamethasone partially rescues hematopoietic stem-cell function in mutant zebrafish. And since MDS is often a precursor to AML, “improving the function of MDS patients’ hematopoietic stem cells could lead to greater numbers of healthy white and red blood cells and potentially prevent patients with MDS from developing AML,” Dr. Bowman notes.

ERTUĞRUL OZBUDAK, Ph.D.:
SEGMENTATION CLOCKS
Ertugrul M. Ozbudak, Ph.D., an associate professor in the department of genetics, studies how backbones develop—the process known as vertebral segmentation. His group and other researchers have identified several genes that play important roles in that process. But some key ones remain to be found.

In all vertebrates, whether zebrafish or zebras, the backbone begins as a clump of cells. This clump must be segmented so that individual vertebrae can form. The segmentation of these cells into vertebral precursors called somites happens at a precise tempo. “As the embryo elongates, try to visualize a pendulum swinging back and forth and slicing the clump of cells into the individual somite segments,” Dr. Ozbudak says.

The timing must be exact. In human embryos, one segment forms every five hours. In zebrafish embryos, the clock ticks faster: a somite forms every half hour. The process relies on oscillating genes—with each swing of the pendulum, expression of some genes rises and for others it falls. Dr. Ozbudak and colleagues have found evidence that zebrafish and other vertebrates use a similar “segmentation clock”—a gene-expression oscillator that paces the rhythmic segmentation of the vertebral column during embryonic development.

In a room jammed with dozens of fish tanks, Dr. Ozbudak searches for one particular kind of fish. It has a kinked spine, the result of a genetic mutation (see image at bottom of page 31). Mutations in genes controlling the oscillator mechanisms are suspected of causing most of the spinal defects afflicting zebrafish as well as people.

Many oscillator-mechanism genes have been identified. But the pace-maker—the crucial gene (or, more likely, several coordinated genes) controlling how fast the pendulum swings—remains elusive. Dr. Ozbudak is in hot pursuit, his search fueled in part by a recent five-year, $1.9 million grant from the National Institutes of Health. One fact helps narrow the list of pacemaker gene suspects: For oscillation to work properly, the pacemaker protein that propels each swing of the pendulum must be short-lived.

Dr. Ozbudak, who trained as a physicist before becoming a biologist,
constructed a mathematical model to estimate how short-lived the pacemaker protein must be for the system to work. While the average protein lasts nearly two days, his model predicted that the pacemaker protein should have a much shorter half-life: six minutes or less.

He and his colleagues have zeroed in on one particular oscillator-mechanism gene, called her7, that appears to repress the expression of other oscillator-mechanism genes in zebrafish embryos. The her7 gene’s protein product, Her7, has a half-life of just three and a half minutes. This, says Dr. Ozbudak, makes her7 a strong candidate to at least be a component of the segmentation clock’s pacemaker. Moreover, her7 has a human counterpart—Hes7—that causes congenital scoliosis when mutated.

Dr. Ozbudak’s lab is now working to identify the genes that regulate Her7’s rapid turnover in zebrafish. Finding those genes should provide a clearer picture of just what makes the segmentation clock tick—and may help reveal the gene defects responsible for congenital spinal disorders.
A look at Montefiore’s innovative wound-care program and an Einstein researcher’s promising wound-healing therapy

BY GARY GOLDENBERG
Mr. Peay sought care at a local hospital, where doctors removed dead and dying tissue that could promote infection or interfere with healing, in the process known as debridement. The pain eased a bit, but the wounds remained raw and troublesome.

“I called the wounds my ‘babies,’” says Mr. Peay, who somehow maintained his sense of humor over the years. “I had to change their dressings every day—and it seemed like they would never grow up and move out.”

There were dark moments, too. At one point, his caregivers hinted that amputations might be inevitable. “That really got me scared. I couldn’t imagine life after that,” says Mr. Peay, a New York City police officer at the time.

His prospects improved a few years ago, when he found his way to Montefiore’s Wound Healing Program. Since his wounds had resulted from sickle cell anemia—a red blood-cell disorder curable only by bone marrow transplantation—he knew his leg ulcers would probably never go away.

“I was just hoping Montefiore would get the wounds under control, to the point where I could live with them comfortably,” Mr. Peay says. He is now participating in a new and unique program: the Sickle Cell Disease Leg Ulcer Clinic, a collaboration between Montefiore’s Wound Healing Program and its sickle cell clinic.

As Mr. Peay’s situation suggests, chronic wounds rarely afflict otherwise healthy people. Instead, they’re often unfortunate consequences of common health problems. For example, the foot numbness caused by neuropathy—a complication of diabetes—encourages foot ulcers that may become chronic wounds. People with impaired mobility, including the elderly and people bedridden or in wheelchairs, may develop pressure ulcers (bedsores) caused by pressure over a bony prominence that can be aggravated by obesity. (The actor Christopher Reeve, immobilized due to a spinal cord injury, died from an infected pressure ulcer.)

Chronic wounds affect an estimated 6.5 million U.S. patients, and treating those wounds costs more than $25 billion annually. With risk factors for chronic wounds on the rise—growing numbers of the elderly and surges in the incidence of diabetes and obesity—it’s no surprise that the burden of treating wounds is increasing. A 2009 report found that the number of hospital patients who develop pressure ulcers had increased by 63 percent over the previous 10 years, and that nearly 60,000 deaths occur each year from hospital-acquired pressure ulcers.

Montefiore’s wound experts tried nearly every available therapy on Mr. Peay’s wounds, from special salves and dressings to skin grafts. Some failed but others helped, and after a few months his wounds improved and stabilized.

“For the first time in years, I had some hope,” says Mr. Peay, who still
makes periodic visits to the Wound Healing Program. “The people at Montefiore seemed genuinely interested in finding a way to help me. I’ve got other serious health problems related to sickle cell disease. Now I have one less thing to worry about.”

The Montefiore Model

Stories like Mr. Peay’s are routine at Montefiore. Its Wound Healing Program offers an unusually comprehensive and coordinated approach to wound care, including preventive screening, early detection and aggressive treatment in settings ranging from the hospital to patients’ homes.

The Montefiore program considers chronic wounds in the context of a patient’s overall health history. As noted earlier, those wounds almost always have an underlying cause—usually a preexisting medical condition but sometimes a change in the patient’s environment such as a new wheelchair, poor nutrition or inadequate self-care.

“It’s critical that we learn the patient’s story—what we in medicine call the patient narrative,” says Anna Flattau, M.D., who is a clinical assistant professor of family and social medicine at Einstein and served as director of the Montefiore Wound Healing Program from 2007 to 2015. (A search is under way for her successor.) “The appearance of the wound is just the latest chapter in that story. Knowing patients’ stories allows us not only to care for the wounds themselves, but to try to alleviate the health conditions or other problems responsible for those wounds.

“The typical model for wound care is an outpatient center with a high patient volume,” says Dr. Flattau. “That model might be good for business, but it makes for substandard care. That’s because
chronic wounds by and large affect the frail elderly, the disabled, the obese—the very people who have trouble getting around. For them, a weekly appointment at the local wound clinic can mean a four- or five-hour ordeal of traveling back and forth. As a result, many patients miss appointments and don’t get appropriate care.”

Montefiore’s innovative approach ensures that chronic-wound patients get care where they need it, when they need it. If patients can’t come to the hospital for outpatient care, the program’s staff coordinates with homecare nurses to make sure care is delivered where patients live.

“They go into patients’ homes like the Marines, examining everything—not just the patient but also the bed, the chairs, looking for anything that might contribute to pressure ulcers, for example,” says Dr. Flattau, who now serves as a senior assistant vice president at NYC Health + Hospitals while retaining her academic role at Einstein. She notes that the wound-care staff also works with clinicians in Montefiore’s outpatient clinics, inpatient services and long-term care facilities.

For Dr. Flattau and her staff, it’s not unusual to see new patients who’ve been suffering from a nonhealing wound for years or—as in Mr. Peay’s case—decades. “Even after all that time, once we get them the right care, many of those wounds can be healed or at least significantly improved,” she says.

An Ounce of Prevention
A major goal of wound care is preventing wounds from turning into calamities. That involves identifying those people at risk for developing chronic wounds and treating them aggressively.

“With proper care, we can heal a small pressure ulcer in a couple of weeks,” says Dr. Flattau. “Without that care, the patient is likely to become septic or develop a bone infection, requiring a hospital stay and perhaps even surgery. Then you have a huge and costly problem.”

Such scenarios are common in poor urban areas such as the Bronx, where rates of risk factors that can lead to wounds—chronic conditions including obesity, diabetes and sickle cell disease—are well above average. The Montefiore system alone has more than 8,000 patients with diabetic neuropathy, and about 15 percent of them develop foot ulcers each year.

“So we’re talking about a lot of patients at risk,” says Dr. Flattau. “The amputation rate for people with diabetes in the Bronx is twice the rate in Manhattan, which says something about the gap in care that we need to address. We can’t prevent all of those ulcers, but we can prevent many of them.”

Montefiore’s Wound Healing Program is beginning to make a significant dent in the problem. Last year, there were about 800 outpatient visits to the wound-healing program, which also cared for about 2,000 inpatients—remarkable numbers considering that the program’s clinical staff consists of just four physicians, three physician assistants and a medical assistant.

“We’re able to take care of so many patients by using existing resources and partnering with staff in plastic and orthopaedic surgery, rehabilitation medicine, the spinal cord clinic, hematology, rheumatology, endocrinology and home care,” says Dr. Flattau.

Montefiore’s comprehensive array of wound therapies includes cleaning and debridement, antibiotics, compression wraps (which increase blood flow in the legs), skin grafts, nutrition counseling, pressure redistribution mattresses, physical therapy and orthopaedic aids such as custom-made shoes. The program also offers the latest wound-healing technologies, such as hyperbaric oxygen therapy (which helps heal wounds by increasing oxygen levels in the blood) and biologic treatments (such as factors that stimulate cell growth).

But more than any single therapy or service, what really counts is comprehensive, coordinated wound care. And that, says Dr. Flattau, requires changing an institution’s culture, so that seemingly simple but crucial measures—routinely assessing patients at risk for pressure ulcers, turning patients frequently in hospital beds to relieve pressure on the skin—are adopted.

“At Montefiore, we’ve seen a huge shift in the importance that our physicians now give to treating pressure ulcers, the most common type of chronic wound,” says Dr. Flattau. “At the same time, our nursing staff has made great strides in
From 2013 to 2015, the rate of pressure ulcers among Montefiore inpatients dropped 66 percent, falling lower than the national average.

"There are a lot of clinical processes that you can't measure well," says Dr. Flattau. "But if your pressure ulcer rate plummets, you know you're doing something right."

Those improvements have attracted attention. In 2012, the Centers for Medicare & Medicaid Services gave a highly competitive Innovation Advisors Program Award to Montefiore’s Wound Healing Program—part of a nationwide initiative to test new models of payment and healthcare delivery. The staff is using the award to develop ways of measuring outcomes stemming from its comprehensive model of wound care.

Training in Wound Care
Unfortunately, the healthcare community is paying scant attention to the worsening wound-care crisis. U.S. medical schools offer students little education about wounds and how to care for them. Many hospitals lack a dedicated wound-care service. National board certification and official fellowship training programs in wound care don’t exist.

“It’s disconcerting that a common, disruptive and potentially fatal health issue such as chronic wounds isn’t a formal component of teaching and training and care in medicine,” says Dr. Flattau. “Some say pressure ulcers are a nursing issue, and to some extent they are, since nurses are best positioned to do a
lot of the prevention and care related to wounds. But you need other clinicians to do debridement, order antibiotics and assess for bone infections, systemic disease and nutritional status. Again, it’s the team approach.”

Montefiore’s wound-care specialists are trying to spread their knowledge by offering electives for medical students and rotations for family medicine residents and geriatrics fellows.

“When I look back at my residency in family medicine, I have very little recollection of patients with pressure ulcers,” says Dr. Flattau. “Statistically, a lot of these patients must have had chronic wounds. We just didn’t look. It wasn’t on the problem list. That’s a part of the culture and practice of medicine that needs to change.”

Dr. Sharp studies microtubules—long, slender structures that provide cells with a skeleton of sorts and help them divide, change shape and move. Defects in cell migration have been linked to various diseases, ranging from mental illness to metastatic cancer, but relatively little is known about the molecular mechanisms that control this process.

Several years ago, scientists found evidence that microtubules are at least partly regulated by enzymes that sever...
them, essentially putting a brake on cell migration when necessary. This suggested the possibility of boosting cell movement—a key component of tissue regeneration—by blocking the action of these enzymes. But which ones?

In 2012, Dr. Sharp found that the enzyme fidgetin severs microtubules during cell division. (Fidgetin is a product of the fidgetin gene, first identified in a mutant strain of mice distinguished by fidgety behavior.) He hypothesized that the enzyme might also have a role outside cell division. Indeed, the following year, he found that fidgetin severs microtubules in nerve cells and that blocking fidgetin’s action promotes nerve regeneration.

In 2014, Dr. Sharp broadened his studies to include skin cells. Working with mice, Dr. Sharp’s postdoctoral fellow Rabab Charafeddine, Ph.D., discovered that another member of the fidgetin enzyme family—fidgetin-like 2 (FL2)—severs skin-cell microtubules. “This suggested that if we could target FL2, we might have a new way to speed the movement of skin cells to injury sites and promote wound healing,” Dr. Sharp explains.

With Joshua D. Nosanchuk, M.D., a professor of medicine (infectious diseases) and of microbiology & immunology at Einstein and an attending physician in infectious diseases at Montefiore, Dr. Sharp found a way to block FL2 using silencing RNAs (siRNAs) specific to the FL2 gene. As their name implies, siRNAs silence the expression of genes. They bind to a

By severing microtubules, the enzyme fidgetin-like 2 (FL2) puts the brakes on cell migration. Dr. Sharp has found that blocking FL2 speeds cell movement and thereby promotes wound healing. The skin cell here was treated with an FL2 inhibitor. To assess microtubule dynamics in the cell, Dr. Sharp’s lab fluorescently labeled the microtubules (red) and microtubule end-binding protein 1 (EB1), found only at the ends of growing microtubules (green). The loss of FL2 has increased the number of EB1-labeled microtubule ends near the cell edge, indicating a localized surge in microtubule growth.

Image courtesy of Rabab Charafeddine, Ph.D.
gene’s messenger RNA, preventing the mRNA from being translated into proteins (in this case, the enzyme FL2).

To learn more about FL2’s role in humans, Dr. Sharp suppressed its activity in human tissue-culture cells. Those cells moved unusually fast when placed on a standard wound assay (for measuring properties such as cell migration and proliferation). “Wound healing in a living organism is much more complex,” he acknowledges. “But healing begins when skin cells move into a wound.”

The discovery, published in the Journal of Investigative Dermatology, was not yet ready for the clinic. “siRNAs on their own won’t be effectively taken up by cells, particularly inside a living organism,” says Dr. Sharp. “They will be quickly degraded unless put into some kind of delivery vehicle.”

Fortunately, a solution was literally just feet away from Dr. Sharp’s laboratory. One of his Einstein colleagues, Joel M. Friedman, M.D., Ph.D., a professor of physiology & biophysics and of medicine, had developed a nanoparticle drug-delivery system. It uses tiny gel particles to encapsulate all sorts of sensitive molecules, including siRNAs, protecting them from degradation while ferrying them to their intended targets.

Nanoparticles with their siRNA cargoes were topically applied to mice with skin excisions or burns. In both cases, the wounds closed more than twice as fast as wounds in untreated controls.

“Not only did the cells move into the wounds faster, but they knew what to do when they got there,” says Dr. Sharp. “We saw normal, well-orchestrated regeneration of tissue, including hair follicles and the skin’s supportive collagen network.” The researchers plan to start testing the therapy on pigs, whose skin closely resembles human skin.

Joseph Peay and millions of other chronic-wound patients will be eagerly awaiting the results.

A Primer on Chronic Wounds

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<th>6.5 million</th>
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<td>people affected by chronic wounds</td>
<td>in annual healthcare expenditures</td>
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Both numbers are expected to escalate as the population ages and more people develop chronic diseases

The Most Common Forms of Chronic Wounds

**Pressure Ulcers or Bedsores**

They often develop in patients during an extended hospital stay and also affect people confined to a bed or wheelchair.

**Venous Skin Ulcers**

Shallow wounds are caused by venous insufficiency. Leg veins don’t adequately return blood back to the heart, allowing blood to pool in the veins, which in turn leads to tissue breakdown.

**Diabetic Wounds**

In diabetic patients, poor circulation and lack of sensation can lead to foot ulcers and cuts that often become infected and are a major cause of hospital admissions. One fifth of diabetic patients who develop infected foot wounds end up with some type of lower-extremity amputation.
One impetus for the new partnership between Albert Einstein College of Medicine and Montefiore was to build on “the decades-long synergy among our educational, research and clinical enterprises,” in the words of Allen M. Spiegel, M.D., Einstein’s Marilyn and Stanley M. Katz Dean. A prime example can be seen in the collaborations among Einstein’s researchers in neurology and Montefiore’s clinicians in geriatrics.

Front and center in this effort is Joe Verghese, M.B.B.S., M.S. His Einstein positions are professor and director of the division of cognitive & motor aging in the Saul R. Korey Department of Neurology; professor of medicine; director of the Jack and Pearl Resnick Gerontology Center; and the Murray D. Gross Memorial Faculty Scholar in Gerontology. At Montefiore he serves as chief of the integrated divisions of cognitive & motor aging (neurology) and of geriatrics. He is also director of the Montefiore Einstein Center for the Aging Brain. Dr. Verghese’s investigations focus on how diseases and aging affect cognitive ability and mobility in older adults.

**Your training and background are in neurology. Why were you appointed chief of geriatrics at Montefiore?**

It was an unconventional appointment, considering that I’m not a geriatrician. However, my work on aging straddles the two disciplines, putting me in an ideal position to build bridges between Einstein’s rich aging-related research in neurology and Montefiore’s extensive clinical services in geriatrics. There had been minimal links between the two sides in the past.

**How are you building those bridges?**

Regarding education, an early initiative was to start a weekly case conference where our researchers share new findings in the field with our clinicians.

We also have a yearly research symposium, which serves as a forum for everyone—researchers, clinicians, fellows, students—to showcase their work.

**What about new bridges between research and clinical care?**

The most prominent example is the new Montefiore Einstein Center for the Aging Brain, a clinical facility in Yonkers where we’re translating the latest dementia research into practice, such as a tool I developed for assessing cognitive abilities. The genesis of this tool comes from a study in India in which I had to measure cognition. One practical problem was that many people there are illiterate or have a low level of education, and most tests for measuring cognition were based on written words. So we came up with a test that uses only pictures. We tested it at Einstein and then implemented it in the center’s clinics, which serve many patients with low literacy skills. All in all, we want the center to serve as a nidus for research—everything from drug trials to large-scale population studies.

**Are you encouraging research from the clinical side?**

Yes. The picture-based tool for assessing cognitive abilities is a great example of the classic loop wherein a clinical observation spurs research, which develops a solution that is fed back to the clinic. We want to encourage that type of
interaction, which is why I appointed one of my previous postdocs, Dr. Helena Blumen, to the geriatrics faculty at Montefiore. Her role is to serve as a resource for clinical faculty members who have ideas for research but may not have the expertise to apply for grants, design a study, make presentations or write papers.

**Will the Einstein-Montefiore partnership help address the shortage of geriatricians?**

That’s a serious issue. It’s estimated that within a decade, we’ll need more than 30,000 geriatricians nationwide to serve our graying population. Today, we have only about 6,000. So while we work to train geriatricians, we’re also trying to increase geriatric awareness—to “geriatricize” the two institutions. I have a clinical faculty of 12, so there’s going to be a limit to how much hands-on care we can actually deliver. But there are other ways to extend our reach.

At Montefiore, we go to various clinical sites to teach clinicians skills such as how to screen for dementia. We’re also working to put screening instruments into the electronic medical record, so that every older patient in the system can get appropriately evaluated. Most older patients with cognitive impairments are seen by a primary care provider, not a geriatrician. But studies show that more than half of these health issues go unrecognized in the primary care setting. There are several reasons—for example, primary care doctors don’t have enough time to fully evaluate older patients—so it will require a multipronged solution. But at least one solution is to give nongeriatricians the right tools to assess older patients.

**Are you collaborating with other departments to “geriatricize” healthcare?**

We have a co-managed service with orthopaedics, where patients who come for surgery are evaluated by a geriatrician as well as by an orthopaedic surgeon. In a pilot study, Einstein-Montefiore geriatrician Dr. Wanda Horn showed that this partnership resulted in fewer complications and a shorter length of stay, compared to the traditional orthopaedics service. Based on this study, we got a grant from the Foundation for Jewish Philanthropies to set up a similar co-management service at Montefiore’s Wakefield campus. In addition, we’re doing consults with nephrology on general geriatrics issues, including palliative care and advanced directives.

We’re also working in cardiology. Heart failure patients who are frail tend to fare much worse than those who are not, so we’re studying possibly introducing assessments of frailty into the heart failure clinic. And we’re working with Montefiore Care Management to expand dementia outreach and research into the Hudson Valley. Montefiore is going to provide the care management, and we’ll provide the consultative services such as teaching primary care physicians how to recognize cognitive and frailty problems and how to use screening tests.

**How many older patients does Montefiore serve?**

Montefiore’s geriatrics services reach about 3,000 patients per year in ambulatory care clinics, inpatient services and nursing homes. But in a broad sense we influence the care of all 300,000 elderly people in the Bronx and, increasingly, in Westchester through efforts to promote screening for cognitive issues and frailty, to create new screening tools for older people and by serving as a resource for local primary care physicians.
Playing to Win for Breast Cancer Research

More than 200 Women’s Division members and friends gathered on October 7, 2015, at the Harmonie Club in Manhattan for the division’s third annual “Girls Just Want to Have Fun” event. The program featured lunch, shopping, mahjong and canasta and raised funds for breast cancer research.

In her welcoming remarks, division executive vice president and event co-chair Andrea Stark highlighted the work of Joseph A. Sparano, M.D., vice chair of medical oncology at the Montefiore Einstein Center for Cancer Care, associate director of clinical research at the Albert Einstein Cancer Center and a professor of medicine and of obstetrics & gynecology and women’s health at Einstein and Montefiore. Dr. Sparano led a groundbreaking study, published last September in the *New England Journal of Medicine*, that may change the way many women are treated for breast cancer (see page 14). The study found that women who have early-stage breast cancer and score low on a gene test for cancer recurrence can limit their post-surgery/radiation treatment to hormonal therapy without the need for chemotherapy. Carol Roaman, Women’s Division president; Jackie Harris, executive vice president; and Bambi Felberbaum, vice president, also served as event co-chairs.

To join the Einstein Women’s Division’s initiative to support research on women’s and men’s cancers, or to learn more about the Women’s Division, please contact Mary Anna Smith at 718.430.4010 or maryanna.smith@einstein.yu.edu.
Touring Montefiore

On November 17, 2015, board members from Einstein’s Professional & Leadership (P&L) Division met at the Moses Campus for a guided tour of Montefiore. Their goal: to learn about clinical services at Montefiore in light of the recent historic agreement between the two institutions.

First stop: the Montefiore Einstein Center for Cancer Care’s new Center for Radiation Therapy, where Shalom Kalnicki, M.D., a professor and chair of radiation oncology and a professor of urology at Einstein and Montefiore, explained how innovative research at Einstein has translated into better patient care at Montefiore. Next, Stuart M. Greenstein, M.D., an adult kidney transplant surgeon and a professor of surgery at Einstein and Montefiore, hosted the group at the Montefiore Einstein Center for Transplantation.

They then met with Daniel B. Sims, M.D., an assistant professor of medicine (cardiology) at Einstein and Montefiore and a specialist in advanced heart failure/transplant cardiology in the Montefiore Einstein Center for Heart & Vascular Care. Final destination: the Children’s Hospital at Montefiore, where Judy L. Aschner, M.D., physician in chief, led them through the emergency department and the pediatric critical care unit. Dr. Aschner is also the Michael L. Cohen, M.D., University Chair of Pediatrics and professor of pediatrics and of obstetrics & gynecology and women’s health at Einstein and Montefiore.

A reception for the visitors and their hosts followed the tour.

Fundraising for Research

On October 13, 2015, P&L Division leaders met with Einstein’s executive dean, Edward R. Burns, M.D. ’76, at the Manhattan law offices of Blank Rome, LLC. The attendees were Martin Luskin, division chair, and fellow board members Raymond S. Cohen, David J. Klein, Jack M. Somer, Andrew M. Weinberg and Peter E. Zinman. They discussed the recent Einstein-Montefiore accord and new strategic plan as well as the Center for Experimental Therapeutics, the division’s current fundraising project.

To learn more about the Einstein Professional & Leadership Division and upcoming events, please contact Eve Marsan at 718.430.4178 or eve.marsan@einstein.yu.edu.
1950s
Harvey Karten, M.D. ’59, formally retired in 2014. He continues to do neurobiological research in the department of physics at the University of California, San Diego. Dr. Karten was recently elected to the National Academy of Sciences in recognition of his long-term contributions to the field of evolutionary neurobiology, particularly his work on avian brains and the evolutionary origins of the mammalian neocortex. He is writing a monograph on the evolution of visual pathways in vertebrates. When not working in the lab, he is “an active single-handed ocean sailor on my 37-foot cutter sailboat, Night Heron.”

1960s
Edward Stim, M.D. ’60, reports, “I am still going strong and, I hope, ‘long’ in Tokyo, Japan. I am a travel medicine consultant for Emergency Assistance Japan, a company that provides health services for overseas travelers in Japan. I would be happy to mentor younger alumni and students and to be acquainted with anyone from Einstein. You can reach me by phone from the United States at 011.81.3.3811.8124.

William Friedel, M.D. ’66, who has been retired for five years, writes, “I am continually surprised by how much I like it . . . between tennis, hiking, volunteering, not to mention the continuing multiple cultural events and classes, I don’t know how I ever had time to work. My wife, Judith, also is very active here in San Diego, and both our married daughters live fairly close by. All in all, 75 and still going strong.”

1970s
Barry M. Schimmer, M.D. ’70, has been elected as a master of the American College of Rheumatology. He continues in his posts as section chief of rheumatology at Pennsylvania Hospital in Philadelphia and as a clinical professor of medicine at the University of Pennsylvania’s Perelman School of Medicine. He and his wife, Naomi, have four grandchildren.
Diane Stover-Pepe, M.D. ’70, reports, “My daughter, Dana, is finishing her internal medicine residency at Georgetown and is applying for a fellowship in infectious diseases. She has worked at both the Centers for Disease Control and the Environmental Protection Agency, has her master’s in public health and is interested in the environment and how it affects our health.”

Henry Klapholz, M.D. ’71, M.E.E., is dean for clinical affairs and a professor of obstetrics and gynecology at Tufts University School of Medicine in Boston, MA. Dr. Klapholz, who is a recipient of the American College of Obstetricians and Gynecologists’ Excellence in Education Award, continues to teach three courses at Tufts. He also oversees the office of faculty affairs and the clinical aspects of the Tufts Physician Assistant Program.

Philip Coffino, M.D. ’72, Ph.D. ’71, has moved from the University of California, San Francisco, where he has had a faculty appointment for more than 40 years. He is now living in New York and is on the faculty of Rockefeller University. He continues his basic research on regulated intracellular proteolysis.

Neal Flomenbaum, M.D. ’73, reports, “I was honored in 2014 when the Neal Flomenbaum, M.D., Prize for Excellence in Emergency Medicine was created by Jeanne and Overseer Herbert J. Siegel to support faculty engaged in clinical care at Weill Medical College of Cornell University.” The prize was established “to recognize the commitment and hard work of physicians in emergency medicine who are on the frontlines of care.” Dr. Flomenbaum is a professor of clinical medicine and emergency physician-in-chief at New York–Presbyterian/Weill Cornell Medical Center, division chief of emergency medicine in the Weill department of medicine and medical director of New York–Presbyterian’s Emergency Medical Service. “This prize,” he writes, “makes a strong statement about the importance of providing excellent clinical care while teaching future Weill Cornell physicians how to do so.”

Jonathan Tobis, M.D. ’73, recently returned to Jacobi Medical Center after 40 years, to speak at cardiology grand rounds. He discussed his work on patient foramen ovale and its connection to migraine with aura and stroke. Dr. Tobis is a professor of medicine (cardiology) and director of interventional cardiology research at the David Geffen School of Medicine at the University of California, Los Angeles. He also works part-time teaching a new percutaneous method of treating mitral regurgitation.
He writes, “I train people in Europe and Australia and travel about one week out of every six. Lots of fun and good food! I recently caught up with Michael Garrett, M.D. ’73, by phone, after 10 years. Warm regards to all.”

Roger Duvivier, M.D. ’74, is a visiting associate professor of obstetrics & gynecology and women’s health at Einstein and Montefiore. Dr. Duvivier has relocated to Antigua, Guatemala, to continue volunteering for WINGS, a Guatemalan nonprofit organization that provides reproductive/sexual health services (contraception, male and female sterilization, cervical screening and treatment) and for Rotary International, which focuses on services for underserved women and girls, on water and sanitation projects and on children’s education. He has been supervising Einstein medical students and Montefiore residents interested in global health in Guatemala “to help them better prepare for the globally interdependent clinical practice of the future.”

Jack Stern, M.D. ’74, Ph.D. ’73, reports that his book Ending Back Pain, published in 2014, continues to be on the Amazon best-seller list of health books.

Harvey Karp, M.D. ’75, is pleased to announce the release of the second edition of his international best-seller, The Happiest Baby on the Block. The book describes a new neonatal reflex—the calming reflex—and how to elicit it to calm crying babies and improve infant sleep. Dr. Karp also reports that more than 3,000 educators have been certified to teach Happiest Baby classes in hospitals and public health clinics in more than 20 countries.

Kenneth Blank, M.D., Ph.D. ’77, has been named a fellow of the National Academy of Inventors (NAI). Election to NAI fellow status is “accorded to academic inventors who have demonstrated a prolific spirit of innovation in creating or facilitating outstanding inventions that have made a tangible impact on quality of life, economic development and the welfare of society.” Dr. Blank, who lives in Philadelphia, also serves as first senior vice president of health sciences at Rowan University in Glassboro, NJ. A professor of biology at Rowan, Dr. Blank holds three patents related to his work as a molecular pathologist and has more than 30 years of experience in research program development, technology commercialization and regional economic development. He was previously senior vice provost for research and graduate education.
Janina Galler fell in love with neurochemistry during high school in New Orleans. Needing to do a science project, she contacted Tulane Medical School and was placed in a lab studying the brain enzyme monoamine oxidase. Her research landed her Westinghouse Science Talent Search honors—an auspicious beginning for the child of two Holocaust survivors from Poland.

Today Dr. Galler is a leading authority on child malnutrition and brain and behavioral development. Among her many titles are professor of psychiatry at Harvard Medical School and psychiatrist in the Chester M. Pierce, M.D., Division of Global Psychiatry at the Massachusetts General Hospital. She served on the National Advisory Council of the Eunice Kennedy Shriver National Institute of Child Health and Human Development.

Dr. Galler is the founder and research director of the Barbados Nutrition Study. This longitudinal study of Barbadian children, started in 1973, examines the effects of childhood malnutrition over life spans and across generations.

Its major finding—the increased prevalence of attention and other deficits that continue into adulthood and can be found among healthy offspring of adults with histories of malnutrition—has helped shape public policy targeting underserved children in the United States and abroad.

She also directs a translational research program relating to preclinical and basic neuroscience studies, including epigenetics, of early malnutrition and its impact on brain and behavioral development.

Dr. Galler was born in Uppsala, Sweden, and immigrated to America with her parents as a child. She grew up in an observant Jewish home and graduated summa cum laude in two years from Sophie Newcomb College, “a small women’s college with no premed program at the time,” she recalls.

Having heard that Einstein welcomed observant Jewish students, she met with the dean of students and was accepted. “Einstein took a risk with me,” she says. “I was very young, female at a time when most medical students were male, and from the Deep South.”

“I had amazing mentors,” she notes. Chief among them were Dominick Purpura, M.D.; Herbert Birch, M.D., Ph.D.; and Isabelle Rapin, M.D. On her second day at Einstein, Dr. Birch, a professor of pediatrics and developmental psychology, invited her to join his lab, and she worked with him until his death in 1973. Her assignment: to establish animal models of malnutrition in young rats. After graduating, she completed her residency in psychiatry at Mass General and a fellowship in child psychiatry.

“Einstein has always been welcoming and inclusive, with a wonderful faculty that’s unusually supportive of its students,” she says. “It values ethics and the social-justice dimension of medicine as much as the clinical and research dimensions. Even in my era, the school helped students pursue their passions and give back to society. I developed the entire basis of my academic, clinical and research career there.” (Einstein is also where she met her future husband, classmate Burton D. Rabinowitz, M.D. ’72.)

A member of the Einstein Alumni Association board of governors since 2011, Dr. Galler became its president in 2015. She and her fellow board members are dedicated to helping Einstein students, strengthening the alumni network and supporting the College of Medicine through alumni programs and events.

Grateful for scholarships she received as a medical student, she’s committed to philanthropy and appreciates the many alumni who share that commitment.

“We’re ready to partner with Dean Spiegel and the Board of Trustees on new ways to support the school and the transition to the ‘new Einstein,’” she says.
education at Temple University and vice provost for research at Northeastern University and Drexel University. He is a member of New Jersey’s Council on Innovation, vice chair of the board of Philadelphia’s University City Science Center and a board member of the New Jersey Innovation Institute. He has been a scholar of the Leukemia Society of America (now the Leukemia and Lymphoma Society) and is currently a fellow of the Philadelphia College of Physicians.

Ira Helfand, M.D. ’77, and Deborah Smith, M.D. ’77, report that Dr. Helfand “had the opportunity to address the United Nations General Assembly on September 10, 2015, about the urgent need for nuclear disarmament, a topic that has been a main theme of his medical career since shortly after we graduated.” (To view the speech, go to https://www.youtube.com/watch?v=fs-WcHc32c.) Dr. Helfand remains active on the board of Physicians for Social Responsibility (PSR) and encourages other alumni to join (www.psr.org). He serves as co-president of PSR’s global federation, International Physicians for the Prevention of Nuclear War, which received the 1985 Nobel Peace Prize. Drs. Helfand and Smith are still in practice in western Massachusetts. Dr. Smith reports that she recently “moved to the new Massachusetts General Hospital Cancer Center at our local community hospital,” and Dr. Helfand continues to work full-time at the urgent care center in Springfield, MA, that he bought a few years ago.

Lynne M. Mofenson, M.D. ’77, has retired from the National Institutes of Health (NIH) after 26 years doing research on pediatric and maternal HIV infection. “It’s time for younger blood to take over,” she writes. She works as an HIV technical advisor in the Elizabeth Glaser Pediatric AIDS Foundation’s research group two days a week. The group is evaluating implementation of the results of many of the studies Dr. Mofenson was involved in at the NIH. She is an active member of the U.S. Public Health Service and World Health Organization guidelines groups, a speaker on pediatric HIV, and a consultant. “Being able to think and to mentor, instead of being an administrator worrying about budget/funds and supervising staff, has been a pleasure,” she adds.

Sten Vermund, M.D. ’77, Ph.D., is a professor of pediatrics at Vanderbilt University School of Medicine in Nashville, TN. Dr. Vermund heads the Vanderbilt Institute for Global Health and serves as assistant vice chancellor for global health. His work is focused on HIV control and prevention in Africa and Asia. He is married to child psychiatrist and classmate Pilar Vargas, M.D. ’77. They have two sons: Julian, 35, and Gabriel, 28.

AAMC Baltimore Reception

Montefiore Health System, in partnership with Einstein’s alumni relations office, hosted a reception at the annual meeting of the Association of American Medical Colleges (AAMC) on November 8, 2015, in Baltimore, MD. More than 50 guests—including alumni, parents, faculty and friends—attended the reception, where they reconnected with Einstein and Montefiore. Guests included members of the Einstein community who live in the Baltimore area as well as those who were in town for the AAMC meeting.
Joseph Barbuto, M.D. ’78, chaired and presented work at a symposium on core concepts in the psychotherapy of cancer patients at the International Psycho-Oncology Society meetings in Lisbon, Portugal, in October 2014. He continues to supervise residents in the department of psychiatry at New York–Presbyterian Hospital and fellows at Memorial Sloan Kettering Cancer Center.

William Breitbart, M.D. ’78, completed residencies in internal medicine and psychiatry at Jacobi Hospital/Bronx Municipal Hospital Center (now known as Jacobi Medical Center) after graduating from Einstein. Then, after completing a fellowship in psychopharmacology at Memorial Sloan Kettering Cancer Center (MSKCC) in Manhattan in 1984, he joined the MSKCC faculty and “was fortunate enough to have a career in psychosomatic medicine and psycho-oncology.” He served for 15 years as fellowship training program director and has been chief of the psychiatric service since 1996. In addition, he chairs the department of psychiatry and behavioral sciences and holds the Jimmie C. Holland Chair of Psychiatric Oncology at MSKCC and is a professor of clinical psychiatry and vice chair of psychiatry at Weill Cornell Medical College. He has received continuous National Institutes of Health research funding for 26 years, has served as editor-in-chief of the journal Palliative and Supportive Care for 14 years and has written more than 350 published papers and 12 textbooks. Dr. Breitbart has received Lifetime Achievement Awards from the Academy of Psychosomatic Medicine, the International Psycho-Oncology Society and the American Psychosocial Oncology Society. “My career has been extremely rewarding,” he writes, “but my most profound rewards have resulted from my 29-year marriage to my beloved wife, Rachel, and from watching my son, Sam, 24, grow into a fine, compassionate young man who is excelling in a career in law.”

Jim Mozzillo, M.D. ’79, M.S., M.P.H., reports, “I am back doing occupational medicine exclusively at U.S. HealthWorks. Love the job. Love the people I work with. Love my boss. What more can a person ask for? I actually enjoy going to work! As always, I have ‘someone upstairs’ calling the plays. He takes great care of me.”

Speakers at the 2015 Stethoscope Ceremony

Alumni leaders and faculty members offered words of wisdom and encouragement to first-year medical students at this annual rite of passage. For more details, see page 6.

1980s

Richard K. Bernstein, M.D. ’83, was an engineer for 24 years before he entered Einstein. He recently produced Dr. Bernstein’s Diabetes University, a series of 70 videos on YouTube focusing on “basic problems associated with diabetes care that are not adequately treated with conventional medical approaches.” Dr. Bernstein, who is 82, pioneered blood-sugar self-monitoring in 1969. He has had type 1 diabetes for 70 years and enjoys good health because, as he puts it, “I insist that diabetics are entitled to the same blood sugars as nondiabetics.” He devised “a simple system” to address this issue 13 years before he became a practicing physician, at age 49, and has written nine books on blood-sugar normalization.

Brian Delaney, M.D. ’83, is an assistant professor of family & social medicine at Einstein and an internist specializing in geriatric medicine at Montefiore and at St. Barnabas Hospital in the Bronx. He is very proud of his daughter, Charlotte Delaney, a member of Einstein’s Class of 2016, a Dean’s Recognition Award recipient and a former musical director of the Lymph Notes, Einstein’s a cappella group.

Vivian Kafantaris, M.D. ’83, has been promoted to professor of psychiatry and molecular medicine at the Hofstra North Shore–LIJ (now Hofstra Northwell) School of Medicine in Hempstead, NY.

Jeffrey Goldberger, M.D. ’84, recently became chief of cardiology at the University of Miami.

Jim Giglio, M.D. ’89, reports: “After serving for more than 16 years as chief of emergency medicine at New York–Presbyterian Hospital/Columbia University Medical Center, I have relocated to Queens and am now building a new team as chair of emergency medicine at the Flushing Hospital Medical Center. Friends (and emergency physicians looking to enjoy unmatched ethnic diversity and the rewards of urban medicine in a hospital that is fully committed to its community) can reach me at 718.670.5766.”

Troy Hailparn, M.D. ’89, is board certified in obstetrics and gynecology, the founder of the Cosmetic Gynecology Center of San Antonio, TX, and the author of a new eModule (online teaching tool) for the American College of Obstetricians and Gynecologists (ACOG) on labiaplasty procedures. The eModule represents “the first time that ACOG has embraced this controversial aspect of gynecology, which is fast becoming one of the most important topics affecting today’s practitioners.” She lives in San Antonio with her husband and son.

Penelope Shar, M.D. ’89, lives and practices in Bangor, ME, where she has a small integrative practice focusing on chelation therapy, heavy-metal detoxification and bio-identical hormone therapy. “I currently work three days a week and love what I do! I still have children and grandchildren in New York, but my heart is in Maine.” She welcomes any classmates who want to visit.

1990s

Yvette Calderon, M.D. ’90, has been appointed medical director for emergency services at North Central Bronx Hospital (NCBH) in the Bronx, NY. In her expanded role, Dr. Calderon has jurisdiction over all NCBH emergency services, including adult, pediatric, psychiatry and emergency care of patients in labor. Dr. Calderon is the immediate past associate dean for diversity enhancement at Einstein.

Sherry C. Huang, M.D. ’94, has been at the University of California, San Diego, School of Medicine (UCSD) since she matched there for her pediatric residency. After finishing a residency and a pediatric gastroenterology fellowship at UCSD, she stayed on as a physician-scientist for 10 years, investigating the genetics of familial colon cancers and polyposis syndromes. In the second decade of her tenure at UCSD, she became involved in education and administration, serving as program director for pediatrics. Recently, at the start of her third decade there, she was promoted to serve as associate dean for graduate medical education and as “the designated institutional official” for the 78 training programs and 950 postgraduate trainees at UCSD. She writes, “Time has passed quickly, but UCSD has been a great place to call home for my medical career and family. My husband and I have two teenagers in high school and enjoy the beach and great weather in San Diego.”

Eric Goldberg, M.D. ’95, has returned to New York City after practicing for three years in Scottsdale, AZ. He now practices internal medicine at NYU
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– Joy Goldstein, Class of 2016, Alumni Scholarship recipient

For more information, please contact the Office of Alumni Relations at 718.430.2013 or alumni@einstein.yu.edu.
Building Connections: Career Speed Networking

Career Speed Networking, a popular annual event co-hosted by the Einstein Alumni Association and the office of student affairs, gives students and alumni a chance to make meaningful connections with fellow members of the Einstein community.

On October 25, 2015, more than 150 students and 50 alumni gathered in the Lubin Dining Hall to participate in Career Speed Networking 2015. Einstein alumni were seated at tables by specialty; second- and third-year medical students dropped by to chat with the alums about their career paths and about life after medical school. Alumni Association president Janina R. Galler, M.D. ’72, thanked the participating alumni, including those who had travelled from out of town to attend.

Students were encouraged to visit https://www.einstein.yu.edu/alumni/student-mentoring/ to find information about individual Einstein alumni willing to provide career advice, expertise and guidance to current students.

Alumni interested in becoming mentors for Einstein students should contact the alumni relations office at 718.430.2013 or alumni@einstein.yu.edu.

Norman Saffra, M.D. ’88, and Jody Piltz-Seymour, M.D. ’84, members of the Einstein Alumni Association board of governors, with a student, at the Career Speed Networking event held in fall 2015.

Langone Medical Center’s Internal Medicine Associates.

Oksana Berkovich, M.D. ’98, has a private internal medicine practice in the Bronx, affiliated with Montefiore Health System and Jacobi Medical Center. She can be reached at 917.647.9322 or via e-mail at valerikazakov2000@yahoo.com.

2000s

Jonathan D. S. Klein, M.D. ’01, F.A.C.S., was honored to be chosen to deliver the keynote address at the graduation ceremony for the Hofstra Northwell School of Medicine’s department of surgery in June 2015. Dr. Klein also has been inducted as a member of the New York Surgical Society.

David Chesler, M.D. ’06, joined the faculty at Stony Brook University Hospital, in Stony Brook, NY, as an assistant professor of neurological surgery and pediatrics and co-director of pediatric neurosurgery in 2014. He lives in Stony Brook with his wife, Brooke, and children, Hayden and Oliver.

Adam Friedman, M.D. ’06, F.A.A.D., is an associate professor of dermatology and the residency program director at the George Washington University School of Medicine & Health Sciences in Washington, DC. Dr. Friedman serves as vice chair of the New York Academy of Medicine (NYAM)’s fellows section on dermatology. He has been selected as a fellow ambassador for NYAM. In that position, he shares his expertise through media interviews, blog posts, op-eds and presentations.
Gary Schwartz, M.D. ’06, reports that after completing his fellowship in cardiothoracic surgery at the Johns Hopkins Hospital in Baltimore, MD, he joined the faculty of the department of thoracic surgery and lung transplantation at Baylor University Medical Center in Dallas, TX. He is “actively growing” the extracorporeal membrane oxygenation program at Baylor, and also has been named surgical director for airway disorders.

Joyce Varughese-Raju, M.D. ’06, and her husband, Robin Raju, welcomed their daughter, Laila Mariam Raju, to the world in May 2015, in Stony Brook, NY. Dr. Varughese-Raju writes, “Laila was a cooperative physician’s child and waited until just after her mommy’s week on call was over to make her appearance. Big brother Joseph loves to play with his baby sister, especially right after she falls asleep.”

Audrey Toda, M.D. ’07, and her husband, Jacques Wilson, welcomed their son, West Zenkou Wilson, in September 2015.

Hannah Rapaport, M.D. ’09, was married in June 2015 to David Kotch. She has joined a private practice in New Jersey, where she practices breast radiology at the Saint Barnabas and Clara Maass Medical Centers. She recently moved to Chatham, NJ.

2010s

Jonah Bardos, M.D. ’13, and his wife, Lauren, announce the birth of their son, Zev Uriel. Dr. Bardos is the co-author, with Jenna Friedenthal, M.D. ’14, and Einstein and Montefiore’s Zev Williams, M.D., Ph.D., of a paper, “Public Perceptions of Miscarriage: A National Population-Based Survey,” published in the journal Fertility and Sterility, and received the Arnold P. Gold Foundation Humanism and Excellence in Teaching Award in June 2015.

Siu Kei (Jacky) Chow, Ph.D. ’13, has been certified as a diplomate of the American Board of Medical Microbiology (ABMM). ABMM certification is the highest credential that a doctoral-level clinical microbiologist can earn.

Vijay Kotecha, M.D. ’14, is in his second year of residency in internal medicine at the University of California, San Francisco (UCSF). He writes, “I am really happy with the program and grateful for my education at Einstein, which prepared me well. Einstein’s wide network of affiliate hospitals helped me make a relatively smooth transition to UCSF’s three-hospital system (UCSF Medical Center, the VA Medical Center and San Francisco General Hospital). San Francisco has been a great city to live in, helped by the fact that I’m living in university-subsidized housing and not contending with the out-of-control real estate market. I play roller hockey in Half Moon Bay, take hang-gliding lessons and see a few Einstein alums on a regular basis in the hospital, including internal medicine interns Saate Shakil, M.D. ’15, and Nick Iverson, M.D. ’15.”

For news about Reunion 2016 and other upcoming alumni programs and events, please visit our website.
When Steven U. Walkley, D.V.M., Ph.D., and his wife, Rebecca, first saw their future home in northern Westchester County, they encountered the then-owner making maple syrup by cooking down sap he’d tapped from trees on the property. That was in 1987, and the joys of backyard sugaring have since become an annual pre-spring ritual for the Walkleys.

“You need the freeze, and where we come from, in the South along the Gulf Coast, freezing weather is rare,” says Dr. Walkley, a professor in the Dominick P. Purpura Department of Neuroscience and in the department of pathology. “It’s time to tap when you have your first thaw. The sap runs as long as temperatures go above freezing during the day and then back down at night.”

A Love of Labor

Last year, the Walkleys tapped 9 of the 15 maples trees on their property and stored the sap in bins on the chilly north side of their house. “We skim off the ice that forms on top and pour the sap into the restaurant-sized lasagna pan that we boil it in,” explains Dr. Walkley, also director of Einstein’s Rose F. Kennedy Intellectual and Developmental Disabilities Research

Living the Sweet Life

BY KAREN GARDNER
Center and a professor in the Saul R. Korey Department of Neurology.

In a makeshift cooking area built largely from cinderblocks and sheet metal, Dr. Walkley sets the lasagna pan in place and hooks up a propane tank for heat. He boils the sap all weekend or even longer, adding new sap as the batch cooks down. Occasional stirring keeps the sap from burning or boiling over. Water in the sap escapes as steam—a big reason the boiling takes place outdoors.

He transfers the resulting syrup to a large pot, where it’s cooked down further, poured through a cloth filter and funneled into bottles, ready to be swirled onto pancakes and waffles.

This year, the couple obtained more than enough sap for their annual cook-down party with members of the Walkley lab. A sweet time was had by all.
Oliver Sacks, M.D., who died last August (see page 12), belonged to Einstein’s neurology faculty from 1967 through 2007 and was the commencement speaker for Einstein’s Class of 1991. He was a noted clinical researcher and author, perhaps best known for his 1973 book Awakenings, which described his work with patients suffering from encephalitis lethargica. Dr. Sacks elaborated on his famous experiment in “Awakenings Revisited,” an article published by Einstein News in 1984.

“I saw wards full of strange frozen figures, human statues, as motionless as stone—a terrible and incredible sight,” he wrote. “I found this vision doubly incredible: first because nothing I had read or heard prepared me in the least. . . . Second, I had not realized that such things could be—they appeared on, or beyond, the verge of the possible. . . . During this time I came to know all our post-encephalitics well, not only as cases, but as persons. I came to see that in every case, there was a vivid, vital personal presence within the immobilizing, anonymizing walls of sleep.”

Dr. Sacks returned to Einstein in 2013 (above) to attend a remembrance for neurologist Saul R. Korey, M.D. (To his left is Isabelle Rapin, M.D., professor emerita of neurology and pediatrics.) His white beard and mischievous eyes were expected, but the black sneakers were a style surprise. He did not ride his motorcycle to Einstein that day.
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Louis Hodgson, Ph.D. (associate professor), and Dianne Cox, Ph.D. (professor), in the department of anatomy and structural biology studied the role of the protein Rac2 in forming protrusions that allow mouse macrophages to migrate. In the upper image, computational analysis “maps” the motion (y axis) of a 50-micron cell-edge section over 10 minutes (x axis). Cyclic edge motion is visible in which protrusions (red areas) alternate with retractions (blue areas). The lower image of the same macrophage shows that protrusive activity correlates with Rac2 activity using fluorescent biosensors that reveal when and where Rac2 is activated in the cell (red = high Rac2 activity, blue = low). The research is described in the April 15 Journal of Immunology, whose cover image resembles the upper image.

Photo credit: Veronika Miskolci, Ph.D., and Gruss Lipper Biophotonics Center